Ministry of Health and Care Services

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Report to the Storting (Norwegian Parliament)

White Paper on Medicinal Products

Correct use – better health

Recommendations from the Ministry of Health and Care Services 22 May 2015, approved by the Cabinet the same day.
(Solberg government)

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3 Development and approval of medicinal products

The Norwegian Medicines Act defines medicines in the following manner:

> "The term 'medicines' is understood to mean substances, drugs and preparations intended for, or used in the prevention, treatment or alleviation of disease, symptoms of disease or pain, to have an effect on human or animal physiological functions, or for the internal or external use in the diagnosis of disease."

Since time immemorial, human beings have been using substances from plants, animals and minerals to treat disease. There is documentation in the form of written records from Mesopotamia and from ancient Egypt and Greece, but it is likely that the practice is even older.

In the early 1200s, the Lateran Council (ecclesiastical councils of the Catholic Church in Rome) banned monasteries from offering medical assistance to most people. It was therefore necessary for medical training and the practice of medicine to take place elsewhere. Around this time, the first universities were established in places such as Bologna, Padua, Montpellier and Paris.

The invention of the printing press and the Renaissance led to major changes in the fields of medicine and pharmacology. During the 1500s, traditional "folk medicine" was practiced alongside a more rational form of medicine. In the late 1700s, scientists began searching for active substances in remedies derived from plants, animals and minerals. This work resulted in the isolation of a number of natural substances, such as morphine in 1805, quinine in 1821, atropine in 1822, and cocaine in 1860. Acetylsalicylic acid from F. Bayer & Co. was the first industrially produced medicine sold on a large scale. This appeared on the market in 1896.

The distinction between medicine and pharmacy most likely arose in Sicily during the first part of the 1200s, because of the so-called "Salerno poem", or the Salernitan Regimen of Health. These regulations determined that there was a clear distinction between physicians and those who produced medicines. Medicines were to be prepared by following a set procedure, and those who carried out this work were required to present physicians with documentation of their skills. The authorities determined the price of medicines, and pharmacies were not free agents, but instead subject to license or privilege.

Pharmacies spread from Italy to the south of France and England throughout the 13th to 14th centuries, and to Germany in the 15th century. These enterprises were regulated by laws, with

the exception of England, that were in accordance with the Salernitan Regimen of Health. Privileges in Italy and France were granted to guilds, while in Germany they were granted to individuals.

The first pharmacy in Norway was established in Bergen in 1595[1]. The distinction between physicians and pharmacies, as well as a law stating that physicians could not own their own pharmacy, was introduced to Denmark and Norway by decree from King Christian V on 4 December 1672.

Until the mid-1900s, Norwegian medicine production largely took place in pharmaceutical laboratories. Independent pharmacies had their own laboratories where they could manufacture medicines that were not industrially mass-produced. For instance, pharmacies produced their own ointments, tablets, oral liquids, eye-drops and injections.

By the late 1960s, regulations for medicine production had become far more stringent. This made it difficult for many pharmacies to maintain production.

3.1 Development of medical products

Today most medicinal products are developed by the pharmaceutical industry, and pharmacy-produced medicinal products are almost a thing of the past. The pharmaceutical industry is a complex industry ranging from high-tech and research-based companies to companies that are based on the production of medicinal products that are no longer patented. There are also significant variations in the size of the companies, from smaller research-based companies that develop individual products to major multinational pharmaceutical corporations. Medicinal product development must meet strict standards for safety, quality control and continuous monitoring after the products have been marketed. The industry is also required to maintain comprehensive monitoring, including reports to the authorities after marketing.

Figure 3.2 indicates the number of active substances that have been granted marketing authorisation[3]. This figure indicates a high number of active substances on the market, and that the number has increased significantly from 2005 to 2014. It has been asserted that there is currently an innovation crisis with respect to new active substances. However, these numbers show no signs of any innovation crisis, at least in terms of quantity.

Figure 3.2 Number of active substances on the market between 2005–2014
Source: Norwegian Medicines Agency

It generally takes somewhere between 10 to 15 years to develop a new medicine. This is a costly process, and estimates of actual costs will vary a great deal and depend on whether one includes

[1]The first Apothecary (Pharmacy) Privilege was given to Nicolaus de Freudt at the Svaneapoteket in Bergen on 13 December 1595 by King Christian IV.

[3] This figure shows the net figure, meaning that the new active substance has been added, while the deregistered active substance has been removed.

research that does not result in a new active substance. There are generally two approaches to the development of new medicinal products. The first approach involves taking known substances and testing these substances within different biological systems to identify signals that could indicate effect.

The other approach involves the focus on the cause of the disease at a molecular level, and based on these findings, try to design new targeted molecules for treatment of the disease. Both processes are demanding, and there are many trace results that do not result in new active substances, at least initially. Sometimes efficacy is discovered at random if an active substance appears to have an effect in other areas than the one first documented. Sildenafil, for instance, which is the active substance in Viagra, was first shown to have a documented effect on pulmonary hypertension (high blood pressure affecting the arteries of the lungs). The effect on erectile dysfunction was a random discovery.

Once researchers have identified a substance that shows promise, they will commence with preclinical trials. This is a phase of research carried out in the laboratory, with animal testing. If preclinical studies are successful, the research continues with clinical trials.

Figure 3.3 shows the process from preclinical studies and industrial authorisation to clinical trials, the application for marketing authorisation, and studies carried out after marketing has been approved (Phase IV trials). This time frame is intended as an illustration of such a process.

The purpose of clinical trials for medicinal products is to find out how the medicine works, potential adverse reactions from the medicine, and how the medicine is metabolised in the body. Clinical trials must be completed before a new medicine can receive marketing authorisation. Clinical trials are discussed in greater detail in Chapter 22.

Figure 3.3 Illustration of preclinical and clinical trials

3.2 Marketing authorisation

Norway participates in the joint European approval processes of medical products through its membership in the EEA and the European Medicines Agency (EMA). As part of the cooperative work, applications for marketing authorisation are jointly evaluated by all member states.

Once a medicine has been granted marketing authorisation, the manufacturer will receive permission to market the medicine in accordance with the conditions specified in the approved summary of product characteristics.

A medicine will be granted marketing authorisation if the benefits of using a medicine are considered to be greater than its potential risks. The assessment of the risk-benefit ratio of a medicine is based on documentation submitted by the manufacturer upon applying for marketing authorisation. In the application, the manufacturer is required to demonstrate the pharmaceutical quality, safety and medical efficacy of the medicine, as well as pharmacovigilance systems and activities designed to minimise and manage potential risk involved while using the medicine. Marketing authorisation applies to the area or areas of use, as well as the dosages specified in the summary of product characteristics. When a medicine is granted marketing authorisation, this does not necessarily imply that it is recommended for use, for instance, through the reimbursement scheme, or as part of an established treatment in hospital. Whether it will be recommended for use and financing will depend on its efficacy, as compared with existing treatment methods. Financing systems are discussed in Chapter 19.

The manufacturer cannot market medicinal products for other use than that for which it has been approved in the marketing authorisation. Nevertheless, such medicinal products are permitted for use in other ways (off-label) than that which has been approved. For all other types of treatment, the use of the medicine must be medically justifiable, based on the regulations stipulated in the Health Care Personnel Act, as noted in the Report to the Storting (Meld. St.) 11 (2014–2015) Quality and Patient Safety 2013.

Box 3.1 Procedures for the approval of medicinal products

Applications for marketing authorisation are evaluated through various procedures depending on the type of medicine for which approval is being sought, and on the market for which the manufacturer is seeking to sell the medicine. In Europe, there are four different procedures for evaluating applications for marketing authorisation.

- *Centralised Procedure* (CP): The product is granted marketing authorisation for most EU and EEA countries. This procedure is mandatory for most new active substances. Here an application is submitted directly to the EMA, and the application is evaluated by two different member states. The application is then discussed in EMA's expert committees before any recommendation for authorisation is made. The EU Commission will then grant marketing authorisation, which will be valid throughout the EU. The Norwegian Medicines Agency will make a corresponding decision to permit the marketing of this medicine in Norway.
- *Mutual Recognition Procedure* (MRP): The product's existing national marketing authorisation will be expanded so that it is valid in two or more member states. Approval by a member state is based on the recognition of the application assessment conducted by the national medicines authority that granted the first authorisation. However, a member state may refuse authorisation if it concludes that the product represents a serious risk to public health.
- *Decentralised Procedure* (DCP): The product will be granted its first marketing authorisation for two or more member states. A member state, or reference state, will evaluate the application on behalf of the others. The other member states can then recognise the assessment made by the reference state. However, the other states may refuse authorisation if they conclude that the medicinal product represents a serious risk to public health.
- *National Procedure*: The product is granted marketing authorisation for one member state. This authorisation can then be used when applying for joint recognition in one or more EEA member states.

The Norwegian Medicines Agency participates actively in the European medicines cooperative, and contributes to the decision-making process, in order to promote the correct use of medicinal products in Europe. Norway is responsible for evaluations, and participates in all scientific committees under the administration of the European Medicines Agency, EMA.

In the European medicines cooperative, each member state must possess its own national assessment competence, and authorisation procedures are coordinated by each individual state. This means that the active professional competence is not located within the central EU system, but rather with the national authorities.

By participating in the EMA committees, the Norwegian Medicines Agency contributes to the EEA cooperation with its national knowledge and expertise. The European cooperative is

founded on a politically selected work distribution principle, in order to utilise EEA resources in the field of medicinal products.

There are requirements for marketing authorisation that must be fulfilled to ensure that medicinal products are of good quality and safe for patient use. The European cooperative in which Norway participates is a vital element in ensuring good quality and patient safety.

Box 3.2 Medicinal products for treatment of rare diseases (orphan drugs)

For medicinal products intended for treatment of rare diseases (orphan drugs) it is generally not commercially profitable to obtain the required documentation for marketing authorisation. Therefore, the EU has a separate set of regulations for rare diseases, in order to provide the industry with incentives to develop such medicinal products[1].

In the EEA, a disease is considered rare if it affects fewer than 5 of 10,000 inhabitants, or when one cannot expect to recoup the costs of developing the necessary medicine in the usual manner. Approximately 300,000 people are living with a rare disease in Norway (30 million in the EU).

Regulations apply to medicinal products intended for use by those with life-threatening or chronic, disabling conditions, where there is no existing approved treatment. If a treatment already exists, the regulations will still apply if the medicinal product is considered of significant benefit to the patients. The EMA provides free regulatory and scientific advisory services for such medicinal products, and application fees for marketing authorisation for these medicinal products is significantly reduced. These medicinal products are also granted ten years of market exclusivity for the approved area of use.

Since 2000, approx. 1400 medicinal products were given status as orphan drugs by the EMA. About 100 of these have been granted marketing authorisation. In 2014, 17 (20%) medicinal products approved through centralised procedures were orphan drugs. It is anticipated that their number and proportion will continue to rise in the years to come.

[1] Regulation (EC) no. 141/2000

The industry itself determines which medicinal products they wish to develop, based on available knowledge of diseases, physiological mechanisms, potential active substances and especially the marketing potential for each new medicine. There are still major disease groups that lack effective treatment. Because of this, the European Medicines Agency EMA now offers special arrangements for medicinal products intended for the treatment of rare diseases, and for antibiotics which are discussed in Box 3.2 and 3.3. These special arrangements have been designed to provide the industry with better conditions for developing medicinal products for these disease groups. New arrangements, such as regulatory advice and adaptive pathways are among the methods intended to provide the industry with incentive to develop and commercialise new medicinal products. This is discussed in further detail in Chapter 23.

In October 2014, the EMA made the decision to make clinical reports from marketing authorisation applications, submitted after 1 January 2015, available to the public. Applications for marketing authorisation must contain all clinical trials, including those that have not yet been published. Publication of these reports will provide researchers and society with a more comprehensive idea of the safety and efficacy of these medicinal products.

Box 3.3 Antibiotics

In Europe, as in the rest of the world, the development and proliferation of antibiotic-resistant bacteria has become a major problem. There is a risk that in the future we will no longer have effective antibiotics against bacteria which causes infections in humans.

There is currently very little research on the development of new, effective drugs against bacterial infections. Authorities are working to facilitate research for the industry, so that it will become more attractive to research new antibacterial substances, and that it will be easier to apply for marketing authorisation. The industry can seek scientific advice from the EMA, and receive assistance in designing research trials. The EMA also offers the opportunity for a more timely regulatory process when applying for marketing authorisation, and both smaller and medium-sized enterprises may be offered fee exemptions. Companies can also request special processing from the EMA in certain cases, for instance for antibacterial medicinal products with entirely new action mechanisms.

Efforts are now underway to compare the summaries of product characteristics for currently marketed antibacterial medicinal products in all EEA countries. This work has been carried out for medicinal products that vary in their indications for use, dosage and contraindications, which have been approved in various European countries. European medicines authorities are cooperating on assessing the safety and efficacy of medicinal products, and are making joint decisions regarding medicinal products that have adequate documentation of indication and dosage.

Norway is actively involved in the decision-making process so that antibacterial substances are consistent with the restrictive Norwegian stance on the use of antibiotics. This means that an infection, which is likely to be cured spontaneously without antibiotic treatment (such as otitis media, or ear infections, and acute bronchitis), will not be approved as an indication for broad spectrum antibiotics.

One project initiated by the EU Commission involved obtaining updated knowledge of older antibacterial medicinal products that were approved with insufficient documentation of safety and efficacy, where there is often a lack of documentation for optimal dose, as well as dosing frequency and duration.

3.2.1 Patents, patent protection, generics and biosimilars

A patent gives the owner the exclusive right to make use of their discovery for business or operating purposes for a certain period of time. This prevents others from copying the discovery, and gives the owner the opportunity to achieve adequate returns from the investment. The term of the patent is 20 years. All new and innovative medicinal products are patented.

A patent is sought at an early stage of medicinal product development, but because development generally takes a long time, and there is often little time left of the patent term when the medicinal product finally receives marketing authorisation. For medicinal products, a patent owner may also apply for a supplementary protection certificate which extends the period of effective protection for patents for an extra five years.

To further secure the manufacturers, there are medicinal product regulations on patent protection. These regulations prevent generic product manufacturers from sending in applications for marketing authorisation until the original product has been on the market for eight years in the EEA area. Marketing authorisations that have been obtained at an early stage will also be valid for up to ten years after the first authorisation has been granted in the EEA.

Generic medicinal products

New medicinal products may receive marketing authorisation in Norway if the collective assessment of quality, safety and efficacy indicates that the medicinal product has a positive risk-benefit ratio, cf. Chapter 3.2. The first approved medicine with a new active substance is called the original medicine. Once the patent term has expired, other manufacturers may produce copies of the medicinal product. Such copies of chemical substances are called generic medicines.

Generic medicines and original medicines always contain the same active substances in the same amount, but may contain different excipients and will differ in appearance. The text on the packaging and in the package leaflet may vary between products. Generic medicines must have their own documentation of quality, while documentation of safety and efficacy will be the same as for the original medicine. In the application for marketing authorisation, manufacturers must provide evidence indicating that the active substance in the medicine is metabolised in the same manner.

The step pricing system is used to reduce prices wherever there is generic competition. This system has resulted in lower prices for medicinal products that have generic competition. The step pricing system is discussed in Chapter 16. Generic medicinal products and pharmacy substitutions are discussed in Chapter 11.

Biosimilar medicinal products

Biological medicinal products are produced with the aid of gene-based technology in live cells. Biological medicinal products are important for the treatment of diseases such as cancer, diabetes, inflammatory diseases and bleeding disorders. These medicinal products have a complex structure which is difficult to characterise. It is therefore not possible to create identical copies of these medicinal products. The term “biosimilar medicinal products” has therefore been introduced to indicate that the product is identical to the original substance in function, but not entirely identical in structure.

Several biosimilar medicinal products have been approved in the EEA. Greater competition

through increased production of biosimilar medicinal products would likely reduce the costs; see Chapter 16.

Box 3.4 Overview of biosimilars with marketing authorisation

Five biosimilar medicinal products are currently being marketed in Norway, in the following medicinal product groups: Filgrastims (stimulate the production of white blood cells), growth hormones (stimulate growth, increased height), epoetin alfa (stimulates the production of red blood cells), follitropin alfa (follicle and gonadal stimulation) and tumour necrosis factor inhibitors (monoclonal antibodies used in treatment of inflammatory diseases). An increase in the number of applications regarding biosimilar medicinal products is anticipated over the next several years, since the patent term for many biological original products will soon expire.

Biosimilar medicinal products undergo the same thorough evaluation process by the EMA as other medicinal products, with the same requirements for quality, safety and efficacy. This means that biosimilar medicinal products must provide the same effect and safety as the original. They are therapeutic alternatives within the same area of indication as the reference product.

There is an ongoing study intended to gain further knowledge of substitutions with biosimilars. This study is discussed in Chapter 11.

3.3 What medicinal products are currently on the market?

Table 3.1 shows that medicinal products for the treatment of arthritis, multiple sclerosis and cancer are among the 25 medicinal products with the highest sales. This table also shows that non-prescription medicinal products such as nose spray and smoking cessation products have high total sales turnover. These medicinal products are not reimbursed by the public health system.

Table 3.1 Overview of the 25 most sold active substances, based on turnover, in 2014

Active substance	**Example of area of use**
Adalimumab	Arthritis
Etanercept	Arthritis
Infliximab	Arthritis
Salmeterol and Fluticasone	Asthma/COPD
Nicotine	Smoking cessation
Coagulation Factor VIII	Bleeding prophylaxis (haemophiliacs)

Formoterol and Budesonide	Asthma/COPD
Sofosbuvir	Hepatitis C
Paracetamol	Pain
Rituximab	Cancer and arthritis
Fingolimod	Multiple sclerosis
Xylometazoline	Nasal congestion
Golimumab	Arthritis
Abiraterone	Prostate cancer
Tiotropium bromide	COPD
Trastuzumab	Breast cancer
Natalizumab	Multiple sclerosis
Somatropin	Growth hormone
Methylphenidate	ADHD
Esomeprazole	Reflux disease
Ibuprofen	Pain
Immunoglobulin, normal human, intravascular administration	Immunodeficiency disorder, leukaemia
Rivaroxaban	Blood clot prevention
Certolizumab pegol	Arthritis
Pregabalin	Neuropathic pain

Source: Norwegian Institute of Public Health (Wholesaler-based medicinal product statistics)

The three medicinal products creating the highest revenue are biological medicinal products for the treatment of inflammatory rheumatic disease, inflammatory bowel disease and psoriasis.

Table 3.2 shows that when use is measured by dose and not by sales, the dominant medicinal products are those intended for treatment of blood clots, high cholesterol and blood pressure. Many of these medicines have been on the market a long time, and generic competition is now possible. This is discussed in further detail in Chapter 3.2.1.

Table 3.2 Medicinal products generating highest turnover, measured in DDD[1], in 2014

Active substance	**Example of area of use**
Acetylsalicylic acid	Blood clots
Atorvastatin	High cholesterol

Simvastatin	High cholesterol
Sodium fluoride	Tooth decay
Paracetamol	Pain
Cetirizine	Allergies
Amlodipine	High blood pressure
Zopiclone	Insomnia
Xylometazoline	Nasal congestion
Ramipril	High blood pressure
Ascorbic acid	Vitamin C deficiency
Candesartan	High blood pressure
Levothyroxine sodium	Hypothyroidism
Metoprolol	High blood pressure
Vitamin B Complex, uncombined	Vitamin B deficiency
Levonorgestrel and Ethinyl estradiol	Birth control
Escitalopram	Depression
Esomeprazole	Reflux disease
Pantoprazol	Reflux disease
Ibuprofen	Pain
Calcium, combined with Vitamin D and/or other substances	Calcium deficiency/ Osteoporosis
Metformin	Diabetes
Desloratadine	Allergies
Losartan	High blood pressure
Furosemide	High blood pressure

[1] DDD stands for defined daily dose, and is a measurement of medicine consumption.
Source: Norwegian Institute of Public Health (Wholesaler based medicinal product statistics)

Statistics from the Norwegian Prescription Database indicate that antibiotics and various analgesics are among those medicinal products with the highest number of consumers, cf. Table 3.3. This often involves short-term treatment. There are also many people who use different medicinal products for the prevention and treatment of cardiovascular diseases, and these are the most frequently used medicinal products, measured by defined daily dose, cf. Table 3.2 Hypnotics, allergy and asthma medicines, and medicines for oesophageal inflammation are on

the list of the 25 medicinal products that are used the most, measured by both the number of users and the number of doses.

Table 3.3 The 30 active substances with the highest number of consumers in 2014 (dispensed by prescription from the pharmacy)

Active substance	**Example of area of use**
Phenoxymethylpenicillin	Infections
Paracetamol[1]	Pain
Acetylsalicylic acid	Blood clots
Codeine, combinations excluding psycholeptics	Pain
Diclofenac[1]	Pain
Zopiclone	Insomnia
Cetirizine[1]	Allergies
Metoprolol	High blood pressure
Simvastatin	High cholesterol
Ethylmorphine	Cough
Salbutamol	Asthma
Ibuprofen[1]	Pain
Atorvastatin	High cholesterol
Pivmecillinam	Infections
Levothyroxine sodium	Hypothyroidism
Pantoprazole[1]	Reflux disease
Chloramphenicol	Infections
Tramadol	Pain
Prednisolone	Inflammatory conditions
Desloratadine	Allergies
Mometasone	Allergies
Esomeprazole	Reflux disease
Levonorgestrel and ethinyl estradiol	Birth control
Doxycycline	Infections
Oxazepam	Anxiety

Amoxicillin	Infections
Amlodipine	High blood pressure
Estradiol	Oestrogen deficiency
Diazepam	Anxiety
Escitalopram	Depression

[1] Does not include prescription sales.
Source: Norwegian Institute of Public Health (Prescription Database)

3.4 What medicinal products can we expect in the future?

The knowledge in the fields of medicine and technology is rapidly developing. A great deal of knowledge and new technology now offers opportunities for the development of new medicinal products. The most important of these is the knowledge of genetics and the possibility of genome sequencing, an increased medical understanding through molecular biological and genetic research, and technologies such as nanotechnology, imaging technology and radiology.

The research strategy that gave us many of the chemical medicinal products throughout the 1980s and 90s involved methods of systematic testing of known substances in biological test models. Over the last decade, the development of gene technology and molecular medicine has resulted in a greater focus on the molecular causes of disease for the current development of medicinal products.

Biological medicinal products

New forms of treatment may include molecularly targeted therapy which can regulate or attack mechanisms causing disease, without disturbing the normal function of the cell or organ. Biological medicinal products may therefore often have less severe adverse reactions than traditional systemic treatment.

Monoclonal antibodies make up the largest group of biological medicinal products. They recognise specific structures on cells or proteins, and can stimulate the immune system to attack these structures. They can also inhibit or block undesirable molecular processes. Monoclonal antibodies targeted at the regulatory mechanisms of the immune system can enhance the treatment with other medicines, rendering them more effective. They are therefore often used in combination with other treatments. Another rapidly developing field is combination therapy, where the immune system is activated to target cancer cells following radiation therapy.

The first monoclonal antibodies were produced 30 years ago, and have since developed to become an important therapeutic tool in the fight against diseases for which there was no previous adequate treatment. Recombinant DNA technology can also be used to create complex proteins that can improve the therapeutic characteristics of the medicine. For instance, there is now a synthetic insulin for the treatment of diabetes that remains in the blood for a much longer

period of time, by fusing with more durable proteins.

Nanotechnology

Nanotechnology is an emerging, but so far underutilised field of technology. In the field of medicine, the purpose of nanotechnology is generally to transport medicines through the body to a specified organ, for diagnosis and treatment. Nanotechnology can help to increase the solubility of an active substance, reduce toxicity and affect biodistribution.

The European Medicines Agency has approved several nanomedical products, where active substances are encapsulated in nano-sized liposomes. Examples from the field of cancer treatment include toxic drugs attached to nanoparticles for achieving targeted delivery of the substance, while reducing the toxic effect of the drug.

Box 3.5 Methods for development of medicinal products

Research is being conducted on new methods for the development and testing of medicinal products, such as modelling and simulation (M&S). These are advanced mathematical and statistical methods that can be used to organise, analyse and simulate data – including pharmacological, physiological and pathophysiological data.

The European Medicines Agency has established a new working group (MSWG) for evaluating modelling and simulation methods (M&S methodology). The group's efforts will contribute towards fulfilling EMA's interest in a stronger integration of modelling and simulation methodology, for both the development of medicinal products and with respect to authorities' regulatory evaluation of medicinal products. The EMA considers modelling and simulation methodology to be an important tool for improving the efficiency of medicinal product development, and for supporting the authorities' evaluation of medicinal products. Modelling and simulation methodology can help to reduce the level of uncertainty in the assessment of safety and efficacy. It can also provide better information, and in some cases, help to reduce the need for clinical trials.

Personalised medicine

Personalised medicine involves procedures that tailor prevention, diagnostics and treatment to the individual patient. [3]

In personalised medicine, medical history, clinical findings, lifestyle factors and environmental influences are all linked to the patient's genetic material (DNA), and to any pathogens such as bacteria and viruses. Genetic material is important for many physiological and pathological processes. Technological development over the past several years has made it possible to collect large amounts of biological data, with a higher level of precision than before. Personalised medicine offers a more precise foundation for treatment, together with increased knowledge of DNA, greater opportunities for genome sequencing and better knowledge of the relationship between genes and development of disease.

Personalised medicine includes medicinal products that have been developed for greater efficacy and highest possible precision. Over the last decade, new, targeted medicines have been developed which either block defects or correct specific errors at a molecular level. Personalised treatment is particularly relevant for patients with cancer, patients with rare hereditary diseases, and patients with infectious diseases. In 2013, 81 new medicinal products received marketing authorisation in Europe. Among these were 16 medicinal products for the treatment of cancer, and most of them are so-called targeted therapies, whereby the diagnostic process and choice of treatment are based on biomarker information. Several of the new medicinal products have been introduced together with diagnostic tools which simplify the diagnostic process and which are essential in determining the patient subgroups that will benefit from targeted treatment. An example of such targeted treatment is Herceptin, used in the treatment of breast cancer.

Box 3.6 Examples of personalised medicine

All trends are indicating a continuing increase in the development and use of personalised treatment. Each year there are new articles being published on studies that examine the relationship between gene expression and disease. DNA sequencing and characterisation of the human genome has revealed thousands of new targets for medicinal products.

Examples of personalised therapies:

Dabrafenib (Tafinlar) for the treatment of patients with a type of skin cancer, a melanoma with a BRAF V600E mutation. Tafinlar attacks proteins produced by the modified BRAF gene and reduces or halts the development of the cancer.

Ataluren (Translarna) for treatment of Duchenne muscular dystrophy, a rare, hereditary disease affecting only boys. Patients with this condition have a mutation in the gene that codes for the protein dystrophin, preventing the dystrophin in the muscles of these patients from functioning. Ataluren is designed to work in such a way that the mutation does not stop protein production in the cells prematurely, thereby enabling the cells to produce normal and functional dystrophin.

Personalised medical treatment is now being offered more frequently. The Norwegian Directorate of Health assigned the Ministry of Health and Care Services the task of preparing a national strategy for personalised medicine in 2015. This national strategy will be based on a report from the national assessment of personalised medicine in health services, conducted by the regional health authorities in 2014. Personalised medicine can offer greater benefits for the patient in the form of more timely and precise diagnostics, as well as better opportunities for an

individually tailored treatment with greater efficacy and fewer adverse reactions.

Advanced therapy

Advanced therapy medicinal products (ATMP) include gene therapy, cell therapy and tissue engineering, and may offer new, ground-breaking and effective treatment for a variety of diseases and injuries, such as cancer, neurological diseases and burn injuries.

Gene therapy involves the delivery of new genetic material to humans, to repair or compensate for a defective gene in certain type of cells. Cell therapy means that cells are given to humans to treat diseases with the aid of the cells' pharmacological, immunological or metabolic action mechanisms. Tissue engineering involves giving cells or tissue to humans to repair or replace human tissue or organs.

Gene and cell therapy and tissue engineering are regarded as medicinal products, and they must therefore be granted marketing authorisation before they can be used. The demand for marketing authorisation is justified by the importance of ensuring good and safe treatment, and for promoting equal access to these forms of treatment for all patients in the EEA area. It is, however, possible to seek exemption from the requirement for central approval, to provide hospitals that are developing new forms of treatment of a more experimental nature with greater flexibility. This so-called hospital exemption applies to products that are not used routinely. In Norway, such exemptions must be approved by the Norwegian Medicines Agency.

Since the regulations regarding advanced therapeutic products came into force in 2009, 14 applications for marketing authorisation have been submitted and 5 forms of therapy have been approved. It is anticipated that 14 new applications will be submitted during the next two years. There is extensive research activity in this area. From 2004 to 2010, 318 clinical trials for 250 different types of advanced therapy were registered. Cell therapy and tissue engineering make up the largest share of the trials, and cancer is the major indication. Both academia and smaller companies are behind most of the trials.

Advanced therapy medicinal products can be used to treat diseases that did not previously have any available treatment methods. One example is the gene therapy product Glybera, which was approved in 2012. This contains a substance that compensates for the inability to produce an enzyme which breaks down fat in the blood. It uses a virus as a messenger to carry the functional gene into the muscle cells, enabling these cells to produce the enzyme. It is possible, for instance, to treat a bad knee by cultivating new cartilage based on the patient's own cells. This is an example of tissue engineering which is already well-established, with two approved products on the market. One example of cell therapy is immune cells which are removed from the body and manipulated to recognise cancer cells, and then replaced, in order to stimulate the immune system to fight the cancer cells. One product of this type of cell therapy has already been approved (Provenge was approved in 2013), and several such treatment methods are currently under development. The first product based on stem cells was approved in 2014 (Holoclar). This is a treatment for eye injuries. Several such products, based on stem cells, are currently being

developed. Many patients who receive treatment with advanced therapy in Norway today are participating in clinical trials at university hospitals, or being treated at such hospitals.

4 Actors in the medicinal product market

There are many different actors in the medicinal product market, the most important of which are the patients, the pharmaceutical industry, prescribers and other health care personnel, pharmacies and health authorities. This chapter provides a brief overview of the key actors and their current functions and responsibilities.

4.1 Patients and service users

The ambition of the government is to create truly patient-centred health services and to enable patients to manage their lives as well as possible. Norway was one of the first countries to adopt laws regarding service-user participation, and service-user or patient participate has now been incorporated into both the Patients' Rights Act and the Health and Care Services Act.

The Patients' Rights Act, Section 3-1 states the following:

> "The patient or service user is entitled to participate in the implementation of health and care services. This includes the patient's right to be involved in the choice between available and medically sound methods of examination and treatment. The form of this participation shall be adapted to the individual patient's ability to convey and receive information."

Patient participation takes place in the encounters between the individual patient and health care personnel, but also at a higher level, whereby patient associations participate in planning processes, evaluation of services, service-user councils, quality committees, etc.

The Report to the Storting no. 26 (Meld. St. 26, 2014–2015), Chapter 12, discusses service-user participation in their report entitled "The Primary health and care services of tomorrow – localised and integrated". Here it was noted that there is a significant need for improvement, especially with respect to knowledge enhancement among service-users, as well as communication between service-users and health care personnel. Peer support and family members are also mentioned.

When service-user participation became a legal right, the roles of patients, users and health care personnel were simultaneously undergoing changes. Just a generation or two ago, medical students were told that they should not provide patients with complete information, in order to spare them unnecessary worry and misunderstanding. In many ways, this was a patriarchal attitude. Physicians viewed most of this information as professional literature, written in manner that required a medical background to understand, and which few patients had the ability to grasp. They therefore felt this information would cause patients to become more confused than informed.

With the rise of the information society and an increasingly more educated population, it has become impossible to prevent people from gaining access to information about medicinal products. Today patients, consumers and health care personnel all have access to comprehensive information about medicinal products through the internet. In 1984 the Norwegian Pharmaceutical Product Compendium was approved for sale to the public, although now patients, consumers and health care personnel all have access to comprehensive information about medicines online. It may, however, be difficult to sort through, interpret and utilise the information available.

In order to create optimal health services for the patient, further efforts will be necessary to develop the communication of knowledge and information systems that help people make good decisions about their own health.

The use of medicines and the challenges associated with the misuse of medicines is discussed in Chapter 5.3. Suggestions on numerous different methods are mentioned in Chapter 7. These are intended to provide patients with more opportunities to exert influence, follow up their own treatment, and manage a life with illness.

4.2 The pharmaceutical industry

The primary role of the pharmaceutical industry is to develop, manufacture and sell medicinal products. The development and manufacturing of medicinal products is discussed in Chapter 3.

The pharmaceutical industry markets its own products and provides information on medicinal products in different ways, for instance through the Norwegian Pharmaceutical Product Compendium (Felleskatalogen). The pharmaceutical industry contributes, in various ways, in achieving many of the objectives of the pharmaceutical policy. Firstly, they are responsible for the development of medicinal products as new methods of treatment, thereby providing a greater opportunity for good quality treatment. Secondly, they follow quality assurance requirements for the development and manufacturing of medicinal products which also ensures good quality.

The pharmaceutical industry is, in practice, a global industry, and constantly undergoing change. The HelseOmsorg21 strategy discusses a global paradigm shift, whereby research and innovation is now more often carried out by smaller companies rather than by larger, international pharmaceutical corporations. Many new active substances have been discovered and researched by smaller drug companies, often originating in academic research environments. In many cases, further development, production and marketing are all carried out through a partnership with one of the major international pharmaceutical companies. Some of the larger international pharmaceutical companies tend to scale down their development of medicinal products during the preclinical phase, and then enter a partnership with these smaller companies, indicating that basic research and preclinical research are important for continued innovation.

The pharmaceutical industry in Norway

In Norway, there are 40 or more research-intensive enterprises, of small or medium size. Their goal is to develop new medicinal products.

The development of new medicinal products is a demanding process, in terms of knowledge, finances and regulations. It is imperative that the Medicines Agency receives acceptable documentation indicating quality, safety and efficacy before it can grant marketing authorisation. To assist smaller companies in satisfying regulatory requirements, authorities provide regulatory advisory services. This is discussed in Chapter 23. Such services can help enhance the capacity for innovation in Norway, in accordance with the objective of facilitating innovation.

Box 4.1 Xofigo

Xofigo (Radium-233) is a medicinal product developed in Norway for patients with castration-resistant prostate cancer that has spread to the bones. This medicinal product stems from cancer research at Oslo University Hospital and the University of Oslo, and led to the establishment of the company Algeta in 1997. In 2006, Algeta was listed in the stock exchange in Oslo. In 2009, they entered a strategic partnership with Bayer for the development and global marketing of Xofigo. The company was assessed at NOK 17.6 billion. In February 2015, a decision forum for new methods determined that Xofigo could be introduced as treatment for castration resistant prostate cancer with symptomatic bone metastases. The production of Xofigo takes place at the Institute for Energy Technology (IFE) at Kjeller.

According to the Association of the Pharmaceutical Industry in Norway (LMI), there are just under 700 employees in member companies working in the area of research and development, while a total of about 3800 people are employed by LMI member companies.

[:figur:figX-X.jpg]

Figure 4.1 The pharmaceutical industry's investments in Research and Development (FoU) in Norway from 2007 to 2012.
Source: LMI

LMI states that the industry invested approximately 30 billion EUR in research and development in Europe, and more than 40 billion EUR in the United States. The industry employs more than 650,000 people in Europe alone.

Marketing and information

The medicinal product legislation defines what should be regarded as advertisement and promotion of medicinal products, and it also determines advertisement design. Advertisements

and promotions are regulated to ensure that they are balanced and that they promote a rational use of medicinal products.

The Health Care Personnel Act and the Regulation regarding gifts, etc. to health care personnel state that health care personnel cannot accept any gifts, commissions, services or other benefits intended to influence health care personnel services in an inappropriate manner. The relationship between health care personnel and the pharmaceutical industry is discussed in the preparatory works to the Act; see Proposition to the Odelsting no. 13 1998–99 (Ot.prp.) regarding the Act relating to health care personnel, etc., pages 64-65.

LMI has internal industry regulations which determine that pharmaceutical companies can only invite personnel who are permitted to receive advertisements for prescription medicinal products. LMI has also entered an agreement with the Norwegian Medical Association regarding guidelines for cooperation and collaboration. The purpose for this is to facilitate a more ethical and trustworthy collaboration between physicians and the pharmaceutical industry.

The pharmaceutical industry has websites with information for patients and health care personnel. Websites for health care personnel must be marked to indicate that they are intended for health care personnel only. Some pharmaceutical manufacturers also offer patient classes and health apps associated with their medicinal products.

The Norwegian Pharmaceutical Product Compendium (Felleskatalogen) is a wholly owned subsidiary of LMI. The company publishes the Pharmaceutical Product Compendium (Felleskatalogen), which is a reference book of human and veterinary medicinal products marketed in Norway. These texts summarise the summary of product characteristics. A paper version of the compendium is available, but the book is also published online, with approx. 9000 unique visitors each day. The Norwegian Pharmaceutical Product Compendium also has an app for tablets and smart phones, and is integrated in the search engine of the Norwegian Electronic Health Library (Helsebiblioteket) and on www.helsenorge.no. The pharmaceutical industry's role regarding information work is discussed in greater detail in Chapter 10.

4.3 Health care personnel

One of the most important ways to achieve high quality treatment with medicinal products is to ensure that all types of health care personnel have the proper education. We will not discuss each education in detail in this report, but will instead refer to the Report to the Storting no. 26, 2014-2015 (Meld.St. 26) The Primary health and care services of tomorrow – localised and integrated. Health care services are personnel-intensive and the quality of these services relies on the qualifications, knowledge and attitudes of its personnel.

Health care personnel groups that are important in terms of the use of medicinal product are those that have the right to prescribe. The same applies to personnel groups that dispense medicinal products to patients and pharmacists, and that have expertise related to medicinal products.

Prescribers

Prescribing is defined as the process of ordering medicinal products for one's own practice, to health care institutions and to patients. Only physicians and dentists are permitted to prescribe prescription-only medicinal products (Health Care Personnel Act, Section 11). The Ministry may, through regulations, determine that other health care personnel should be permitted a limited or restricted right to prescribe. Veterinarians may prescribe prescription veterinary medicinal products (cf. the Act related to veterinary surgeons and other animal health personnel, Section 17).

The restricted right to prescribe means that health care personnel other than physicians and dentists will be permitted to prescribe specific medicinal products.

Regulations regarding the requisition and dispensing of medicinal products from a pharmacy in Chapter 2 includes decisions concerning the right to prescribe.

Examples of the restricted right to prescribe include pharmacists who may prescribe medicinal products for pharmaceutical wards at hospital, and midwives who may requisition vaccines for approved vaccination programmes and all hormonal contraceptives for women from the age of 16 (the latter enters into force on 1 January 2016).

Health care personnel who prescribe medicinal products are responsible for considering the interests of the patient and major public resources. The primary requirement of such prescribing practices is that they must be medically justified, in accordance with the Health Care Personnel Act, Section 4.

General practitioners have several responsibilities regarding the follow-up of medicinal product use among their patients who live at home. A general practitioner shall coordinate medicinal treatment for patients on his or her list, in accordance with the Regular General Practitioner (GP) Scheme, Section 25. When a general practitioner changes a medicine, or receives information that treatment with the medicine has changed, the list of the patient's medicines must be updated.

Patients on the GP's list shall receive an updated list of medicines at each consultation with their GP if the medicine use has been changed. For patients that are using four or more different medicinal products, their GP shall conduct a medication review whenever this is considered necessary, based on a medical assessment.

A general practitioner must give other service providers in the health and care services an updated list of the patient's medicinal products when necessary, to provide patients with medically sound services.

Care personnel

Care personnel have an important role in ensuring the correct dispensing of medicinal products. They also have an important role in observing and following up patients' use of medicines. Medicine management regulations for health care enterprises and personnel who provide health

care services from 2008 were amended on 1 January 2015. This revision took into consideration the problems associated with inadequate information about patients' medicine use when they are transferred between different levels of health care. Leaders in health care institutions and enterprises are now required to ensure an adequate system for internal control.

The Norwegian Directorate of Health produced a new circular (IS 7/2015) for the regulations, which contains a detailed description of how these regulations are to be interpreted, as well as guidelines that provide advice and practical examples of good routines. Medicine management is described in greater detail in Chapter 12.

Pharmacists

The field of pharmacy encompasses knowledge related to medicinal products and medicine use. Pharmaceutical knowledge is key to the pharmacy system, and in other areas where it is necessary to supervise and follow up the use of medicines. This knowledge is also a part of a broad spectrum of research areas, forming the foundation for the pharmaceutical industry.

Pharmacists are employed throughout the health care sector, in public administration, education and research. The majority of pharmacists work in pharmacies, ensuring that patients are regularly receiving the medicinal products prescribed by their physicians. Pharmacists also have central roles in the pharmaceutical industry. Clinical pharmacists, primarily those at hospitals, contribute in multidisciplinary teams together with responsible physicians to ensure optimal pharmaceutical treatment for each individual patient.

An experience-based master's degree in clinical pharmacy was established at the University of Oslo in the autumn of 2009. The University of Oslo has now discontinued this experienced-based master's degree and instead incorporated a new specialisation in clinical pharmacy into the framework of the 5-year master's degree in pharmacy.

Multidisciplinary cooperation has been included in most of the curriculums, and most new pharmacists have received training in talking with patients about medicinal products, medication reconciliation, and medication review . There is also an increased focus on the identification and management of medicine-related problems to ensure correct use of medicinal products.

There is a need to assess how pharmacists' competency can best be utilised to improve the quality of treatment with medicines.

Box 4.2 Pharmacy education in Norway

Norway has five schools offering educational programmes in pharmacy. The University of Oslo and the University of Bergen each have a 5-year integrated master's degree programme. The University of Tromsø has a 3-year bachelor's and 2-year master's programme. The Nord-Trøndelag University College and Oslo and Akershus University College each have a 3-year bachelor's programme, while NTNU, the Norwegian University of Science and Technology offers a 2-year master's programme.

The 3-year bachelor's programme qualifies for authorisation as an assisting "reseptar" pharmacist, while the master's programme qualifies for authorisation as an authorised "provisor" pharmacist. Only the master's degree fulfils the requirements for Article 44 of the EU Directive 2005/36/EC, and is the equivalent of the term "pharmacist" in the European and international sense.

Pharmacy technicians

Pharmacy technician is a vocational education programme at an upper secondary school level. A pharmacy technician assists pharmacists in the pharmacy and has tasks related to customer service and counter sales. Pharmacy technicians cannot independently dispense medicinal products requiring prescriptions or requisitions.

4.4 Pharmacy

A pharmacy sells medicinal products, but in some cases, it may also manufacture medicinal products. Pharmacy activities are regulated by the Pharmacy Act. The Pharmacy Act shall ensure the proper dispensing of medicinal products to the end user. It shall contribute towards the correct use of medicines and ensure that all parts of the country have access to quality medicinal products and pharmaceutical services at a reasonable price.

In accordance with the statutory objective, the primary activity of the pharmacy can be divided into two categories: the first is to have an efficient and safe distribution and dispensing of medicinal products. This contributes towards achieving the objective of an equal and timely access to medicinal products. These tasks and their further development are discussed in Chapter 18.

The second activity is to ensure the correct use of medicines by providing advice for consumers and patients. Pharmacy employees have a key role in the communication of medicine information. They meet consumers face to face, and the pharmacy's medicine competence is available in pharmacies all over the country. Consumers need no appointment to receive information about their medicines, to ask questions, or to discuss medicine-related problems. The further development of these tasks is discussed in Chapter 7.1.4.

4.5 Regional health authorities and municipalities

Both regional health authorities and the municipalities are stakeholders in the pharmaceutical market. A large part of the prescription and use of medicinal products takes place within these areas.

The Medicine Management Regulation for health care institutions/enterprises and health care personnel providing health care places certain demands on these enterprises. Medicine management is discussed in Chapter 12. Responsible medicine management is essential for ensuring quality treatment and patient safety.

Information and training

Learning and mastery training has been established in specialist health care services in all health authorities. Learning and mastery training for municipal health care services is still at an early stage. The organisation of municipal learning and mastery services varies considerably. These services may, for instance, be provided in learning and mastery centres or "healthy-living centres", centres including healthy-living and mastery initiatives, at local medical centres, or in health institutions.

Many health authorities and municipalities collaborate on learning and mastery services, for better quality and integrated patient care pathways.

Patients who suffer from long-term health problems may have general worries, practical challenges and lack of knowledge about their own illness that can exacerbate their situation and reduce their quality of life. Learning and mastery initiatives can provide patients and their families with greater insight into their situations, so that they are better able to cope and to manage their daily lives. These initiatives not only address medical conditions, but also issues associated with work, family and friends. Equal cooperative efforts between health care professionals and user representatives ensure that learning and mastery services place the needs of the patients and their families first, in accordance with the Report to the Storting no. 26 2014-2015 (Meld. St. 26) The Primary health and care services of tomorrow – localised and integrated.

4.6 Public administration

Public administration oversees tasks related to the issue of marketing authorisation for medicinal products, as discussed in Chapter 3.2. Administration also deals with tasks and initiatives designed to help achieve the objectives specified in Chapter 2. The Ministry of Health and Care Services has the overarching responsibility, but many other actors have important roles.

4.6.1 The Norwegian Medicines Agency

The Norwegian Medicines Agency is the government authority for medicinal products and is responsible for the approval of medicinal products, including the evaluation of marketing authorisation applications. They also evaluate applications for clinical trials of medicinal

products. The Norwegian Medicines Agency is responsible for the regulatory administration of the supply chain for medicinal products, including permits for manufacturing, import and export, wholesaler enterprises, and sales of medicinal products. The Norwegian Medicines Agency also determines the price of prescription medicinal products, to evaluate reimbursement through the reimbursement scheme and conduct health technology assessment of medicinal products financed by regional health authorities. The Norwegian Medicines Agency also oversees pharmaceutical surveillance and monitors manufacturers, wholesalers, pharmacies, clinical trials and advertising. Last, but not least, the Norwegian Medicines Agency provides informational and advisory services. These are discussed in more detail below. The Norwegian Medicines Agency is responsible for initiatives intended to contribute towards the achievement of medicinal product policy objectives, as discussed in Chapter 2.

Information about medicinal products

Once a medicinal product is granted marketing authorisation, the Norwegian Medicines Agency must also approve package leaflets and a summary of product characteristics (SPC), which sums up the knowledge that provides the basis for the approval of the medicinal product. Information on the package leaflet is intended for the patient, while information in the SPC is directed at health personnel. These documents also provide the legal framework for manufacturer marketing.

The Norwegian Medicines Agency publishes reviews of new medicinal products, where the risks and benefits of the new medicinal product is assessed against existing treatment. These reviews are published on the Norwegian Medicines Agency's website and in the "News about medicines" in the Journal of the Norwegian Medical Association.

The European Medicines Agency publishes information about medicines that are authorised through the centralised procedure described in Chapter 3. It also publishes assessment reports describing evaluations that formed the basis for authorisation.

The Norwegian Medicines Agency has developed an electronic prescription support system (FEST). For more information about FEST, see Chapter 7.2.1.

The Norwegian Medicines Agency publishes current information on its website and in social media. This is information regarding the quality, safety, efficacy and availability of various medicinal products.

4.6.2 The Norwegian Directorate of Health

The Norwegian Directorate of Health is a government agency in charge of implementing adopted policies on behalf of the government and the Storting (Norwegian Parliament), and the administration of existing legislation.

The Directorate is also a specialist body that oversees monitoring conditions that may have an impact on public health and the development of health and care services. The Directorate shall

compile knowledge and experiences, setting national standards in different areas. The Norwegian Directorate of Health is an expert body which acts as an autonomous and independent advisor.

The Norwegian Directorate of Health has a statutory responsibility for the development, communication and maintenance of national professional guidelines and protocols. There are currently 50 national professional guidelines and about 120 protocols. The purpose of national professional guidelines is to contribute towards appropriate and quality priorities, and to prevent undesirable inequality between the services. Many of the guidelines do not contain specific information about medicines, but instead indicate when medicinal treatment may be relevant, compared with prevention and other forms of treatment.

The Directorate has prepared several protocols which are relevant for the appropriate use of medicines, such as the protocol for correct use of medicines for the elderly, and the protocol for conducting medication reviews.

The Directorate oversees e-health, including e-prescriptions and core medical records. The Directorate is also the secretariat for the national system for introduction of new methods in specialist health care services, as well as the secretariat for the patient safety programme. The Norwegian Directorate of Health shall also develop measures for monitoring, evaluating and conveying information about the use of new methods. The Norwegian Health Economics Administration (HELFO) is the Directorate's external agency. Its tasks include the processing of applications for individual reimbursement and administration of the contribution scheme.

In 2011, the Norwegian Directorate of Health established the web portal "helsenorge.no". Helsenorge.no offers quality assured information about diseases, treatment, health advice and services offered by the healthcare system. The page "My health" (Min helse) on helsenorge.no gives patients access to their own health information, and will in time provide patients with the opportunity to communicate digitally with health services.

4.6.3 Norwegian Knowledge Centre for Health Services

The Knowledge Centre provides research summaries, conducts health economic analyses, measures the quality of selected services, works towards better patient safety, promotes the application of research results, develops methods, and provides instruction. The Knowledge Centre also conducts full health technology assessments of medicinal products in the system for new methods in specialist health services.

Information about medicinal products

One of the key initiatives for information and advice, which is operated by the Knowledge Centre, is the Norwegian Electronic Health Library (Helsebiblioteket). Helsebiblioteket.no is a publicly funded website that offers health care personnel and internet users access to numerous central sources of knowledge, free of charge. Most of the contents are available to all residents of Norway, while some of the contents are limited to health care personnel and health care service

employees.

The purpose of the Health Library is to enhance the quality of health care services by offering free access to useful and reliable knowledge. The Health Library purchases access to licensed resources, such as reference material, databases and journals. The Health Library also offers services for clinicians and decision-makers in health care services, where they can submit inquiries concerning the efficacy of measures, and receive help in locating research summaries which address the issue. The Health Library also publishes Norwegian guidelines, protocols, clinical procedures and other material developed by public services.

The Health Library helps to reduce duplication, improve quality and promote sharing of knowledge within the health care system.

The Health Library at helsebiblioteket.no provides links to important, quality assessed information about medicinal products. The Health Library has also developed a special search tool for medicinal product information which obtains information from FEST, the Norwegian National Formulary, the Norwegian Pharmaceutical Product Compendium, HELFO, regional medicine information and pharmacovigilance centres (RELIS), Micromedex, UpToDate with Lexicomp, etc.

4.6.4 Point of contact for interdepartmental medicine information

The point of contact for interdepartmental medicine information was established in 2006, as a follow-up of the proposal in the Medicinal Product Policy report (Report to the Storting no. 18, 2004-2005), presented in 2005. Today this point of contact consists of representatives from the Norwegian Medicines Agency, The Norwegian Directorate of Health and the Norwegian Knowledge Centre for the Health Services. The point of contact also has a reference group composed of representatives from the Norwegian Institute of Public Health, the Norwegian National Formulary for health care personnel, RELIS, Colleague-based therapy supervision and the Medicinal Product Procurement Cooperation (LIS).

The objective of this point of contact is to ensure proper and efficient information concerning the correct medical and socio-economic use of medicinal products, and to ensure that the resources that public facilities use for this information are well-utilised.

The point of contact has carried out an evaluation on the preparation of this report.

Box 4.3 British National Formulary for Children

The British National Formulary for Children (BNFC) is a standard reference publication which offers practical information on the use of medicinal products, including off-label use, from birth to puberty. There is free access to BNFC through helsebiblioteketet.no, financed by the National Competence Network for Medicines for Children. The international medicines drug reference, Micromedex Solutions is accessible to everyone in Norway, free of charge, through

the Health Library. Lexicomp is a reference guide providing information about medicines, and is integrated in the medical reference resource UpToDate.

4.6.5 Norwegian Institute of Public Health

The Norwegian Institute of Public Health is a state-run administrative agency, subordinate to the Ministry of Health and Care Services. The institute acts as a national competence institution in the following areas:

- infectious disease control,
- mental and somatic health,
- environmental factors, drugs and alcohol, tobacco, nutrition, physical activity, and other conditions that have an impact on health and health inequality,
- health-promoting and preventive initiatives for the public,
- international health and
- forensic medicine.

The Institute of Public Health shall first and foremost provide knowledge about public health and rule of law. Knowledge underpins the Institute's activities regarding preparedness, advice and guidance, health analyses, research and services.

The Institute of Public Health oversees pharmacoepidemiology, the operation of the Norwegian Prescription Database, and a WHO centre for the classification of medicinal products. The Prescription Database is discussed in further detail in Chapter 8.

The Institute is a professional body for vaccines. The need for a better system for the evaluation of vaccines is discussed in Chapter 19.6.

The Institute is also in charge of the Norwegian Poison Information Centre, which is a national advisory and competence agency that provides information about acute poisoning and poisoning hazards. The agency's core function is a 24-hour phone service, which receives just under 40,000 inquiries annually. Around 40% or 16,000 inquiries concern medicinal products. Approximately two-thirds of these inquiries come from the public and one-third from health care services. As part of its information service for health care services, the Poison Information Centre publishes treatment recommendations for various types of poisoning in its own subject library at helsebiblioteket.no, the Electronic Health Library. The Poison Information Centre has also composed a list of antidotes with recommendations for the storage of antidotes at Norwegian hospitals. The Poison Information Centre provides information for patients at helsenorge.no. The Centre also prepares and distributes brochures and other written informational material.

4.6.6 Supervisory authorities

Supervisory authorities include the Norwegian Board of Health Supervision, and the county

governors. The Norwegian Board of Health Supervision is the superior national supervision authority. County governors are assigned authority to oversee health and care services in their own counties, and are directly subordinate to the Board of Health Supervision.

Supervisory authorities determine whether services are being delivered in accordance with regulations, including regulations regarding sound professional practice. Supervisory authorities are important bodies in terms of uncovering and documenting deficiencies in services. Supervisory authorities handle complaints, and provide supervision and advisory services, in order to meet the public need for services, and to prevent, uncover, and follow up any deficiencies in these services.

4.7 Other actors that compile and convey knowledge about medicinal products

One of the most important elements for ensuring good quality treatment with medicinal products is relevant knowledge about medicinal products and how these should be used. This applies to all actors involved in this field. This section provides an overview of all remaining actors that were not mentioned in Chapter 4.6. In addition to these actors, there are professional associations, sector associations and patient associations that all provide information and guidelines used by health and care services. Many patient associations make major contributions in the form of education and training. In many cases, the information they use is compiled in collaboration with the Norwegian Medical Association and with support from the pharmaceutical industry. Proposals for improvement of knowledge and information about medicinal products are discussed in Section III of this report.

The Norwegian National Formulary

The Norwegian National Formulary for health personnel is a reference book for treatment with medicinal products, and is fully funded by the national budget. It is primarily intended for use by general practitioners and nursing home physicians. There is therefore an emphasis on conditions which are generally treated in primary healthcare services.

The Norwegian National Formulary is published in print, but also has its own website and an app for smart phone and tablets. The website for the Norwegian National Formulary can be found by searching the Health Library.

RELIS

RELIS is a national network of regional medicines information and pharmacovigilance centres in Norway, and is a part of the health authority system. University hospitals are responsible for its operations. The Norwegian Medicines Agency has a central role in the management of these centres. RELIS was established to contribute towards a rational and correct use of medicinal

products through manufacturer-independent medicine information. RELIS offers a question-and-answer service, where health care personnel can inquire about medicine use for their patients. These information centres have a joint homepage (relis.no) where they publish news and various issues. This homepage provides access to the question-and-answer database (relis.no/database), and is intended for health care personnel.

RELIS also has two online advisory services for the public, Safe Medicine (Trygg Medisin) and Safe Mamma Medicine (Trygg mammamedisin), and offers individual guidance in the use of medicinal products.

RELIS also has an important role in the surveillance of adverse reactions, by accepting reports on adverse reactions, evaluating causal relationships, and by reporting causal relationships to physicians. Together with reports on adverse reaction events from EU countries and WHO, reports by RELIS provide the basis for updated information on medicinal products.

Box 4.4 Safe Mamma Medicine

Safe Mamma Medicine (tryggmammamedisin.no) is an online service for woman who are either pregnant or breast-feeding, and who have questions about medicines. The service is directed at healthy individuals seeking more detailed information about the use of medicines during pregnancy or when breast-feeding. The service started in June 2011 by RELIS, and around 8000 inquiries had been replied by the end of April 2015. Medicinal products that generated the most inquiries in 2014 included paracetamol, ibuprofen and cetirizine. Replies are promised within 2 business days. Those who send in inquiries remain anonymous and the service is free of charge. Questions are answered by pharmacists and physicians working at university hospitals in Tromsø, Bergen, Trondheim and Oslo. The Bergen Health Authorities at RELIS Vest oversees operations and has received licensing from the Norwegian Data Protection Authority to run the service.

The Norwegian Electronic Medical Reference Book and Norwegian Health Informatics (nhi.no)

The Norwegian Electronic Medical Reference Book (NEL) is a medical reference book that offers decision-making assistance for diagnostics and treatment. NEL is a product offered by subscription, and 95% of all Norwegian general practitioners are subscribers. Other subscribers include a number of hospitals, universities, colleges and municipalities. Content is continuously updated and quality assured by nearly 200 professionals in the health and care services and educational institutions. The reference book currently contains about 7000 articles which cover broad areas of the medical profession. NEL information for patients is freely available on NHI.no. This website is financed through advertising.

5 Health status and the use of medicinal products

Medicinal products comprise an important factor at all levels of health care services, as a preventive measure and in terms of treatment. Figures from the Norwegian Prescription Database indicate that approximately 3.5 million Norwegians, (70% of the Norwegian population), were dispensed at least one medicinal product during 2014. Medicinal products are the most common form of medical treatment in the industrialised world. Around 60% of consultations in Norwegian general practices result in the prescription of medicinal products.

In addition to prescription medicines, there is the use of medicinal products for patients admitted to hospitals and nursing homes, as well as the use of non-prescription medicinal products, natural remedies, herbal medicinal products, herbal substances and food supplements. Use of medicinal products varies with age: Around 40% of the 10–14 age bracket was dispensed at least one prescription medicine, while around 95% of the over-70 age bracket received the same.

5.1 Health status

According to the recently presented Report on Public Health, the health status of the Norwegian population is extremely good. Life expectancy is high and likely to increase over time. Social inequalities in life expectancy have also increased, however there are signs that these inequalities are about to flatten out. The major portion of premature deaths and the loss of quality-adjusted life years in the Norwegian population were due to non-communicable chronic diseases such as cardiovascular diseases, diabetes (type 2), chronic lung diseases and cancer.

The Institute for Health Metrics and Evaluation (IHME) published data on the global burden of disease, which shows that cardiovascular diseases and traffic injuries were significantly reduced between 1990 and 2010, while substance abuse and Alzheimer's disease had the sharpest increase.

5.1.1 Communicable diseases

Serious communicable diseases are less common in Norway than in most other countries. However, this situation may change. International trade with food products and animals, migration and travel may all have consequences for public health in Norway as well, as they pose a higher likelihood of infection. One out of 20 patients in health institutions are affected by hospital infections. Approximately 20,000 people are chronic carriers of hepatitis B, and most were infected prior to their arrival in Norway. Around 20,000 people are carriers of hepatitis C, and most of these were infected through sharing needles. The number of new incidences of tuberculosis has increased by about 400 cases per year. Antibiotic resistance is also becoming a problem.

5.1.2 Non-communicable chronic diseases and NCD strategies

In May 2012, the World Health Assembly (WHA) declared its goal of a 25% reduction in

premature mortality from NCD diseases, including cardiovascular diseases, diabetes, chronic lung diseases and cancer, by 2025. Norway has adopted this goal. This is also why Norway formulated its own NCD strategy in 2013, where the objective was more cohesive and unified efforts in the work with these diseases at all levels, while simultaneously addressing the unique characteristics of each disease group. This strategy was divided into a joint section with common challenges and measures, and a section defining specific challenges, goals and measures for each individual disease group.

In order to achieve the goals of this strategy, it is necessary to implement a variety of different measures. Preventive measures at the population level are generally the same for all four disease groups. The Report on the Public Health Policy addresses this issue. There are also many common challenges and solutions for health care services in the areas of prevention, diagnostics, treatment and rehabilitation. There must be a stronger focus on preventive services, education, active follow-up and good patient care pathways than is currently the case. Far too many people are unaware of the fact that they have a disease, such as diabetes or COPD. Once they become aware of the risk of a disease, patients and their family members will be in need of education which could enable them to stop or slow down the development of the disease. Individuals with established diseases must be followed up in accordance with professional guidelines, and must also receive patient education to help them manage their lives and allow them to live with the disease, and also prevent the disease from growing worse.

5.2 Use of medicinal products

Health registries are an important source of knowledge of a population's health status and the quality of services. Information about the use of medicinal products can be found in both medical quality registries and central health registries. The Norwegian Prescription Database, established in 2004, is the database containing the most comprehensive information on the use of medicinal products at an individual level. The system of reporting adverse reactions is an important tool for pharmacovigilance, and is used to uncover signs of adverse reactions which were unknown at the time the medicinal product received marketing authorisation. The need for registries for research, health analyses and quality assurance is discussed in Chapter 8.

5.2.1 Adverse reactions

Adverse reactions are one of the major challenges of medicinal use. As mentioned above, the registration of adverse reactions is essential for gaining knowledge about the effect of medicinal products in clinical practice, and possibly also for warning certain patient groups against specific types of medicinal products. Below are two examples of how the registration of adverse reactions and new knowledge has resulted in prescription recommendations.

Birth control pills and the risk of blood clots

The risk of blood clots associated with the use of birth control pills has long been recognised.

Previously this risk was associated with the oestrogen component of these pills, while the importance of the progestin component was unknown. During the first several years, when products containing the new progestogen – drospirenone – were on the market, the Norwegian Medicines Agency received numerous reports concerning blood clots, including several reports of pulmonary embolisms and deaths.

Oral contraceptives with drospirenone were placed on Norwegian Medicines Agency's watch list. Based on data from the adverse reaction registry, and data that eventually came in from epidemiological studies, it was recommended that prescribers select birth control pills with the lowest risk of blood clots as their first choice. These recommendations led to a significant change in prescription patterns in Norway. A European review of the data has later shown that various progestogens counteract, to a varying extent, the risk of blood clots presented by oestrogen.

Adverse reactions associated with the transition from digitoxin to digoxin

Digitalis glycosides (digitoxin and digoxin) are often used in the treatment of heart failure and heart rhythm disorders. In Norway, digitoxin has traditionally been used by adults, while digoxin has been used by children. This was a different practice than for the rest of the Western world, where digoxin was the primary substance of choice. These two products are equally efficacious, but are distributed and metabolised differently in the body. It is particularly important to be aware than digoxin is eliminated via the kidneys, which means that patients with reduced renal function must be given a lower dose.

After a period of delivery problems, digitoxin was deregistered in December 2011, and all patients using digitoxin had to switch to digoxin.

For digitalis glycosides, there is a relatively narrow safety window between a therapeutic dose and a toxic dose. Digitoxin was used by a high number of elderly patients with reduced renal function, and there was therefore a major concern of potential overdose when switching to digoxin.

The Norwegian Medicines Agency, in cooperation with health authorities, provided information on how to proceed with the switch. Despite this, there was a rise in adverse reactions reports for digitalis glycosides from 2011 to 2012. Switching medicines became a problem in clinical practice. Several rounds of information were eventually required, which illustrates the importance of such information. Since the switch from one medicine to another was only relevant for Norway, this demonstrates the need for a well-functioning national system.

5.2.2 Children

From a global perspective, Norwegian children have excellent health. Figures from the Norwegian Prescription Database show approximately 494,000 children and teenagers between the ages of 0 and 17 (45% of the children in this age group) were dispensed one or more prescription medicines in 2014. The proportion of users is highest among children ages one to

two (around 60%) and lowest among children ages 8 to 11 (around 37%). Medicinal products most often used by children and teenagers include antibiotics, anti-asthmatic agents, allergy and cold medications, and eye drops, which also reflects the most common diagnoses for these age groups by general practitioners: asthma, allergies, otitis (ear infections), upper respiratory infections and conjunctivitis (eye infections).

About 15–20% of children and teenagers between the ages of 3 and 18 experience reduced function due to mental health issues such as anxiety, depression or behavioural problems. Approximately 8% of children and teenagers are experiencing symptoms of such severity that they meet the criteria for a psychiatric disorder. Over the last decade there has been an increase in the total use of psychoactive medicinal products in the 0–17 age bracket. This increase was found among both boys and girls. See Chapter 13.2 for a more detailed discussion. Both the Report on Public Health and the Report on The Primary Health Care Services discuss mental health among children and teenagers, and both place emphasis on improving conditions for children's upbringing to promote better mental health. This includes measures to improve public health care clinic services for children and pregnant women, as well as school health services. Additional subsidies are needed for psychologists in the various municipalities. There is a need for more research-based knowledge on the use of medicinal products among children and teenagers, particularly with respect to psychoactive medicinal products.

5.2.3 The elderly

People in Norway are living longer than ever before, and although this implies additional healthy years of life, an aging population will inevitably include a greater number of people with chronic diseases. Diseases which previously meant an early death, such as type 2 diabetes, cardiovascular diseases, and cancer, have now become chronic health conditions, and their incidence increases with age. Elderly individuals often have several diseases at the same time, which has a collective impact on function, quality of life and mental health.

According to the Norwegian Institute of Public Health, there is an extensive use of medicinal products among the elderly. Among those who are 65 or older, 92% were dispensed at least one prescription medicine in 2014. People over the age of 65 compose approximately 15% of the population, but they use nearly half of all medicines, measured by defined daily dose. The 65 and older age group uses 47% of all hypnotics and sedatives. This age group also uses 44% of medicines for musculoskeletal disorders, and 63% of medicines for cardiovascular diseases.

Many elderly people have several diseases or disorders and use several different medicinal products at the same time (polypharmacy). This increases the risk of unnecessary medication and unfortunate medicine combinations. Data from 2011 indicates that 57% of older medicine users (≥ 65 years) were dispensed more than five different medicinal products over the course of a year, while 21% received more than ten different medicinal products.

Elderly patients are more vulnerable to adverse reactions and other medicine-related problems. Residents at nursing homes use an average of seven different medicinal products, and one out of

three residents use at least one unnecessary medicinal product.

Several studies have indicated an incorrect use of medicinal products, for both patients in hospitals and those living at home. Although research criteria vary, there have been reports on prescription errors for medicinal products given to elderly patients, in 10 to 25 per cent of all prescriptions. Studies also indicate that nearly 10% of all hospitalisations of elderly patients in general medicine wards are due to medicine-related problems. There is a need for more research on the use of medicinal products among the elderly, as well as the development of new innovative solutions that can contribute towards the reduction of medicine-related problems among the elderly.

Statistics from the Cancer Registry of Norway indicate that the number of new cancer cases (incidence) has remained stable for the oldest age groups over the past decade, with the exception of breast cancer and prostate cancer, where the number has increased (partly due to screening examinations). However, the proportion of elderly living with cancer (prevalence) has increased in the population, perhaps because more patients begin treatment at an earlier stage. They also receive better treatment, and have a higher survival rate.

Over the past decade, mortality associated with cardiovascular diseases among the elderly has declined in Norway. It is expected that many more people will continue to live with cardiovascular conditions due to a higher rate of survival.

Each year, approximately one-third of those over the age of 65, and half of those over the age of 80 will be injured in falls. In 2012, 479 people died from falls and subsequent complications from fractures. Among these, 70% were over the age of 80. The incidence of fractures in Norway is among the highest in the world. The reason for this is unknown. About 70% of all hip fractures occur in women. Many of these fractures are due to low bone density (osteoporosis), combined with fall injuries.

The risk of developing an infection requiring treatment with antibiotics is relatively high among the elderly. It is estimated that six per cent of all antibiotics used in Norway are given to residents of nursing homes, despite the fact that less than 40,000 people are living in such institutions.

Studies on health and living conditions conducted by Statistics Norway suggest that mental health problems are less pervasive among the elderly than among young people. The prevalence of anxiety and depression is evenly distributed throughout adult life.

The proportion of dementia increases with age. Risk factors for dementia appear to be the same as for cardiovascular diseases. An estimated 70,000 people in Norway are living with dementia.

5.2.4 Gender differences in the use of medicinal products

Figures from the Norwegian Prescription Database for 2014 indicate that 76% of all women and 62% of all men are using prescription-only medicinal products. More women than men use

hypnotics, medicines for mental health disorders and analgesics.

However, a higher proportion of men than women use medicinal products for diabetes and the prevention of cardiovascular disease. Gender differences in the use of medicinal products have remained constant over time. It is unclear whether the reason for this involves differences in terms of morbidity, age distribution, use of health care services, or health behaviour. The utilisation of data from various registries offers the opportunity to examine possible reasons for these differences in use.

When applying for marketing authorisation for a new active substance, a company must determine whether gender differences may have significance for medicine dosage. Weight-related differences are often an issue between the genders, but this seldom has any importance for changes in medicine dosage. The morbidly obese, pregnant women and other subpopulations with characteristics that deviate from the main population, but that can have an effect on the metabolism and safety profile of medicinal products currently present a greater challenge than gender differences.

During 2015, the Norwegian Directorate of Health will begin work on a summary of knowledge on gender-related differences regarding the effect and adverse reactions to medicinal products.

5.3 Incorrect use of medicinal products

The correct use of medicinal products was also the subject of the previous Report to the Storting no. 18 (2004–2005) “On course towards more correct use of medicine”. It was also a topic in the Report to the Storting no. 16 (2010–2011), “The National Health and Care Plan” (2011–2015), and it was a topic in the Report to the Storting no. 10 (2012–2013) “High Quality – Safe Services” (quality report).

The incorrect use of medicinal products may have serious consequences for individual patients, in the form of adverse reactions, and possibly even death. Repercussions for society involve sizeable additional costs associated with absenteeism and unnecessary use of health care services. Only 20–30 % of medicines are taken as recommended. Although the research criteria may vary, there have been reports of incorrect prescriptions in 10–25 % of all cases. The previous medicinal product policy report indicated that 5–10 % of all acute internal medicine hospitalisations at hospitals were a result of an incorrect use of medicinal products, and that about half of these hospitalisations might have been avoided.

Box 5.1 Definition of a medicine-related problem

Medicine-related problems (MRP) can be defined as an incident or situation which occurs in association with treatment with medicinal products, and which interferes, or may potentially interfere with the desired medicinal effect on the individual's health. A potential problem is defined as a situation which may lead to a medicine-related illness or death if it is not followed up, while an actual problem is one that has already manifested itself with signs and symptoms[1].

[1] Ruths S, KK. Viktil, HS Blix. *Klassifisering av legemiddelrelaterte problemer.* Tidsskriftet for Den norske legeforening. 2007.

Several studies indicate that medicine-related problems occur at all levels of health care services. Examples of medicine-related problems include patients who needlessly use too many medicines, patients using too high or too low a dose, or patients using an unfortunate combination of medicines. In one study among nursing home residents in Bergen, patients used an average of 11.5 different medicinal products, and the study found 5.5 medicine-related problems per nursing home resident. All in all, 33% of the medicine-related problems were due to the use of unnecessary medicinal products. Three out of four patients in nursing homes had one or more medicine-related problems. One multicentre study of hospitals in Norway showed that more than 80 per cent of patients had an average of 2.1 relevant medicine-related problems.

Many studies have shown that people who have begun medicinal treatment will continue with this over time, even when the indications for treatment are no longer present. Many elderly patients have several illnesses and use many medicinal products at the same time (polypharmacy). Elderly people are particularly vulnerable to adverse reactions and other medicine-related problems. Both international and Norwegian studies clearly indicate an inadequate quality of medicinal treatment for this group.

The simultaneous use of many medicinal products increases the risk of incorrect medication. Combinations of medicinal products can also either enhance or cancel out the effect of the medicines. The risk of medicine-related problems for a patient increases when being treated with medicinal products for several illnesses simultaneously.

In accordance with Section 3-3 of the Specialist Health Care Act, specialist health care services have a mandatory duty to report any significant personal injuries to a patient due to problems with health care services, as well as incidences that might potentially have led to significant personal injuries. The purpose of this mandatory duty to report is to improve patient safety by using these reports to determine the cause of such incidences, and to prevent similar incidences from occurring. The Norwegian Knowledge Centre for the Health Services overtook the responsibility for this system from the Norwegian Board of Health Supervision on 1 July 2012.

In 2013, 19% of the reports of failure or errors in the health care system were associated with the

use of medicinal products. The most common error involved the dispensing of medicines with incorrect doses, in terms of strength and frequency. In 9% of these cases, the incident resulted in significant injury to a patient, or death. Specialist health care services also have a duty, in accordance with Section 3-3 of the Specialist Health Care Services Act, to notify the Norwegian Board of Health Supervision of any serious incidences, including death or significant injury to the patient, where the outcome was unexpected, based on foreseeable risk.

Medicine confusion is a common problem in health care services. The term “confusion” means that the patient has received the wrong medicinal product due to a similar name, similar spelling, packaging or labelling. Medicine confusion is an undesirable incident at a systems level, and has been defined as a medicinal error which can be prevented. The reporting system has received 50 notifications concerning incidents where patients have been given the wrong medicinal product due to medicine confusion. Most of the confusion errors have occurred during the preparation and dispensing of medicinal products. Reports show that 10 to 50% of all medicinal errors involve confusion due to similar names of drugs and 35% are due to packaging or labelling similarities. The development of new technology for decision-support and control routines would help to reduce these types of errors.

Patient injuries occurring at all Norwegian hospitals have been assessed through the Patient Safety Campaign and Programme since 2010. In 2013, approximately 11,000 patient stays were examined. At least one patient injury was found in 13% of the stays, and 15% of these injuries were associated with the use of medicinal products. It is estimated that about half of medicine-related injuries can be prevented.

Primary challenges associated with undesirable incidences from the use of medicinal products may be associated with the following:

- health care personnel lack an overview of the patient’s actual medicine use
- a physician prescribes the wrong medicine, too many medicines, an unfortunate combination of medicines, wrong dosage or provides poor follow-up
- care personnel distribute the incorrect medicine, incorrect dose, or do not ensure that the patient actually takes the medicine
- the patient does not receive adequate supervision, uses medicines incorrectly, or does not follow up treatment because he/she does not have confidence in them

5.3.1 Uncertainty regarding medicinal products in use

One of the main challenges associated with the correct use of medicinal products is that both health care personnel and patients are often uncertain as to which medicinal products the patients are using. This problem is of significant consequence for the most seriously ill patients, patients who use many different medicinal products simultaneously, and patients who have been transferred between different health care services or levels of care. A large proportion of these patients are recipients of care services.

One study found that 39% of patients admitted to an emergency ward had no updated list of medicinal products. The study states: "Obtaining essential information about patients' use of medicinal products was both difficult and time-consuming for all personnel involved. The quality of information was viewed as variable and unreliable." Another study indicated a lack of consistency between the GP's list of medicinal products and the home health care nurse's list, for more than 60% of the patients. These patients used 25% more medicinal products than the GP was aware of.

The uncertainty regarding patients' use of medicinal products increases the risk that problems will arise during medical treatment. When the treating physician lacks an adequate basis for decision-making regarding medical treatment, there is a chance that the patient will receive improper or unsuitable treatment, or an unfortunate combination of medicinal products.

Measures intended to gain greater certainty with respect to medicinal products in use is discussed in further detail in Chapter 6.2.

5.3.2 User-friendly information about medicinal products for health care personnel

Health care personnel, particularly those who prescribe medicinal products, require updated knowledge about medicinal products. There is a lot of good and quality assured information about medicinal products directed toward health care personnel, however, information is often not made available to personnel in an efficient manner, for instance through medical record systems and hospital record systems. Patients often receive concurrent and overlapping information concerning medicinal products, and there may also be challenges associated with the coordination, roles and responsibilities involved in the production of such information for health care personnel. This is discussed in further detail in Chapter 7.2.

5.3.3 Treatment adherence

In medicine, "adherence" is used to describe the extent to which a patient collects medicinal products from the pharmacy, takes the correct dose at the correct time, and completes the recommended treatment.

Research literature indicates that poor adherence to treatment with medicinal products is a major problem, especially among the elderly and patients with chronic diseases. A report by the World Health Organization states that as many as 30 to 50% of all patients fail to follow recommended treatment. This same report states that one out of three patients refrain from taking medicines for fear of adverse reactions.

A Norwegian review of the literature for seven common medicine groups (antidiabetics, antiepileptics, antihypertensives, statins, psychoactive medicinal products, antibiotics and analgesics) showed a wide variation in adherence for all medicine groups, regardless of diagnosis. Adherence varied between 20 to 80 per cent, and generally decreased over time. A

few key factors are associated with poor adherence:

- more than one dose per day
- complicated treatment routines
- reduced cognitive function and depression
- inadequate follow-up

Measures directed at these types of factors could possibly improve adherence. Such measures include simplified dosage (e.g. depot tablets, combination medicinal products), assistance with practical problems (e.g. dosage administration aids, alliance with family members, home care services involvement), and better follow-up (e.g. frequent appointments, shorter waiting times).

A 2003 report from the World Health Organization indicates that about 50% of patients with chronic diseases have poor adherence to treatment. For instance, patients with COPD or asthma often use their inhalation medicines incorrectly. Some patients who are uncertain about their treatment and afraid of adverse reactions may refrain from taking their medicines as prescribed. There are patients who reduce their use of a medicinal product during a phase where they are feeling better, in order to reduce possible adverse reactions, while other patients simply forget to take their medicines.

There is a lot of good and quality assured information about medicinal products, but the problem is that this information is often not adapted to the patient group, and it may therefore be difficult for them to understand. There is concurrent and overlapping information about medicinal products directed towards the patient, and there may be challenges associated with the coordination, roles and responsibilities involved in the production of such information.

Adapting information about medicinal treatment to the patient, and developing tools for patient participation, may result in improved communication between health care personnel and patients, as well as better adherence to treatment. This is discussed in further detail in Chapter 7.

5.3.4 Management of medicinal products

In 2009/2010 the Norwegian Board of Health Supervision carried out inspections with regard to treatment with medicinal products and the management of these in nursing homes and home-based care services. The Board found non-compliances in nursing homes in 40 of the 63 municipalities, and in home-base care services in 9 of 12 municipalities. The Norwegian Board of Health Supervision considered these findings to be serious enough to report them to the Ministry of Health and Care Services, expressing concern over the poor monitoring of treatment with medicinal products. Key findings included an unclear division of roles and responsibilities, personnel with inadequate professional competence, as well as a lack of routines for ensuring correct information about the type of medicinal products used by the patients.

As a follow-up of these non-compliances, the Norwegian Directorate of Health prepared a report in 2011, entitled “Correct use of medicinal products for elderly patients/residents at nursing

homes and in home health care services". This report was directed towards municipalities and municipal physicians, general practitioners, health care management, and other health care personnel in charge of dispensing medicinal products to elderly individuals. To improve the use of medicinal products among the elderly within and outside health care institutions, the report called for greater focus on health care management responsibilities, a clear and appropriate distribution of roles and responsibilities, teamwork, enhanced professional competence, good communication, and collaboration. This is described in more detail in Chapter 12.

5.3.5 General challenges

In Norway, as previously noted, the predominant diseases are generally non-communicable, chronic diseases. These diseases require treatment and follow-up over a long period of time. In many cases, individuals will require treatment and follow-up throughout most of their lives.

A growing number of service users with major and complex needs are receiving home care services in care homes, often collocated care homes, which in many ways function as a nursing home. Proper follow-up of service users with the most complex needs requires adequate information flow. This is especially important during the critical phase after discharge from hospital, so that health care personnel who will take over the responsibility for patient follow-up have the correct information about the type of treatment given. This will enable them to continue the patient's treatment in an appropriate manner.

There is evidence to suggest that the information provided is not always adequate, and that follow-up after hospital discharge is not sufficiently systematic. Patients with complex needs are discharged from hospital to home health care services, often needing advanced medical treatment but without any established cooperation between the general practitioner and home health care services for medical follow-up. Examples include complex medical treatment with intravenous antibiotics, analgesics and cancer treatment. Hospitals notify municipalities when a patient requiring municipal services is ready for discharge, but few hospitals or other institutions have routines for notifying general practitioners about the need for medical follow-up. According to Section 14 of the Regular General Practitioner (GP) Scheme, this is something they are required to do prior to discharging a patient, whenever there is a need for GP follow-up. The Ministry of Health and Care Services will take the initiative to develop a protocol for the follow-up of patients with a major and complex need for municipal services. Reference is made to the discussion and proposal for measures in the recently presented Report to the Storting no. 26, (2014–2015) "The Primary health and care services of tomorrow – localised and integrated". It may be necessary to assess how available health care personnel can be utilised in a more efficient manner, possibly with new tasks and responsibilities for several different types of health care personnel. A different distribution of responsibilities and different organisation of services would demand national measures to ensure good information flow and competence with respect to medicinal products.

There are also challenges associated with antibiotic resistance, mentioned in Chapter 13.1, which

will be followed up with a separate strategy. This will most likely be presented during the first half of 2015, while the plan of action will be presented sometime during 2015.

Section III

Good quality in medicinal products treatment

6 Quality treatment with medicinal products

Figure 6.1

All treatment with medicinal products must be of good quality. This includes the best possible effect, the fewest possible adverse reactions, and the assurance that patients undergoing treatment can continue to manage their lives in a satisfactory manner. Good quality means that patient safety is ensured, and that patients are not needlessly harmed by their use of medicinal products.

In the preparation of this report, the Ministry of Health and Care Services assigned the Point of Contact for interdepartmental medicinal product information with the task of evaluating information and decision support systems for diagnostics, treatment choice and adherence to medicinal treatment. The Directorate of Health was tasked with evaluating pharmacy services and assessing adherence to treatment with medicinal products, while the Institute of Public Health was given the task of preparing a report on the use of addictive medicinal products, based on the data from the Prescription Database.

As part of the work with evaluating information, adherence and pharmaceutical services, an open council was held to ensure input from all involved actors. There was an opportunity to submit ideas and input both prior to, and subsequent to the consultation.

Section III describes both new and existing measures and initiatives which may contribute to improved quality and patient safety.

6.1 Quality and patient safety

The Report to the Storting no. 18, 2004–2005, “On course towards more correct use of medicine”, proposed several initiatives aimed at the improvement of treatment with medicinal products. The purpose of these initiatives was to strengthen information efforts by the Norwegian Medicines Agency, and to establish cooperation between several agencies in the Point of Contact for interdepartmental medicinal product information. Another important area has been the development of e-prescriptions and the electronic prescription support system (FEST), as well as core medical records.

Box 6.1 Medicines for Children Network, Norway

The Medicines for Children Network's activities include patient safety, competence enhancement, and the communication and exchange of knowledge. The Network has developed detailed instructions for the practical use and preparation of numerous different medicinal products, and has compiled information for parents on the use of medicinal products among children, in cooperation with external expertise. The Medicines for Children Network aims to contribute towards scientific competence enhancement and knowledge reviews, in collaboration with national and international expertise. The Network is the secretariat for a national research network for medicinal products intended for children (NorPedMed).

The Medicines for Children Network is composed of physicians, nurses and pharmacists, all of whom are working to ensure that the topic of medicinal products for children has priority among manufacturers, pharmacies and health care personnel. All regional health authorities are represented in the Network, and a committee has been established to address medicinal products for children in all paediatric wards in the country. Primary health care services are a central part of the Network. This is to secure the correct use of medicinal products for children among general practitioners, public health clinics and emergency health care services, and to ensure collaboration.

The use of medicinal products in children has also become an important area of priority after the previous white paper on medicinal products. In 2009, the Medicines for Children Network was established. This is a multidisciplinary network which works towards the safe and appropriate medicinal treatment of children, based on documented knowledge. The Network is working to ensure that all those involved in medicinal treatment for children will have access to essential and relevant knowledge, so that they can act and collaborate in an appropriate, correct and safe manner.

Many of the challenges associated with the use of medicinal products in children are due to the lack of approved medicinal products for children provided in a suitable formula. This may result in an extensive use of unapproved medicinal products, or the use of medicinal products outside approved application areas, particularly in hospitals. Expertise regarding medicinal product formulas and knowledge of the use of medicinal products in children is essential in solving medicine-related problems. This includes knowledge regarding the possibilities and limitations of preparing formulas that were created for adults. There are major challenges in the areas of neonatal medicine, paediatric intensive care and paediatric oncology, where there is frequent use of intravenous treatment with potent medicines.

Box 6.2 Patient safety programme

The national patient safety programme "In Safe Hands", was initiated and implemented on commission by the Ministry of Health and Care Services in the period 2011–2013. The overall objective of the campaign was to reduce patient harm, establish lasting structures for patient safety, and improve the patient safety culture in health and care services. The campaign has been working along two axes:

- competence enhancement in improvement efforts for health care personnel and leaders.
- the implementation of measures aimed at reducing harm and improving patient safety in selected target areas.

Eleven target areas were identified, based on knowledge of what causes the most patient injuries. Intervention packages were developed, which were composed of the most important measures for achieving improvement. Three of the target areas deal with the correct use of medicinal products: reconciliation of medicine lists, the correct use of medicinal products in nursing homes, and the correct use of medicinal products in home care services.

The campaign was a national initiative, carried forward in the National Patient Safety Programme (2014–2018). Specialist health care services are required to participate in the programme and implement the intervention packages, while municipalities are encouraged to participate. By the end of 2014, 55% of all municipalities were involved in one or more of the target areas in the patient safety programme.

The intervention packages for correct use of medicinal products in nursing homes and home care services became the most widespread. These measures resulted in a much higher proportion of regular medication reviews for patients in participating nursing homes. The intervention package for medication reconciliation requires active participation among general practitioners – something which has been difficult to achieve.

The programme involved the preparation of posters and brochures, aimed at patients and medicine users, encouraging them to ask for their medicine lists. Intervention packages from the patient safety programme are useful tools in ensuring that patients have updated and synchronous medicine lists, and they can help to facilitate the correct use of medicinal products. It is therefore important to continue the implementation of medicinal product measures of the national patient safety programme "In Safe Hands". The programme itself does not initiate research, but it does support research to obtain increased knowledge about patient safety efforts conducted in Norway.

Patients, users and family members must have safe, high-quality health and care services. Better quality and patient safety is secured through the improvement of systems, leadership and culture within these services. It is important to ensure that all hospitals are implementing the measures

from the patient safety programme, and to encourage all municipalities to implement the programme's intervention packages. Over the past several years, many measures have been carried out to ensure that the work with quality and patient safety is being conducted.

As a follow-up of the government platform, the government made the decision to publish annual reports on quality and patient safety. The first one, Report to the Storting no. 11, (2014–2015) "Quality and Patient Safety 2013", was presented in December 2014, and reviewed by the Storting (Norwegian Parliament) on 17 March 2015, cf. Recommendation 195 S (2014–2015). The report provides an overview of the status and challenges associated with quality and patient safety in health and care services, as they are presented in annual reports by Patient and Service User Ombudsmen, the Norwegian Board of Health Supervision, the Norwegian System of Patient Injury Compensation, as well as from the reporting system of the Norwegian Knowledge Centre for the Health Services, the final report from the Norwegian Patient Safety Campaign, and both national and international quality indicators.

6.2 Shared medicine lists

One of our goals is for health information to be made available for health care personnel whenever there is a professional need, regardless of where the patient was previously treated. The various types of medicinal products a patient is using, or has used, offers important health information. Another goal is for patients to have access to their own information, and that data is made available for quality improvement, health analyses, governance and research.

Status and challenges

One of the primary challenges of the medicinal product field is that there is no real-time sharing of the lists of medicinal products used by a patient, between health care facilities and treatment levels (see Chapter 5.3.1). Today, information relating to medicinal product use is registered in IT-systems belonging to different health care facilities, but this information cannot be accessed if the patient is transferred from one clinician or health care facility to another. Manually gathering information about medicinal products from a variety of different sources is time-consuming, and involves a risk of error and inconsistencies. A review conducted in an internal medicine ward at Oslo University Hospital uncovered discrepancies in the list of medicinal products for 77 % of the patients, and most of these were associated with medicines that were taken regularly [4].

Uncertainty regarding the use of medicinal products reduces the level of patient safety if, for instance, the wrong medicine is administered, necessary medicines are not administered, or the correct medicine is administered in the wrong dosage. These all examples of situations

4 The hospital pharmacy in Oslo.

that can result in incorrect treatment or adverse reactions. Uncertainty regarding medicinal products means that both health care professional and patients will have a poor basis for

knowledge and decision-making with respect to continuing treatment. Any group of health care personnel that prescribes and dispenses medicinal products, or that provides advice on such products, has a need for access to a real-time sharing of the medicinal products used by patients. This is often referred to as “Medicines in Use”.

Today’s systems for electronic prescriptions, or e-prescriptions, have contributed towards better communication between physicians and pharmacies. They also provide the patient with a good overview of valid prescriptions through “My Health” at helsenorge.no. E-prescriptions do not, however, provide historical data for prescriptions that are no longer valid. E-prescriptions were nationally introduced in February 2013 among general practitioners, subsidised specialists, and emergency health care services. The electronic prescription functionality is now gradually being introduced in hospitals throughout the country. The plan is to develop the e-prescription function to include new groups of prescribers, such as dentists. This system is being developed with support for the use of multidose-dispensed medicines in care services. See the discussion on multidose-dispensing in Chapter 12.

All regional health authorities have initiated various projects involving the electronic medical record (EMR), but the rate at which such tools are being implemented differs between health authorities. A medical record is a tool used by physicians to note medicine dosages, the type of treatment the patient is receiving, blood test results, observations, and other relevant information. An electronic medical record would be an important tool for managing medicinal products in hospitals.

A core medical record is an electronic system that gathers specific health information considered to be especially vital, including information about the use of medicinal products. The intent is for core medical record to be available for both patients and health care personnel. This system has been tested in various parts of Norway since autumn 2013, and will now gradually become available throughout the rest of the country. The core medical record would assist in achieving improved patient safety, better collaboration, and better patient involvement. General practitioners and health care personnel in the acute care medical chain will initially be given quick and secure access to such information in a portal system connected to the health record system. Core medical records with correct and updated information about medicinal products will help to ensure improved patient safety as both health care personnel and patients themselves will have access to the list of medicinal products dispensed to the patient from Norwegian pharmacies over the previous three years.

A National Action Plan for E-Health (2014–2016) has been drawn up, presenting all planned and ongoing e-health initiatives of national importance for this period, including those in the field of medicinal products.

Furthermore, the Ministry of Health and Care Services has asked the Norwegian Directorate of Health to assess how the objective of “One Citizen – One Record” may be realised. A feasibility study report will be submitted by the end of 2015. This report will include recommendations regarding long-term target goals for future health information systems.

Initiatives

The Ministry of Health and Care Services propose to evaluate a shared medicine list, in other words, a shared infrastructure which would make information about a patient's use of medicinal products available from both primary and specialist health care services. A shared infrastructure must be viewed in association with ongoing work on the assessment of "One Citizen – One Record", and other relevant activities in the National Action Plan for E-Health, including e-prescriptions and core medical records.

This type of conceptual system (see figure 6.2) will provide health care personnel with secure access to information regarding the medicinal products patients are using (Medicines in Use), and the medicines they should not use, and will also provide important data for population-level studies of medicinal product use, as well as for quality assurance and research. To ensure good treatment, health care personnel will want to examine the patient's use of medicinal products in association with other clinical information such as allergies, ongoing treatments, recent examinations, previous medical history, etc. Access to medicinal products (and other clinical information) will require a shared infrastructure which can handle a large volume of traffic, uptime requirements, and strict demands for security.

Figure 6.1 Shared medicine list

A shared medicine list should also provide access to information about medicinal products that have been in use (a specific period of time), medicines that were ineffective, and medicines that should be avoided due to allergies or contraindications. This information should also include a plan that determines how long the patient should continue to use the medicinal products before a new evaluation is carried out, and whether any changes should be made to treatment or dosage, etc.

Privacy policies and information security must be an integrated part of the development and implementation of all IT-initiatives. The public must be able to trust that the information is managed in a safe and secure manner. Health information must be made available, while simultaneously safeguarding the confidentiality and integrity of the information. Health information is to be secured through technical functions, training and structural systems designed to prevent unauthorised use.

In both the short and long term, and pending access for health care personnel to a real-time shared list of medicinal products in use, there will be a need for greater focus on the importance of medication reconciliation. It is also important to clarify the responsibility of the general practitioner in this work, for instance, through an informational campaign aimed at prescribers, health care personnel and patients. Furthermore, it will be necessary to utilise the potential inherent in the current national electronic systems, such as e-prescriptions and core medical

records.

Medication reconciliation is often performed with outdated information, because a comprehensive list of the patient's use of medicinal products is either not available, or there are delays in the exchange of information between different health care personnel or enterprises. According to the Regulations relating to the Regular General Practitioner (GP) Scheme, the general practitioner is responsible for maintaining an updated list of the medicinal products used by the patient, cf. Chapter 4.3.

Box 6.3 Medication reconciliation

Medication reconciliation involves compiling a list of all medicinal products used by the patient. This list is called "Medicines in Use". The list would contain information regarding product names, active substances, type of medicinal product, strength, dosage and area of use.

Box 6.4 Medication reconciliation project

The Norwegian Association of General Practitioners has developed an electronic tool to assist general practitioners in updating medicine lists in patient health records.

Notifications regarding changes in the patient's use of medicinal products occurring elsewhere in the health care system are sent to the general practitioner through discharge reports. Since a discharge report is submitted textually, the general practitioner will have to manually integrate his or her own list of medicinal products that are in use with the information the physician receives from various cooperative partners. This tool will help to simplify the task through electronic medication reconciliation. General practitioners who have begun using the tool are very pleased with it, but there are currently very few users.

The Ministry of Health and Care Services intends to place greater emphasis on efforts to reconcile medicine lists, including efforts to follow up and continue the implementation of medication reconciliation initiatives through the Patient Safety Programme.

Patients currently have access to an overview of those medicinal products they are prescribed through the "My Prescriptions" system, as well as access to their own core medical records that can be found at helsenorge.no. However, this does not provide patients with a list of medicinal products they are actually using. Changes in dosages, for instance, would not be visible after a prescription has been written or after the medicines have been dispensed in health institutions (nursing homes, hospitals). There is a need to make patients more aware of the importance of an updated list of medicinal products in use, and patients must be encouraged to request this from their general practitioners.

6.3 Medication Review

After the Report to the Storting no. 18 (2004–2005) "On course towards more correct use of medicine", the Norwegian Directorate of Health funded several projects related to medication reviews in hospitals, nursing homes, home health care and pharmacies. In the Report to the Storting no. 16 (2010–2011) The National Health and Care Plan, it was recommended that methodical medication reviews be conducted at nursing homes and for home care patients with an extensive use of medicinal products. In 2012, the Norwegian Directorate of Health completed the national guidelines for medication reviews. This is now being implemented through the National Patient Safety Programme's initiatives for the correct use of medicinal products in nursing homes and in home health care. The Norwegian Medicines Agency, the Norwegian Directorate of Health and the Patient Safety Programme prepared a checklist in 2014, to be utilised in medication reviews. This checklist is a practical tool for conducting medication reviews. A medication review requires a correct list of all medicinal products used by the patient.

Box 6.5 Medication Review

The Medication Review is a systematic review of patients' use of medicinal products, for ensuring appropriate use and for preventing patient harm. Medication reviews are conducted by the physician, either alone or with a pharmacist and/or nurse. The patient and family members can participate. A medication review is carried out whenever there are changes in a patient's condition or care services and on an annual basis for patients using more than three medicinal products.

Section 25 of the Regulation relating to the Regular General Practitioner (GP) Scheme, which entered into force on 1 January 2013, states that the general practitioner must conduct a medication review for all patients on their lists who use four or more medicinal products, whenever this is considered necessary, based on a medical assessment. Since May 2013, general practitioners have been able to use a separate tariff when conducting medication reviews (2ld).

During the first year of the agreement (2013–2014) this tariff was used approximately 100,000 times. Upon the introduction of the tariff, the Ministry had anticipated a significantly higher figure. However, this tariff does not present the entire picture with respect to the general practitioner's work with medication reviews, since the general practitioner can also use other tariffs while performing medication reviews. It would, however, be better if this were used more frequently, and there will be continued focus on this development in the years to come.

Box 6.6 Medication reviews at nursing homes in Oslo municipality

The Nursing Home Agency for Oslo Municipality carried out a comprehensive medicinal product project with three subprojects: Medication reviews, a compilation and presentation of medicinal product data, and competence enhancement for physicians and nurses working at nursing homes in Oslo.

A subproject for medication reviews involved carrying out 2464 standardised medication reviews for long-term care patients for two periods (2011–2012 and 2013–2014). Medication reviews were conducted in teams, each consisting of a nursing home physician, nurse and pharmacist. Preparation, implementation and follow-up of medication reviews were described in detail. Pharmaceutical expertise was hired in from external suppliers during both periods of the project.

- The average patient age was 85.
- Patients used an average of 7.2 regular medicinal products and 3 “when required” (PRN) medicinal products prior to the medication review in 2011–2012. Corresponding numbers for 2013–14 were 7.6 and 3.
- The medication review in 2011–2012 resulted in an average reduction in 1.3 medicinal products per patient. This included 0.7 regular and 0.6 “when required” (PRN) medicinal products. The reduction in 2013–14 was 0.1 and 0.3 respectively. The modest reduction during the latter period may be due to the need for new medicinal products, since it was discovered that a relatively high number of patients had Vitamin D deficiencies in the latter period.
- Each patient experienced an average of 2.7 medicine-related problems prior to the medication review in both periods. Most of these were resolved during the medication review.

Project results:

- Increased energy and improved quality of life for many of the patients.
- A reduction in the proportion of unnecessary medicinal products.
- Nursing homes reduced the use of sleeping pills, antidepressants, diuretics and anticoagulants.
- Nursing homes began using a greater number of analgesics (paracetamol) and medicinal products for symptoms of dementia, such as medicinal products for restlessness and confusion.

After the project was completed, the Nursing Home Agency in Oslo instituted new regulations, stating that medication reviews should be conducted within three weeks after admission for long-term care patients and semi-annually thereafter. Oslo municipality has also carried out projects involving medication reviews in home health care services and in care homes. Results from this project indicate that the use of medicinal product statistics increases

the utility of the collective efforts to improve the quality of medicinal product use in the nursing homes.

Several nursing homes have carried out medication reviews, either through the Patient Safety Programme, or through separate medicinal product projects. Results show a reduction in the number of medicinal products for most patients following the review. Medication reviews can lead to improved health and quality of life for patients, and can also contribute towards fewer hospitalisations.

A reduction in the use of medicinal products will also result in reduced expenses for medicinal product for municipalities. A comprehensive medicinal product project by the Nursing Home Agency in Oslo indicated a reduction in expenses, and concluded that the introduction of medication reviews and inclusion of medicinal product statistics were influencing factors.

The government intends to establish regulations for municipalities to ensure systematic medication reviews for patients in nursing homes. This makes it clear that efforts towards the implementation of medication reviews in nursing homes and home health care services must become a priority. Reference is made in this context to ongoing efforts by the Norwegian Directorate of Health, regarding the development of quality indicators for municipal health and care services, where the area of medicinal products is a priority.

6.4 Correct use of medicinal products in specialist health care services

Figures from the Patient Safety Programme indicate that undesirable incidents occurred in 13 % of all admissions to specialist health care services in 2013. These led to patient injuries or extended hospital stays, necessitated special measures, or resulted in serious consequences for patients. In 15 % of these cases, patient injuries were caused by medicinal products. It is assumed that about 50 % of these undesirable incidents might have been avoided.

Clinical pharmacy has been introduced at several hospitals as one of several initiatives to ensure the correct use of medicinal products, due to greater focus on patient safety and increased knowledge about the potential problems of medicinal products.

Box 6.7 Clinical pharmacy

Clinical pharmacy is defined as pharmaceutical knowledge applied to a patient's pharmacotherapeutic problems, based on clinical data, whereby the pharmacist has direct or indirect contact with the patient. Here the pharmacist focuses on the patient's use of medicinal products, and pharmacists work together in interdisciplinary teams together with other health care personnel[1].

[1] Definition from the Master of Clinical Pharmacy programme

The Diakonhjemmet Hospital began using pharmacists in their clinics as early as the 1980s. Pharmacists were included in multidisciplinary teams at the Department of Rheumatology, and later in other hospital departments, based on a model from England and Scotland. At the Diakonhjemmet Hospital, medication reviews are carried out daily, as part of the pre-rounds in the hospital wards. Participants in these reviews include a physician, nurse, pharmacist and other health care personnel as needed.

Clinical pharmacists' work is based on the IMM method (Integrated Medicine Management). This is a research-based, multidisciplinary and standardised method. The model was developed in Northern Ireland and commenced in 2000. It is also used in other countries, including Sweden. The objective of IMM is to improve treatment with medicinal products for each individual patient, with emphasis on interdisciplinary collaboration. The purpose of IMM is to increase patient safety and improve the quality of treatment with medicinal products. It is a systematic method with a focus on the following:

- Quality assurance of the patient's list of medicinal products (medication reconciliation).
- Individualised and optimised treatment with medicinal products (medication review)
- Ensure the transfer of information to other levels of care.
- Provide advice and counselling for the patient to ensure that they understand the medicinal treatment (medicine dialogue upon discharge).

Studies from both Sweden and Ireland indicate that IMM is a good method for uncovering medicine-related problems in patients, and it has an impact on the length of hospital stays and readmissions. Clinical pharmacists engage in interdisciplinary work, and it is the physician's responsibility to set a diagnosis and make decisions regarding treatment with medicinal products. The pharmacist acts as a consultant to ensure the best possible treatment.

Box 6.8 Clinical pharmacy in the Central Norway Regional Health Authority

The Regional Health Authority for Central Norway (Helse Midt-Norge RHF) has made the decision to use IMM and clinical pharmacists as a tool for ensuring the correct use of medicinal products. Since 2010, hospital pharmacies in the Health Authorities in Central Norway have continued to develop this method in collaboration with hospital health authorities and the regional health authority. Clinical pharmacy has now been introduced in all hospitals in the region.

Clinical pharmacists are employed at hospital pharmacies, which are also responsible for the training and professional guidance of pharmacists. Health authorities and hospital pharmacies regulate the activity of clinical pharmacists through data processing agreements and cooperative agreements.

Up until 2014, these services were fully funded by the health authorities. As of 31 December 2014, there were 11.5 positions for clinical pharmacists. Ten of these pharmacists have master's degrees in clinical pharmacy.

To ensure that clinical pharmacy is expanded and strengthened in accordance with the IMM model, the Regional Health Authority for Central Norway has agreed to increase its funding for clinical pharmacy for a five-year period from 2015, through annual framework grants in the amount of NOK 20 million. This would mean twice the amount of activity compared with 2014.

Several hospital pharmacies have entered cooperative agreements with health authorities to supply clinical pharmacy as a service. This may be in the form of a central agreement with the health authority, or an agreement with an individual department. It would be up to each regional health authority, as owner of the hospital pharmacy and health authority, to determine the structure of such a service.

Because pharmacists possess vital expertise on medicinal products which may be of benefit to the patient, all pharmacists should have a role in patient treatment. This is especially important in more complex medicinal treatment in specialist health services. Clinical pharmacy is an essential initiative which can help ensure a more correct use of medicinal products and improve patient safety.

Medicinal products committees

For many years, it has been common practice to establish medicinal products committees in hospitals, but such committees are not mandatory for health authorities. The mandate and activities of medicinal products committees may vary from hospital to hospital, but they are usually multidisciplinary, and often advise management on issues regarding medicinal products.

Medicinal products committees have the overarching mandate to promote rational, safe and cost-effective use of medicinal products, and to ensure an efficient supply of medicinal products and prudent medicine preparedness in the health authorities. The Regional Health Authority for South-Eastern Norway has established a Regional Medicine Forum which assists in the regional coordination of medicinal products and acts as an advisory body for the CEO of the Regional Health Authority for South-Eastern Norway. The goal of the Regional Medicine Forum is to ensure that regional practice in the field of medicinal products becomes as uniform and consistent as possible.

Box 6.9 Reconciliation of medicinal product lists at Oslo University Hospital

In the general internal medicine ward at Oslo University Hospital, discrepancies were uncovered in lists of medicinal products for 77 % of the patients, and most of these were associated with regular medicines. A study is now being conducted with a pharmacist who follows the entire hospitalisation process, from hospital admittance to the time the patient is discharged. There is also a project that has a pharmacist training nurses in medication reconciliation.

Oslo University Hospital purchases clinical pharmacy from Oslo Pharmaceutical Trust (Sykehusapotekene Oslo), in the amount of seven full-time equivalent positions. Oslo University Hospital and Oslo Pharmaceutical Trust have also entered an agreement resulting in six full-time equivalent positions. Tasks under this agreement include the preparation and maintenance of clinical support tools (drug compatibility tables, antibiotic tables, tablet crushing and splitting table, etc.), assisting Oslo University Hospital by preparing and implementing routines, training, measures for medication reconciliation, etc.

In 1996, a law was passed in Sweden requiring all counties to have at least one medicinal products committee. Stockholm County established a medicinal products committee and a system of cooperative efforts throughout the region to ensure the rational use of medicinal products. The Stockholm County Drug and Therapeutics Committee is an advisory expert body working towards a safe, rational and cost-effective use of medicinal products. The committee has prepared the “Wise List”, for recommended essential medicines for patients in Stockholm County, with an evidence-based compilation of cost-effective medicinal products. This applies to the entire health care system in the county, and is part of a collective medicinal product strategy for the county. The list includes about 200 medicinal products for use with the most common diseases.

Box 6.10 Pharmaceutical Advisory Service Polyclinic at Diakonhjemmet Hospital

Diakonhjemmet Hospital has established pharmaceutical advisory services in a polyclinic at the Department of Geriatrics. Patients can be referred by a general practitioner, nursing home physician, or by physicians at the hospital. The patient is actively involved at all stages. A nurse assesses the patient's function while performing everyday tasks, and a clinical pharmacist talks with the patient and conducts a medication review. A specialist in geriatric medicine performs a medical evaluation of the patient. The visit is concluded by an interdisciplinary meeting with the patient, where they agree on measures and further follow-up.

6.5 Correct use of medicinal products in municipal health and care services

There is a growing trend towards transferring more advanced patient treatment to municipal health and care services, and this is a positive trend. It will require greater competence in the field of medicinal products, both on a system and patient level, as well as competence in the preparation of medicinal products. Pharmacists can have an important role in this interdisciplinary cooperation, which is organised by municipal health and care services in a variety of ways. Pharmacists can also participate in teams that follow up patients with complex needs.

The delivery of medicinal products and pharmaceutical services is also conducted in many different ways. The most common is for municipal health and care services to announce tenders for the purchase of such services. These are services that require expertise with respect to medicinal products, and are primarily carried out by pharmacists. Services include the supply of medicinal products, medicine management, and medicine use, on both a system and patient level. The system level involves general advisory services for management on the use of medicinal products (including preparation, mixing and administration), clinical audits, supervision, education and training. The patient level involves medication reconciliation, systematic medication reviews, multidose dispensing, and educational services for patients and their family members.

Certain municipalities have established medicinal products committees, which assist units in the development and maintenance of a quality system for medicine management.

Municipalities with prioritised target areas in the Patient Safety Programme report that medication reconciliation and medication reviews have contributed towards better medicine management and a better use of medicinal products in the municipalities. The implementation of these initiatives demands a prioritisation of resources and expertise in the field of medicinal products. The use of teaching nursing homes and pharmacists has helped to make the initiatives

of the Patient Safety Programme more widespread.

Municipalities that have begun utilising pharmaceutical expertise in municipal health and care services report positive results. Some municipalities, such as Trondheim, Stavanger and Drammen, have hired their own municipal pharmacists. Oslo municipality has hired a pharmacist for a project period to conduct medication reviews among patients in home health care services and in care homes. In smaller municipalities, it may be more appropriate to cooperate with other municipalities in sharing a municipal pharmacist when cooperating with special health care services, or when purchasing services from the local pharmacy. Reports from municipalities that have hired pharmacists indicate an increased interest in a more correct use of medicinal products, improved quality of medicine management and greater competence with respect to medicinal products.

Box 6.11 Municipal pharmacist in Stavanger municipality

Reports from Stavanger municipality indicate that the employment of a municipal pharmacist has resulted in a better integration and increased availability of the pharmacist in the municipal organisation. It provides the opportunity to become acquainted with the municipal structure, which is important for a constructive cooperation. A municipal pharmacist improves the management of medicinal products in the municipality through the close monitoring of routines, competence enhancement measures and the implementation of proper tools to ensure a safe and correct use of medicinal products.

The municipal pharmacist in Stavanger works at a higher system level with medicine management and treatment, both within and across the organisation and various enterprises in the municipality. This applies to everything from nursing homes to home health care services, emergency medical services, prison health services, schools and preschools or day care centres. The municipal pharmacist is also involved in direct patient-centred tasks to ensure a correct use of medicines for individual patients, for instance, in a nursing home. This work involves everything from preparing and revising routines, conducting medication reviews as part of an interdisciplinary team, teaching health care personnel, and providing advice and guidance by replying to questions from municipal enterprises and personnel. The municipal pharmacist is also a key person in the municipal medicine committee, as well as in various quality committees that handle reports of deviations, complaints and supervisory issues, and is also a possible resource for general practitioner services in terms of expertise on medicinal products and medication reviews.

7 The need for information about medicinal products among patients and health care personnel

The need for information about medicinal products among patients and health care personnel is contingent on many different factors, including previous experience with, and knowledge of disease and treatment with medicinal products. This need will vary, depending on the phase of treatment.

Figure 7.1 Need for information in different phases of treatment

The need for information about medicinal products among patients and health care personnel can be divided into three different phases, where information will provide support for various purposes:

Choice of treatment – decision support

Once a diagnosis has been made, there are often several relevant forms of treatment or measures to choose from. The patient's perception of the seriousness of the disease, the effect of the measure, and the willingness to accept risk will all have an impact on the choice of treatment, and on treatment motivation and adherence. Before choosing between various measures it is necessary to have information about the disease, the efficacy of the measure (benefit), the risk of the measure (adverse reactions), and practical feasibility. The measure may either be medicinal or non-medicinal (such as nutrition and lifestyle counselling). For physicians, access to professional guidelines and information about what would be reimbursed by the state, faccording to the Regulation for reimbursement (where the patient does not pay the full cost of the medicine), would be important in this phase. For patients and family members, information obtained through electronic shared decision making would be important for becoming more actively involved in the treatment.

Completing and managing treatment – motivation and skills

Once the medicinal treatment has been selected, it is essential for the patient to receive practical information and instruction in the correct use of the medicinal products. Health care personnel must also determine whether the patient has understood the content of the communication. The prescribing physician is obligated to inform patients about their treatment, and the pharmacy is required to provide instructions and advice upon dispensing medicinal products. This includes information regarding the importance of taking medicines, how medicinal products should be used (for instance, by inhalation or injections), how the treatment will affect or be affected by aspects of daily life (food, driving, alcohol, etc.), how medicines affect or are affected by other medicines the patient is using, what could happen if the patient does not adhere to treatment,

assistive devices that can facilitate adherence (dosette boxes, reminders, etc.), advice on the prevention of adverse reactions, as well as symptoms of adverse reactions or problems with treatment that might necessitate contacting a physician.

Monitoring and evaluating treatment – experience and learning

The choice of treatment and expectations of risk and benefit are based on the average effect of medicinal products on the population. Nevertheless, there are major individual variations in both effect and adverse reactions. The evaluation of effect on the individual patient is therefore essential. Useful forms of evaluation include objective assessments (such as blood pressure measurements and blood tests), and more subjective registrations (such as patient records). Quality registry data provides information about efficacy and adverse reactions associated with the various treatment options for any given group of patients, while registry data provides the opportunity to monitor and analyse the use of medicinal products on a population level.

Phases may overlap to some degree, but the need for information will vary across the different phases. Current available information about medicinal products is not structured in such a way that it satisfies the need for information in the various phases.

7.1 The patient's need for information about medicinal products

The purpose of treatment with medicinal products is to improve patient health. Information and decision support for patients is meant to ensure better patient adherence to treatment and to reduce the risk of error. Modern IT solutions can assist patients in making active choices regarding their health and treatment.

Good communication between patients and their treating physicians is essential in ensuring the correct use of medicinal products (adequate adherence). Proper dialogue between physician and patient offers the opportunity to personalise information, and it is important to find measures that facilitate proper communication.

The primary objective is to create patient-centred health and care services. This must be facilitated if the rights of the patient and medicine consumers are to be recognised. Patient involvement in the choice of treatment, as well as informed consent to examinations and treatment recommended by health personnel are vital. A few simple control questions may be of help in enabling patient involvement and consent based on relevant knowledge:

1. Should I use this this medicine? What is the alternative? What is the benefit of this treatment, and what are the risks?
2. How should I use this medicine to get the best possible effect of treatment with the least amount of adverse reactions (side-effects)?
3. How can I determine whether the treatment works, and what adverse reactions (side-effects), if any, should I report?

A decision made together will often result in better adherence. The accommodation of practical conditions, simplified doses, and better follow-up may also lead to increased adherence. Communication with patients and information about medicinal products must be adapted to the patient group. For instance, language barriers or poor reading skills may present a challenge among some minority groups. Furthermore, it is important that clinicians ensure that patients have understood the content of what has been communicated. Adherence is particularly challenging for patients with chronic disorders who use several different medicinal products simultaneously.

Cochrane reviews from 2008 and 2014 concluded that it was difficult to find scientific documentation showing that individual measures lead to improved adherence. It has, however, been shown that several simultaneous and customised measures do affect adherence, and can improve the effect of treatment. It is therefore important to personalise measures to suit everyone. Also vital are system-level initiatives that offer health care personnel and patients the opportunity for proper treatment follow-up.

7.1.1 Patient involvement – shared decision making

Adequate information regarding the effect and adverse reactions of treatment provides the basis for informed choices, and is essential in giving the patient ownership of his or her treatment. Shared decision-making means that patients are involved in decisions regarding their treatment, to the extent that is important for them. Several electronic tools for shared decision-making are being developed, including programs for tablets and smartphones for patients with asthma, coagulation disorders and bipolar disorder. Shared decision-making tools can also be used when determining medicinal treatment, but they are perhaps particularly relevant in situations where the choice and follow-up of medicinal products will have major consequences for the patient, and where the choice depends on factors that are important for the individual patient.

Box 7.1 Shared decision-making tools for bipolar disorder, under development by the Norwegian Knowledge Centre for the Health Services and Innlandet Hospital Trust

A variety of treatment measures may be relevant for the treatment of bipolar disorder, including the use of medicinal products. Medicinal products vary in terms of desired effect and adverse reactions. Determining the best treatment for each individual requires knowledge about efficacy, and involves weighing the advantages and disadvantages – deciding on that which is most important for each individual patient. Shared decision-making tools, developed for long-term treatment of bipolar disorder, enable patients and clinicians to cooperate on determining the best treatment. These are interactive tools, which makes it possible for both patient and clinician to explore patient's own judgments and how they influence the choice of suitable treatment choices. It is also possible to compare the effects of various medicinal products and medicine combinations. Possible alternative treatments and treatment effects considered to be important by both the patient and the clinician can be tailored to the individual patient. Knowledge of previous treatment, as well as important aspects for the patient, can be entered into the programme, serving as a basis for the decision. Text and graphics promote a shared understanding of the decision. This tool enables a more systematic treatment follow-up, with regular measurements of the effects that are of greatest importance to the patient. Adherence to treatment can also be monitored over time.

The Ministry of Health and Care Services proposes a pilot study to determine how shared decision-making tools can be utilised to a greater extent when choosing the medicinal treatment. Objectives include greater patient involvement in the choice of treatment, facilitating better communication between the patient and physician, better adherence, and contributing towards a treatment that is adapted to the patient's individual preferences.

7.1.2 Information about medicinal products to strengthen adherence to treatment

During treatment, the patient and family members will require information about the correct use of medicinal products. This may involve the way in which the medicines are taken (swallowed whole, taken with food, use of inhalers), the prevention of adverse reactions and what reactions one should be particularly aware of, precautions regarding driving, alcohol use, etc. Reminders for dosage times, multidoses, medicinal product subscription plans, etc. can make it easier to adhere to treatment.

There may be challenges associated with poor reading and writing skills, as well as language issues in the immigrant population. This makes good communication even more important, but also more difficult. Studies show that language barriers between patients and services represent a risk to patient safety. Language barriers can reduce the patient's ability to understand recommendations and aspects of his or her own disease, and this may in turn result in the patient being less likely to follow recommended treatment. The lack of communication between

clinician and certain immigrant groups may cause patients to avoid taking their medicines, or to use them incorrectly, both of which may have fatal consequences. For patients with poor or no reading skills, it may be advantageous to use pictures to convey information. Cultural differences may also be a factor, whereby individuals from other cultures may have different attitudes towards medicinal products than those who are born and raised in Norway. There is a need for greater knowledge regarding the presentation of information on medicinal products for certain minority groups.

Sami patients have the same right to equal health and care services as the rest of the Norwegian population. Equal health and care services for Sami patients requires services that are adapted to the Sami people, so that the Sami language and cultural background do not impede the provision of adequate services. This is discussed in greater detail in the Report to the Storing no. 26 (2014–2015) "Primary health and care services of tomorrow – localised and integrated".

The Norwegian Official Report, NOU 2014: 8 "Interpreting in the Public Sector", describes several initiatives for improving language and communication. The Report to the Storing no. 26 (2014–2015) "Primary health and care services of tomorrow – localised and integrated" presents ways in which NOU 2014: 8 Interpreting in the Public Sector should be followed up. Proposals in this report may enable better communication between services and various patient groups.

Current patient-centred information about medicinal products is not sufficiently customised to patients, and it may prove difficult for many to understand. Package leaflets are produced for the patient and provide a summary of the knowledge that the marketing authorisation for the medicinal product is based on. The package leaflet contains information about the benefits of the treatment and a great deal of information about the risks involved in treatment, as well as practical advice regarding correct use. However, this information is rarely accommodated to the consumer, and may be difficult to understand. A package leaflet describes both common and rare adverse reactions. This may prove alarming to the patient, and studies have shown that patients who read the package leaflets sometimes refrain from carrying out treatment. It is essential that the English to Norwegian translation is of high quality, and that the information is coherent and accommodated to the patient. The Norwegian Medicines Agency should be a driving force in the European cooperation on medicines in terms of changing regulations so that information in the package leaflets and summary of product characteristics are accommodated to the needs and circumstances of patients and health care personnel. In autumn 2014, the Norwegian Medicines Agency conducted a pilot project, where package leaflets were supplemented with an information sheet (medicine advice). This provided a brief summary of the information with an emphasis on those areas of medicine use which patients themselves have control over to get the best possible effect from the medicinal treatment. Figure 7.2 illustrates an example of medicinal product advice.

Figure 7.2 Medicinal product advice - Penicillin
Norwegian Medicines Agency

Results from the pilot study indicate that both health care personnel and patients found the format and information to be both useful and relevant. The Ministry of Health and Care Services will assess ways in which the current information format can be reworked, or determine if a new format can be developed to enable patients to understand the information intended for them.

The United States has been testing out the use of a "Drug Facts Box". This provides a summary of the expected absolute effect of the medicinal product, as well as the frequency of adverse reactions, compared with placebo or some other form of treatment. These summaries are brief, with tabular data, using a simplified language. Studies have shown that Drug Facts Boxes provide patients with a better understanding of the benefits and risks involved in using medicinal products. By indicating a medicine's absolute effect and frequency of adverse reactions, compared with placebo or other form of treatment, it may be easier for patients to evaluate the clinical relevancy of such a treatment, and to determine the differences between alternative treatments. The implementation of the Drug Facts Box or similar summaries is currently being evaluated by American medicine authorities. The Ministry of Health and Care Services will assess and prepare a national standard for the presentation of information about the benefit and risk of medicinal products.

Many different actors offer useful information on medicinal products for patients, including the Norwegian Medicines Agency, the Norwegian Directorate of Health, the Norwegian Pharmaceutical Product Compendium, patient organisations, patient information the Norwegian Electronic Medical Reference Book, Safe Medicine and Safe Mamma Medicine from RELIS, helsenorge.no, pharmacies, etc.

Box 7.2 The Diabetes Hotline

The Diabetes Hotline is an advisory service offered by the Norwegian Diabetes Association, and is intended for anyone who has questions about diabetes. This service is intended as a widely-known, low-threshold service, and a supplement to public health services. With the Diabetes Hotline, anyone can ask questions by phone, or at: diabeteslinjen.no. In 2014, the Diabetes Hotline received about 3000 inquiries, 73% by phone, and 27% on the website. Approximately 440 of the inquiries in 2014 regarding medicinal products and the use of medicinal products, and about 330 of the inquiries involved treatment. The service is available in different languages (Norwegian, English, Urdu/Punjabi, Turkish, Somali and Arabic). Inquiries to the Diabetes Hotline are answered by a first-line support staff (90%) with experienced advisors or by a second-line support staff, an expert panel composed of health care personnel and professionals. The expert panel has extensive health care expertise and is composed of a general practitioner, paediatrician, specialist, pharmacist, clinical nutritionist and psychologists.

It will be necessary to coordinate this public information for patients, as there are many different

actors providing the same type of information. To achieve higher quality, an appropriate division of tasks, user testing and user involvement, the Ministry of Health and Care Services will evaluate the possibility of establishing a network to ensure standardisation and the development of patient-centred information. This type of network should be connected to the existing network, such as the National Network for Clinical Procedures, and the point of contact for interdepartmental medicinal product information. The Ministry has proposed to invite the pharmaceutical industry to join this cooperative effort. See Chapter 10 for further information. Patient organisations should also be invited as representatives for patients and medicine consumers, and as an important actor with respect to the distribution of information.

7.1.3 Digital medicine information

Norwegians are active internet users, accustomed to obtaining information and conducting services on their own. Although the health and care sector has been slower in providing online services than other sectors, these services are continuously being expanded.

Helsenorge.no was established in 2011 and will be part of a shared portal to online public health care services. In the course of just a few years, helsenorge.no has become an important source of information and an important channel of communication for patients and other users. The portal has self-service options that provide access to patients' personal medical information, including prescriptions and core medical records. This is an important step towards the vision of "One Citizen – One Record". Several services are currently under development, including a solution for digital communication between patients and their general practitioners. Here it will be possible to carry out electronic consultations, book appointments, renew prescriptions, and generally make it easier to contact the doctor's office. Work is currently underway to develop similar solutions for specialist health services.

Public data regarding medicinal products will be made available for the development of applications and online services. Helsenorge.no has already been adapted for open sets of data in certain areas. Once data is made available, businesses can be invited to develop good digital services. In this manner, it will be possible to achieve an innovative cooperation between patients, public health care services, and private suppliers. The result could be the development of customised, online health care services and apps, which authorities should not develop on their own.

Box 7.3 Patient app from the Norwegian Pharmaceutical Product Compendium AS

The Norwegian Pharmaceutical Product Compendium AS is developing a patient application for medicinal products. This app will consist of nearly 3000 package leaflets and nearly 2000 photos of capsules and tablets, as well as patient warnings from the Norwegian Medicines Agency. It will be possible to build up a personal list of medicinal products in use. Medicinal products can easily be added to the list by scanning the barcodes on the medicine packages. Dosages and warnings can also be added.

The Norwegian Pharmaceutical Product Compendium AS is now converting all package leaflets to a structured format (XML). This will provide entirely new opportunities for displaying package leaflets, both online and on patient apps. It will also provide new opportunities for others using package leaflets from the Norwegian Pharmaceutical Product Compendium, such as the Norwegian Medicines Agency, the Norwegian Directorate of Health (helsenorge.no) and the pharmacy chains.

Pharmaceutical manufacturers can request QR codes on their packages, and there is already an approved use of QR codes on some medicinal product packages. A QR code is a two-dimensional barcode that can be scanned using a mobile phone camera. Use of the QR code or other references to the package can simplify access to approved patient information about medicinal products in digital formats. Digital formats make it possible to enlarge text size, add audio text and provide video instructions. This can improve legibility and make the text easier to understand. Digital patient information also ensures access to updated information.

7.1.4 Pharmacy advice for enhancing adherence to treatment

Pharmacies must ensure that medicinal products are responsibly dispensed to the end user. Pharmacies are subject to stringent laws and regulations that apply to businesses. Pharmacy personnel include primarily pharmacists and pharmacy technicians. Both groups are authorised health care personnel, and subject to the regulations of the Health Care Personnel Act. Only authorised pharmacists are permitted to dispense medicinal products in Norwegian pharmacies. As of 15 December 2014, there were 8,186 employees in Norwegian pharmacies (6,516 full-time equivalents), including 3,361 pharmacists and 3,495 pharmacy technicians with professional training.

The pharmacy is a low-threshold service for health care services, which inform consumers about the correct use of medicinal products. Pharmacy personnel have a key role in providing advice on the correct use of medicinal products.

The primary activity of a pharmacy is to dispense medicinal products and ensure that these products are used correctly. The Pharmacy Act requires pharmacies to make certain that those who purchase medicinal products (both prescription and non-prescription) have sufficient

information about the correct use of these medicinal products (Pharmacy Act, Sections 6-6 and 6-7). Many pharmacies have developed standards for the type of information given. However, it is generally up to each individual pharmacy employee to determine who may need certain types of information in each case. Studies from Sweden, as well as information from patient associations indicate that information provided from pharmacies tends to vary in content and scope. There should therefore be greater focus on the systematisation of information.

Because the pharmacy is a good low-threshold service for health care services, it is important to assess the way in which the pharmacist's advisory role might be enhanced, to promote better patient adherence to treatment.

Current pharmacy services

There are currently no services from Norwegian primary pharmacies that are reimbursed by authorities. Some pharmacies offer services for the assessment of health risks, such as blood pressure readings, cholesterol tests, blood sugar tests, mole scanning, chlamydia tests, bowel cancer tests, and tests to assess the risk of cardiovascular disease. The use of these paid tests varies, but feedback from pharmacies indicates that customers are interested in these services.

Some pharmacies also offer personal medicinal product advice. This service is based on questions posed by the patient regarding his or her own use of medicinal products. The pharmacist attempts to discern medicine-related problems and offers the patient advice and guidance.

Pharmacies in other countries that are comparable to Norwegian pharmacies, offer various types of services. These services can be divided into four categories, and examples of such services are shown in Table 7.1.

Table 7.1 Pharmacy services in other countries

Category	Service
Disease prevention	Vaccination Syringe dispensing Help to quit smoking Lifestyle advice
Health risk assessment	Blood pressure reading Tests of cholesterol levels Allergy tests Skin cancer screening

	Other tests
Start-up of treatment, or changes in treatment	Start-up dialogue Technical advice Pharmacist prescription
Treatment follow-up	Medication review, to promote adherence Clinical medication review Pharmacist prescription Technical advice

The opportunity for pharmacies to promote correct use of medicinal products should be utilised to a greater extent here in Norway. One good example of this is the campaign that was carried out by pharmacies in collaboration with the Norwegian Medicines Agency regarding the switch to new anticoagulants (NB2013). Results from the campaign were positive. The Norwegian Pharmacy Association conducted a pilot study on “Start-up Consultation” (“Oppstartsveiledning”), based on the model from New Medicine Service, which was established in the UK.

Box 7.4 New Medicine Service (Start-up Consultation)

New Medicine Service (NMS) was introduced in England in 2011. The goal of this service is to improve patient adherence to treatment. The service is offered to patients who are beginning new long-term treatment in the therapeutic areas of asthma/COPD, type 2 diabetes, anticoagulents, or hypertension.

Patients who meet the criteria can receive these services from a pharmacist in the pharmacy, or they may be referred by a physician or other health care personnel. Patients must sign a consent form that will permit the pharmacist to share the information with the patient's physician and NMS.

These services consist of two consultations: one intervention consultation and one follow-up consultation. These consultations are intended to increase the patient's sense of security and motivation to continue the recommended treatment. The consultations may be carried out in person in the pharmacy or over the phone, and last about 10 – 15 minutes each.

The intervention consultation takes place approximately two weeks after the new medicinal product has been dispensed. During this consultation, the pharmacist attempts to uncover whether the patient is adhering to recommended treatment, or if there are any medicine-related problems. The patient's need for information and education is also evaluated. Based on this information, the pharmacist provides personalised advice and information. The consultation concludes with an agreement on a follow-up plan for the patient.

The follow-up consultation takes place 2–3 weeks after the intervention consultation. In this consultation, the pharmacist again tries to determine the patient's adherence to treatment. Previously noted problems are followed up. Any new medicine-related problems are registered and discussed, and the pharmacist and patient agree on new measures.

During both consultations, the pharmacist determines whether the patient has medicine-related problems that require the attention of a physician. This can be done by referring the patient back to the physician or by reporting this information to the physician after the consultation.

Results published by the New Medicine Service indicate that a greater amount of information and more frequent follow-up associated with the start-up of new medicinal products helps more patients to use their medicinal products as recommended. The study also indicates that this service can lead to additional life years and improved quality of life for the patient, and that it is cost-effective.

From the autumn of 2014 the Norwegian Pharmacy Association will begin a research project (Medicine Start) to examine the effects of start-up consultations. This is a further development of the pilot study "Start-up Consultation". The goal of this study is to examine whether the service increases adherence to prescribed treatment. The study will determine whether these start-up

consultations have any benefits for the patient, society or for pharmacies. Planning for a 12-month recruitment period is underway, and results are expected by the spring of 2016. The Ministry of Health and Care Services will evaluate whether start-up consultations may be an appropriate service, if the study on Medicine Start shows positive results.

Increased adherence to medicine treatment necessitates several individual and system-oriented services. Prescribers, pharmacies, patient organisation and learning and mastery centres are all arenas where patients can receive information regarding the correct use of medicinal products.

Expanded information services should particularly be directed at patient groups with the greatest need for advice and guidance. Studies indicate that more than 50% of patients with COPD have poor treatment adherence [3]. Patients with asthma and COPD make regular visits to pharmacies to pick up their medicinal products. Pharmacists provide information and advice on correct use and good inhalation techniques, but there are no routines for regular patient follow-up. Monitoring of inhalation techniques and providing advice on how inhalation medicines should be used could prevent incorrect use and result in better treatment adherence. Pharmacies in Denmark offer a similar service, which involves checking whether asthma inhaler users are using their medicinal products correctly.

Box 7.5 Inhalation checks in Denmark

Pharmacies in Denmark offer a service that involves checking whether asthma inhaler users are using their medicinal products correctly to achieve the greatest treatment benefit. This service is offered to all first-time users, but also for more experienced users if a patient has problems with their inhalation technique or with the use of the medicinal products. Physicians may also refer patients to this service.

This service includes personalised instruction in inhalation techniques and a demonstration of correct inhalation techniques. Pharmacies provide advice on correct use, and if necessary, referrals to other services. The consultation takes about 10 minutes. All pharmacy employees can identify and refer patients to this service, but only pharmacists and pharmaconomists[1] with special training can perform the service. Special checklists have been prepared for this consultation. Completed checklists are stored for 5 years as documentation to show that the service was performed, and patient consent is essential. This is a publicly funded service. Between 50,000 and 60,000 inhalation checks have been performed at Danish pharmacies over the last several years.

1 A pharmaconomist has a three-year education from upper secondary school, and does not have the right to dispense medicines. Only Denmark has this profession.

[3] Lareau SC, *Improving adherence with inhaler therapy in COPD,* INT J Chron Obstrct Pulmon Dis. 2010 Nov 24; 5: 401-6. Doi: 10.2147/COPD.S14715

The Ministry of Health and Care Services will evaluate the possibility of introducing standardised advisory services. One possible service involves pharmacist consultations for patients with asthma and COPD. In time, it may also be possible for other actors, such as learning and mastery centres, nurses in future primary health care offices, and patient organisations to offer these services. However, this type of advisory service, information about technical inhalation procedures in the pharmacy, would exceed the current obligation to provide information.

To provide good advice on the correct use of medicinal products, there must be access to information about patients' actual use of medicinal products. In the Report to the Storting no. 9 (2012–2013) "One Citizen – One Record", the objective is for health information to be accessible to health care personnel whenever there is an official medical need for this information, regardless of where the patient was previously treated. Such access must also be given to pharmacists when dispensing medicinal products.

7.2 The need for medicinal product information for health care personnel

The previous report to the Storting on medicinal products proposed that information provided by from authorities should aim to balance out information from the pharmaceutical industry, and furthermore, authorities must become more efficient in this area. The report also stated that there is a need for information about medicinal products from both authorities and from independent professional environments. This report concluded that tasks regarding public medicinal product information should be distributed between three different public sources of information:

1. Knowledge reviews of medicinal products and access to independent sources of information (Norwegian Electronic Health Library) – ensured by the Norwegian Knowledge Centre for the Health Services
2. Information on authorised medicinal products, adverse reactions and reimbursement status – ensured by the Norwegian Medicines Agency, and
3. The authorities' therapeutic recommendations, including the use of medicinal products – ensured by Norwegian Directorate of Health.

Today, health care personnel can seek and find information on medicinal products from a variety of sources. At a national level, there are reference publications and national professional guidelines and protocols being developed. This is information of high professional quality, but the information is often difficult to access and not sufficiently user-friendly. In addition to the information from the three actors mentioned above, there are several other information resources including: The Norwegian National Formulary, The Norwegian Electronic Medical Reference Book (NEL), the Norwegian Pharmaceutical Product Compendium, RELIS, etc. The various information resources are discussed in Chapter 4. There are many good sources of medicinal

product information that should be further developed and preserved. Several different sites and publications have been developed over the years, all of which have plenty of knowledge of this field, as well as a good idea of what health care personnel tend to request and use. The content of the various information resources often overlap one another, and the information is not always suitable for sharing through a variety of channels. There is reason to consider whether publicly funded medicinal product information could be coordinated and structured in a more effective manner. This would likely reduce the need to search for information from several different sources.

The Ministry of Health and Care Services will evaluate how to coordinate the production of information, and how authorities can ensure, preserve and offer good sources of information to health care personnel. The point of contact for interdepartmental medicinal product information, cf. Discussion in Chapter 4.6.4, should participate in the assessment.

In Norway, we have access to several good reference publications in both Norwegian and English, but there is a need for additional high quality medicinal product information in Norwegian. The Norwegian Electronic Health Library offers health care personnel access to central international reference publications. It is important to continue to develop the content and services offered at helsebiblioteket.no and to maintain the access to international reference publications.

7.2.1 Electronic decision support function for health care personnel

The Report to the Storting no. 9 (2012–2013) "One Citizen – One Record" points out that IT tools in the health and care sector should offer a decision and process support system function. This would assist health care personnel in their work processes, based on guidelines, protocols and research-based knowledge. This type of function should be made available for health care personnel through the electronic patient medical record. Such a support function could be useful in diagnostics, treatment planning, medicine prescriptions and referrals. Quality assured information and decision support for prescribers, other health care personnel and for patients themselves, may reduce the risk of incorrect use of medicinal products and improve treatment adherence. Electronic tools such as e-prescriptions and, in time, core medical records, would likely result in better communication about medicinal product use between the various actors in health care services and to patients and consumers.

Medication reconciliation would make it easier for physicians to gain an overview of their patients' use of medicinal products. This would also be important for making correct decisions about treatment. In order for information about patients' medicinal product to lead to informed and correct decisions, electronic chart systems in hospitals and electronic medical records must all offer decision and process support functions. For a decision support function to work, there must be an increased utilisation of structured knowledge sources, where information is divided up and made available for various purposes and systems. A standardised coding system and terminology for IT systems would be essential in ensuring the sharing and reuse of the

information.

The Norwegian Medicines Agency manages structured information on medicinal products with the use of FEST, an electronic prescription support system. FEST is a database and the primary source of information regarding medicinal products and reimbursement policies in physicians' record systems, pharmacy dispensing systems, electronic prescriptions, core medical records, etc. With FEST, the Norwegian Medicines Agency can send out alerts with vital information directly to physicians' record systems, including information about serious adverse reactions, withdrawn products, and medicine interactions, etc.

Many new groups have started using FEST, including hospitals and nursing homes. This requires a reliable, flexible and accessible FEST service. The current FEST set-up is not suitable for meeting future needs. FEST must be developed as an open source of data. This means that information must be made far more accessible, and data must be presented in a manner that allows for direct inquiries.

Hospitals also need information which currently cannot be found in FEST. Examples of such information include protocols which provide an overview of all medicines that can be combined. Hospitals also need additional information about dosage. While general practitioners measure medicine by the amount in an entire bottle, hospitals must deal with smaller amounts, such as millilitres. In order to meet these needs, the data in FEST must be accessible as linked open data.

Information from the Norwegian Electronic Health Library can be presented as structured information, and is available as open data, to achieve better integration with structured information in other services. A pilot project has been proposed, whereby contents from the Norwegian Electronic Health Library, such as clinical procedures, would be made available as open data. Such data can be more easily integrated with medicinal product information from sources such as FEST.

Such information sources should be further developed to include information that is adapted to various user groups, including hospitals and general practitioners, and to offer structured and open data. This development would be consistent with DIFI recommendations (Agency for Public Management and eGovernment) which propose that national share components should be made available as open data. It would also be an important factor in encouraging sharing, reuse, decision support and the innovation of new services.

7.2.2 Academic detailing

Physicians have good access to a great deal of high professional quality information, but this information is not always available or user-friendly, which may have consequences for the implementation of national guidelines and protocols. There is a demand for greater competence with respect to medicinal products among physicians and other health care personnel, and several publications have indicated that the incorrect use of medicinal products and adverse reactions from medicinal products might be prevented by maintaining and improving prescriber competence.

Academic detailing, or service-oriented educational outreach, is a process that involves the face-to-face or group education of prescribers by trained health care professionals, who offer knowledge-based, up-to-date information about treatment with medicinal products within a key therapeutic area. This method is utilised on a national level in both Australia and Canada. In the United States, Kaiser Permanente uses academic detailing as a cost-effective method of communicating information about medicinal products. Clinical pharmacologists, pharmacists and other professionals with special expertise can communicate knowledge adapted to various groups of health care professionals within the framework of the academic detailing programme. This service can be offered to both primary health care services and special health care services.

The Department of Clinical Pharmacology at St. Olav's Hospital has carried out academic detailing on a smaller scale with positive results, through its education programme for general practitioners in the Trondheim region.

Box 7.6 Pilot project – Academic detailing in Norwegian general practice

The Ministry of Health and Care Services and the Norwegian Directorate of Health has assigned RELIS in the Central part of Norway the task of conducting a pilot project in academic detailing in collaboration with the Department of Clinical Pharmacology at St. Olav's Hospital and RELIS in the Northern part of Norway. This pilot project is entitled "KUPP", and stands for kunnskapsbaserte oppdateringsvisitter. The subject of the pilot project is the correct use of NSAIDs, and academic detailing will be conducted with all general practitioners in Trondheim and Tromsø. It is anticipated that the project will result in increased knowledge about these medicinal products among general practitioners, which may lead to a change in prescription patterns. These changes will be evaluated based on prescription data. Results from the project will form the basis for an evaluation of the method to determine whether it is suitable for implementation on a national level.

There is a need for the development of comprehensive and systematic educational training services for health care personnel that is adapted to Norwegian conditions. This service can be utilised to achieve a more rational use of medicinal products, as well as a swifter implementation of guidelines and protocols. If the pilot shows good results, the Ministry of Health and Care Services will assess whether academic detailing (in Norwegian, Kunnskapsbaserte oppdateringsvisitter - KUPP) should be utilised as a permanent educational training method.

8 Medicinal product information for research, health analyses and quality assurance

The Norwegian Prescription Database is the current prescription-based medicinal product registry, and was established in 2004. It contains data regarding pharmacy-dispensed prescription medicines. The purpose of the Norwegian Prescription Database is to obtain greater knowledge of how medicinal products are prescribed and used in the population, and to research both the short-term and long-term effects of medicinal product use by linking the registry to other central health registries (secondary use of health care data). The Norwegian Prescription Database is currently the country's most important source of data at an individual level in the population, and it has been used for more than a decade for research, health analyses and quality assurance of prescriptions and use of medicinal products.

The Norwegian Prescription Database is a pseudonymised registry. Pseudonymisation was chosen as the form of encryption for personal privacy reasons. The technology needed for a pseudonymised registry involves limitations in juxtaposing this data with other registries and/or databases, and prevents important research on medicinal products or adverse reactions from medicinal products, from being conducted. This type of registry format has made it difficult to pursue the aims and objectives of the Norwegian Prescription Database. Personal privacy could be secured in other acceptable ways, with encryptions that allow for reuse, and a more optimal utilisation of data. The Norwegian Patient Registry and the Norwegian Cardiovascular Disease Registry have used other forms of encryption to ensure personal privacy.

Another objective of the Norwegian Prescription Database is to enable prescribers to use prescription data extracts as a basis for internal control and quality improvement measures. Studies indicate that peer review groups reviewing prescriptions by individual physicians can have a permanent impact on prescribing practices, and can also improve them. A number of major projects have shown interest in using data from the Norwegian Prescription Database to provide clinicians with feedback on their prescribing practices, as a basis for quality improvement. A lack of technology solutions means these types of data extractions must be performed manually by prescribers who require an overview of their own medicinal product prescriptions.

Box 8.1 Feedback on prescribing practices

A project at the University of Oslo will be investigating whether a simplified version of the project entitled "Colleague-based therapy supervision" could change prescribing patterns and promote a prescribing pattern for antibiotics that is more consistent with national guidelines. Interventions will be directed towards Norwegian general practitioners and will utilise colleague-based supervisory groups (specialists in general practice must participate in these to maintain their specialisation), and both high-consumer and low-consumer municipalities are included in the study. The intervention involves a course meeting which offers up-to-date knowledge about antibiotics, and a subsequent discussion. The focus is on the amended National Guidelines for the Use of Antibiotics in General Practice. Participants are also offered a package with IT tools and pop-up reminders concerning the Guidelines, in addition to patient brochures. Physicians discuss their own practices with the aid of feedback from the Norwegian Prescription Database (accommodated for antibiotic prescribing) in colleague-based groups. Then, with the assistance of the Norwegian Prescription Database, the following is evaluated: Total number of antibiotics, frequency of penicillin compared to amoxicillin, macrolides and doxycycline, as well as the frequency of ciprofloxacin compared to trimethoprim, pivmecillinam and furadantin. There is particular emphasis on the prescription of antibiotics for children under the age of 12.

The Norwegian Prescription Database currently lacks patient-level information about medicinal products that are prescribed internally and dispensed to patients in hospitals, nursing homes and other health care institutions. It is therefore not possible to measure the systematic quality of internal prescribing practices for medicinal products, or the consequences of medicinal treatment and use among patients in institutions. Neither is it possible to assess and analyse the continuity of medicinal treatment when patients are transferred to another level of care.

Shared information about medicinal products in health care services, regardless of the level of care or the location of patient care, would provide data and analyses of medicinal product use throughout the entire patient care pathway. This would include patients in nursing homes, hospitals and other health care institutions.

Measures

Extensive efforts are underway to modernise and coordinate central health registries and medical quality registries, by the National Health Registry Project. The National Health Registry Project is implemented through biennial action plans, and registry activities are coordinated through eHealth. The integration of the Health Registry Project with national eHealth efforts involves the development of shared technology for reporting and data capture, transfer to national health registries, feedback systems, technology solutions for publications and other user services.

One of the prioritised areas of the Action Plan for Health Registries 2014–2015 is the collection of information about the use of medicinal products in institutions such as hospitals and nursing homes. The Norwegian Institute of Public Health, which oversees this action plan, conducted a feasibility study which recommended the modernisation and expansion of the Norwegian Prescription Database. This type of solution would be consistent with long-term goals in electronic health services, which involves the routine collection of structured data from health services for health registry purposes to avoid separate data collections, to the extent it is possible. The development towards a seamless reporting system to health registries requires technology to enable health registries to be synchronised with technological solutions from other areas of the health care sector. A shared infrastructure, rendering all information on medicinal products available, would be consistent with the Norwegian eHealth Action Plan, which will assess the opportunities for a better monitoring of medicinal products in use. Standardised and structured information on medicinal product use found in electronic medical charts and electronic medical records is essential in ensuring a uniform exchange of medicinal product information throughout the patient care pathway. This is also important in terms of expanding the Norwegian Prescription Database with data from institutions.

More automatic data extraction solutions are needed for medicine product prescribers who are seeking access to get an overview of their own prescriptions. This type of extraction system would also provide prescribers with a basis for comparison with the prescribing patterns of other physicians. The use of antibiotics, for instance, is an area for which an automatic reporting system would be an important tool in achieving more appropriate prescription practices. See the discussion in chapter 13.1.

A new law regarding health registries and the management of health care information (Health Registry Act) entered into force on 1 January 2015. Changes as a result of this law will make it easier to use the registries for research, health analyses and quality assurance, by permitting exemptions from the duty of confidentiality upon the provision of indirectly identifiable personal information. The government is interested in developing and expanding today's prescription registries, in order to meet future needs, and will evaluate the possibility of establishing a person-identifiable database for medicinal products, based on the current prescription database, supplemented with data on the use of medicinal products in institutions, when this is made available through a shared medicine list, cf. the establishment of a shared medicine list and assessment of "One Citizen – One Record". In this evaluation, personal privacy issues associated with a person-identifiable medicinal product database must be thoroughly examined. Personal privacy must be emphasised, weighing the advantages and disadvantages of such a database. The Norwegian Data Protection Authority must be involved in this evaluation.

8.1 System for reporting adverse reactions

Authorities receive information about adverse reactions to medicinal products in a variety of ways:

- Health care personnel are required to report adverse reactions they encounter in their daily work.
- Marketing authorisation holders for medicinal products are also required to report adverse reactions of medicinal products to the authorities.
- Patients can report adverse reactions directly.

There is an online reporting system for patients, and reports are sent electronically to the Norwegian Medicines Agency. Health care personnel must send reports of adverse reactions to their regional medicinal product information centre (RELIS) whenever the connection between a medicinal product and a reaction is suspected.

Adverse reaction reports from health care personnel are essential for the monitoring of medicinal products. Reports from health care personnel, the pharmaceutical industry and from patients are collected in a national adverse reaction database, which is designed to uncover signals of new adverse reactions. All adverse reaction reports received are coded in accordance with an international coding system, so that symptoms, diseases and medicinal products all have a standardised format. This coding makes it possible to search for signals of new adverse reactions, also internationally. Once reports are coded, they will no longer contain directly identifiable personal information. Reports that are added to the national adverse reaction database are also sent to the marketing authorisation holder for the product. These companies collect adverse reaction reports in standardised formats from various countries, and continue to search for new adverse reaction signals.

Controlled clinical trials of medicinal products are intended to ensure that these marketed medicinal products are safe and effective. Such studies form the basis for the authorisation and marketing of new medicinal products. Yet knowledge of these new medicinal products is relatively limited when they first arrive on the market. Rare adverse reactions are difficult to detect before the medicinal product has been in general use, since there are relatively few patients being treated in these clinical trials, and since the patients included the trials have been specially selected, based on certain criteria. To discover unforeseen adverse reactions of a medicinal product as quickly as possible, most countries have established a system for reporting serious and unknown adverse reactions to medicinal products (spontaneous reporting). The purpose of the spontaneous reporting of adverse reactions is to detect the signals of adverse reactions which were unknown at the time the product received marketing authorisation. Spontaneous reports will be collected in the new system for reporting adverse reactions (the National Register of Adverse Reactions).

The legal basis for a system of reporting adverse reactions has been included in a new Health Registry Act, Section 11. Registration of adverse reactions will not require consent. It is stated in the provisions that more detailed rules must be drawn up for these regulations.

One of these regulations will stipulate rules regarding the type of information the National Register of Adverse Reactions would contain. This may be information about adverse reactions

or suspected adverse reactions to medicinal products, or directly identifiable personal information concerning the individual who had experienced these adverse reactions.

The monitoring and assessment of adverse reaction signals is conducted on national, European and international levels. Information concerning adverse reactions may necessitate a revised summary of product characteristics and updated package leaflet with new safety information, or require the medicinal product to be withdrawn from the market.

Spontaneous reporting is effective in detecting adverse reactions which occur soon after treatment has commenced. The system is less effective in identifying adverse reactions which occur after prolonged use, such as the increased risk of cancer.

Systematic analyses based on links between the Norwegian Prescription Database and other central health registries and quality registries can also provide new knowledge regarding the positive and negative effects of medicinal product use over time.

9 Quality indicators

The Norwegian Directorate of Health intends to develop, communicate and maintain national quality indicators to assist health care management, promote the improvement of quality in health care services, and enable patients to protect their rights. A national quality indicator system would help to ensure the population equal access to quality health care services by providing valid and reliable information about the quality and capabilities of the Norwegian health care system, with regard to both status and long-term trends. When quality indicators are combined with patient reports on targeted effect and the results of patient and user surveys, this provides a more complete picture of the quality of services.

A quality indicator is an indirect goal, an indicator which says something about the quality of the subject or area under evaluation. Quality indicators are based on one or more of the dimensions of quality, and can provide a measurement of the available resources in health care services, patient care pathways, and the outcome of health care services for the patients. Quality indicators must be viewed in context, and offer an overall impression of the quality of a service. These are usually divided into three types of indicators:

- Structure indicators (framework and resources, expertise, available equipment and facilities, databases)
- Process indicators (activities in the patient care pathway, including diagnostics and treatment)
- Result indicators (survival, health benefits, satisfaction)

There is no established measurement to determine the highest level of use for a medicinal product for various indications or medicinal product groups. When the work on the Norwegian National Strategy Against Antibiotic Resistance is underway, cf. discussion in Chapter 13.1, it may be appropriate to determine goals and indicators for the use of antibiotics. The national

quality indicator system also involves the development of indicators for infections and the use of antibiotics.

The Norwegian Directorate of Health is working on an evaluation of national quality indicators to determine whether medication reviews are being conducted in accordance with the Protocol for Medication Reviews (IS-1998). The proposed indicators are:

- The proportion of residents in institutions (≥ 65 years of age) who have had a medication review, in accordance with the Protocol for Medication Reviews IS-1998, over the last six months.
- The proportion of patients with home-based health care services (≥ 65 years of age) who have had a medication review, in accordance with the Protocol for Medication Reviews IS-1998, over the last six months.

In accordance with the plan, the pilot project will commence in January 2016.

10 The role of the Association of the Pharmaceutical Industry in Norway in providing information

The Pharmaceutical Industry provides information on prescription medicines to health care personnel who prescribe or dispense medicinal products. It is permitted to direct advertising towards this group of health care personnel. Advertising in this context applies to activities which are designed to promote the sale or use of the medicinal product. Advertising for non-prescription medicinal products may also be directed towards the public.

These regulations are based on the EU Directive on Medicinal Products, which has been implemented into Norwegian law as a result of the EEA agreement. There are clear restrictions on the advertising content. The advertisement must be neutral and objective, and promote the rational use of medicinal products. The advertisement must be not be misleading, it should not exaggerate the qualities of the medicinal product or its medical value, and it should not encourage use of the product for anything other than medical purposes. The advertisement must be consistent with the content of the summary of product characteristics, and is only permitted if the medicinal product has been granted marketing authorisation.

The supervisory activities of the Norwegian Medicines Agency associated with the industry's medicinal product marketing are of importance to the public, and reports from this supervision are published on the Norwegian Medicines Agency's website.

Box 10.1 Medicinal product advertising for health care personnel

Advertising for prescription medicines may only be directed at health care personnel who can prescribe medicinal products, or that have the right to dispense medicinal products.

Many groups of health care personnel have pharmacology educations, and they work with medicinal products, yet they do not prescribe or dispense these products, under the provisions of Directive article 91 (Directive 2001/83/EEA). Health care personnel included under Section 13-7 of the Norwegian Medicinal Products Regulations, is therefore a small group, compared with health care personnel under Section 48 of the Health Care Personnel Act. The health care personnel groups included under Section 13-7 of the Norwegian Medicinal Products Regulations are defined based on their right to prescribe or to dispense medicinal products.

Health care authorities have adopted a broad understanding of activities that should be viewed as advertising, based on the definition of advertising. The Association of the Pharmaceutical Industry in Norway (LMI) is of the opinion that regulations regarding medicinal product information must be adapted to today's information society, and that the pharmaceutical industry should be permitted to communicate information about disease and medicinal products to both health care personnel and the general public. According to the LMI, the liberalisation of practice could contribute towards a more well-informed patient population through the use of patient brochures, mobile apps and instructional brochures for specific medicinal products.

Over the past year, authorities have given the pharmaceutical industry a greater opportunity to inform the public about disease, health and medicinal products. For some medicinal products, it may be useful to have material that demonstrates injection techniques and inhalation techniques. The Norwegian Medicines Agency has therefore given the pharmaceutical industry permission to create instructional videos and illustrations for the practical use of medicinal products, as long as demonstrations are consistent with the text and any illustrations in the package leaflet.

In autumn 2014, the Ministry also gave the pharmaceutical industry permission to supply information about certain diseases, together with information about medicinal products at a group level. The basis for this new policy is a provision in the Regulations on Medicinal Products, which state that rules for advertising do not apply to information concerning health or disease when it is not directly or indirectly related to one or more medicinal products. The guidelines by the Norwegian Medicines Agency, states that this information must be correct, easy to understand, and adapted to the general public. It should emphasise information regarding health and disease, and should not focus on the choice of treatment. Medicinal products can be mentioned as one or several treatment options, but it is not permitted to mention product names or specific active substances.

TV advertising for non-prescription medicinal products

Television advertising for medicinal products is not permitted in accordance with Section 13-4 of the Norwegian Medicinal Products Regulations. This restriction is based on a public health perspective.

Television advertising for non-prescription medicinal products is permitted in several European countries, including Sweden and the United Kingdom. The “sender country principle” applies to advertising sent from other countries. Regulations concerning sender countries determine the type of advertisements that can be shown on television. Certain Norwegian TV channels send advertisements from other countries that are aimed at the Norwegian market, which undermines the ban on advertising for medicinal products on Norwegian television.

Norwegian restrictions are no longer as purposeful for non-prescription medicinal products, and it is determined that a repeal of these restrictions would not have any major negative consequences for public health. A proposal to allow advertising for non-prescription medicinal products on television has now been presented for public consultation.

Information on medicinal products for the general public

LMI believes that information brochures from the Pharmaceutical Industry, which are distributed after a medicinal product has been prescribed, should not be viewed as advertising. LMI refers to the practice in Denmark, Sweden, Finland, the Netherlands and the UK, where this is permitted. Other countries in the EU consider these patient brochures to be advertising for prescription medicines, as does Norway.

A patient brochure that is distributed after the medicinal product has been prescribed could potentially influence the physician’s prescription practices and the use of the medicinal product. This type of activity is therefore subject to the advertising ban. This decision must be viewed in light of the EU Directive on Medicinal Products, where advertising is defined as any form of door-to-door information, canvassing activity or inducement designed to promote the prescription, supply, sale or consumption of medicinal products.

Box 10.2 Decision by the European Court of Justice

The scope of the definition or concept of advertising is evident in the decision delivered by the European Court of Justice in 2011. The Court stated that it was apparent from the wording of the provision that the concept, in *any form*, would result in a very broad conception of advertising[1]. Furthermore, the Court stated than the broad concept is justified by the need to safeguard public health, and prevent serious health risks which may arise from improper use or overconsumption of prescription medicines.

The Court referred to the fact that the concept of advertising involves only activities intended to promote the prescription, supply, sale and consumption of medicinal products. In this case, the Court determined that making package leaflets available on the pharmaceutical company's website could not be considered advertising. Had the manufacturer selected certain sections of information from the package leaflet, or reworded the information, the activity would, according to the Court, have an advertising intent. The Court emphasised that the information was made available to anyone who sought to obtain it, and not forced on those who did not wish to receive the information.

[1] See Case c-316/09.

The practice of the European Court of Justice shows that the distribution of patient brochures, in its very wording, is encompassed by the definition of advertising, and publications of such brochures on the manufacturer's website would be considered as advertising. Is it possible, however, that such patient brochures could be of such value that they should be provided by health care personnel after a medicinal product has been prescribed?

- The pharmaceutical industry has a great deal of knowledge about their own medicinal products, and a patient brochure might, on its own, provide some valuable information for the patient.
- Physicians and their patients must often choose between medicinal treatment and the use of other measures. A patient brochure from the industry, distributed after a medicinal product has already been prescribed, could potentially relieve physicians of their duty to inform their patients, and might make it more appealing to choose a medicinal solution to the problem. Such activities would therefore be inconsistent with the recommendations of the authorities.
- In practice, the pharmaceutical industry generally tends to offer information about patented (and expensive) medicinal products.
- The supervision of medicinal product marketing indicates that the information offered is often biased, and the positive aspects of the medicinal product are often excessively emphasised.

At the present time, the Ministry of Health and Care Services must consider informational material from the pharmaceutical industry, distributed to patients who have received prescriptions, as advertising.

The pharmaceutical industry is a knowledgeable actor, and its interest in providing better information to the public should be utilised. Chapter 7.1.2 contains a proposal to assess the opportunity to establish a network which would ensure the standardisation and facilitation of good information for patients. The Ministry of Health and Care Services proposes to invite the pharmaceutical industry to collaborate with health care authorities on preparing patient-centred information on medicinal products.

It is essential, however, that this information is made available for all medicinal products, including those that are no longer under patent protection.

11 Generic and biosimilar medicinal products

11.1 Generic medicinal products and pharmacy substitution

The Norwegian Medicines Agency assesses whether approved generic medicinal products should be placed on the substitution list. The substitution list can be found in a searchable database, and contains an overview of medicinal products that can be substituted with generic medicinal products in the pharmacy at any given time. This list is updated each month, and published on the Norwegian Medicines Agency's website.

Before placing generic medicinal products on the substitution list, the Norwegian Medicines Agency must evaluate whether a generic alternative would be safe, in terms of:

- disease
- patient group
- risk of serious problems due to improper use
- need for special equipment

Generic substitution was introduced to pharmacies in 2001 and led to a reduction in the cost of medicinal products which are financed through the National Insurance scheme, cf. discussion in Chapter 16.5. Pharmacies can only offer to substitute medicinal products with generic alternatives that are on the substitution list. Physicians may decline the substitution when there are medical reasons for doing so, and patients may decline a substitution without stating a reason. Physicians and patients decline substitutions in about 7-8 per cent of all cases.
Two Norwegian studies have shown that generic substitutions may generate some concern. Some patients may become confused about their medicinal products, the most common problem being that the patient uses both the original and the general medicinal product at the same time. Håkonsen found that five per cent of Norwegian patients, and ten per cent of first generation immigrants were using both original and generic medicinal products for a certain period after the generic substitution. Language barriers and experience with false medicinal products in their homelands may cause uncertainty and improper use among some immigrant groups.

The Norwegian Medicines Agency made extensive efforts to spread information regarding generic substitutions in pharmacies. In 2008, the Norwegian Medicines Agency conducted a major information campaign on generic substitutions in pharmacies. This campaign was aimed at pharmacies, physicians and patients, employing methods such as letters, posters, brochures and animation videos. Various aspects of generic substitutions have later been repeated and elaborated on the Norwegian Medicines Agency's website, and in Journal of the Norwegian Medical Association, on the Norwegian Medicines Agency's regular information page, "News about Medicinal Products" (Nytt om Legemidler).

There is still very little knowledge about the actual costs and problems associated with generic substitutions. There have been no systematic studies involving physicians' experiences with generic substitutions.

More knowledge is needed about measures that might counteract the negative consequences of the scheme, such as standardised labelling for medicinal product packages, as well as home visits to patients who use several different medicinal products. In Sweden, for instance, home visits will now be conducted for all 75-year-old patients.

The Swedish Medical Products Agency has, in collaboration with the Swedish Dental and Pharmaceutical Benefits Board and the Swedish eHealth Agency, begun to allow pharmacists in pharmacies to refuse generic substitutions from 1 January 2015. The opportunity to refuse generic substitutions may be utilised if the pharmacist believes that a substitution would pose a significant disadvantage to the patient.

Standardised labelling of medicinal product packaging with the names of active substances

The Norwegian Medicines Agency has noted the need for common European regulations to ensure that names of active substances are given a prominent and standardised placement on medicinal product packaging. The Norwegian Medicines Agency has presented this proposal at an EMA meeting (CMDh in 2013) at several international congresses. The Norwegian Medicines Agency, in cooperation with the Institute of Psychology at the University of Oslo, conducted an experimental study which indicated that clear and standardised labelling with the name of the active substance makes it much easier to determine whether the two packages contain the same or different active substances.

The Norwegian Medicines Agency should continue its efforts in the EMA, possibly in collaboration with WHO, to develop international regulations which would ensure that active substance names are given a prominent and standardised placement on all medicinal product packages.

Generic prescriptions

The term "generic prescription" implies that the physician prescribes the name of an active

substance instead of a product name. Generic prescriptions are permitted in Norway, and are used in approximately two per cent of all prescriptions (figures from 2007).

New European regulations demand that active substance names must be noted in all prescriptions (possibly together with a product name), to make it easier for the patient to use the prescription in other countries. Generic prescriptions are mandatory in Portugal as well as in certain areas of Spain, and they are used in approximately 80 per cent of all prescriptions in the UK. At the University Hospital of North Norway, generic prescriptions have been introduced as a standard.

The Norwegian Medicines Agency is making efforts to increase the use of active substance prescriptions. The central argument for using the names of active substances is that it would facilitate communication among various health care personnel, and between health care personnel and patients. Using names of active substances would also minimise misunderstanding and uncertainty regarding generic substitutions in pharmacies, and when patients require health care services abroad.

Active substance names are also part of a shared medical language used by health care professionals and in scientific literature all over the world. To increase the use of active substance prescriptions, it is essential that the Norwegian Medicines Agency database of medicinal products (FEST) is adapted to include the prescription of active substances. Patient record systems must also be able to facilitate active substance prescriptions by physicians. The Ministry of Health and Care Services will evaluate methods of information for physicians, pharmacies and patients, as well interest organisations, in order to promote generic prescriptions.

11.2 Biological and biosimilar medicinal products

There has been in increase in the use of biosimilar medicinal products in Norway. Once European medicinal product authorities authorise a biosimilar medicinal product, this confirms that the product has the same effect as the original product. However, the authorisation does not apply to the substitution of original medicinal products with biosimilar medicinal products while the patient is undergoing treatment with the original product. Scientific research on substitutions would be important in terms of gaining greater acceptance for treatment with biosimilar medicinal products in Norway and in other countries. The Norwegian Pharmacy Act does not permit pharmacy substitutions between biological and biosimilar medicinal products.

The Norwegian Parliament’s decision on Proposal 1 S (2013–2014) included a grant of NOK 20 million for clinical research on switching biological medicinal products with biosimilar products. The study NOR-SWITCH is being conducted in collaboration with the regional health authorities under the leadership of the South-Eastern Norway Regional Health Authority. This study will provide information on the safety and efficacy of switching from the biological medicinal product Remicade to the biosimilar medicinal product Remsima. The study will include about 500 patients from all health authority regions.

Efforts are currently underway in the EU to develop an identification system (2D Data Matrix

marking) for biological medicinal products, to identify exactly what type of medicinal product the patient has received. To improve the safety associated with biological medicine use, it is essential to be able to identify the product (original product or biosimilar, trade name, batch number, etc.) which is being administered.

12 Medicinal product management

Amendments to the Norwegian Regulation related to Medicinal Product Management were adopted and entered into force on 1 January 2015. The revision stipulates that management of a health care enterprise must ensure that their enterprise employs routines that include quality assurance for information regarding patients' use of medicinal products upon admittance and discharge, as well as when transferring to other services within the enterprise. Section 5 also requires that "an updated and reconciled list of medicinal products in use shall, by agreement with the patient, always accompany the patient when transferring to a different level of care".

Box 12.1 Welfare technology

Welfare technology involves technological solutions and products designed to improve patients' self-reliance, independence and security in their daily lives. Welfare technology is one of several methods of meeting the future challenges in health care and social services. Participants in the Welfare Technology Project include the Oslo districts of St. Hanshaugen, Gamle Oslo, Grünerløkka and Sagene, as well as the Lovisenberg Diakonale Hospital, in collaboration with the Norwegian Directorate of Health and the Norwegian Confederation of Municipal Employees. Ten electronic medicinal product dispensers (called "Pilly") are being tested in the district of St. Hanshaugen. Pilly alerts patients with sound and light when it is time to take their medicine. Patients can receive reminders, such as text messages on their mobiles, and family members or home health care services can also receive reminders. Medicine dispensers are normally filled for a seven-day period of use, and one medicine dispenser can save home health care services 20 minutes a day in visiting time. In order to use Pilly, patients must be able to understand how to take their medicine once they hear the beeping sound or notice the blinking lights. Proper training of the staff and the organisational system is essential for this to function.

These two regulations support the provisions of the Regular General Practitioner (GP) Scheme, Section 25, which stipulate that a general practitioner must ensure that his or her patients have an updated list of medicinal products in use. A general practitioner must give other service providers in the health and care services an updated list of the patient's medicinal products, if this is necessary for providing the physician's patients with medically justified services.

Box 12.2 Closed Loop Medication Management

Closed loop medication management has been considered as an important system improvement initiative in Norway, Europe and the United States for reducing instances of adverse reactions, after acquiring and implementing new hospital IT systems. Closed loop medication management (CLMM) is a method to ensure that hospitalised patients receive the correct medicinal product, in the correct dose, at the correct time and in the correct manner, using new technology.

Primary requirements for the use of CLMM are as follows:

- An electronic medical chart (e-chart) with an electronic decision support function for prescriptions, preparation and dispensing of medicinal products
- Electronically and manually identifiable medicinal products
- Electronic communication and documentation systems

The primary intention is for medicinal product management and logistics to interact in a way which improves patient safety.

Norwegian hospitals have yet to implement closed loop medicinal management, although Østfold Hospital Trust is working towards the implementation of CLMM in their new hospital. Akershus University Hospital and St. Olavs Hospital are both working on solutions for a more individualised system of receiving medicinal products, whereby medicines would be prepared by an automatic system for each individual patient. This would satisfy the demand for a closed loop medicinal management when electronic chart technology is in place.

Regulations emphasise quality and competence requirements for the preparation of medicinal products in institutions, including hospitals and municipal health care services. A risk assessment is also required prior to the preparation of medicines.

The Norwegian Directorate of Health has prepared a new circular (IS 7/2015) for the regulations in their current wording. This circular contains a more detailed description of how to interpret the regulations, and includes guidelines that provide advice and practical examples for maintaining good routines and ensuring the quality of medicinal product management.

12.1 Multidose

Multidose dispensing refers to tablets or capsules that are packaged together for each dose. This system is well-suited for patients who live at home, who use several different medicinal products, and who are on stable medicinal treatment. It is most often used when the home health care nurse is responsible for medicine management. The purpose of multidose is to reduce the risk of dispensing errors and the waste of medicinal products, and to help nurses save time.

Multidose as a system was recommended as an improvement initiative in the previous White Paper on medicinal products, where the goal was to implement multidose to a greater extent. In 2002 there were 3000 patients using multidose, while in 2014 there were nearly 70,000 users. The majority (80 per cent) of the 70,000 multidose users receive municipal home health care services. Nursing homes also utilise this system, and a few patients have taken the initiative to use the system on their own.

HELFO (the Norwegian Health Economics Administration) offers municipalities a subsidy of NOK 500 per year for each patient using multidose in home health care services. This subsidy is equal to about 20 per cent of the cost of each multidose package. Private individuals using multidose cannot receive reimbursements for multidose packages.

When there are frequent changes to medicine dosages, multidose is not a suitable solution. Medicinal products that are used as needed, such as addictive medicinal products, must be managed without the use of multidose. In its National Clinical Protocol for Addictive Medicinal Products, the Norwegian Directorate of Health recommended that addictive medicinal products used as needed should not be offered in multidose packages.

Multidose is a good, quality system, and an important method for ensuring the proper use of medicinal products. The introduction of multidose has been shown to provide better medication reconciliation, improve patient treatment follow-up, simplify patient management of medicinal products, and lead to increased adherence to treatment.

Nevertheless, health care service actors have noted certain features in need of improvement. Studies indicate that patients' medicinal product lists are seldom revised, that patients are using unnecessary medicinal products over a long period of time, and that patients and home health care nurses tend to become less concerned with the type of medicinal products the patient is using. Physicians also tend to disagree on who should be responsible for a medicinal product list when several physicians are able to prescribe multidose systems for one specific patient.

Until now, multidose has been a paper-based system, using fax to convey information about medicinal product lists between the various actors (physician, home health care services or nursing homes, and pharmacies), in a medicinal product chain. This process involves several undefined, manual controls.

There is a need to ensure the electronic communication of medicinal product information between general practitioners and the multidose pharmacy when packing a multidose. A pilot study on electronic multidose prescriptions for patients is underway. New electronic prescription technology will replace today's paper prescription and use of fax as a communication channel between physician and pharmacy. This solution will not apply to patients who receive multidose as part of an internal prescription system (such as in nursing homes). An evaluation of the multidose pilot study indicated that medicinal products lists from pharmacies were consistent with general practitioners' medicinal products lists in 30 per cent of all cases. There was 64 per cent consistency in cases where pharmacies sent medicinal product lists to GPs in advance, with

prior medication reconciliation. A national implementation of electronic prescriptions for multidose is scheduled to commence sometime during 2015.

There may be a need for regulatory, structural, financial and IT-related changes to ensure that multidose will be a good tool for future use. During 2015, the Norwegian Directorate of Health will assess which corrective measures must be implemented, as well as how these shall be implemented, if they are to improve the quality of multidose.

13 Special groups

13.1 The use of antibiotics and antibiotic resistance

Antibiotics are medicines used in the treatment of bacterial infections. There is a clear correlation between the use of antibiotics in humans and animals and the development of antibiotic resistance. The prevalence of antibiotic resistant bacteria is increasing, and this presents a serious threat to public health, animal health and food safety. However, the development of new types of antibiotics appears to be at a standstill. Good strategies for counteracting of antibiotic resistance development are therefore crucial in ensuring that existing antibiotics can continue to be effective in the future.

The EU has determined a need for greater knowledge about antibiotic resistance, which would necessitate joint European research efforts. This is the reason for the establishment of the Joint Programming Initiative on Antimicrobial Resistance (JPIAMR).

The government intends to present an intersectoral strategic action plan on antibiotic resistance by the end of June 2015. This is in line with recommendations from the World Health Assembly and expert group, which has advised the government on how Norway should manage the challenges of antibiotic resistance. This expert group was appointed in 2013 by the Ministry of Health and Care Services, the Ministry of Agriculture and Food, the former Ministry of Fisheries and Coastal Affairs, and the Ministry of the Environment. The expert group has especially noted the need for a broad professional approach and a broad collaboration across sectors to confront the problems.

The use of antibiotics is relatively low in Norway, among both humans and animals. In 2013, 87 per cent of antibiotics were sold for human consumption, while 12 per cent were intended for animals, and 1 per cent for farmed fish. There has been a gradual increase in the use of antibiotics by humans in recent years. The use of penicillin, estimated by dose, has doubled since the mid-1970s. Antibiotics are too often used in inadvisable doses, and for too long. Furthermore, the antibiotics prescribed are not always those with a favourable resistance profile. Antibiotic resistance development is a consequence of overuse, and can be restricted by using these medicinal products in the appropriate manner. It is therefore essential to develop measures designed to reduce consumption and ensure a more rational use of antibiotics in Norway.

The systems for monitoring the use of antibiotics in Norway are inadequate. The few sources available indicate a possible overprescription of antibiotics to women, children, adolescents and the elderly. Consumption is about 50 per cent higher among adult women than among men in the same age groups. There are also geographical differences. For instance, antibiotic use is lower in the Northern Norway Regional Health Authority (Helse Nord) than in the three southern health authorities. Differences in consumption may be due to different prescribing practices, and to some extent also to public expectations. Access to medical services and pharmacies may also play a role.

As part of the operationalisation of the strategy on antibiotic resistance, the government will present an action plan for health care services on antibiotic resistant bacteria in 2015, where the goal is to reduce the public's use of antibiotics by 30 per cent by the end of 2020. The Ministry of Health and Care Services has commissioned the Norwegian Institute of Public Health to prepare a draft for this action plan. Central features of the action plan will involve the implementation and organisation of initiatives, and the method of measuring the reduction of antibiotic use (indicators). Effective instruments are essential if they are to have an impact on the use of antibiotics.

Many studies have indicated the difficulties involved in influencing physicians' prescribing practices. Projects that have physicians discussing their own prescribing practices in colleague-based supervisory groups have shown to be effective measures, cf. Chapter 8.

Two competence centres in Norway, one for primary health care services and one for specialist health care services, are working to promote a rational and restricted use of antibiotics. The Antibiotic Centre for Primary Care (ASP) oversees the revision of guidelines for antibiotic use in general medical practice. The Centre is working to promote a better understanding of the appropriate use of antibiotics with information directed towards prescribers and the public, as well as through research, quality assurance, competence enhancement and short courses for physicians in primary health care services. The National Competence Centre for Antibiotic Use in Specialist Health Care Services (KAS) encourages a responsible and appropriate use of antibiotics in hospitals, with support for the implementation and revision of national guidelines.

Nearly 90 per cent of all antibiotics are prescribed in primary health care services. Dentists are accountable for about 5 per cent of all antibiotic prescriptions, measured in DDD. The most recent edition of the 2013 National guidelines for antibiotic use in primary health care services, includes a new chapter about antibiotic treatment of children.

Box 13.1 Antibiotic-free prescriptions

The Norwegian Institute of Public Health has prepared several fact sheets: "When your child has a…throat infection / fever / ear infection / bronchitis", for physicians to distribute to parents of young children during consultations. These fact sheets validate the message that infections in children usually go away by themselves – without antibiotic treatment. These fact

sheets are therefore known as “antibiotic-free prescriptions”.

These antibiotic-free prescriptions contain information about the child’s condition, and explain why antibiotics would have no effect. They also inform parents of what they can do to relieve their child’s symptoms, and mention symptoms that warrant special attention.

It is essential to have objective goals and good instruments for measuring the use of antibiotics. Sweden has recently introduced a system to measure the number of antibiotic prescriptions (250 prescriptions per 1000 citizens per year). In comparison, Norway had 428 antibiotic prescriptions per 1000 citizens per year in 2014. Concrete goals for antibiotic prescriptions will be crucial in the efforts against antibiotic resistance in Norway as well. A working group has been established for the national quality indicator system (cf. Chapter 9), which will formulate various quality indicators for the use of antibiotics and healthcare-acquired infections. Four quality indicators have been planned which can provide an idea of the use of antibiotics on a municipal level. These will be published on the helsenorge.no website in 2015.

In hospitals and nursing homes, it is more common to use broad-spectrum antibiotics, in higher doses. Transferring patients between institutions can result in the spread of antibiotic resistance. There is currently an overview of antibiotic use in hospital wards, but no comprehensive overview over the use of antibiotics in nursing homes, cf. Chapter 8.

The Norwegian Prescription Database has a good overview of the use of various types of antibiotics that have been dispensed to patients by prescription. This data is distributed by age, gender and geographical location. Diagnostic information is not available in the Norwegian Prescription Database, making it difficult to assess whether current prescribing practices are consistent with guideline recommendations. By requiring diagnostic codes to be added to all antibiotic prescriptions, or by ensuring that diagnostic information is entered in the Norwegian Prescription Database, the registry would contain useful statistics for the quality assurance of antibiotic use, management and planning. Diagnostic codes would also facilitate better feedback to the prescriber, and raise greater awareness of prescription patterns for peer review discussions. Physicians would be able to use this knowledge as a basis for internal control and quality improvement.

On 17 February 2015, the Norwegian Parliament (Stortinget) adopted a resolution (no. 425), requesting that the government: “introduce requirements for diagnostic codes to be noted on all types of prescriptions for antibiotics, in a manner that maintains personal privacy”. The Ministry of Health and Care Services has commissioned the Norwegian Directorate of Health to evaluate possible solutions for the introduction of diagnostic codes on all antibiotic prescriptions, within legal and technical parameters.

13.2 Use of medicinal products for mental illness and pain

The government is making efforts to strengthen services for people with mental illness and

substance abuse problems. This is exemplified by the reintroduction of the "golden rule" that there must be more development in each of these two areas – mental health care and substance abuse treatment, than in the entire area of somatic health care. This necessitates an increase in the municipal sector's free income, to improve mental health care services, public health care and school health care, with earmarked funds in the amount of NOK 100 million for municipal substance abuse efforts in the national budget for 2015. In recent years, there has been a marked increase in research efforts in the mental health sector, including health research programmes under the Research Council of Norway and the regional health authorities.

The Report to the Storting no. 26 (2014–2015), "The Primary health and care services of tomorrow – localised and integrated" presents several initiatives that can contribute towards strengthening services for people with mental illness and substance abuse problems. The most important initiatives include mandatory psychologist positions in municipal health and care services, the introduction of mandatory payment by patients ready for discharge from mental health care services to municipal services, and interdisciplinary specialised substance abuse treatment (TSB). In addition, the municipal duty to provide 24-hour emergency services will also apply to people with mental illness and substance abuse problems. A pilot scheme for municipal operational responsibility for district psychiatric centres (DPS) will also be implemented, and there will be an escalation plan for substance abuse treatment services during 2015.

These initiatives are meant to create greater regularity and more solid professional services for people with mental health and substance abuse issues. By moving competence, follow-up and treatment closer to the areas where service users live, the threshold for receiving help will be lowered, increasing the possibility of immediate and early interventions.

The government will also include mental health care as an equal recipient of public health efforts. The Report to the Storting no. 19 (2014–2015) "Report on Public Health", describes several initiatives. The goals of these initiatives include good mental health and well-being for a greater share of the public, and the reduction of social inequality in mental health.

Several patient and service-user mental health organisations have established a joint action for medication-free mental health care services. The Ministry has followed up on this through its tasks for regional health authorities in 2015.

13.2.1 Use of psychoactive medicinal products

Medicinal products for the treatment of mental illness are called psychoactive medicines. In addition to hypnotics and sedatives, cf. Chapter 13.2.2, these primarily include medicinal products for depression (antidepressants), and antipsychotics for the treatment of psychotic disorders such as schizophrenia.

Medicinal treatment is one of several treatments for depression, and should always be used in combination with other measures such as psychotherapy, psychosocial interventions, etc. Patients who are beginning treatment with antidepressants should receive both verbal and written

information that is easy to understand. Patients must also be monitored for effect and adverse reactions.

In 2014, 314,000 individuals over the age of 18, or 7.8% of the Norwegian population, were dispensed at least one prescription for antidepressants. This proportion of antidepressant users has remained nearly constant from 2005 to 2014. The number of antidepressant users is higher among women than men.

I 2014, 2.7% of the adult population were dispensed an antipsychotic medicine at least once. There was an equal distribution of women and men in the 18 – 39 age group, but a higher proportion of women in older age groups. Gender differences increase with age, and are greater in age groups over 65. In this age group, the number of people using antipsychotic medicines was somewhat lower from 2005 to 2014, for both women and men.

The use of addictive medicinal products is more frequent among antidepressant users than in the general population. This applies to both women and men in all age groups. Patients with mental illnesses comprise a vulnerable patient group. This group experiences many problems and requires various forms of treatment. More research is needed in terms of linking the use of these medicinal products with diagnoses.

From 2005 to 2014 there was a sharp increase in the number of people using antidepressants in the 15 to 19 age group, based on figures from Norwegian Prescription Database. During this 10-year period, there was 28% increase in the number of young men using antidepressants, and an 37% increase in the number of young women. This increase was much lower in other age groups. Changes in the use of medicinal products are influenced by many different factors, and this cannot be used solely as an indicator of change in morbidity.

In 2003, both the Norwegian Medicines Agency and the European Medicines Agency warned against the increased use of antidepressants among young people. The Norwegian Institute of Public Health carried out a cohort study which indicated that this warning led to a temporary 17% reduction in the use of antidepressants among children and adolescents in the period 2004–2005.

Competent authorities are well aware of the fact that the use of antidepressants may increase the risk of adverse psychological effects among young people, and this information has previously been communicated by the Norwegian Medicines Agency, as well as through other channels. Adverse psychological effects among young people, including suicidal thoughts and behaviour, have been listed in the summaries of product characteristics and package leaflets of antidepressants sold in Norway.

The Norwegian Medicines Agency is continuously evaluating the risk-benefit ratio of medicinal product use. These evaluations are conducted on both a national and international level, based on information from all reported adverse reactions (spontaneous reports), as well as information from clinical studies. All medicinal products are intermittently reported through Periodic Safety Update Reports (PSUR) which summarise the available data on adverse reactions for a specified

period of time. Most antidepressants are evaluated in cycles of three to five years. Based on the information uncovered through these continuous risk-benefit evaluations, authorities can implement measures, such as posting new warnings or changing prescription regulations. These risk-benefit evaluations will often result in a revised summary of product characteristics and package leaflets, with updated information for health care personnel and patients.

There is still a need for more knowledge regarding the use of antidepressants among young people. There are few good, clinical longitudinal studies on the use of antidepressants, and there is significant publication bias in this area. The Norwegian Directorate of Health will evaluate the need for a revised evidence base for medicinal treatment of depression, especially for young people. By using the Norwegian Prescription Database, possibly also connecting to other sources of data, the Norwegian Institute of Public Health will conduct further studies on the use of antidepressants among young people to learn more about the users and prescribers of these medicinal products.

13.2.2 Use of addictive medicinal products

Addictive medicinal products primarily consist of hypnotics, sedatives, anxiolytics, centrally acting analgesics (opioids), central nervous system stimulants (medicinal products used in the treatment of ADHD and narcolepsy), medicinal products for the treatment of opioid dependency, and certain cough suppressants.

Psychological disorders and various pain disorders are widespread, and it is crucial to provide appropriate treatment for patients with these disorders. Many patients with these disorders are treated with different types of medicinal products, and several of the prescribed medicinal products are potentially addictive. When used responsibly, these medicines can be of great benefit, but they can also prove harmful, especially when combined with alcohol and/or illegal narcotics, and may lead to addiction. Use of addictive medicinal products may also result in adverse short-term effects such as reduced coordination, the risk of falls, reduced cognitive function, and intoxication.

Figures from the Norwegian Prescription Database indicate that around 900,000 Norwegians are dispensed at least one prescription for analgesics, anxiolytics or hypnotics/sedatives in one year. A large portion of (30 to 60%) users are dispensed such medicinal products only once in one year. Some use these medicinal products over a longer period. The proportion of the population using addictive medicinal products increases with age, with more women than men using these products.

Analgesic opioids are the addictive medicinal products used most often in Norway, and more than half a million people were dispensed opioids from pharmacies in 2013, with approximately 54,000 people receiving strong opioids.

Hypnotics and sedatives are the second most commonly used groups of medicinal products. There are two groups of hypnotics and sedatives: benzodiazepines and z-hypnotics

(benzodiazepine-related hypnotics). More than 350,000 people received z-hypnotics in 2013, while just under 30,000 were given sedatives that contained benzodiazepines. A large group of people also use medicinal products containing benzodiazepines to relieve symptoms of anxiety. Around 250,000 people were dispensed these medicinal products in 2013.

After a gradual increase in the use of opioids from 1999, the total use of opioids remained relatively stable from 2010 to 2013. There was, however, an increase in the use of strong opioids from 2005 to 2013. This may in part be due to the focus on optimal pain relief for patients with non-cancer related chronic pain. Opioid use among this group has become more accepted, which may explain the increased use.

The use of benzodiazepines as sedatives declined after the introduction of z-hypnotics in the 1990s. Use of z-hypnotics had an initial sharp increase, and these medicinal products now dominate the hypnotic and sedative market. However, this use has flattened out, with a slight decline over the past few years. Around 20% of new users of z-hypnotics are long-term users (at least 4 years). More than half of those who are long-term users have a level of consumption equivalent to almost daily use. This indicates that prescribing practices often deviate from recommended use. In situations where general practitioners become aware of long-term use, beyond recommended indications, it would be expedient to seek advice from specialist health care services. There is a need for further research to learn more about possible adverse effects of such use.

There are some major regional differences in the use of addictive medicinal products in Norway, and these differences appear to remain stable over time. There is nothing to indicate that this is due to differences in morbidity. Geographical differences most likely reflect different prescribing practices or therapeutic traditions.

The consumption of addictive medicinal products in Norway is not significantly different from consumption in the other Nordic countries. The consumption of opioids in Norway is higher than in Finland, but on the same level as the other Nordic countries. Norway has a higher consumption of benzodiazepines for the treatment of anxiety than that of Sweden and Denmark, but lower than Finland and Iceland. The consumption of hypnotics and sedatives varies between the Nordic countries. Iceland has the highest level of consumption, Denmark the lowest, while the other countries are basically on the same level.

Even short-term use of addictive medicinal products can result in adverse reactions. This may involve a greater risk of falling, reduced driving skills, short-term memory loss and emotional reactions. It is important that physicians inform their patients from the start about the benefits and risks of treatment, and that they make an agreement with patients on a specified treatment duration with these products.

In 2014, the Norwegian Directorate of Health published a protocol on the prescription and responsible use of addictive medicinal products. The goal of the protocol was to provide good professional support for health care personnel who prescribe addictive medicinal products, to

avoid dependency and to assist patients in have already developed dependencies in gradually reducing their use.

One of the important recommendations in the protocol is for prescribers to assess non-medicinal measures or treatment with other types of medicinal products before prescribing treatment with addictive medicines. These assessments must be made in agreement with the patient.

The simultaneous use of several addictive medicinal products is a problem for many patients. The new protocol recommends that prescribers only prescribe one addictive medicinal product per patient, since the simultaneous use of such medicinal products can lead to enhanced effect and adverse reactions. Furthermore, the protocol recommends that only one prescriber – the general practitioner – should be permitted to prescribe addictive medicinal products, and that there should be a plan for treatment duration and reduction from the start. It will be necessary to monitor the development of the use of combined addictive medicinal products, although this would require good registry data as a basis for research.

A revised national protocol for the use of opioids for long-term, non-cancer-related pain was published by the Norwegian Directorate of Health in October 2014. The protocol emphasises that general practitioners are responsible for this type of treatment, and that individual treatment plans must be prepared in cooperation with the patient.

As part of the implementation of the protocol, the Norwegian Directorate of Health will grant funding for a separate advisory system for general practitioners on the use of addictive medicinal products during the spring of 2015. The protocols for the use of addictive medicinal products and opioids will be applied to the Norwegian Directorate of Health's new publication tools for guidelines in 2015. The new publication tools will involve a structured content, which will facilitate decision support by showing these recommendations in electronic medical record systems.

In many ways, the prescription and use of addictive medicinal products present a threat to patient safety, and is a frequent topic in supervisory cases. The responsibility of the Norwegian Board of Health Supervisions includes general supervision and surveillance of the area, and event-based and planned supervision, including supervisory guidance. A report of concern regarding unwarranted prescriptions/prescribing practices must be submitted before supervisory authorities can establish a supervisory case. Most reports of this type are submitted by pharmacies. The pharmacy sector has stated a need for a more regulated case management of reports of concern with the County Governors offices, and the wish for the submitting party to remain anonymous. The pharmacy sector has also stated the need for more concrete guidance on how pharmacies should deal with suspicions of unwarranted prescribing practices and harmful use.

The National Protocol for prescription and use of addictive medicinal products, describes various actions that pharmacy employees may take, while also noting the uniqueness of each situation. This means that pharmacy staff must evaluate the most suitable measures for each individual situation. Pharmacy staff must therefore have the experience and knowledge necessary to

manage such situations in the best possible manner. The Norwegian Pharmacy Association's competence and resource centre, Apokus, will offer a competence enhancement course on addictive medicinal products for pharmacy employees in 2015.

Often when there is suspicion of unwarranted prescriptions of addictive medicinal products, it becomes clear that the physician has not had an adequate overview of the amount prescribed for each individual patient. Supervisory authorities therefore face the challenge of securing prescription data in a uniform and simplified manner, since this calls for a medical record function that can provide an overview of the prescribed amount. Some physicians do not have sufficient knowledge regarding the appropriate use of addictive medicinal products, particularly the long-term effects of treatment, and are not fully aware of how addiction develops. The updated protocol is expected to result in better practices among prescribing physicians.

The Norwegian Board of Health Supervision has been utilising electronic tools for the collection and compilation of prescription data in supervisory cases since 2005, but has noted that it can be difficult to gain access to essential data in physicians' record systems. The Norwegian Prescription Database contains data on physicians' prescriptions, but the use of this data is restricted from access to personal information, cf. Section 1-3, point 3 of the Regulations relating to the Norwegian Prescription Database (NorPD Regulation), which only provides access to supervisory authorities. When evaluating the use of a shared medicine list, it should be considered whether supervisory authorities may also have access to data within the area of supervisory responsibilities.

Box 13.2 Withdrawal of Somadril

Data from the Norwegian Prescription Database and other Norwegian studies indicated an increased risk of intoxication, abuse or addiction with the use of Somadril (carisoprodol). This resulted in the withdrawal of Somadril from the Norwegian and EU markets in 2008. More recent studies have shown that withdrawal of Somadril has reduced the problems associated with the use of the product. Few former Somadril-users began using other medicinal products with potentially harmful effects.

13.3 Medication-Assisted Treatment

Medication-assisted treatment (MAT) refers to medicinal treatment used in the rehabilitation of individuals who have developed opioid addictions. MAT involves the use of medicinal products (methadone or Subutex/Suboxone) which prevents abstinence symptoms. In addition to these medicinal products, the patient must be followed up by a general practitioner, municipal services, and specialist health care services if necessary.

Medication-assisted rehabilitation in its current form was first offered in 1991 as a pilot project

(HIV-MET) for 25 HIV-positive patients with opioid addictions. The purpose of methadone treatment was to stabilise patients and assist in a better utilisation of medicinal treatment for HIV. The results of HIV-MET were positive, and the pilot project was expanded to include 50 patients in 1994 (MiO). The results of the MiO project were also positive, and in 1997, Norwegian Parliament determined that MAT would become a nationwide service from 1998.

With the "Substance Treatment Reform" in 2004, the responsibility for the treatment of patients with addiction issues (including MAT) was transferred from county councils to regional health authorities. Since 2010, MAT has been regulated by regulations governing medication-assisted treatment and rehabilitation. The Norwegian Directorate of Health also prepared the National Guidelines for Medication-Assisted Rehabilitation of Opioid Addiction.

Around 10,000 patients with opioid addictions participated in the MAT programme between 1998 and 2014. By the end of 2014, more than 7430 patients were undergoing active treatment. From 2004, the regional health authorities have been responsible for dispensing costs. The 2014 status report from SERAF (Norwegian Centre for Addiction Research at University of Oslo) indicates that 52% of MAT patients were dispensed MAT medicinal products in pharmacies, 28% from municipal services, 16% from general practitioners and correctional services etc., and 4% through MAT initiatives.

The report also shows that 43% of MAT patients were treated with methadone, while 57% received buprenorphine treatment (35% with Subutex and 21% with Suboxone).

The Norwegian Directorate of Health recommends buprenorphine as the first choice of treatment. The high proportion of patients using methadone is partly due to the fact that methadone was the first medicinal product used in MAT, while buprenorphine did not become available until several years later. There is a higher risk of adverse reactions, overdose and fatalities associated with methadone than with buprenorphine.

MAT is the form of treatment for opioid addiction which has the best documented effect. The dropout rate with MAT is much lower than in non-medicinal treatment of patients with opioid addictions. The 2013 status report from SERAF (Norwegian Centre for Addiction Research at University of Oslo) indicates that two-third of the patients are either abstinent or they have achieved significant improvements in their living conditions.

For many years, Norway had one of the highest rates of overdose fatalities in Europe. In recent years, the number of overdose fatalities has declined, but there are still many deaths each year due to overdose. An increase in the number of fatalities from methadone overdose has also been registered. In 2013 there were just as many overdose fatalities from methadone as from heroin. There is reason to believe that legally prescribed methadone through MAT has been sold illegally. The Norwegian Directorate of Health has been commissioned with a five-year overdose strategy, where overdoses from methadone are an essential element. The Norwegian Directorate of Health will also revise the national guidelines for MAT, where the pick-up scheme for MAT medicinal products will be evaluated.

In January 2015, Stavanger Health Trust (Helse Stavanger) called for tenders from pharmacies for the dispensing of MAT medicinal products from pharmacies. Oslo University Hospital attempted a tender process in 2014, but received no offers from the pharmacies. Aside from this, no tender competitions for the dispensing of MAT medicinal products have taken place in any health authority region. In February 2015, the Ministry of Health and Care Services submitted a letter to the Norwegian Medicines Agency, stating that the unconditional right to the free choice of pharmacy does not apply to pharmacies dispensing MAT medicinal products on commission from specialist health care services. In such cases, the patient's choice of pharmacy would be limited to those pharmacies that have a special dispensing agreement with specialist health care services.

In 2012, the Norwegian Directorate of Health published the National treatment guidelines for pregnant women in opioid maintenance treatment, and for family follow-up until the child reached school age. These guidelines recommended that women who become pregnant while undergoing medication-assisted treatment of opioid addiction (MAT) should continue with this treatment. The guidelines also recommend that pregnant women who are addicted to opioids and are not receiving medication-assisted treatment should apply for this treatment. These recommendations build on research results indicating that foetuses and neonates do best when pregnant women are stabilised through MAT. There is a significantly higher dropout rate among patients receiving non-medicinal treatment compared with those receiving MAT. There is therefore a significant risk of an overdose occurring during relapse to active substance abuse.

In accordance with these guidelines, women who receive MAT and who become pregnant must be offered help in gradually reducing their use of these medicines if they wish to do so, although medication tapering must be conducted under safe conditions. The Ministry of Health and Care Services submitted a letter to Norwegian Parliament, stating that relevant professional environments involved in medication-assisted treatment agreed that there was inadequate knowledge of how the foetus is affected by MAT medicinal products during pregnancy.

There is also inadequate knowledge of how infants born to mothers who received MAT continue to develop during their school years. The need for more research in this area was emphasised in the letter to Parliament.

14 Veterinary medicinal products

14.1 Authorisation of veterinary medicinal products

Veterinary medicinal products for animals have the same requirements and must go through the same procedures for authorisation as medicinal products for humans. This means that the application for marketing authorisation must include documentation of the medicinal product's quality, safety and effect, and marketing authorisation can only be granted if this documentation indicates a positive risk-benefit ratio. Safety documentation must show that the medicinal

product is safe for animals being treated, for the environment, and for those who consume food from the animals being treated with the medicinal product. Most veterinary medicinal products are authorised in cooperation with the European Medicines Agency (EMA) and other medicines agencies in the EEA.

The impact of medicinal products on the environment is an important part of the authorisation assessment, and environmental effects are emphasised in the final risk-benefit assessment of the medicinal product. An application for marketing authorisation for veterinary medicinal products for herd animals must therefore include extensive environmental documentation

Norwegian medicine authorities are permitted to argue their views in this European cooperation. However, they will not always receive acceptance for these views, and therefore have a limited opportunity to influence the authorisation of antibiotic agents. Some authorised medicinal products do not have a natural place in Norwegian antibiotic therapy traditions, yet these substances may be marketed here as well.

14.2 Proposal on new EU regulations for veterinary medicinal products

On 8 September 2014, the European Commission presented a draft for new regulations regarding the authorisation and use of veterinary medicinal products. This proposal was sent to the Parliament and the Council. It is anticipated that the new regulations will be adopted in 2017, at the earliest. This proposal would carry forward the existing regulations, but it also contains important changes which are discussed below.

The purpose of the proposal is to increase the availability of veterinary medicinal products, ensure a more efficient authorisation process, stimulate competitiveness and innovation, improve the functioning of the internal market, and prevent the development of antimicrobial resistance.

Applications for antibiotics must include proposals for measures that would prevent the development of resistance. Authorities would then gather and report data on the sale and use of antibiotics. To ensure continued efficacy for humans, the European Commission would have the right to restrict or ban the use of specific antibiotics for use in animals. Measures against the development of resistance is also supported by the European Commission’s proposal for new regulations regarding medicated feed.

The market for veterinary medicinal products is limited for groups of animals that have fewer individuals. This offers less opportunity for profit, and it has therefore been proposed to extend the protection against generic competition, as an incentive to develop new medicinal products. Today, medicinal products generally have a 10-year period of marketing protection against generic competition. This protection is reserved for medicinal products for larger animal groups, such as cattle, sheep, pigs, chickens, dogs and cats. For smaller animal groups, such as fish, this protection is extended to 14 years, and the same period of protection applies to new antibiotics. Manufacturers may receive extended protection if they receive authorisation for medicinal

products for other species, with a maximum period of 18 years. The proposal also states that several medicinal products can and will be authorised through EU's centralised procedures.

Through these cooperation procedures, cf. Chapter 3.2, the CMDh would be able to make majority decisions on authorisation. The Coordination Group CMDh is comprised of representatives from the medicines agencies of EEA countries. In the event of disagreement, such cases must be handled by the EMA, and final decisions are made by the European Commission. As stated in the proposal, affected countries would not receive the application. They would receive only the reference country's evaluation and proposal for information.

It has also been proposed to permit the authorisation of medicinal products with limited documentation of safety and effect if the medicinal product is intended for a limited market. In the presented proposal, this would apply to medicinal products for animal species apart from cattle, sheep, pigs, chickens, dogs and cats. Medicinal products for farmed fish could therefore be authorised in this manner.

The Ministry's evaluation of the proposal

This proposal contains several provisions which would help to achieve the stated goals. New veterinary medicinal products are needed. It is problematic for aquaculture, animal husbandry and pet owners that so few medicinal products have marketing authorisation.

The government's fundamental position on the proposal is therefore positive. Here there is emphasis on proposed measures for preventing development of resistance, as well as incentives for developing new antibiotics and medicinal products in general. The proposal that gives the European Commission the right to restrict or ban specific antibiotics for animals could, in the long-term, prevent the development of resistance, and ensure that people receive the necessary treatment for disease.

In some countries outside the EEA, veterinarians are permitted to sell antibiotics. There must be professional justification for the prescription and use of antibiotics. If veterinarians are able to profit from sales of antibiotics, it would result a more frequent and widespread use of antibiotics. The Ministry therefore plans to present arguments to the EU in support of banning veterinarians from selling antibiotics.

The centralised procedure is an effective authorisation, which involves subjecting the application to a thorough scientific evaluation. More frequent use of a centralised procedure might therefore result in greater availability of veterinary medicinal products. This is a positive development, although increased centralisation may cause the downscaling of national medicines agencies due to few tasks and taxation. Local knowledge, which is essential in the authorisation of veterinary medicinal products, would then be lost.

In cooperation procedures, the quality of the authorisation is a sum of the reference country's evaluation and input from the other national medicines agencies. The quality of authorisation would be reduced if the affected countries are not given access to the application and rely only

on the report from the evaluating country. This would also reduce opportunities for Norwegian medicines authorities to assess the risk-benefit ratio of the medicinal product when used on animals in Norway. Norwegian medicines authorities have long been a driving force in restricting the development of resistance through their efforts to limit the approved area of use for antibiotics. Without access to the application, this work would be difficult.

The proposal for the new EU regulations allow for medicinal products for fish to be authorised with limited documentation. If this is approved, it may result in claims that fish from the Norwegian aquaculture industry are unsafe. There is a sizeable aquaculture industry in Norway and in the EU, and there should be an economic basis for demanding that manufacturers of medicinal products for salmon present full documentation of the safety and effect of these products.

When there is disagreement between the countries involved in cooperation procedures, cases should continue to be brought to the EMA and the European Commission. Here the disagreement would be discussed by the Committee for Medicinal Products for Veterinary Use (CVMP) which has expertise in the field of veterinary medicinal products. Experts from Norway also participate in this committee. A final decision by the Commission would also ensure that this decision is firmly rooted in law. If not, the CMDh must be provided with significant scientific expertise. The Danish government has stated that they view this provision as contrary to the Treaty of Lisbon.

The Norwegian government will be closely following the negotiations on new regulations on veterinary medicinal products, and Norwegian views have already been conveyed to the European Parliament, the European Commission and EU member states.

14.3 Responsible use of medicinal products

In intensive livestock production, good operating routines and optimal nutrition and feeding are important factors in the prevention of disease. The use of medicinal products must promote animal health, prevent the unnecessary development of resistance, and must not have an unnecessary negative impact on the environment.

If an infection breaks out in an aquaculture facility, the entire facility must undergo treatment. In exceptional cases, treatment of all animals may also be necessary for land animals, such as a flock of several thousand broiler chickens. Both diseased and healthy animals would then undergo treatment, and the use of medicinal products would therefore be more extensive than in treating individual animals. Preventive efforts to avoid disease and the need for treatment is even more important for large animal flocks than in cases where individual animals may be treated.

The proper use of medicinal products can be a major challenge when treating animal flocks, since it involves a higher number of animals, and the absolute number and weight of each animal is unknown. It would therefore be important to administer medicinal products with sufficient spacing between the therapeutic dose and the dose that may have an adverse effect to avoid underdosing.

Cooperation on the handling of applications for marketing authorisation may result in the authorisation of medicinal products in Norway that have no natural place in the Norwegian antibiotic therapy tradition. The same applies to many of the antiparasitic agents that are authorised for use, especially those for dogs and cats, and that have no natural place in the antiparasitic treatment of Norwegian livestock. There is also a risk of resistance for antiparasitic medicinal products. The situation in Norway is currently favourable, compared with many EU countries. It is essential to avoid unnecessary antiparasitic treatment if we are to prevent or halt the development of resistance. This is best done by only providing treatment after parasites have been detected and identified by veterinarians. If these medicinal products are authorised as non-prescription products in the EEA, Norway will no longer have the right to manage antiparasitic treatment of livestock through veterinarians. It is therefore crucial that Norwegian therapy recommendations for livestock and pets are regularly revised.

To promote the use of antibiotics and antiparasitics in accordance with Norwegian traditions and genuine medical requirements, regulations must ensure that animal health authorities and pharmaceutical authorities can present concrete and binding recommendations for the use of new medicinal products on animals. Summaries of product characteristics for such medicinal products assume that each individual country will provide recommendations based on national and local conditions.

In Norway, aqua medicine biologists, in addition to veterinarians, have the right to prescribe medicinal products for aquatic animals, apart from marine mammals. This is intended to ensure sufficient personnel with competence in diagnosing disease and the ability to responsibly prescribe medicinal products for use in fish.

The use of antibiotics in Norwegian livestock is among the lowest in Europe. From 1995 to 2013, use of antibiotics in land animals was reduced by 35%. For pets, however, there was an 18% increase during the same period. The relative consumption of narrow-spectrum penicillin in land animals increased to 50% of the total sales in the same period. This is a positive development, since narrow-spectrum antibiotics are less likely to lead to resistance than broad-spectrum antibiotics. For pets, penicillin made up 87% of the total consumption in 2013. In the aquaculture industry, the use of antibiotics has been significantly reduced due to effective vaccines against the most common serious fish diseases.

All use of prescription medicinal products used in animals must be reported to the Norwegian Food Safety Authority, through its reporting portal. This is stipulated in the regulations and provides authorities with a good overview of the use of medicinal products. The Veterinary Medicinal Product Registry, Vetreg, is the Norwegian authorities' instrument for monitoring the prescription and use of medicinal products for animals. Systems for registering and managing this data must be further developed before they can easily be utilised for the control of medicinal product use.

The Norwegian Food Safety Authority oversees the supervision of prescribing practices by animal health care personnel, to ensure responsible prescriptions of medicinal products for both

land and aquatic animals. Through this supervision, the Norwegian Food Safety Authority is able to safeguard animal welfare, animal health and food safety, and detect possible risks of resistance development associated with the use of medicinal products. The use of medicinal products in the aquaculture industry is still necessary for the prevention and treatment of disease, and to reduce the spread of infection. The use of medicinal products for farmed fish is also important for protecting wild stock. For instance, the authorities' strict requirements for low levels of salmon lice in salmon farm facilities are in place to avoid exposing wild salmon to unacceptable levels of salmon lice.

The extensive use of medicinal products against salmon lice, as well as the increasing resistance among salmon lice, is the single, biggest challenge associated with the use of medicinal products in animals in Norway. The situation cannot be solved by continuing to develop new medicinal products. It is essential to find solutions that are based on other principles, to significantly reduce the need for routine medication. As long as fish farms are located in marine facilities, it will be necessary to use medicinal products for sporadic medicinal treatment when other measures prove insufficient. The breeding of new aquatic animal species will result in new diseases that will require vaccines and curative medicinal products.

14.4 Research and development

The development of new fish vaccines was a determining factor in gaining control of cold water vibriosis and furunculosis in the late 1980s and early 1990s, and has been crucial for the growth of the Norwegian aquaculture industry. There is still a need for new vaccines against viral infections and parasitic diseases. Although there are major efforts underway to find alternatives to chemical delousing, there is still a need for new agents against salmon lice. The breeding of new aquatic animal species will result in new diseases that will require vaccines and medicinal products.

Development of diagnostic instruments that can provide quick results would mean a great deal for the correct choice of medicinal product for the disease.

14.5 Medicinal products and environmental effects / environmental impact

The Pharmacy Act states that pharmacies are required to accept the return of medicinal products for destruction at no expense for the patient. Pharmacies receive residual medicinal products, sort them and send them off for responsible destruction. Some are sent for incineration, while other medicines are treated as hazardous waste. The Norwegian Pharmacy Association conducted a study in 2010, which indicated that only 48% of a total of 474 individuals who reported the disposal of medicinal products, had handed these medicinal products in to a pharmacy. The rest were disposed of in the environment. Studies conducted in Sweden showed that 69% of those interviewed had delivered medicinal products to pharmacies, however this figure increased to

75% after an informational campaign.

Medicinal products in the environment pose a problem, especially for aquatic organisms, and eventually also for humans. Humans use approximately 3000 different medicinal products, and there are additional medicinal products used for animals. Medicinal products and metabolites of medicinal products formed in the body are eliminated via excrements and urine, and end up in the environment. Medicinal products and their decomposition products can have an impact on aquatic life. There is a lack of knowledge regarding the prevalence, characteristics and effects of medicinal products' active substances and their metabolites in the environment.

A report on the risks of environmental effects of medicinal products was submitted to the EU in December 2013, and will form the foundation for an EU strategy for medicinal products in the environment. It is anticipated that this will be adopted in September 2015. The EU also plans to present a legislative proposal at some point in 2017. This could change regulations regarding the authorisation of medicinal products, and could eventually be incorporated into the EEA agreement and Norwegian law.

The EU has placed Ethinyl estradiol (EE2) (contraceptives), Beta estradiol (E2) (contraceptives and medicines for the treatment of menopausal symptoms) and Diclofenac (anti-inflammatory agent) on its Watch List under the Water Framework Directive. This means that member states must monitor these substances in bodies of water. Environmental impact is emphasised in decisions regarding marketing authorisation for veterinary medicinal products. There are comprehensive requirements for the environmental documentation of medicinal products for herd animals. It is essential that environmental impact is monitored over time when new medicinal products for herd animals are in use.

Wastewater treatment facilities are not designed to remove medicinal products or other environmentally harmful substances from wastewater. Environmentally harmful effects caused by medicinal products, and the infrequent use of scheme for returning medicines for destruction, indicates a need for public information on how to dispose of unused medicinal products. In health care services, there is a need for clear disposal routines and correct waste disposal, and this should be included in the environmental certifications for health care institutions.

Ministry of Health and Care Services proposes a commission for the Norwegian Medicines Agency to implement an informational campaign in cooperation with the Norwegian Pharmacy Association, the Association of the Pharmaceutical Industry in Norway, and Norwegian Water, on the return of unused medicinal products to the pharmacy.

Box 14.1 To ensure good quality of medicinal product treatment the government will:

- Evaluate a shared medicine list.
- Stipulate regulations for municipalities to ensure systematic medication reviews for patients in nursing homes.
- Assess a pilot project using shared decision-making tools when choosing treatment with medicinal products, for instance, for patients with bipolar disorder.
- Assess the implementation of NOU 2014: 8 Interpreting in the public sector.
- Evaluate the way in which information about medicinal products should be formulated, so that patients understand the information intended for them.
- Evaluate the possibility of establishing a network to ensure the standardisation and development of patient-centred information.
- Assess whether start-up consultations may be an appropriate service, if the project Medicine Start shows positive results.
- Evaluate the possibility of introducing standardised advisory services, such as providing pharmacists at pharmacies with advice on patients with asthma and COPD.
- Evaluate whether the production of information can be coordinated, and how authorities can ensure, preserve and offer good sources of information to health care personnel.
- Continue to develop content and services at helsebiblioteket.no.
- Facilitate open, structured data (for instance, FEST and the Electronic Health Library).
- Assess whether academic detailing (KUPP) should be utilised as a permanent educational training method, if pilot projects show positive results.
- Consider developing and expanding the current Prescription Database in order to meet future needs.
- Evaluate the possibility of establishing a person-identifiable database for medicinal products, based on the current prescription database, supplemented with data on the use of medicinal products in institutions, when this is made available through a shared medicine list.
- Continue to use the current concept of advertisement.
- Propose that pharmaceutical industry be invited to collaborate with health care authorities on preparing patient-centred information on medicinal products.
- Assess information initiatives to increase the use of generic prescriptions.
- Assess regulatory and organisational changes that could improve the quality of multidose.
- Closely follow the negotiations on new regulations for veterinary medicinal products.
- Conduct an information campaign on the return of unused medicinal products to the pharmacy.

Part IV

Lowest possible price

15 The need for price regulation

Prices of prescription medicinal products for humans are regulated by authorities. There are a variety of circumstances that necessitate government price regulations. The National Insurance scheme reimburses a large portion of patients' medicine expenses, and there is therefore a risk that physicians will show little consideration for price when prescribing a medicinal product. Many medicinal products are also protected against competition under patent legislation and the provisions of the Norwegian Medicines Act pertaining to document and market protection.

One of the goals of medicinal product policy is to ensure the lowest possible price for medicinal products, cf. Chapter 2.2, to ensure that neither patients nor the authorities will pay an unreasonably high price for medicinal products. This goal must be weighed against adequate access to the products. If prices are too low, the industry may decide against marketing their products in Norway, and pharmacies would not have the necessary conditions for performing their tasks.

Non-prescription medicinal products and medicinal products for animals are not price-regulated.

16 Current price regulations

16.1 Maximum price system

The Norwegian Medicines Agency determines a maximum price (pharmacy purchase price = PPP) for all prescription medicinal products with marketing authorisation. This price is determined as the mean of the three lowest market prices of the medicinal products in the following reference countries: Sweden, Denmark, Finland, Great Britain, Ireland, Germany, Austria, Belgium and the Netherlands.

The Norwegian Medicines Agency regularly reevaluates these prices so that Norwegian prices reflect currency fluctuations and changes in European prices. Generic medicinal products with the highest turnover are re-evaluatedd annually. In 2015, there were 246 reevaluations of generic medicinal products.

The Norwegian Medicines Agency has drawn up guidelines for price-setting in Norway. These guidelines allow for deviations from the general rule of maximum price as a mean of the three lowest prices among the reference countries. Deviations from the guidelines are acceptable if there is a significant chance that the estimated maximum price will lead to the medicinal product's removal from the market, and if the absence of this medicinal product would have

negative consequences for access to beneficial, cost-effective medicinal products. Should these conditions apply, the Norwegian Medicines Agency will consider a higher maximum price, while also considering documented production costs and any special conditions associated with the foundation for the price estimate. This may either be done when determining the price of a new medicinal product, or when reevaluating the price.

16.2 Reimbursement price and reimbursement contract

Reimbursement prices must be determined for medicinal products that have been preapproved for reimbursement. Currently, this price is equal to the maximum price. Occasionally the industry will accept a reimbursement price that is lower than the usual maximum price. Today's practice and regulations restrict the latitude of the industry, partly because reimbursement prices are made public and are therefore subject to international reference pricing.

In accordance with Section 6 of the Norwegian Medicines Act, the government and the applicant may enter a reimbursement contract which specifies that the applicant will provide a full or partial reimbursement of National Insurance scheme expenses, if the medicinal product is prescribed to more patients than anticipated when reimbursement is decided.

In 2004, the Norwegian Medicines Agency signed a reimbursement contract for the diabetes medicines Actos and Avandia. These could only be prescribed directly by physicians as reimbursed medicinal products for combination therapy, and only to patients who had not obtained sufficient control of their disease through established treatment.

In this case, the Medicines Agency determined that there was a considerable risk that prescriptions would not meet the criteria for reimbursement. The contract required the companies to provide information concerning the reimbursement criteria for prescribing Actos and Avandia as reimbursed medicinal products. If reimbursement prescriptions did not comply with these conditions, the companies would be required to repay a portion of the additional costs to the authorities.

Prescriptions that did not comply with the reimbursement conditions were followed up by annual claims for repayment. The contract formulation made it difficult to determine the scope of prescription errors, and estimations had to be based on an extensive set of data from the Norwegian Prescription Database. Enforcement was therefore a challenge. Future reimbursement contracts must be formulated with simpler criteria for repayment. For instance, repayment rules could be linked to sales volume.

16.3 Pharmacy markup

The pharmacy's maximum retail price is based on maximum purchase price by the pharmacy, added to the pharmacy's maximum markup and VAT. The pharmacy's maximum markup is currently NOK 25 per package plus a supplement charge of 7 per cent of the pharmacy's

purchase price, up to NOK 200, and 3 per cent of the pharmacy's purchase price over NOK 200. For class A and class B medicines, there is an added markup of NOK 10 per package. The pharmacy must pay a medicinal product turnover fee, so markup is actually somewhat lower. The fee is 0.55% of the maximum retail price.

Table 16.1 Price and markup for medicinal product with a retail price of NOK 400

Mean of the three lowest prices in the reference group (pharmacy purchase price)	NOK 278.64
Pharmacy markup: 25.00+(200x0.07) +(78.64x0.03)	NOK 41.36
VAT (320x0,25)	NOK 80.00
Pharmacy retail price	NOK 400.00

16.4 Profit-sharing model

If pharmacies obtain a lower purchase price than the set maximum purchase price, cf. Chapter 16.1, they may retain half of the discount price. This profit is an addition to the basic maximum markup. Pharmacies may retain NOK 0.50 of each NOK 1 they receive as a discount, while the other 0.50 goes to the patient or National Insurance scheme, in the form of a lower retail price. The purpose of the profit-sharing model was to give the pharmacies an economic incentive for negotiating lower purchase prices, thus simultaneously ensuring a lower retail price.

16.5 Step pricing ("trinnpris")

When a medicinal product has generic competition, and the Norwegian Medicines Agency decides that the medicinal product can be substituted with the generic product in the pharmacy, cf. Chapter 3.2.2 and 11.1, a step price ("trinnpris") is generally determined. This step price is based on the medicinal product's maximum pharmacy purchase price (PPP). This is reduced by a specific percentage rate. These rates depend on the turnover from the medicinal product, and reductions or cuts are made in two or three steps. This is illustrated in Table 16.2.

Table 16.2 Step pricing cuts

Turnover prior to generic competition	1st step price cut (immediately)	2nd step price cut (after six months)	3rd step price cut (no earlier than 18 months)	
Under NOK 100 million	35 %	59 %	Turnover > NOK 15 million	69 %
Over NOK 100 million	35 %	81 %	Turnover > NOK 30 million	88 %

			Turnover > NOK 100 million	90 %
atorvastatin	94 %			
simvastatin	96 %			

This table illustrates how the price is reduced step by step, depending on the turnover from the medicinal product. The pharmacy's retail price (step price) becomes apparent when the pharmacy's markup and VAT is added.

Pharmacies dispense at least one medicinal product at a retail price that is equal to the step price in each substitution group.

Figure 16.1 illustrates step pricing for two medicinal products, both of which had a maximum pharmacy retail price (PRP) of NOK 165 prior to generic competition. One medicinal product had a turnover of less than NOK 100 million prior to generic competition, while the other had a turnover of more than NOK 100 million.

[:figur:figX-X.jpg]

Figure 16.1 Step pricing with different reduction rates

When the step pricing model was introduced in 2005, it applied to 20 generic medicinal products. Step prices have been set for more than 100 generic medicinal products in 2015. This model is based on negotiations between pharmacy chains and the various suppliers, and pharmacies can obtain low purchase prices by making the medicinal product the pharmacy chain's "step price product", thereby securing a high sales volume. Today's step pricing system offers the pharmacy and the wholesaler a higher markup through the sale of substitutable medicinal products, than the markup from sales of other prescription medicinal products. However, substitutions involve more work for the pharmacy, since patients will require for additional advice and information.

Biosimilar medicinal products, cf. Chapter 3.2.1 and 11.2, are currently not available for substitution in pharmacies, and these medicines are not regulated by the step pricing model. This means that the price is based on the maximum price system. Biological and biosimilar medicinal products are primarily financed by the hospitals. Through established hospital cooperation on the purchase of medicinal products, it is possible to obtain discounts on biosimilar medicinal products. Information on price determination for hospital medicinal products can be found in Chapter 16.7.

16.6 Non-prescription medicinal products

There is no regulation of non-prescription medicinal product prices. One of the goals of the scheme for medicinal products sold outside pharmacies, cf. Chapter 18.2.7, was to facilitate competitive pricing on non-prescription medicinal products. To determine whether this goal was achieved, the Norwegian Medicines Agency carried out a survey on the prices of non-

prescription medicinal products sold at various points of sale. The most recent survey was conducted in 2010. The Norwegian Medicines Agency found significant differences in prices between the different outlets (pharmacies, supermarkets, kiosks and petrol stations). Supermarkets had the lowest prices on the most common product brands. Petrol stations and kiosks had the highest prices. Pharmacies generally offered similar alternatives to the brand products. Pharmacy prices for generic products were basically the same as the prices for known brand products in supermarkets.

Revisions to the Pharmacy Act have permitted pharmacies to offer online shopping and delivery of non-prescription medicinal products. Pharmacies are now also permitted to advertise medicinal product prices. These revisions were effective from 1 January 2010, and are intended to facilitate competitive pricing for this segment.

16.7 Price regulation for hospital medicinal products

A Medicinal Product Procurement Cooperation has been established for medicinal products that are financed by the regional health authorities. The purpose of this cooperation is to lay the foundation for contracts regarding the purchase and supply of medicinal products and other pharmacy products on commission from the health authority, which would reduce the costs of these products. The Medicinal Product Procurement Cooperation obtains offers on medicinal products used by the health authorities. It also calls for tenders and negotiates agreements on behalf of the health authorities, in accordance with the Public Procurement Act. An agreement is signed by the individual health authority, which is legally accountable for its own contracts. The medicinal products are then sold to hospitals via wholesalers and pharmacies.

The Medicinal Product Procurement Cooperation has established its own council that offers advice on competitive tendering, while it also evaluates offers and answers questions about financial issues and medicinal product consumption.

The council is comprised of individuals with backgrounds in medicine, pharmacy and procurement. The Medicinal Product Procurement Cooperation has also established specialist groups for specific medicinal product areas, such as TNF-inhibitors, MS medications, and a few cancer medicines.

Each health authority has a Medicinal Product Committee, which works to contribute towards a rational, safe and cost-effective use of medicinal products. These committees are involved in the development of therapeutic guidelines, choice of purchase agreements for medicinal products, the establishment of medicine lists, etc.

The health authorities define the criteria for procurement. The primary criteria for basic medicinal products are currently the following:

- Price
- User-friendliness, packaging and product range

- Reliable delivery
- Service

The sole criterion for medicinal products in the H-prescription scheme is price, since the products are considered to be equal in terms of regular use.

Each individual health authority is party to a framework contract, which is binding for both the supplier and the purchaser. Identical agreements are made with regional health authorities for medicinal products that belong to the H-prescription group, including TNF and MS medicines,

Medicinal products other than contract products may be used if there are medical reasons for doing so. These contracts shall not preclude clinical trials or research on medicinal products.

In 2014, hospitals achieved a price reduction of just over NOK 1.5 billion for medicinal products, in comparison to the maximum price. Medicinal Product Procurement Cooperation prices are not accessible until the agreement has been made, and these are “national” in the sense that they cannot be used to compare prices with those of other countries. The maximum price is the basis for reference pricing with other countries. There can be no parallel exportation of medicinal products at the price agreed with the Medicinal Product Procurement Cooperation.

Medicinal Product Procurement Cooperation activities are financed by an annual fee which is paid by the regional health authorities. See Chapter 19.3.4 for further details on the establishment of a cooperative authority for procurement coordination.

17 The need for changes in the pricing systems

17.1 Reimbursement contracts and discounts

The maximum price scheme functions well with respect to medicinal products financed by the National Insurance scheme (reimbursed medicinal products), paid by the patients themselves (standard medicinal products), and as a basis for price agreements between the industry and the health authorities/municipalities (medicinal products used in institutions and H-prescription medicines). It is essential to have a pricing system that applies to all medicinal products, and the current maximum price scheme is reliable and relatively simple in its administration.

Nevertheless, problems may arise with respect to expensive medicinal products for therapeutic areas where there is no comparable treatment. This is treatment which is often financed by hospitals in reference countries. The listing price of these medicinal products, which forms the basis for the determination of maximum prices in Norway, is probably not the actual price paid in the reference countries. In Norway, the possibility of obtaining discounts should therefore be managed through tenders and price negotiations, or through reimbursement contracts.

There is a need to increase the possibilities for negotiating discounts on medicinal products that are financed by the National Insurance scheme. Experience has shown that the pharmaceutical industry would not be willing to reduce the maximum price. In many cases these companies are

willing to make agreements on discounts, but usually only on the condition that these discounts do not result in reduced maximum prices or listing prices. This is partly to prevent parallel export, and partly to prevent low prices in Norway from being exported to other countries through reference pricing systems. Parallel export is the exportation of medicinal products which is organised by independent actors, and not by the company holding the marketing authorisation for the medicinal product.

If the industry provides discount rates that increase with higher sales, this would conflict with the provisions of Section 6 of the Norwegian Medicines Act, which states that it is not permitted to offer discounts that have not been determined at the time of the sale of the medicinal product.

The statement "discounts that are determined at the time of the sale of the medicinal product" means discounts that can be tied to each individual item number and its volume in the order. Discounts that are calculated after the sale of the medicinal product has been completed are known as rebates, and are not permitted.

The background for this restriction was the price index system, which was used to reduce the price of certain generic substitution medicines from 2003 to 2005. The price index (maximum retail price) for a medicinal product was determined by reported net purchase price from the wholesaler. For this system to work as intended, it was necessary to ban rebates. This ban was formulated in a general manner, so that it also applied to medicinal products that were not covered by the price index system. When the price index system was discontinued, the ban on rebates continued.

The Norwegian Medicines Agency's handling of reimbursement cases is regulated by Section 14 of the Norwegian Medicinal Products Regulations. The Norwegian Medicines Agency assesses whether the four criteria have been met (serious disease, long-term treatment, effect, cost-effectiveness). Reimbursement contracts between authorities and the pharmaceutical industry can be instrumental in ensuring cost-effective treatment in cases other than those described in Chapter 16.2. The government will evaluate potential revisions in the regulations that may facilitate this, including lifting the ban on rebates.

In the autumn of 2014, a report was presented on future Nordic cooperation on medicinal products. Nordic cooperation on negotiations and the purchase of medicinal products would lend these countries negotiating power which would be difficult to achieve independently. However, experience from previous exploratory discussions between the Nordic countries demonstrates the complications of a binding cooperation, partly because health care services are organised and financed differently from country to country. No decisions were made on pursuing this matter at the Ministerial Council meeting in the autumn of 2014. The Ministry of Health and Care Services will evaluate the possibility of following up the proposal from the report on future Nordic cooperation on medicinal products

17.2 Review of pharmacy markup and the step pricing system

Several price surveys have shown that Norway has relatively low prices on medicinal products that are not subject to generic competition, compared with the rest of Western Europe. For medicinal products with generic competition, several of the surveys show that prices in Sweden and Denmark are lower than prices in Norway. Sweden and Denmark have a type of tender process whereby medicinal product suppliers report to authorities on the price they are willing to offer. The least expensive medicinal product is the product that will be reimbursed by the authorities in pharmacies during the following period. These periods have a duration of one month in Sweden and two weeks in Denmark. Price differences between the two countries is most likely due to the fact that pharmacy chains (pharmacies and wholesalers) make a high profit from sales of these medicinal products in Norway. There is no evidence that the purchase prices from the industry are significantly higher in Norway than in Sweden or Denmark.

Step prices have been substantially reduced over the last few years. Although there are no updated price surveys, the prices of substitutable medicinal products are most likely higher in Norway than in Sweden or Denmark. It is appropriate for pharmacy chains to make a higher profit from the sale of substitutable medicinal products, since this offers an incentive to promote substitutions in the pharmacies, and pharmacies receive compensation for the extra work involved in providing information and advice to the patients.

The Norwegian Association of Pharmaceutical Manufacturers (NIGeL) are interested in abolishing the step pricing system and prefer to replace it with a tender model, similar to the Swedish or Danish model. NIGeL has presented its arguments to the Ministry, pointing out that today's system gives pharmacy chains incentives to enter agreements with the original industry, which results in lower sales for generic manufacturers. Generic manufacturers also have financial risks associated with failed deliveries. These conditions, in NIGeL's view, make the Norwegian market less attractive for generic manufacturers. NIGeL claims that the introduction of a tender model would likely lead to increased competition and lower retail prices.

In the step pricing model, there is no direct connection between wholesalers' purchase price and pharmacy retail price. This makes it unclear whether the pharmacy chain markup is reasonable, and may result in an unreasonably high price for certain medicinal products. One benefit of the step pricing model is that pharmacy chains are more likely to enter long-term agreements with suppliers, and patients who are regular pharmacy customers would not need to switch medicines in frequent intervals. This may be difficult to achieve with a tender model. Furthermore, a step pricing model is easier to administrate, with low administration expenses.

The level of pharmacy markups for the sale of medicinal products has remained virtually unchanged for many years. Pharmacy sales of items other than prescription medicines represent an increasingly higher portion of pharmacy earnings. Over the last several years there has also been a significant increase in the number of pharmacies. This indicates that there are other factors that are important for the establishment of pharmacies than simply profit from the sale of prescription medicines, cf. Chapter 18.2.5.

The Norwegian Pharmacy Association is interested in a reliable markup system which covers the actual costs of prescription dispensing in the pharmacy. The Pharmacy Association would also like to see a shift towards a higher markup in NOK and less in percentage. The Pharmacy Association wishes to continue utilisation of the step pricing system, and believes that increased pharmacy markups can partially finance step price cuts.

Box 17.1 Central elements in the review of price and markup systems:

- Evaluation of the step pricing system
  - Is generic competition being sufficiently utilised with respect to the lowest possible prices in the most efficient manner with this pricing model?
  - Does this pricing model contribute towards reducing the risk of incorrect use due to substitution?
  - Assessment of alternative models
- Pharmacy markups
  - Evaluation of the total framework conditions for pharmacies
  - The relationship between markups for substitutable and non-substitutable medicinal products
  - Changes in markups that better reflect pharmacy costs (transition from markup percentage to markup in NOK), including consequences for hospital pharmacies
  - Evaluate the profit-sharing model

Restructuring pharmacy markups by NOK and not by percentage would provide more structure for the markups, which would better reflect the actual costs for the pharmacies in terms of the dispensing and sale of medicinal products. If markups are reduced for the most expensive medicinal products, this would have an impact on hospital pharmacies that sell a relatively high share of expensive medicinal products.

Several changes have been made over the last few years, especially in the step pricing system. Major restructuring was conducted, effective from 1 January 2014. Here the markup in NOK for the pharmacy markup was raised, and step prices were reduced. Further reductions in step prices were effective from 1 January 2015.

The Norwegian Medicines Agency has proposed to abolish the profit-sharing model, cf. Chapter 16.4, so that pharmacies are free to determine whether a possible discount on the maximum purchase price will affect retail prices. The opportunity to negotiate down the purchase price primarily applies to substitutable medicinal products. By introducing the step pricing model, cf. Chapter 16.5, the purpose of the profit-sharing model would be ensured to a major extent. However, the profit-sharing model is of little practical significance for today's pharmacy structure. Most pharmacies are integrated with a wholesaler, and pharmacy chains can take out

their entire profit at the wholesale level if they do not wish to reduce the pharmacy retail price. Whatever significance the profit-sharing model has, it applies only to those pharmacies that are independent from the major pharmacy chains.

Ministry of Health and Care Services will conduct a review and evaluation of the step pricing system and pharmacy markups in 2016.

Box 17.2 To obtain the lowest possible price for medicinal products, the government will:

- Evaluate changes in the regulations, including removal of the restrictions on rebates, which are necessary for facilitating price discounts for medicinal products financed by the National Insurance scheme.
- Conduct a review and evaluation of the step pricing system and pharmacy markups in 2016.

Part V

Equal and fast access to effective medicinal products

18 Secure access to medicinal products

The objective of equal and fast access to effective medicinal products, cf. Chapter 2.3, can be divided into two categories. Firstly, these medicinal products must be available on the Norwegian market for distribution among patients all over the country. This will be discussed in Chapter 18. Secondly, there must be a financial system that secures equal access to effective medicinal products regardless of patients' ability to pay. This will be discussed in Chapter 19. The goal of fast access is partly ensured through Norway's participation in the European cooperation on medicinal products. This ensures that medicinal products receive marketing authorisation in Norway through the same authorisation procedures as those in the rest of the EEA. Furthermore, it is important that the handling of reimbursement and new health technology in specialist health care services do not result in unnecessary delays in patients' access to medicinal products.

Access to medicinal products is ensured by the supply chain. This consists of manufacturers / suppliers, wholesalers and pharmacies, as well as other points of sale, (see Chapter 4). The authorities cannot force the industry to market its medicinal products in Norway. Norway is a relatively small market, and there are substantial costs involved in marketing medicinal products. Chapter 18.1 discusses medicinal products with marketing authorisation in Norway, and the access to medicinal products that do not have marketing authorisation. Chapter 18.2 discusses pharmacies and other points of sale. Initiatives for easier access to medicinal products are discussed in Chapter 18.3. Secure supply and delivery in cases where the ordinary supply chain may fail, is discussed in Chapter 18.4. Falsified medicinal products represent a threat to public health. This is discussed in Chapter 18.5.

18.1 Access to medicinal products in Norway

18.1.1 Medicinal products with marketing authorisation in Norway

Authorised medicinal products contain altogether more than 1500 active substances. Another 57 active substances were registered in 2014, while 27 were withdrawn. All the new active substances were given marketing authorisation through the centralised procedure. There were 2276 different medicinal product brands in Norway by the end of 2014.

The number of medicinal products on the market in Norway increases each year. Active substances and medicinal product brands are divided among approximately 15,000 marketing authorisations. This is because different strengths, medicinal product packaging, and package sizes each require a marketing authorisation.

Not all medicinal products that are authorised through centralised procedures and cooperative procedures end up on the Norwegian market. This may be because the medicinal products are not intended for use in Norway, or because the market is so small that the manufacturer cannot market the product here. However, access to the medicinal products used in Norway is still considered to be satisfactory.

18.1.2 Compassionate use on a named patient basis ("spesielt godkjenningsfritak")

Medicinal products must have been granted marketing authorisation before they can be placed on the market. Health care personnel are generally only permitted to prescribe medicinal products that have marketing authorisation in Norway. This ensures:

- that authorities have determined that the medicinal products have a positive risk-benefit ratio when used as described in the approved summary of product characteristics.
- equal competitive conditions for the industry, by not placing non-authorised medicinal products in competition with authorised medicinal products.
- that the prescribed medicinal products are price-regulated (this does not apply to medicinal products without marketing authorisation).

Patients may not always be able to use medicinal products that have marketing authorisation. This may be the case if there are no authorised medicinal products in Norway that are effective against the disease or condition being treated, or if the patient cannot use the authorised medicinal products for some other reason.

Compassionate use named patient basis enables the use of medicinal products that do not have marketing authorisation in Norway. The scheme is based on rules of exemption in the Medicinal Products Directive.

Medicinal products without marketing authorisation can only be used when medicinal products with marketing authorisation cannot meet the patient's need for medical care. The prescriber must therefore apply for an exemption and submit medical justification for refraining from using the marketed product.

Medicinal products that have marketing authorisation in the EEA area, the United States, or countries where requirements are on the same level as those in Norway, are available through a so-called notification system. The same applies to biological medicinal products on a separate list determined by Norwegian Medicines Agency. For other medicinal products, a physician must

apply for exemption from authorisation before the medicine can be dispensed to the patient. It is possible to apply for exemption online, through the e-prescription system.

The Norwegian Medicines Agency has recently reviewed medicinal products dispensed by compassionate use named patient basis, and the medical need associated with their use:

The use of these prescribed medicinal products for meeting medical needs has been well-founded in most cases.

- Some of these medicinal products are prescribed when authorised medicinal products cannot be supplied due to shortage.
- Exemptions have also been made for substances considered to be medicinal products, but that do not have marketing authorisation as products.

Based on this review, the Ministry has determined that the use of compassionate use on a named patient basis in Norway is consistent with overarching principles, which state that this system should only be utilised when there is a compelling medical need, and when medicinal products with marketing authorisation cannot be used. Initiatives in this area are therefore seen as unnecessary.

18.1.3 Compassionate Use

In some cases, a pharmaceutical company may offer and finance the use of an unauthorised medicinal product for a certain group of patients (compassionate use). This must be approved by the Norwegian Medicines Agency prior to treatment. There are, however, certain conditions. The medicinal product can only be offered to patients with chronic, life-threatening or severely disabling diseases, who cannot participate in clinical trials, and who will not benefit from treatment with medicinal products that have marketing authorisation. Furthermore, sufficient documentation of the safety and efficacy of the medicinal product is required, and the manufacturer must submit an application for marketing authorisation and/or have ongoing clinical trials for the medicinal product. Since 2010, the Norwegian Medicines Agency has received 13 applications for Compassionate Use. The Ministry of Health and Care Services wish to raise greater awareness of this system among patients and health care personnel, possibly through the helseNorge.no portal.

18.2 Pharmacies and other points of sale

Pharmacies must ensure responsible dispensing of medicinal products to the end-users. This is stated in the provisions of the Pharmacy Act. Furthermore, pharmacies must facilitate the correct use of medicinal products in the population, as well as adequate access to medicinal products and pharmaceutical services in all parts of the country. The pharmacy is an important channel of

channel of information for patients regarding the correct use of medicinal products, regulation for reimbursement, co-payments, generic substitution, and it can also refer patients to physicians or other health care personnel. Dispensing medicinal products enables the pharmacy to evaluate a prescription, pick up on any errors, and ensure that the medicinal product is dispensed in accordance with the physician's instructions. The pharmacy's role in ensuring high quality medicinal treatment is discussed in further detail in Chapter 7.1.4.

18.2.1 The organisation of pharmacies in Norway

Prior to the Pharmacy Act of 2001, all pharmacies, apart from public hospital pharmacies, were privately owned, and organised as sole proprietorship companies. Since 2001, there has been an extensive establishment of pharmacy chains with wholesalers. Three major chains dominate the market today.

In January 2015, there were18 independent pharmacies in Norway which had no ties to the three pharmacy chains. The Pharmacy Act stipulates that licensing is required for both pharmacy ownership (pharmacy licensing) and pharmacy operations (operating license). Permission to operate a pharmacy requires at least a master's degree in Pharmacy (authorised "provisorfamasøyt"). A branch pharmacy is a pharmacy that is subject to the same operating licence as a main pharmacy. A branch pharmacy can be managed by an assisting "reseptar" pharmacist who has a bachelor's degree in pharmacy. As of 3 December 2014, there were 71 branch pharmacies in Norway.

A hospital pharmacy is a pharmacy located in a hospital. Its primary task is to supply the hospital with medicinal products. Most hospital pharmacies are owned by the regional health authorities. Two hospital pharmacies are owned by non-profit foundations.

Table 18.1 Overview of pharmacies

Year As per 1 January	Boots Norway AS, wholly owned	Apotek 1, wholly owned	Vitusapotek, wholly owned	Hospital pharmacy	Independent pharmacy and partly owned pharmacy chain	Total
2001	-	-	-	28	369	397
2002	66	77	91	28	199	461
2003	89	130	100	30	153	502
2004	109	155	106	30	120	520
2005	114	168	113	30	110	535
2006	120	180	120	31	103	554

2007	127	185	132	31	98	573
2008	137	202	149	33	92	613
2009	138	215	163	33	87	636
2010	144	226	168	33	91	662
2011	146	236	172	33	95	682
2012	147	243	179	32	106	707
2013	147	252	190	32	117	738
2014	150	263	195	32	127	767
2015	151	282	210	32	125	800

The Norwegian Pharmacy Association

Box 18.1 Pharmacy licenses

Section 2-3 of the Pharmacy Act states that manufacturers of medicinal products and persons with the right to prescribe medicinal products cannot be granted a pharmacy license. This rule of ownership is intended to prevent an inappropriate influence on pharmacy sales of medicinal products. In the current situation, where most pharmacies are owned by major international actors, it may be difficult to manage these regulations. The Norwegian Medicines Agency believes that this rule is unnecessary for achieving policy goals regarding medicinal products and competition. The Ministry will consider a proposal for amendments to the Pharmacy Act. It is important to maintain consumers' trust in the pharmacy industry as an objective and independent specialist trade service for medicinal products, and that pharmacies continue to ensure the availability of all medicinal products and pharmaceutical services.

Medicinal product points of sale

Districts without pharmacies can establish points of sale for medicinal products ("medisinutsalg"). A medicinal product point of sale is a separate delivery point for a local pharmacy. A medicinal product point of sale is often located in a supermarket. Many medicinal product points of sale have an agreement with a pharmacy which delivers packages of patients' prescription medicines to the outlet, once the prescription has been expedited from the pharmacy. There are currently close to 1000 medicinal product points of sale in Norway.

18.2.2 Pharmacy supervision

The Norwegian Medicines Agency oversees the supervision of pharmacy operations, while the Norwegian Board of Health Supervision oversees the supervision of health care personnel, as stipulated in the Health Care Personnel Act. These two agencies cooperate on pharmacy supervision.

Supervision by the Norwegian Medicines Agency is aimed at uncovering illegal marketing, manufacturing and sales, and it provides authorities with important knowledge for the administration and further development of regulations in this area.

The Norwegian Medicines Agency inspects approximately 40 pharmacies each year. These inspections have focused on certain types of pharmacies. Some inspections have also been initiated after concerned reports from members of the public, county medical officers, pharmacy staff, etc.

After an inspection has been carried out, most pharmacies implement measures to correct identified deviations. These inspections are not concluded until the pharmacy in question has submitted documentation to the Norwegian Medicines Agency to indicate that all deviations have been followed up. Should a pharmacy neglect to follow up identified deviations, the Norwegian Medicines Agency may impose sanctions.

18.2.3 Medicinal products manufactured in pharmacies

There is also a need for medicinal products that cannot be obtained through the pharmaceutical industry. This applies to medicinal products that are not manufactured by the industry due to low demand (e.g. replaced by more modern medicinal products), medicinal products in different dosage strengths or in a different form that that which is manufactured by the industry (e.g. dosage strength for children), or the market may have a temporary shortage of important medicinal products (e.g. morphine injections in 2014). The pharmacy's obligation to supply products is not limited to those that are obtained from the industry/wholesaler. If feasible, the pharmacy has a responsibility, in these cases, to manufacture such medicinal products, or to have other pharmacies manufacture the products for them. These medicinal products are commonly known as "pharmacy-produced" medicines, although most of the manufacturing process is conducted by companies that specialise in the production of medicinal products on commission from pharmacies. There is no government authorisation of these medicinal products. There are, however, demands for quality, while safety and efficacy must be assessed by the prescriber, possibly in cooperation with the pharmacy.

Pharmacy-produced medicinal products currently make up just 1% of all medicinal product sales in Norway. Earlier, all pharmacies were permitted to produce medicinal products, but in the 1960s, pharmacy production was "industrialised" whereby the industry centralised the production of the most commonly used medicinal products. The Norwegian Association of Pharmacies (NAF) overtook responsibility for these medicinal products. These products are therefore now known as NAF-products, and are produced through a service production system. There are currently 110 different medicinal products manufactured through this system. In addition to NAF-products, there is also a demand for several hundred other pharmacy-produced medicinal products. Most pharmacies ensure their obligation to supply these medicinal products through an agreement with a pharmacy that has production facilities, while some pharmacies, such as hospital pharmacies, generally produce these medicines themselves. There is no

overview of the number of pharmacy-produced medicinal products, however a rough estimate suggests just over 1 million packages per year, whereby most are NAF-products.

Authorities want to be certain that prescribers and pharmacy personnel understand the difference between industrially-produced and pharmacy-produced medicinal products, and that pharmacy-produced medicinal products do not compete with approved medicinal products (medicinal products which have marketing authorisation). For instance, it is not permitted to advertise pharmacy-produced medicinal products.

It may be difficult for both prescribers and pharmacy personnel to understand the principal importance of this distinction when pharmacy production is centralised, and when pharmacy-product products are given an item number and can be purchased through a wholesaler.

The Norwegian Medicines Agency is now evaluating the need to restrict its practice in order to clarify the distinction between industrially-produced and pharmacy-produced medicinal products. At the same time, it is acknowledged that pharmacy production is entirely necessary for safeguarding medical needs, and some of these medicines are also on the authorities' emergency preparedness list. The Norwegian Medicines Agency is also considering whether these medicinal products should be given some form of government approval.

18.2.4 Pharmacy availability

Pharmacies ensure that the population has access to medicinal products throughout the country. Pharmacies are required to carry all medicinal products that are permitted for sale in Norway, and provide storage for medicinal products that are regularly prescribed. The pharmacies' obligation to supply means that they must, if necessary, also product the medicinal products that are not available from the pharmaceutical industry.

During its handling of the Report to the Storting, no. 18 (2004–2005) "On course towards more correct use of medicine", the Norwegian Parliament determined that the supply of medicinal products was functioning adequately. As of 1 January 2005, there were 535 pharmacies in Norway. Ten years later, this figure rose to 800, cf. Table 18.1 in Chapter 18.2.1. Many new pharmacies have been established in central areas, but pharmacy availability has also improved in the outlying districts. The Ministry of Health and Care Services therefore sees little reason to implement new initiatives to stimulate the establishment of additional pharmacies.

18.2.5 Pharmacy economy

In 2014, pharmacies had a total turnover of more than NOK 28.2 billion, including VAT, which is an increase of 9% compared with 2013. During the previous years, this rate of growth was significantly lower. The high rate of growth during 2014 may, to a large extent, be a result of increased sales of prescription medicinal products. This is largely due to the weak Norwegian Krone which led to higher maximum prices, cf. Chapter 16.1.

The average turnover per pharmacy was approximately NOK 36 million. The medicinal product

share of the total turnover declined after 2004. In 2014, medicinal products comprised 75.8% of pharmacies' total turnover, compared with 83.5% in 2004.

If hospital pharmacies are taken out of the equation, the average turnover per pharmacy was NOK 29.5 million, and the medicinal product share of the turnover was 72.2% (62.2% for prescription medicinal products and 9.9% for non-prescription medicinal products). Pharmacies have a significantly lower sales margin for prescription medicinal products than for other items. In 2014, the sale of prescription medicinal products constituted 41.2% of the total gross earnings for primary pharmacies, while non-prescription medicinal products and other pharmacy items made up 18.8%, and 40.0% respectively. Pharmacies' markup on sales of medicinal products is discussed in Chapter 16.3.

The Norwegian Medicines Agency obtains annual account figures from every pharmacy in the country. In 2013, operating results made up 3.3% of operating income, as opposed to 6.2% in 2012 and 3.4% in 2011. 30% of primary pharmacies had negative operating results in 2013, as opposed to 16% in 2012 and 25% in 2011. Pharmacies in central districts are overrepresented among pharmacies that had negative operating results. Pharmacies owned by a pharmacy chain post a share of the chain's total overhead costs in their accounts. Based on the Norwegian Medicines Agency's pharmacy statistics, cost principles for goods have changed for a few of the pharmacy chains over the past several years. This has had an impact on results, although it is not possible to assess whether the actual financial basis for the pharmacies has changed. To get a complete picture of the industry's financial status, the financial results for the associated companies (holding companies, chains and wholesalers) must be included. Key figures indicate a stable economic growth over the past few years.

Table 18.1 indicates a significant increase in the number of pharmacies over time. Since 2005, there has been a yearly net growth of 20 to 40 pharmacies. However, there has been relatively modest growth in pharmacy turnover during the same period, and the medicinal product share of the turnover has declined. When measured by defined daily dose, pharmacy sales of medicinal products have increased by an average of 2% since 2010. The number of packages sold by pharmacies has remained constant. Increased demand for pharmacy services cannot, therefore, explain this significant growth.

18.2.6 Shipping medicinal products from pharmacies – online pharmacies

The Norwegian Regulation on Medicinal Products, Section 41, second paragraph, states that a pharmacy cannot send prescription medicinal products outside the pharmacy's geographic customer area. Current solutions for online pharmacies in Norway are therefore generally limited to the sale of non-prescription medicinal products and other merchandise.

The Ministry wishes to revise these regulations to allow the establishment of online pharmacies in Norway. Secure conditions must be in place for the use of online pharmacies, and these must be regulated to ensure that patients receive proper information and secure deliveries. The Ministry will submit a proposal for a public consultation. The establishment of online

pharmacies, combined with solutions for electronic prescriptions, would provide the public with improved access to safe and effective medicinal products.

18.2.7 Sale of medicinal products outside pharmacies (LUA)

The LUA scheme was introduced in 2003, and permits the sale of certain non-prescription medicinal products outside the pharmacy, in places such as supermarkets, kiosks and petrol stations. This scheme is intended to provide improved access to common non-prescription medicinal products and facilitate price competition between pharmacies and other point of sales.

The Norwegian Medicines Agency oversees this scheme and determines the type of medicinal products that can be sold. Each year, the Agency reviews a list of items that could be sold outside the pharmacy (the LUA list).

A reference group for the LUA scheme has been established, consisting of representatives from the Norwegian Pharmacy Association, the Consumer Council of Norway, the Competition Authority, the Association of the Pharmaceutical Industry in Norway, the Norwegian Association of Wholesale Grocers, the Norwegian Association of Pharmacists, and the Norwegian Medicines Agency. The intention of this group is to strengthen agency management of the LUA scheme, and to provide a forum for discussion on the further development of the scheme.

Medicinal products sold outside the pharmacy must meet certain criteria:

- The medicinal product and its area of use must be very familiar to the public.
- The individual consumer must be able to diagnose his or her symptoms and condition, and assess the need for treatment, as well as safety and effect.
- Information on the use and safety must be easily found on the package and in the package leaflet, and this information must be sufficient to ensure safe use.
- The stated contraindications (when a medicine should not be used) for use of the medicinal product should not be too extensive or complicated.

The risk of overuse or misuse of the medicinal product must also be taken into consideration. Consumers must be at least 18 to purchase medicinal products outside the pharmacy. Personnel in LUA outlets are not permitted to provide customers with advice on the choice of medicinal product or information on the characteristics and use of the medicinal product.

The Norwegian Food Safety Authority oversees the outlets to ensure that they comply with regulations. In 2014, the Norwegian Food Safety Authority conducted 815 inspections of LUA outlets, compared with 776 inspections in 2013.

The two most common deviations were the lack of an internal control system, and outlets that did not have the required minimum range of medicinal products. In 2014, 16 outlets were temporarily banned from sales, indicating that serious deviations from the regulations are

relatively rare.

There is no complete and updated overview of the number of enterprises selling medicinal products outside the pharmacy. In 2010 the registered wholesaler reported sales of medicinal products to 6365 enterprises/outlets.

Box 18.2 Paracetamol tablets removed from LUA in Sweden

Swedish medicines agencies have decided to stop the sale of paracetamol tablets in stores, partly because there has been an increase in the number of reports of paracetamol poisoning to the Swedish Poisons Information Centre. This ban will be in effect from 1 November 2015. There has been a significant increase in the total consumption of paracetamol in Norway over the last few years. This is due to increased prescriptions of the product. The use of non-prescription paracetamol has remained unchanged, and even declined over the past ten years. The Norwegian Medicines Agency recommends paracetamol as a first-choice medicine. The goal is therefore to increase the use of paracetamol while reducing the use of other analgesic medicinal products, such as NSAIDs (ibuprofen, naproxen and diclofenac, etc.).

The sale of non-prescription paracetamol has remained stable since 2003, and half of all non-prescription paracetamol is now sold outside the pharmacy.

There is no indication that the sale of paracetamol in stores lead to a greater number of serious poisonings or deaths. Based on the current evidence, the Norwegian Medicines Agency finds no basis for new restrictions on the sale of this product in Norway. The Norwegian Medicines Agency does not, therefore, share the view of the Swedish authorities.

18.3 Easier access to medicinal products

18.3.1 Right to prescribe medicinal products

Section 11 of the Health Care Personnel Act states that only physicians and dentists have the right to prescribe prescription medicinal products to humans. Other groups of health care personnel may have a limited right to prescribe, cf. discussion in Chapter 4.3.

During the flu pandemic of 2009, regulations were put in place to give pharmacists in pharmacies the temporary right to prescribe antiviral medicines. Econ Pöyry evaluated this arrangement on commission from the Norwegian Directorate of Health. Econ Pöyry concluded that the goal of increased access had been achieved, and that the very rapid implementation had been successful. Whether pharmacist prescriptions are a suitable instrument for permanent use must, according to Pöyry, be assessed for each individual medicinal product.

Evidence from abroad

There are currently only a few countries that permit pharmacists to prescribe medicinal products. The United Kingdom, Australia and New Zealand have a system known as "Pharmacist Only Medicines". Medicinal products included in this system are divided into non-prescription and prescription categories. Patients may be dispensed these medicinal products by a pharmacist without prescription. Pharmacists must ensure that patients meet the criteria, and must provide standardised information on how to use these medicinal products. The Danish Healthy Authority has recently been tasked with evaluating whether to develop regulations for pharmacist-dispensed medicinal products without prescription from a physician.

Both England and Canada have introduced pharmacist dispensing. England has a system with two categories of prescribers. Independent prescribers include health care personnel who are responsible for assessing a patient's health condition and making clinical decisions on treatment for the patient. Supplementary prescribers are responsible for following up treatment after an assessment of the health condition and implementation of a clinical management plan. Supplementary prescribers can prescribe any medicinal product, as long as it is within their area of competence, and part of the clinical management plan. Pharmacists may act as supplementary prescribers after undergoing training, while independent prescribers must have completed an accredited programme.

18.3.2 Pharmacist dispensing ("Farmasøytutlevering")

Regulations regarding the prescription and dispensing of medicinal products from the pharmacy require the pharmacy to ensure that customers have received enough information about the medicinal products to use them correctly, as well as information on possible adverse reactions. The Norwegian Medicines Agency has determined that the need for such advice from the pharmacy is unnecessary for medicinal products included in the LUA scheme. Pharmacist dispensing means that certain non-prescription medicinal products can only be dispensed by a pharmacist in a pharmacy. Pharmacist dispensing may be necessary for certain non-prescription medicinal products where there is a particular need to inform customers about a medicinal product's effect, adverse reactions, area of use, etc.

- The Norwegian Medicines Agency has been tasked with determining whether there are prescription medicinal products that can be dispensed without a prescription, but that must be dispensed by a pharmacist, and
- if there are non-prescription medicinal products that should only be dispensed with special information from the pharmacy (pharmacist).

Preliminary feedback from the Norwegian Medicines Agency suggests that this may be the case. The government will therefore evaluate a system for pharmacist dispensing from pharmacies.

18.3.3 Pharmacist prescribing

Pharmacist prescribing refers to permission for pharmacists who work in pharmacies to prescribe medicinal products, as was the case with the temporary system of pharmacist prescriptions of the antiviral medicine (Tamiflu) during the pandemic of 2009. The Norwegian Directorate of Health has reviewed medicinal products that may be appropriate for pharmacist prescribing, and concluded that only a limited number of medicinal products would be suitable. This applies to medicinal treatment in cases where the patient has a clear diagnosis, and where there is little need for a clinical assessment by a physician.

The primary benefit of pharmacist prescribing involves easier access to medicinal products for the public, and it may possibly also free up resources for the physician. Pharmacist prescribing can also result in a better utilisation of pharmacist competence.

The introduction of pharmacist prescribing would also involve numerous financial, legal and practical challenges:

- The role of decision-maker and seller is unfortunate and violates the principles of the Pharmacy Act.
- If pharmacists are given the right to prescribe, Section 2-3 of the Pharmacy Act must be amended.
- This provision would mean that personnel with the right to prescribe medicinal products would not be able to receive pharmacy licensing.
- The Norwegian Medicines Agency and the Norwegian Directorate of Health would need additional resources for case management and administration of the scheme.
- This scheme would result in more time-consuming dispensing for the pharmacies, which could result in financial loss if no tariff is added for the activity.
- Pharmacist prescribing would require the use of medical records, in addition to regular pharmacy records, cf. the Pharmacy Act.
- There would be challenges associated with prescriptions processed through the e-prescription scheme, and it must be determined whether pharmacists would be able to prescribe medicinal products encompassed by the reimbursement scheme.
- It must also be determined whether all pharmacists should have the right to prescribe, or if some type of certification should be involved in obtaining the right to prescribe.

A certain volume would be necessary for establishing good routines for management and recording in the pharmacy. It is also essential to have a scheme which is well-managed, and easy for the public to comprehend. The preliminary assessment conducted by the Norwegian Directorate of Health indicates that pharmacist prescribing would only be suitable for a small number of medicinal products.

The government believes that pharmacist dispensing is, for the time being, a more appropriate solution that pharmacist prescribing.

In the Report to the Storting no. 26 (2014–2015) "The Primary health and care services of tomorrow – localised and integrated", the government has indicated that it will assess whether selected groups should be given an extended right to prescribe medicinal products, medical consumables and food stuffs under the regulation for reimbursement, and whether additional groups should have the right to refer patients to other health care service providers. This proposal also opens for the assessment of prescription rights for pharmacists, and the Ministry believes that it may be appropriate to consider the right to prescribe for pharmacists who work with clinical pharmacy in hospitals or primary health care services.

18.3.4 Prescription renewal – extended validity period for prescriptions

Pharmacist prescriptions would involve the right to renew certain prescriptions. Prescriptions are generally only valid for one year, although prescriptions for contraceptives are valid for three years. The Norwegian Directorate of Health and the Norwegian Medicines Agency have been commissioned to assess the need for revised regulations regarding the dispensing of medicinal products from pharmacies. The Ministry of Health and Care Services will consider whether regulations governing the validity period of prescriptions should be revised when viewed in context of the work on e-health. It may be possible to give some prescriptions a validity period of more than one year, while other prescriptions would, for medical reasons, have a shorter period of validity. Prescriptions may be valid "until further notice" or "until change is reported or the use of the medicine is discontinued". "Wait-and-see prescriptions" should also be facilitated. This would be especially relevant for antibiotic prescriptions. More flexible regulations governing the period of validity for prescriptions would reduce the need for a doctor's appointment if the sole purpose of the appointment is to renew a prescription. This will also reduce the need for prescription renewal by pharmacists.

18.4 Supply and delivery security

The population must be ensured access to important medicinal products, assuming a normal situation where there is a stable and secure supply of medicinal products. However, emergency preparedness is also needed for possible accidents, disasters and critical situations, in addition to preparedness for situations that involve a shortage of certain medicinal products and failed deliveries.

The supply and delivery of medicinal products generally functions well in Norway. Nevertheless, there have been an increasing number of failed deliveries over the past few years. A change in treatment due to a shortage situation is a resource-intensive task for health care services, although normally this would not represent a medical problem for the patients. The most common reasons for a shortage situation are production problems, the withdrawal of a medicinal product from the market, or an inordinately high demand for the product, making it difficult to supply an adequate amount. The shortage of medicinal products is a growing international problem and European cooperation is essential for addressing this development.

Most shortage situations are dealt with by using packages intended for other countries, or by using alternative medicinal products that have a similar effect. In cases of shortage, the Norwegian Medicines Agency can grant approval for the sale of medicinal products that do not have Norwegian marketing authorisation.

National production expertise and manufacturing facilities for medicinal products may reduce the level of vulnerability in the event of failed deliveries. One example is the national production of morphine products. From 2013 to 2015 there was reduced access to industrially manufactured morphine products. Here the supply to the Norwegian market was covered by the pharmacies' service production system. The Ministry has asked the Norwegian Directorate of Health to assess where specific measures should be implemented to ensure necessary production capacity in Norway.

When pharmacy manufacturing is needed due to a long-term supply shortage of medicinal products, it may be difficult to sell the surplus stock of replacement medicinal products when the supply shortage is over. The Norwegian Pharmacy Association has proposed that industrially manufactured medicinal products should, in such cases, be quarantined until the emergency pharmacy-manufactured products have been sold out. This is equivalent to a temporary withdrawal or suspension of the medicinal product's marketing authorisation, which would not be consistent with the EU directive on medicinal products. The Ministry has asked the Norwegian Directorate of Health, in cooperation with relevant stakeholders, to assess alternative measures to reduce the risk of surplus stock from the emergency production of medicinal products.

Pharmaceutical companies are not obligated to deliver medicinal products, but they must inform the Norwegian Medicines Agency of all cases of interruptions in the supply and distribution of medicinal products. Clearly, the industry has a financial interest in supplying the market. Wholesalers are obligated to deliver the medicinal products they carry to all pharmacies within 24 hours. In areas where transport may be difficult, the maximum delivery time is 48 hours. Pharmacies are obligated to carry all medicinal products authorised for sale in Norway.

Medicinal product preparedness is based on the fundamental principles of preparedness: responsibility, proximity and equality. This means that the responsibility for preparedness and management of extraordinary circumstances will lie with the party organising the services under normal circumstances.

In Norway, the Norwegian Directorate of Health manages the emergency preparedness stockpile of medicinal products for both specialist and primary health care services. It is neither practical nor financially possible to have a medicinal product stockpile in Norway that can compensate for a shortage of medicinal products in every conceivable situation. Preparedness solutions have been fragmented, with no overall plan for ensuring that the composition of the stockpiles is based on updated, professionally sound assessments. The Norwegian Directorate of Health has therefore recently determined certain medicinal products that would be needed the most in a potential emergency situation.

In 2014, the regional health authorities were commissioned to oversee the preparedness management of medicinal products used by the specialist health care services, from 1 January 2015. Meanwhile, the national stockpile, under administration by the Norwegian Directorate of Health was dismantled. The regional health authorities were also asked to describe the challenges and strategies for national medicinal product preparedness for specialist health care services, in a report to the Ministry of Health and Care Services, submitted by 1 July 2015.

The Norwegian Directorate of Health has extended its agreement with the Norwegian Medicinal Depot on the preparedness stockpile of medicinal products for primary health care services for the remainder of 2015. The Norwegian Directorate of Health has recommended that this system be discontinued and replaced by a requirement for wholesalers of medicinal products to have a preparedness system. The Norwegian Medicines Agency has been commissioned to evaluate the way in which preparedness management of medicinal products for primary health care services may be ensured, and how this can be rooted in actual regulations. The Ministry will follow up the Norwegian Medicines Agency's evaluation with plans for implementation from 1 January 2016.

The Norwegian Institute of Public Health oversees the supply of vaccines, and is responsible for preparedness with respect to vaccines, immunoglobulins and immunosera, in accordance with the Control of Communicable Diseases Act.

In 2012, the Ministry of Health and Care Services submitted the white paper, Report to the Storting no. 16 (2012–2013) Preparedness for Pandemic Influenza, which presented the knowledge gained from the influenza pandemic in 2009/2010, the way in which this knowledge has been followed up, and the most important principles of a revised contingency plan for pandemic influenza. The government adopted a new national contingency plan for pandemic influenza in October 2014. This contingency plan determines responsibilities and distributes planning and management tasks among several different bodies, both within and outside health care services.

Following a tender competition, the Norwegian Institute of Public Health entered an agreement with GlaxoSmithKline AS and Novartis Norway AS on the reservation of production capacity, and the purchase of vaccines for fully vaccinating Norway's population in the event of another influenza pandemic. The release of this agreement depends on a WHO pandemic declaration. The contracts, which are valid for four years, will require manufacturers to deliver a percentage of their weekly production to Norway during a given time frame.

Many different stakeholders have tasks related to medicinal product preparedness. Among the government agencies, the Norwegian Directorate of Health, the Norwegian Medicines Agency and the Norwegian Institute of Public Health each have specific tasks and responsibilities. The supply chain has commercial stakeholders such as pharmaceutical manufacturers, wholesalers and pharmacies. In the final link of the chain, medicinal products must be prescribed and used in health care services. A safe and secure supply of medicinal products requires optimal interaction and dialogue between all these actors. Cases of delivery failure will often require the use of

alternative medicinal products, and this often involves new procedures and routines. Health care services have called for earlier alerts and more immediate dialogue with government agencies so that such cases can be handled more efficiently. The Norwegian Directorate of Health has therefore established a Medicinal Product Preparedness Committee in 2014, to enable improved cooperation and better dialogue between the various stakeholders.

18.5 Falsified medicinal products

In recent years, there has been an alarming increase in the number of falsified medicinal products throughout the EU. Innovative and life-saving medicinal products have also been falsified and channelled through the ordinary distribution chain.

The sale of falsified medicinal products without authorisation from authorities through the supply chain has also become a major problem. In recent years, medicines authorities have warned against purchasing medicinal products online, since there is a substantial risk that these products are falsified or illegal. Such products may also be ineffective, because they do not contain the necessary active substances. At worst, they could be harmful. WHO estimates that more than 50% of all medicinal products purchased online are falsified or illegal products.

The EU Directive 2011/62/EU is intended to prevent falsified medicinal products from entering in the legal distribution channels and being sold in pharmacies. This directive has been incorporated in the EEA agreement, and implemented in Norwegian law through amendments to the Pharmacy Act and its provisions. The Norwegian Parliament has previously been informed of the directive in Prop. 168 L (2012–2013) regarding amendments to the Pharmacy Act (measures to counteract falsified medicinal products). Based on the proposals in this document, the Norwegian Parliament made the decision to seize and destroy medicinal products which are imported illegally by private persons, without involving the police and prosecuting authorities, pursuant to the Norwegian Medicines Act.

WHO has overseen efforts to identify and prevent the export and import of falsified medicinal products since 1988. Nevertheless, the problem has been steadily growing. In 2011, the working group under WHO recommended that the World Health Assembly establish a member state mechanism to bring a halt to falsified medicinal products. The proposal specifies that consideration for trade and protection of immaterial rights should not be assessed with this mechanism. The purpose of this mechanism is to protect public health. The first meeting in the member state mechanism was held in autumn 2012. The ongoing work has been demanding, as the various member states have different interests. The United States and the EU have special interests in protecting their own industry against falsified medicinal products produced in breach of patent rights, while developing countries with a significant production of counterfeit medicinal products view this as an impediment for their own industry. Countries with a large production of generic medicinal products have a major interest in obstructing the process, since they wish to protect their national pharmaceutical industry. Lack of funding for the mechanism makes it difficult to carry out these efforts.

On 8 December, the Council of Europe adopted the convention on counterfeiting of medical products and similar crimes involving threats to public health. That members of the Council will criminalise falsifications of medicinal products and medical equipment, protect the rights of the victims of these crimes, and promote national and international cooperation. Many of the convention regulations were already contained in Norwegian law through provisions in the Pharmacy Act and the Norwegian Civil Penal Code.

The term “falsified” refers to fake medicinal products that purport to be authentic. Falsified medicinal products also include medicinal products with a false or unknown background. The quality of medicinal products hinges on the control of storage conditions. Consumers are unlikely to discover that the medicinal product is damaged if the damage is due to storage at the wrong temperature, for instance. The EU imposes strict demands for control of the medicinal product seller.

In recent years, there have been numerous cases of authentic medicinal products going astray, only to return through the legal distribution channel for medicinal products. These batches were then withdrawn from the market.

- In Italy, there have been several thefts of medicinal products from hospitals and lorries. Many of these medicinal products have turned up again in different countries through parallel importation of Italian packages.
- In Romania, a wholesaler purchased medicinal products from a pharmacy. This was not legal, but many of the products were sold to other countries, and two batches were delivered to Norway.
- There have been instances where expensive medicinal products, or packaging for expensive medicinal products were reused. This was the case with the breast cancer medicine, Herceptin. After this medicine was delivered in Finland, it was found that some of the packages contained only the remaining fluid added by the hospital prior to use, and no dry goods. Hospital waste may have been the source of these falsified medicinal products. There have been many recent examples involving several different countries. Norway has thus far not been affected by this problem.

These examples indicate the importance of monitoring the wholesaler link throughout the EEA area. Adoption of the Falsified Medicines Directive 201/62/EU will contribute towards a more intensified monitoring.

19 Equal access – financing of medicinal products

Public financing of medicinal products is currently threefold.

- Regional health authorities cover expenses for medicinal products used during hospitalisation and out-patient treatment.
- Municipalities are responsible for medicinal product expenses in municipal institutions.

- The National Insurance Scheme finances medicinal products used outside hospitals and municipal institutions.

In 2014, the total turnover from medicinal products with marketing authorisation was NOK 14.8 billion (PPP – pharmacy purchase price), including NOK 1.0 billion for veterinary medicinal products. This is equivalent to a retail price (PRP) of NOK 22.3 billion. The turnover for medicinal products for human use increased by 8.9% from 2013 to 2014. This increase was due to exchange rate fluctuations, which resulted in higher prices upon annual maximum price reassessments. New medicinal products for the treatment of hepatitis C and various types of cancer, in addition to new anticoagulants, also contributed toward this increase.

From 2006 to 2008 the financial responsibility for several biological medicinal products (TNF-inhibitors and MS medicines) was transferred from the National Insurance Scheme to regional health authorities. In 2014, financial responsibility for certain cancer medicines was also transferred to the health authorities.

The turnover from medicinal products through the reimbursement scheme totalled NOK 10.7 billion in 2014. The share paid by the National Insurance Scheme, including patient co-payments covered by the health care exemption card system, was NOK 9.7 billion, while patient co-payments were in the amount of NOK 1.0 billion.

National Insurance also covers certain medicinal product expenses beyond the contribution scheme. Girls between the ages of 16 and 19 receive full or partial contribution for hormonal contraceptive expenses, which amounted to NOK 24 million in 2014. Expenses for infertility treatment are also partially contributed, and National Insurance expenses amounted to NOK 24 million in 2014. National Insurance also contributes for certain non-reimbursed medicinal products, which amounted to NOK 23 million in 2014.

In 2014, hospitals' medicinal product expenses totalled NOK 5.4 billion. Of these, NOK 3.2 billion involved ordered products, while expenses for medicinal products through H-prescriptions amounted to NOK 2.0 billion.

There are no good statistics on municipal expenses for medicinal products used in nursing homes. Figures from the Norwegian Pharmacy Association for 2014 indicate that nursing homes, other health care institutions, doctors' offices and dentist offices ordered medicinal products from primary pharmacies for NOK 619 million (including non-prescription medicinal products). Most of these went to nursing homes.

Medicinal products on standard, non-reimbursed prescriptions are primarily covered by the patients themselves. Turnover from standard prescriptions amounted to NOK 2.9 billion in 2014. Non-prescription medicinal products were sold for NOK 2.1 billion in pharmacy retail prices (excluding sales of ordered products), and for approx. NOK 330 million (purchase price) through the LUA system. The above-mentioned figures are collected from different sources and cannot be summarised.

Figure 19.1 illustrates the turnover from medicinal products in Norway from 2006 to 2014, listed

in nominal NOK. The top line is the estimated total turnover, calculated from pharmacy purchase price turnover, reported by wholesalers to Norwegian Institute of Public Health. Veterinary medicinal products are not included in these figures. National Insurance expenses (red column) consist of medicinal products encompassed by the reimbursement scheme, Sections 2, 3 and 4, and include co-payments reimbursed by the health care exemption card system. Hospital expenses (green column) include sales of ordered products and H-prescription medicinal products. The difference between the columns and the total turnover is the turnover from standard prescription medicinal products, non-prescription medicinal products and co-payments for reimbursable prescriptions, as well as ordered products for nursing homes, doctors' offices, etc.

Figure 19.1 Medicinal product turnover by NOK 1 billion (pharmacy retail price), 2006–2014

Wholesaler-based statistics for medicinal products. Norwegian Institute of Public Health, Norwegian Directorate of Health, Hospital pharmacies' medicinal product statistics

19.1 Financing of the National Insurance Scheme

Provisions of Section 5-1 of the National Insurance Act stipulates that full or partial reimbursement for health care expenses will be given for necessary expenses for health care services due to illness, injury, etc.

Section 5-14 also stipulates the provision of financial support for essential medicinal products. The terms state that the medicinal product must be required for long-term use, and that the product must be prescribed by a physician for use outside the hospital. These terms are described in more detail in the Regulation for reimbursement for long term diseases.

In accordance with Section 5-14 of the National Insurance Act and its provisions, medicinal products may be reimbursed through three different systems: general reimbursement for preapproved medicines (Section 2), individual reimbursement (Section 3), and reimbursement for medicinal products for communicable diseases (Section 4).

Reimbursed medicinal products require a co-payment from the patient, which is 38% of the prescription amount, but no more than NOK 520 per prescription. Section 5-14 of the National Insurance Act places these co-payments in the maximum co-payment category 1. This means that co-payments exceeding NOK 2185 (maximum for 2015) in the course of one year will be reimbursed by the National Insurance Scheme.

19.1.1 National Insurance expenses for medicinal products

General or preapproved reimbursement (Section 2 in the Regulation for reimbursement) is the primary system in the reimbursement scheme, with nearly 2.3 million unique users, and a total reimbursement (including co-payments covered by the health care exemption card system) in the amount of NOK 7.1 billion in 2014. National Insurance expenses for individual reimbursements

(Section 3), was NOK 1.9 billion, with just under 110,000 unique users. Medicinal products for communicable diseases, (Section 4), were sold for NOK 672 million to approx. 35,000 users.

National insurance expenses for medicinal products encompassed by the reimbursement scheme increased from NOK 8.6 billion in 20014 to NOK 9.7 billion in 2014, which is a nominal increase of 13%. From 2006 to 2008, the financial responsibility for several biological medicinal products (TNF-inhibitors and MS medicines), were transferred from National Insurance to the regional health authorities. In 2008, several other medicinal products were also transferred from the contribution scheme to the reimbursement scheme. When corrected for these transfers, the expenses for medicinal products encompassed by the reimbursement scheme remained stable from 2004 to 2008. Automatic health care exemption cards were introduced in 2010, which led to an increase in expenses, since many more people received reimbursements for co-payments that exceeded the exemption card cap. The increase in expenses between 2012 and 2014 was partly due to new medicinal products for the treatment of hepatitis C, MS, cancer, and the prevention of blood clots. In 2014, the financial responsibility for certain cancer medicines was transferred to the Regional health authorities.

The use of reimbursed medicinal products, measured by defined daily doses (DDD) increased by 42%, from 1.2 billion DDD in 2004 to 1.7 billion DDD in 2014. The reason for this growth is the number of inhabitants and the consumption per inhabitant.

19.1.2 Preapproved reimbursement – Section 2 in the Regulation for reimbursement

Section 2 in the Regulation for reimbursement states that reimbursement will be granted for medicinal products on the reimbursement list, if the medicinal products have been prescribed in accordance with conditions and restrictions noted in the reimbursement list.

Generally, it is the pharmaceutical company (holding the medicinal product's marketing authorisation) that applies for preapproved reimbursement.

The Norwegian Medicines Agency assesses these applications based on the provisions of Chapter 14 of the Medicinal Products Regulation. In 2014, the Norwegian Medicines Agency reviewed 102 applications for preapproved reimbursement, whereby 96 were granted preapproved reimbursement or extended reimbursement. 98% of these applications were reviewed before the 180-day deadline.

38 of the reimbursement applications involved new active substances, new indications, or a new formulation. The criteria for cost-effectiveness were met in 37 of these cases, and the medicinal products were granted preapproved reimbursement. In several of the cases, the price of reimbursement was either negotiated down or reimbursement was granted with certain restrictions, to ensure cost-effective use.

Five of the 37 granted reimbursement applications were originally sent to the Ministry for budgetary reasons. All these medicinal products were granted preapproved reimbursement from

1 January 2015, when the defined minimum threshold ("bagatellgrensen") was raised from NOK 5 to 25 million.

The medicinal products that were granted preapproved reimbursement were for the treatment of various diseases, including diabetes, COPD, breast cancer, lung cancer, heart failure, hand eczema, ADHD and schizophrenia.

Treatment of serious medical conditions

A medicinal product may only receive preapproved reimbursement if it is intended for use in the treatment of serious medical conditions, or in the treatment of risk factors which are highly likely to lead to or exacerbate a serious medical condition.

The Royal Decree from 6 June 2003 states that preventive measures are not encompassed by Section 5-1 of the National Insurance Act. This means that medicinal products for the prevention of disease in healthy individuals cannot be covered through the reimbursement scheme. However, risk factors that are highly likely to lead to, or exacerbate serious medical conditions should be viewed as pathological, and would therefore be encompassed by the reimbursement scheme. This means that medicinal products intended for the treatment of such risk factors, which would therefore prevent serious disease or exacerbation of a serious disease, are included in the reimbursement list. Examples include medicinal products for hypertension, and for lowering cholesterol.

Repeated, long-term treatment

Medicinal products can only be granted preapproved reimbursement if the disease (or the risk factor) results in the need for long-term treatment.

Criteria for long-term treatment have been determined, through administrative practice, to include the need for the use of one or more medicinal products for at least three months in one and the same year for the same disease. It is not necessary for this three-month period to be continuous. The Royal Decree of 6 June 2003 states that the risk of long-term treatment would be sufficient. This opens for the reimbursement for medicinal products which would replace or prevent long-term treatment.

In cases where chronic disease makes it necessary to have a medicinal product readily available throughout most of the year, this would also satisfy the criterion of long-term medicinal treatment, such as medicines for anaphylactic shock.

Well-documented and clinically relevant effect

The medicinal product must have a well-documented and clinically relevant effect on a specific patient group, and documentation must be provided to indicate that clinical effect is also relevant for Norwegian conditions. Generally, the medicinal product must have marketing authorisation

for the indication for which reimbursement is being sought. Regulations include certain exceptions to this rule. Reimbursement can also be granted for a narrower area of use than for the authorised indication.

Cost-effectiveness

The cost of using the medicinal product must be reasonable when compared with the benefits, and with the costs of alternative treatment. Applications for preapproved reimbursement must include documentation of the medicinal product's cost-effectiveness. This is generally done through a pharmacoeconomic analysis, included with the reimbursement application. The Norwegian Medicines Agency has established guidelines for pharmacoeconomic analyses.

In this analysis, the medicinal product's cost and health benefits are compared with the most relevant alternatives in a Norwegian context. Data on efficacy is obtained from clinical trials. The analysis contains the cost of the medicinal product itself, as well as other costs associated with treatment and follow-up, such as control appointments with a physician or through hospitalisation. Other consequences for society, such as the benefits of a healthy patient who can continue working, are also assessed.

19.1.3 Defined minimum threshold ("Bagatellgrensen")

The Norwegian Medicines Agency may grant preapproved reimbursement for medicinal products, if the expenses for National Insurance do not exceed a certain cost limit. This is often referred to as the defined minimum threshold ("bagatellgrensen"). Prior to 2015, this limit was set at NOK five million per year, and had at that point remained unchanged since 2003. The estimated amount is based on anticipated sales of the medicinal product five years after the reimbursement decision. If the costs exceed the minimum threshold, the Norwegian Medicines Agency must send its recommendation to the Ministry, and reimbursement for the medicinal product must be approved by the Norwegian Parliament.

The government submitted a proposal for the 2015 National Budget to raise the minimum threshold to NOK 25 million, as the low threshold was preventing quick financing of new and effective medicinal products. Parliament adopted the government's proposal. Many other medicinal products can now be introduced without prior approval by Parliament, and patients will have faster access to new and effective medicinal products.

A total of nine medicinal products, including five medicinal products with applications submitted in 2014, were preapproved for reimbursement once the minimum threshold was raised. Among these were seven medicines for the treatment of type 2 diabetes.

19.1.4 The Norwegian Medicinal Products Regulation Section 14-14

Section 14-14 of the Norwegian Medicinal Products Regulation refers to medicinal products that cannot be granted preapproved reimbursement:

> "A medicinal product cannot be granted preapproved reimbursement if it will primarily be used in the treatment of:
>
> a. Substance abuse
> b. Nicotine addiction
> c. Natural hair loss, or
> d. Erectile dysfunction
>
> Should the Norwegian Medicines Agency receive an application for a medicinal product encompassed by the first subsection, the case must be sent to the Ministry, which will assess the need for an evaluation of a special reimbursement system. The Ministry can, in its conjunction with its assessment, request that the Norwegian Medicines Agency evaluate reimbursement worthiness in accordance with Section 14-31."

Such medicinal products are not currently reimbursed. Medicinal products used for smoking cessation or peroral medicinal products for use with erectile dysfunction are also exempt from coverage through the contribution scheme, however, contributions have been granted for medicinal injections used to treat erectile dysfunction, and for medicinal products for the treatment of substance abuse.

Section 14-14 of the Norwegian Medicinal Products Regulation was included since these conditions were not viewed as a disease, in accordance with the National Insurance Act. The government does not wish to have a special reimbursement system for these medicinal products. Any public reimbursements for medicinal products encompassed by Section 14-14 should be introduced via an amendment in the regulation which would give the pharmaceutical industry the opportunity to apply for preapproved reimbursement.

The Norwegian Medicines Agency will then assess whether the criteria for reimbursement are met. This would involve an assessment of the severity of the condition, the need for long-term use, any available documentation relevant to Norwegian conditions, and the cost-effectiveness of the treatment.

The government believes that the reimbursement of expenses for the treatment of substance abuse, beyond that covered by MAT initiatives, should be assessed in the same manner as preventive treatment that is currently covered through the reimbursement scheme. The Royal Decree of 6 June 2003, addresses preventive treatment in the following manner:

> "Section 5-1 of the National Insurance Act stipulates that the purpose of reimbursement in accordance with this chapter is to provide compensation for "necessary expenses for health services due to illness, injury, disability, family planning, pregnancy, childbirth and abortion". Preventive treatment is not mentioned, and reimbursement therefore not be granted for the prevention of disease in healthy individuals, in accordance with this chapter."

This is also stipulated in the regulation. The medicinal product must be intended for use in treating "serious medical conditions or risk factors that are highly likely to lead to, or exacerbate serious medical conditions". Serious risk factors should, in the context of reimbursement, be

viewed as pathological, and covered by the reimbursement scheme. In such cases, medicinal products intended for the prevention of disease and prevention of relapse (treatment of risk factors) could be encompassed by the reimbursement scheme.

Currently, reimbursement is granted for medicinal products used to treat risk factors such as hypertension and high cholesterol. Substance abuse is considered a risk factor that is similar to, and perhaps even more serious than risk factors that are currently treated with reimbursable medicinal products.

A 12-week course of treatment with varenicline costs about NOK 2200, or NOK 26 per day. In comparison, the average smoker spends NOK 50 per day on tobacco, which is the equivalent of about NOK 18,000 per year. The individual patient would therefore have strong financial incentives to stop smoking in order to finance this treatment. The government will therefore not, at the present time, prioritise reimbursement for medicinal products for the treatment of nicotine addiction.

In 2007, the Norwegian Medicines Agency evaluated the issue of reimbursement for medicinal products used in the treatment of erectile dysfunction. The Norwegian Medicines Agency concluded that erectile dysfunction could be considered a serious medical condition, which based on its severity would be encompassed by the reimbursement scheme The Norwegian Medicines Agency also stated that reimbursement for peroral medicinal products such as sildenafil could be cost-effective treatment for certain patient groups, for instance, in cases where erectile dysfunction was caused by another serious disease. Erectile dysfunction can often be a consequence of diseases such as diabetes, multiple sclerosis, spinal cord injuries and prostate cancer. The Norwegian Medicines Agency have concluded therefore that it is unreasonable to provide contributions for injections and urethral pellets, but not tablets, which is the case today.

The government propose to repeal Section 14-14, Subsection 1, letter a, of the Norwegian Medicinal Products Regulation (substance abuse) and letter d (erectile dysfunction). A proposal for an amendment to the regulation will be submitted for public consultation in autumn 2015.

19.1.5 Individual reimbursement – Regulation for reimbursement, Section 3

Section 3 of the Regulation for reimbursement allows for reimbursement for medicinal products even if criteria for preapproved reimbursement have not been met. According to this regulation, reimbursement is granted by individual application to HELFO (Norwegian Health Economics Administration).

Individual reimbursement can be granted for medicinal products intended for the treatment of medical conditions included in the preapproved system (Section 3, Subsection 1, letter a), and for rare conditions (section 3, Subsection 1, letter b).

A circular that provides more detailed information on the provisions of the regulation has recently been prepared.

Rare diseases and medical conditions are defined as diagnoses that have a prevalence of less than 1 per 10,000 inhabitants, corresponding to fewer than 500 individuals in Norway. If the degree of severity of a disease is considered rare, it would equate a rare disease or medical condition.

As with individual reimbursement in general, these conditions must meet the criterion of long-term use.

Documented effect

Scientific documentation must be provided to show that the medicinal product listed in the application is effective in treating the corresponding diagnosis.

The requirement of documented effect has already been met for medicinal products that were granted marketing authorisation in Norway or the EEA, if the medicinal products are used for the authorised indications. The same applies to medicinal products that are recommended for use in national treatment guidelines for the corresponding condition. In other cases, there must be published, scientific documentation of effect for the condition.

Requirements for instituting treatment

An application for individual reimbursement is generally submitted by a physician on behalf of a patient. The primary rule is that the treatment must be instituted (initiated) by a specialist in the field of medicine pertinent to the disease, or a corresponding hospital unit. In July 2014, regulations permitted specialists in general medicine to initiate the treatment of conditions that were previously only treated in primary health care services, such as asthma, COPD, type 2 diabetes, hypertension and high cholesterol. The government wishes to revoke the requirements for instituting treatment. This is discussed further under the heading “Requirements for specialist assessment for reimbursement by individual application”.

Reimbursements for medicinal products that are not included in the reimbursement list under the corresponding reimbursement code – special cases

Section 3, Subsection 1, letter a of the Regulation for reimbursement states that reimbursement can be granted for medicinal products by individual application, for use that is indicated by a reimbursement code, in special cases. This is a safety valve for patients who for medical reasons cannot be treated with a preapproved medicinal product. To prevent this individual system from undermining the system of preapproved reimbursement, treatment must first have been attempted using one or more preapproved medicinal products.

Special cases include instances where preapproved medicinal products have not been adequately effective, or they have resulted in adverse reactions which render the product unacceptable for use in further treatment, or a patient has another serious disease, another medical condition, or uses other medicinal products preventing the use of preapproved medicinal products.

The use of relevant marketed medicinal products must also be attempted before applying for

reimbursement of expenses for medicinal products which are not marketed.

When applying for reimbursement in cases where there is no suitable, preapproved treatment, reimbursement may be granted based on documented effect.

Public consultation on proposals for amendments in the regulation

In accordance with the current regulation on individual reimbursement, certain patients with serious diseases will not be covered by the reimbursement scheme. A proposal for a new regulation regarding individual reimbursement for medicinal products was submitted for public consultation in October 2013. The primary intent of the proposed amendment was to ensure that patients whose medicinal product expenses are currently not encompassed by the reimbursement scheme would be reimbursed for medicinal product expenses in the same manner as other patients with serious diseases and conditions. The proposal for this consultation includes four fundamental conditions for individual reimbursement: the severity of the disease, documentation of the medicinal product's effect, cost-effectiveness of the treatment, and treatment duration. The proposal also seeks to remove the distinction between letter a and letter b of the current Section 3, Subsection 1.

The proposed changes touch on topics which are key to the White Paper on prioritisation. This will be presented by the government in 2016. Possible amendments to the regulation regarding individual reimbursement for medicinal products will be assessed in conjunction with the White paper on priority setting.

Specialist requirements regarding individual reimbursement for addictive medicinal products to treat chronic, severe pain

Since 2008, individual reimbursement in accordance with Section 3 has been granted for addictive analgesics for patients with chronic, severe pain and significantly reduced quality of life and function. Previously, an appropriate specialist was required to prepare the application for reimbursement and to institute treatment.

The Norwegian Directorate of Health's treatment protocol for the use of opioids for long-term, non-cancer related pain (the Opioid Protocol) from 2014, recommends that only one physician should be responsible for prescribing addictive medicinal products. Normally this would be the patient's regular general practitioner, who has contact with the patient over time. The general practitioner should therefore be responsible for applying for the reimbursement of addictive medicinal products, and for their prescriptions.

The Ministry of Health and Care Services has determined that new conditions for individual reimbursement should be established, as stated in the recommendations of the Opioid Protocol. Applications for low opioid doses for use in diagnosed pain conditions must be submitted by the patient's general practitioner. Should there be a need for higher doses and/or if the pain is undetermined, the patient should be assessed by a specialist at an interdisciplinary pain clinic. In

such cases, applications for reimbursement must be submitted by a physician at the pain clinic.

These revisions also allow for decisions without a time limit for the second application, and universal decisions which apply to all marketed opioids up to a specified amount. These new conditions will provide an easier and less bureaucratic reimbursement system for patients, physicians and HELFO. At the same time, responsibility for treatment and follow-up will lie with the general practitioner.

Requirements for specialist assessment for reimbursement through individual application

One of the basic requirements for granting reimbursement for medicinal products by individual application is that the treatment is instituted by a specialist in the field of medicine pertinent to the disease, or a corresponding hospital unit. The reason for this requirement is that treatment with a medicinal product that has not been preapproved for the specific diagnosis deviates from that which is considered cost-effective treatment. In these cases, it has been necessary for a specialist to quality assure appropriate treatment. This requirement also ensured a general threshold for the prescription of medicinal products without preapproved reimbursement, to maintain control over the use of the medicinal product and to limit expenses, cf. Report to the Storting no. 18 (2004–2005) “On course towards more correct use of medicine”.

The requirement of instituting treatment implies that a specialist or a physician at a hospital unit must initiate the treatment, or assess whether the patient should be treated with the medicinal product in question. However, an application for individual reimbursement may in some cases be prepared by the patient’s general practitioner or other physician providing treatment. The application must state the name of the physician who has instituted treatment. In practice, a phone consultation with a specialist will also qualify as instituting treatment. Certain medicinal products are exempt from the requirement of instituting treatment. This applies to certain allergy medications. Since July 2014, specialists in general practice have also been considered appropriate specialists in various areas of treatment. Examples include the treatment of hypertension, high cholesterol, osteoporosis, diabetes and allergies.

Health care legislation has provisions to ensure that patients are treated by qualified personnel, and in the most appropriate area of health care services. The current regulation for individual reimbursement results in a high number of referrals to specialist health care services which are formally, but not professionally justified. These referrals are often viewed as unnecessary and troublesome for both the referring party and the recipient, and the practice conflicts with the intentions of Sections 4 and 6 of the Health Care Personnel Act, and the guidelines of the Coordination Reform.

The opportunity for specialists in general practice to institute treatment in certain treatment areas will simplify this system. However, it may also lead to differential treatment of patients, since only around half of all general practitioners in the country are general practice specialists.

The current requirements for instituting treatment are inexpedient, and contrary to the principle that treatment should be carried out at the appropriate treatment level, and should not place an unnecessary burden on specialist health care services. The government will therefore revoke the general requirement for treatment to be instituted by a specialist. This means that basically all physicians will have the same right to institute treatment and apply for individual reimbursement of expenses for medicinal products. The standard principles regarding sound medical judgment and cooperation will determine when a physician must seek advice from another physician or specialist.

In some areas, it may still be natural for specialist health care services to have the primary responsibility for initiating treatment, and in certain cases also treatment follow-up. In such cases, the Norwegian Directorate of Health, or the organ determined by the Norwegian Directorate of Health, will decide whether only certain specialist groups should be permitted to institute treatment and apply for individual reimbursement. Cancer treatment, treatment with orphan drugs and treatment of rare diseases may be areas demanding specific expertise. It may also be necessary to maintain the specialist requirement with respect to treatment with medicinal products outside the approved indications.

Revoking the general requirement for specialist initiation of treatment will help to reduce the unnecessary burden on specialist health care services, and will simplify this process for both general practitioners and patients.

19.1.6 Discontinue the “Forskningsblå” scheme

The primary rule of the reimbursement scheme is expenses can only be reimbursed for medicinal products with documented safety and effect. For this reason, medicinal products used in clinical trials are usually not included in this scheme.

“Forskningsblå” is a system whereby expenses for medicinal products in clinical studies can be financed through the reimbursement scheme. The scheme finances use of the medicinal product outside the terms of the product’s approved area for reimbursement. This scheme appears to have originated in a circular for Section 5-14 of the National Insurance Act by the former National Insurance Administration, but the objective of the scheme is unclear. The Norwegian Directorate of Health has received two to three applications per year. “Forskningsblå” covers only the costs of the medicinal products. Other expenses involved in conducting these trials must be covered by other sources. The budgetary consequences have been in the amount of just under NOK 1 million per year.

The “Forskningsblå” scheme is little known and rarely used. It can ensure public funding for studies that are unable to obtain funding through the ordinary channels. Since these medicinal products would be prescribed as a reimbursable prescription, which patients must pick up at the pharmacy themselves, the scheme could only be used for non-blind trials. The Ministry of Health and Care Services cannot see any compelling reasons to continue this scheme, and proposes the discontinuation of “Forskningsblå”.

19.1.7 Regulation for reimbursement, Section 4 – medicinal products for treatment of communicable diseases

According to Section 4 of the Regulation for reimbursement, the National Insurance scheme grants reimbursements for medicinal products through the reimbursement scheme for the treatment of communicable diseases that pose a threat to public health. This applies to everyone residing in Norway, even if residents are not members of the National Insurance Scheme. In this case, no co-payments are required by patients, and medicinal products without marketing authorisation may be prescribed. When the Regulation for reimbursement was revised on 1 November 2014, revisions included the requirement for membership in the National Insurance Scheme for reimbursement of expenses for medicinal products for hepatitis C infections.

Reimbursement is granted for anti-infective medicinal products, as stated in Section 4, no. 2 and Section 4a of the Regulation for reimbursement, as well as for vaccines, immunoglobulins and immunosera, as stated in Section 4, no. 3 of the Regulation for reimbursement. The regulation specifies reimbursement criteria for certain medicinal product groups, and list conditions for prescribing, reimbursement and dispensing for certain groups.

Section 4 of the Regulation for reimbursement is pursuant to the Act relating to the Control of Communicable Diseases. The purpose of separate provisions for these medicinal products is to treat the individual patient infected with a communicable disease that poses a threat to public health, and to prevent further infection. Co-payment is not required for medicinal products prescribed in accordance with Section 4, since financial circumstances must not be an obstacle to completing treatment and preventing the spread of a communicable disease to the public. The main purpose of treatment for hepatitis C infections and HIV infections, currently covered by Section 4, is to treat the individual patient. Hepatitis C is generally incurred by individuals who inject illegal substances, and there is a substantial risk of infection within this group. Treatment is generally offered to patients who have developed liver damage. The Ministry has commissioned the Norwegian Institute of Public Health to develop a proposal for a national strategy for efforts against viral liver infections (hepatitis).

Section 4 of the Regulation for reimbursement has no current prioritisation criteria for reimbursement, however, there are requirements regarding cost-effectiveness for medicinal products in the treatment of hepatitis C.

There are several aspects of the current system that make it difficult to produce adequate statistics, and to control whether prescriptions stated in Section 4 are in compliance with the regulations:

- Medicinal products are regulated by the assignment of an ATC code (not at a medicine or active substance level).
- The prescription does not reveal the infectious disease being treated.
- Physicians can prescribe HIV medication for themselves to ensure patient anonymity.

There are currently established, special requirements for dispensing certain medicinal products

for treatment of tuberculosis. These medicines can only be dispensed from a hospital pharmacy, and a special notice of dispensed medicinal products must be sent to the Norwegian Institute of Public Health. Such notices rarely include additional information beyond that which is already registered in the Tuberculosis Registry.

The government proposes a review of the current financial management systems for vaccines, cf. Chapter 19.6. A revision of Section 4 of the Regulation for reimbursement should be included in these efforts. The purpose of reimbursement should be clarified in the revision. Furthermore, it should be evaluated whether medicinal products for the treatment of communicable diseases that pose a threat to public health can be evaluated in the same manner as other medicinal products encompassed by the reimbursement scheme, i.e. with the same requirements for efficacy and cost-effectiveness. Consideration for control of communicable diseases must also be emphasised in an assessment of cost-effectiveness.

19.1.8 Contribution Scheme – National Insurance Act, Section 5-22

Section 5-22 of the National Insurance Act states that the National Insurance Scheme can contribute to expenses for health care services when these expenses are otherwise not covered by the National Insurance Act or other legislation.

Contributions are also provided for marketed, prescription medicinal products which are not encompassed in the reimbursement scheme. This contribution scheme functions as a safety net for patients who are not dispensed reimbursable medicinal products. The scheme does not require an assessment of effect, and there are no costs involved in the granting of contributions. The only requirement is that the medicinal product must be marketed in Norway, prescribed, and purchased at a Norwegian pharmacy.

This system also provides contributions for medicinal products associated with infertility treatment and for contraceptives for women between the ages of 16 and 20. Non-prescription medicinal products (creams, ointments and oil preparation etc.) for treatment of chronic and serious wounds, fistulas and skin conditions are also subsidised. Expenses for treatment of the condition epidermolysis bullosa (a skin disease) were previously paid through the contribution scheme, but on 1 January 2015 these expenses were transferred to the reimbursement scheme.

19.2 Municipal financing of medicinal products

The current financing and user payment systems for municipal health and care services vary, depending on whether the service recipient lives at home or in an institution. Services provided in the home or in the institution are primarily financed through the municipality's free income and through service user payment. The government finances housing allowances and assistive devices, and provides some funding for medicinal products and medical services for users outside the institution. Municipalities are responsible for medicinal expenses for residents of municipal institutions and housing with around-the-clock care services.

Individuals who receive services in their own home (including care housing) pay for each service they receive, while residents in institutions pay a regular share of their income for a comprehensive service. Today's regulations may result in users paying different amounts for the same services, depending on whether the municipality offers the individual a place in an institution or whether services are provided in the individual's own home.

When Norwegian Parliament reviewed Report to the Storing no. 29 (2012–2013) "Care services of tomorrow", approval was given for the evaluation of financing and co-payments for various forms of housing. The objective is to determine a set of regulations that are fair, predictable and simple to understand for users, family members, and the municipalities. These regulations should also encourage municipalities to assess and plan their capacity needs based on the real needs of the populations, as well as what is most socioeconomically sensible.

These evaluation efforts must be seen in conjunction with the point in the government platform regarding a government operating subsidy scheme to prevent an unequal distribution of care housing and nursing homes, and to ensure quicker construction of additional nursing home places.

Medicinal products can present unpredictable costs for municipalities. This may occur when patients using new and costly medicinal products suddenly need 24-hour care and nursing services. Some of the costliest medicinal products are those used for treating rare, hereditary diseases that have a higher prevalence in certain local communities.

New, costly and specialised medicinal products can be administered outside the hospital due to simpler administration and increased competence in the municipalities. New medicinal products offer increased life expectancy for several patient groups, enabling them to live as long as the average population. These patient groups may in time need 24-hour care and nursing services.

19.3 Financing of medicinal products in hospitals

19.3.1 Financing of health authorities

Section 2-1 of the Specialist Health Care Service Act stipulates that the government has the overall responsibility for ensuring that the population receives essential specialist health care services. This means that the government must provide the regional health authorities with framework conditions that make it possible to comply with the imposed responsibility. A central goal of government ownership of the regional health authorities is to secure comprehensive governance specialist health care services and the proper utilisation of resources to operate and develop these specialist health care services for the population.

In 2015 the government transferred approximately NOK 130 billion to regional health authorities. Financing of the regional health authorities is primarily twofold, and consists of a basic allocation and activity-based financing (performance-based financing and out-patient reimbursements). There are also allocations for specialists with operating agreements, private

laboratories and radiological institutions. The most important goal of the financing system is to support the responsibilities imposed on the regional health authorities. Specialist health care service financing is done in several steps. The government transfers funds to the regional health authorities, which distributes incomes to the owned health authorities, and to private stakeholders, all of which provides financial support for the imposed responsibilities.

19.3.2 Basic allocations

In 2015, the basic allocation was in the amount of NOK 96 billion. This allocation provides basic financing that enables regional health authorities to conduct their activities in accordance with the Health Authorities and Health Trusts Act, other regulations, and political decisions. Basic allocations are also intended to finance investments. The distribution of the basic allocation between the four regional health authorities is determined by the number of inhabitants in the different regions, as well as the age composition, various socioeconomic criteria and cost statistics.

19.3.3 Performance-based financing

Performance-based financing (PBF)is the largest of the activity-based systems, and constituted approximately NOK 30 million in 2015. Through performance-based financing, part of the budget for regional health authorities hinges on the number and type of patients receiving treatment. The purpose of this system is to ensure that activities are carried out as cost-effectively as possible. If there is less activity than anticipated, subsidies for the regional health authority will be reduced. If there is greater activity than anticipated, subsidies for the regional health authority will be increased. Greater activity can only be compensated through performance-based financing. Reimbursements through PBF are meant to cover some of the costs of expanded treatment capacity. The rest must be covered by the basic allocation to the regional health authorities. Activity-based financing encourages cost assessment and it identifies and remove bottlenecks that prevent cost-effect patient treatment. The PBF rate covers 50% of the unit price.

Expenses for medicinal products, for which the regional health authorities are financially responsible, must be covered by health authorities' regular income system (basic and PBF).

Medicinal product expenses for hospitalised patients are distributed by specific diagnosis-related groups (DRG) based on the duration of hospitalisation, while expenses for out-patient treatment with medicinal products are largely based on information about the medicinal products that are actually used. There are DRGs for medicinal out-patient treatment of cancer, multiple sclerosis (MS), inflammatory bowel disease, inflammatory arthritis, and severe psoriasis. This includes the costs of both consultations and medicinal products.

PBF also covers treatment with specific medicinal products administered by patients themselves, including those medicines use in the treatment of cancer, MS and severe psoriasis.

19.3.4 Medicinal Product Procurement Cooperation

The Medicinal Product Procurement Cooperation was established for medicinal products that are financed by the regional health authorities. The purpose of the Medicinal Product Procurement Cooperation is to provide the basis for agreements on the procurement and supply of medicinal products and other pharmacy goods on commission by the health authorities, thereby reducing the costs of these products. This activity is financed by an annual fee paid by the regional health authorities.

Market and hospital developments demand an increasingly specialised procurement and negotiation expertise. This means that the type of expertise needed has gradually changed and become more cutting edge than before. Regional health authorities have been delegated the task to present a plan for the establishment of a jointly owned authority for procurement, to coordinate current units and resources, including the Procurement Services for Health Enterprises Ltd., and the Medicinal Product Procurement Cooperation (LIS). A national procurement function could benefit from a coordinated expertise base where there is room for increased specialisation, use of best practice, and the development of standardised processes, thereby providing even better support for the core activities of the hospitals. This work must be viewed in context with the health authorities meeting in 2013, where regional health authorities were asked to assess the role of the Medicinal Product Procurement Cooperation in the national system for the introduction of new methods in specialist health care services. The organisation and development of a national procurement function should include an assessment to determine whether the tenders offered by the Medicinal Product Procurement Cooperation should consider other criteria than those included in the current allocation criteria, cf. Chapter 16.7.

Reference is made to the more detailed discussion on the National System for the Introduction of New Methods in Chapter 19.4.

19.4 National System for Managed Introduction of New Health Technologies within the Specialist Health Care Services

A new system for the introduction of new and costly technology in specialist health care services was described in the Report to the Storting no.16 (2010–2011) “National Health and Care Plan” (2011–2015) and in the Report to the Storting no. 10 (2012–2013) “High Quality – Safe Services”.

The system was established in 2012, and introduced in January 2013. A secretariat has been set up in the Norwegian Directorate of Health, in addition to a national working group composed of all the major stakeholders, a reference group with representatives from user and patient organisations, the industry, as well as an Ordering Forum for the regional health authorities. A Decision Forum for new technology was established in May 2014.

The purpose of the system is to improve quality and patient safety in the treatment by ensuring that patients are quickly able to gain equal access to new and effective technology, and to ensure

that obsolete or harmful health technologies are disinvested. For medicinal products that have marketing authorisation, and therefore also a documented positive risk-benefit ratio, the system will help to promote an economically and medically appropriate use of these medicinal products in specialist health care services.

The system utilises internationally recognised standards for the assessment of health technology (Health Technology Assessment – HTA) which ensures that decisions are based on the best possible evidence-based platform. Health technology assessment is a systematic summary and assessment of available scientific literature. These assessments often involve medical equipment and devices used in prevention, evaluation/diagnostics, treatment and procedure follow-up, medicinal products, care and nursing, as well as the organisation of services and other interventions.

19.4.1 Structure

The system is built on the principles of accountability and transparency, and is implemented and developed within current governance structures and legislation.

The implementation of the system is a long-term enterprise, which requires significant coordinated efforts between the involved parties. There is also a need for cooperation between users and patient organisations, primary health care services, other relevant agencies, innovation and research environments, and technology manufacturers, as well as the pharmaceutical industry.

Figure 19.2 Local and national processes

The system is based on the current responsibilities of the various parties. At the local level, health trusts are responsible for conducting local health technology assessments and are supported by regional health authorities in these endeavours through local competence, academic environments and experts.

Decisions made by regional health authorities will be based on national, single technology assessments conducted by the Norwegian Knowledge Centre for the Health Services (for medical equipment, procedures, etc.) and the Norwegian Medicines Agency (for medicinal products). The Knowledge Centre performs all full health technology assessments for all technology categories. Full health technology assessments are used when it is necessary to compare several different treatment options, and when the focus is on the entire area of treatment rather than on single products.

A systematic assessment of medicinal products is conducted once the regional health authorities have placed their orders. This is financed by the health authorities/hospital. The assessment is based on current criteria which determines priority, and is handled in a Decision Forum for new technology.

The regional health authorities, the Norwegian Knowledge Centre for Health Services, the Norwegian Medicines Agency, the Norwegian Directorate of Health, the Norwegian Radiation Protection Authority, the Medicinal Product Procurement Cooperation (LIS) and the Procurement Services for Health Enterprises Ltd. (HINAS) all collaborate on the implementation and development of the system in specialist health care services, and participate in a national working group. The Ministry of Health and Care Services is an observer, and the Norwegian Directorate of Health functions as the secretariat.

Regional health authorities are responsible for ensuring that the populations in their respective regions are offered specialist health care services. Both the responsibility for providing patients with medically sound services and the responsibility for strengthening their own health trusts means that the regional health authorities can provide the health trusts with guidelines for prioritising resources and treatment technology. In this way, regional health authorities maintain the overarching responsibility for medically sound specialist health care services. This also gives patients access to new and effective technology, and ensures that obsolete or harmful health technologies are disinvested.

The four regional health authorities make a joint decision on whether to introduce a new technology to the entire country, after performing a national health technology assessment, cf. Chapter 19.4.3 under “Decision-making”.

The Ordering Forum (Bestillerforum RHF) meets monthly to review submitted proposals for health technology assessments. They determine which health technology assessments will be conducted on a national level, and then delegate the task of conducting the assessments to the Knowledge Centre or Medicines Agency. The Ordering Forum is composed of the medical directors from each of the four regional health authorities, as well as two representatives from the Norwegian Directorate of Health. Representatives from the Knowledge Centre, the Norwegian Medicines Agency and the Norwegian Radiation Protection Authority have observer status.

The reference group is a forum for feedback and ideas that contribute towards quality assurance, further development and evaluation of the system. The reference group consists of representatives from patients and service user organisations, professional associations, university and research environments, health and care services, primary health care services, the industry and health technology manufacturers/suppliers.

19.4.2 Principles and overarching guidelines

One of the goals is to make all processes, procedures, treatment courses, documents and structures of the system available to the public on the system’s website: www.nyemetoder.no. This shall provide a better overview of the system, greater transparency of the processes, optimal dialogue during the ongoing processes, and greater predictability for the entire health care service, included all involved stakeholders. This website was introduced in February 2015.

In some cases, the pharmaceutical industry has demanded that negotiated discounts remain

undisclosed. Non-disclosure of prices is one of the reasons the Decision Forum for new technology have held closed meetings. The Decision Forum includes one representative from the regional user committees as an observer with the right to speak at the Forum meetings.

Comments and input on the system from medical profession communities is an important factor in ensuring the proper professional understanding of assessments and introduction of new technology. During the first year of operation, a panel of experts was established from several professions. It is also essential to include patients' perspectives in this part of the assessment process. To improve quality and to legitimise the use of technology assessments in health care services, it is important that both expert and patient roles are clarified and enhanced in the work on technology assessments. Professional environments will also play an important role in the technology notification function of the system.

The national budgets for 2013, 2014 and 2015 have all allocated funds for strengthening the capacity of health technology assessments, for both the Norwegian Medicines Agency and the Norwegian Knowledge Centre for Health Services.

19.4.3 The main stages of the system

The system can be divided into four main stages, cf. Figure 19.3. All four stages of the system are under development and gradually implemented. It will be appropriate to evaluate the system when all steps have been implemented and tested. The system for new health technology is under development and will be continuously evaluated and improved through dialogue with stakeholders, patient organisations, professional communities and the industry. The Ministry will be assessing any changes to the system, including the need for possible exemption arrangements, during the work on the White paper on priority setting.

Figure 19.3 Main stages of the national system for the introduction of new methods

The following describes initiatives that have been, or are currently being implemented, with particular emphasis on the area of medicinal products.

Proposals, technology notification and assessment

Anyone can submit a proposal indicating the need for a technology assessment at a national level for technologies that are relevant to specialist health care services. Health technology assessments for medicinal products must always be conducted at a national level. A total of 72 proposals for national health technology assessments were submitted by December 2014. Of these 72 proposals, 55 were with respect to medicinal products. The Ordering Forum for regional health authorities gave instructions for a single technology assessment in most of the cases, and for a full technology assessment of three therapeutic medicinal product areas to compare the treatment options.

Horizon scanning reports are reviews of new and potentially significant technology. Horizon scanning is intended to ensure that new and important technologies/methods are identified and prioritised for health technology assessment as early as possible. The Ministry has commissioned the Norwegian Knowledge Centre for Health Services to lead and develop the efforts on implementing the horizon scanning system. The project plan was completed in the autumn of 2014, and the horizon scanning notifications were piloted in December 2014. The horizon scanning system is now in its first pilot stage in 2015, and will be evaluated after one year of operation.

Horizon scanning reports are carried out by the Knowledge Centre in cooperation with the Norwegian Medicines Agency. It is estimated that around 10–15 horizon scanning reports will be made per month. When the technology has come far enough in its development that it may be appropriate to conduct a technology assessment, this will be reported to the Ordering Forum in a proposal for technology assessment. One of the goals of the horizon scanning is to shorten the system's response time to new technologies, so that they can be applied as soon as possible.

Assessment agencies have a maximum period of 180 days to complete a single technology assessment. This deadline applies from the time the documentation is received from the suppliers.

To ensure the best possible basis for decisions, suppliers are given the opportunity to comment on conducted health technology assessments reports. Any comments from the suppliers will be published in the case documents. It will later be determined whether this will also apply to comments from other stakeholders in the future.

Decisions

Once a health technology assessment has been made, the Decision Forum makes a joint decision for the regional health authorities on whether the technology will be used as a standard treatment method throughout in the entire country. The Decision Forum is comprised of the directors from each of the four regional health authorities, and the Forum was established after a joint board decision made by the regional health authorities.

The Decision Forum has determined that the decisions that are made will be based on the current criteria for prioritisation in the Norwegian health services. The Decision Forum has monthly meetings, and its decisions are made public. The Norwegian Directorate of Health is responsible for incorporating these decisions in the national clinical guidelines and cancer action programmes.

The Decision Forum has determined that new technology undergoing health technology assessment cannot be implemented or used in the evaluation phase. This ensures equal treatment of patients, regardless of where they receive treatment, or who their treating physician is, and follows the principle of one door in for medicinal products for ordinary clinical use. The Decision Forum is still open to exceptions to this rule, if all the directors of the regional health

authorities approve previous use. Such an exception was made to allow temporary permission for autologous stem cell transplants as treatment for MS in the Helse Bergen health trust, pending the assessment of this technology and its decision.

The regional health authorities are conducting negotiations with suppliers for new health technologies. The Decision Forum for the regional health authorities has stated that they will carry out an evaluation of the negotiation structure and take a closer look at the conduction of future negotiations as a basis for creating a good framework for agreements with suppliers, and for streamlining the negotiation processes. The system for introducing new technology must be viewed in relation to the task the regional health authorities were given in the health trust protocol in January 2015, with respect to the establishment of a national procurement organisation.

Implementation

The Norwegian Directorate of Health is working to develop measures for the evaluation and monitoring of the use, adherence to, and the effect of new methods and health technologies. Evaluations and the use of quality registries will also be important instruments in implementing the system. The system will also be able to detect the need for a better evidence base for making final decisions, or when it is necessary to conduct follow-up trials after the technological method has been implemented, cf. discussion in Part VI. In the event of new or better data, through Phase IV clinical trials, for instance, it may be necessary to re-evaluate the health technology assessments, cf. Chapter 22.

19.4.4 International cooperation

International cooperation has been established for the development of cooperative platforms and networks for the systematic introduction of medicinal products and technology in general, Health Technology Assessment (HTA), work on guidelines, etc. Stakeholders in the national system are participating in these efforts. One of the networks that include all EU member states, as well as Norway and Iceland, has developed a joint European strategy meant to encourage a more consistent use of HTA and to optimise the use of resources by avoiding duplications of technology assessments.

WHO has emphasised the significance of HTA in a global perspective through the resolution “Health intervention and technology assessment in support of universal health coverage” which was adopted at the World Health Assembly on 24 May 2014. This resolution refers to the 2010 World Health Report, which indicates that as much as 40% of the resource efforts in the field of health are ineffective, and that there is a need to strengthen the rational use of health technology.

19.4.5 Initiatives for continued development

Based on experiences with this system, there is a need for continued development of the following selected areas:

- Transparency, accountability and user involvement.
- Clarification of structure and capacity.
- Systematic and predictable selection of methods for health technology assessment.
- Coordination of the national system and procurement processes and organs in the regional health authorities.
- Systematic use of professional and patient environments in health technology assessments.
- Systematic evaluations of new and existing technology
- Use of health technology assessments that have already been performed in other countries, to avoid duplication.

19.5 Division of financial responsibility between National Insurance and regional health authorities

Financing of medicinal products is currently divided between the regional health authorities, municipalities and the National Insurance Scheme. Generally, the regional health authorities are responsible for expenses for medicinal products used under hospitalisation and for out-patient treatment. Municipalities are responsible for medicinal product expenses in municipal institutions, and the National Insurance Scheme provides reimbursement for medicinal products used outside the hospital and municipal institutions.

Box 19.1 Principles for transfer of financial responsibility

The following principles underlie the Norwegian Parliament's decisions on the transfer of financial responsibility for medicinal products from National Insurance to hospitals, cf. Prop. 1 S (2013–2014):

- Risk of a shift in consumption: Different financial systems can result in choosing medicinal products based on economic and not medical considerations.
- More correct prioritisations: Hospital physicians are often the best qualified for making correction prioritisations for patient treatment in their area of expertise.
- Lack of price competition: It will be possible to achieve price competition between medically equal medicinal products through, for instance, hospital tenders.

In more recent years, there have been exceptions to the primary rule that the National Insurance Scheme covers medicinal products used outside the institution, whereby certain medicinal products that are picked up from the pharmacy by the individual patient are financed by the hospital. In 2006, the Norwegian Parliament made the decision to transfer financial responsibility for the medicinal product group of TNF-inhibitors from National Insurance to the regional health authorities. This is a group of biological medicinal products used in the treatment of certain

inflammatory conditions, such as rheumatoid arthritis. In 2008, financing for medicinal products used in the treatment of multiple sclerosis was transferred to the regional health authorities, and in 2014, the financial responsibility for certain cancer medicines was transferred from National Insurance Scheme to the regional health authorities.

These medicinal products are prescribed by hospital physicians or private practice specialists that have agreements with health authorities. Patients pick up these medicinal products at the pharmacy. The Norwegian Directorate of Health is considering new medicinal products for these areas of use, and whether these may represent alternatives to the existing medicinal products already financed by the hospitals. The Norwegian Directorate of Health will make decisions regarding the financial responsibility for these new medicinal products, and whether it should be placed with the health authorities.

Box 19.2 H-prescription scheme

The H-prescription scheme was established for medicinal products that can be administered by patients themselves, but where the expenses are covered by the regional health authorities.

The H-prescription scheme builds on a solution involving direct payment between the pharmacy and health trust (hospital). The patient receives the H-prescription and can pick up the medicinal product from the pharmacy of his/her choice. Both prescriptions and invoices exchanged between the health trust and pharmacy are currently paper-based. Once invoice information is received, the health trust performs random control checks before reimbursing the pharmacy.

In December 2014, the Ministry submitted a proposal for public consultation regarding the regulations on health trust-financed medicinal products for use outside the hospital. The purpose of the regulations is to facilitate the follow-up of physician prescriptions and correct financial reimbursement from the health trust to the pharmacy. These will regulate the prescribing and dispensing of H-prescription medicinal products, and the management of health information in relation to the financial reimbursement. The regional health authorities are preparing an electronic reimbursement system for H-prescriptions and plan a pilot project that will start up in 2015.

It is difficult to define clear criteria to determine the division of financial responsibility for medicinal products between the National Insurance Scheme and the regional health authorities. Medical technology and treatment are continuously undergoing changes, resulting in grey areas with respect to responsibility, as well as shifting boundaries for this responsibility over time.

The government wishes to continue its efforts to define criteria for the transfer of financial responsibility for medicinal products from the National Insurance Scheme to the health

authorities in those cases where there are challenges with a division of financial responsibility. The government is aware that transferring financial responsibility for single medicinal products or groups of medicinal products may be expedient, even if all three conditions are not apparent (cf. Box 19.1). This may be relevant when it is obvious that the initiation, evaluation and conclusion of patients' medicinal treatment is performed by a physician in specialist health care services, and there is competition between several medicinal products within one therapeutic area. Possible proposals for the transfer of financial responsibility for medicinal product groups will be reviewed in the annual national budget, and thereafter submitted to the Norwegian Parliament.

19.6Vaccines

19.6.1 Current system for reimbursement of expenses for vaccines

Vaccines in Norwegian Childhood Immunisation Programme are currently covered by public authorities in accordance with the provisions of the National Immunisation Programme. The Norwegian Institute of Public Health provides professional guidelines for the implementation of the National Immunisation Programme, including the vaccines that should be offered through the programme, and the target groups for vaccination. The Norwegian Institute of Public Health procures vaccines after a tender competition and distributes these at no cost to the municipalities. Vaccines are offered for free to the public, usually through the public health station and school health services.

Regulations regarding the National Immunisation Programme also apply to vaccines against seasonal influenza (and pandemic influenza). These vaccines are offered each year to individuals with a high risk of complications from influenza. The Norwegian Institute of Public Health identifies the risk groups, procures the vaccines following a tender competition, and sells these at full cost to the municipalities. The municipality organises the vaccinations in the most suitable manner, to ensure the highest possible vaccination coverage. Municipalities are permitted to charge a fee for such vaccinations. The vaccination process is either organised by the municipality at the public health stations, in the form of a mass vaccination programme, or they are performed by general practitioners who may also charge for this service.

The National Insurance Scheme reimburses medicinal products used for communicable diseases for those who reside in Norway, even if the individual is not a member of the National Insurance Scheme, in accordance with Section 4 of the Regulation for reimbursement. Vaccines are reimbursed in accordance with Section 4, point 3 of the Regulation for reimbursement. The regulation includes a table listing the vaccines, etc. that are reimbursed for various diseases and indications. For hepatitis A and hepatitis B, the table refers to indications in the guidelines by the Ministry of Health and Care Services. As specified in the regulation, these vaccines are requisitioned from the Norwegian Institute of Public Health, which will assess whether the indications are in accordance with the provisions of the regulation. Vaccines prescribed through

the reimbursement scheme are not procured through tender, due to low volume, and because there is often only one supplier. These vaccines are dispensed by the Norwegian Institute of Public Health and sent at no cost to health care personnel who will be administering the vaccine.

The regulation allows for the reimbursement of vaccines, as stated in the general provisions of the Regulation for reimbursement, Sections 2 and 3. It is necessary for each individual patient to meet the criteria for a serious disease, or the risk of a serious disease. Vaccines intended for use on large population groups will normally not meet these criteria. Travel vaccines are not reimbursed by the authorities.

Detailed information about the Norwegian Childhood Immunisation Programme

The Act Relating to the Control of Communicable Diseases states that the Ministry shall establish a national programme for vaccination against communicable diseases. The Childhood Vaccination Programme is regulated by the Norwegian Regulation relating to the National Immunisation Programme. This programme is offered to all children of preschool and compulsory school age, and is carried out at the public health station and in school health services.

The Norwegian Childhood Immunisation Programme was set up in 1952, and currently recommends vaccines against 11 different diseases: diphtheria, tetanus, pertussis, poliomyelitis, measles, mumps, rubella, infections from Haemophilus influenzae type b (Hib), The Norwegian pneumococcal vaccine, human papillomavirus (HPV) and rotavirus infection. Vaccines against tuberculosis (BCG) and hepatitis B for children in risk groups are also offered.

To offer a medically sound childhood vaccination programme, there are systems that monitor vaccination coverage, incidences of adverse reactions (side-effects) after vaccinations, as well as the effect of vaccinations. This is achieved through the following:

- The SYSVAK registry is a nationwide electronic vaccination database containing an overview of the vaccination status of individuals and the vaccination coverage throughout the country.
- Adverse reactions to vaccines are followed up by use of the SYSVAK registry and the adverse reaction registry through cooperation between the Norwegian Institute of Public Health and the Norwegian Medicines Agency.
- Effects of the vaccines that are included in the Childhood Immunisation Programme are currently monitored by comparing data from the SYSVAK registry with the data from MSIS (the Norwegian Surveillance System for Communicable Diseases).

When combined with international data, this provides a solid evidence base for information activities associated with the Child Immunisation Programme. It is essential to make this knowledge available to parents to help them make informed choices, and to maintain public trust in the programme.

Figure 19.4 MMR vaccines in the various age groups

Norwegian Immunisation Registry SYSVAK

Figure 19.5 HPV vaccines, 16-year-olds fully vaccinated

Norwegian Immunisation Registry SYSVAK

We have a high level of participation in the Child Immunisation Programme in Norway, and there are continuous efforts to maintain this level. A review of the national vaccination coverage in 2014 (SYSVAK registry), shows that most children and adolescents in Norway are receiving the vaccines recommended by the Child Immunisation Programme. Vaccination coverage against measles, mumps and rubella (MMR) has remained stably high. As per 31 December 2014, 94% of the country's 2-year-olds, 95% of the country's 9-year-olds, and 94% of the country's 16-year-olds were fully vaccinated against measles, mumps and rubella. The vaccine with the lowest coverage is the vaccine against human papilloma virus (HPV), which was introduced as a vaccine for all schoolgirls in year 7, from the 2009/2010 school year (girls born in 1997). The 2014 SYSVAK registry shows an increase in the proportion of 16-year-old girls who are fully vaccinated against HPV infections of 9% compared with the previous year. However, this coverage is still under 80%.

One of the success factors of the vaccination coverage and Child Immunisation Programme, is the personal contact between public health nurse and parents. Parents are given suitable information, and can ask questions and discuss any concerns or express any scepticism they may have.

19.6.2 Assessment of new vaccines

The Norwegian Institute of Public Health shall, in accordance with the Act Relating to the Control of Communicable Diseases, monitor the epidemiological situation and advise authorities of communicable diseases, infection control, and the choice of infection control measures. In accordance with the Regulation of the National Immunisation Programme the Norwegian Institute of Public Health provides professionals with guidelines for conducting the National Immunisation Programme, including the vaccines that should be offered through the programme, as well as the target groups for vaccination. It may, however, be somewhat unclear as to which vaccines are recommended, and which vaccines are paid by the authorities. Several new therapeutic vaccines are also anticipated in the coming years. Specific criteria for vaccine coverage, as stated in the Regulation for reimbursement, and the date for including the vaccines in the National Immunisation Programme, should therefore be reviewed.

Furthermore, it has not yet been determined which provisions of Regulation for reimbursement

are to be used for possible reimbursements for the new therapeutic vaccines. The government must review the current financial systems for vaccines.

When a new vaccine is considered for introduction into the Child Immunisation Programme, the Norwegian Institute of Public Health establishes a working group with internal and external participants. This working group prepares a report to be submitted to the Ministry of Health and Care Services. Health economic assessments are generally not one of the working group's mandates. These are usually carried out by external institutions, such as the Knowledge Centre for Health Services. The Council for Quality Improvement and Priority Setting in Health Care will participate in the assessment of population-centred measures such as screening and vaccines. The Ministry of Health and Care Services will consider the recommendation and possibly submit a proposal to the Norwegian Parliament defining the way in which the vaccine should be included in the Child Immunisation Programme. If a vaccine is to be removed from the programme, or if different population groups are to receive a vaccine that is already in the programme, the process will be handled in a similar fashion.

The current system functions adequately, but with certain deficiencies:

- There is no mechanism for assessing new vaccine needs, including a system for the early identification of potential vaccine candidates (horizon scanning).
- There is no long-term plan for continuous updates to the National Immunisation Programme.

The government will evaluate the establishment of a more robust system to assess the introduction of vaccines by public authorities. This must be viewed in context with systems for new methods in specialist health care services and systems for the assessment medicinal products through the reimbursement scheme.

19.6.3 Vaccination across the life span – an immunisation programme for adults

There are currently no standardised programmes for vaccinating the population apart from the Child Immunisation Programme, apart from seasonal influenza vaccines for the elderly and specific target groups. Young adults in need of vaccinations are a difficult group to reach. Standard vaccination of adults may be needed for both immigrant groups and ethnic Norwegians alike.

By following the success of the Child Immunisation Programme, and establishing an adult immunisation programme, it would be easier to follow through on recommendations especially aimed at adults. Examples include meningococcal vaccinations for adolescents and young adults, HPV vaccinations for young women, and vaccines against influenza and rubella for pregnant women. Recommended vaccines for the elderly would also be easier to provide through an adult immunisation programme, such as pneumococcal vaccines, seasonal influenza and herpes zoster.

The government will evaluate the establishment of an adult immunisation programme, similar to the Child Immunisation Programme. Its facilitation and prioritisations must be further evaluated.

Box 19.3 To ensure equal and fast access to effective medicinal products, the government will:

- Evaluate the system of pharmacist dispensing in pharmacies.
- Propose that the Norwegian Medicinal Products Regulation, Section 14-14, subsection 1, letter a (substance addiction) and letter d (erectile dysfunction) be revoked. This proposal will be submitted for hearing in the autumn of 2015.
- Discontinue the general requirement of specialist instituted treatment for applications regarding individual reimbursement.
- Discontinue the Forskningsblå scheme.
- Revise Section 4 of the Regulation for reimbursement.
- Continue efforts to define criteria for transferring financial responsibility for medicinal products from National Insurance Scheme to the regional health authorities in those cases where there are problems with shared financial responsibility.
- Allow certain medicinal products or medicinal product groups, for which specialist health care services have medical responsibility, to be transferred from the National Insurance Scheme to the regional health authorities, subsequent to special assessment, even if certain criteria for transfer have not been met.
- Review the current funding system for vaccines.
- Evaluate the establishment of a more robust system for assessing the introduction of vaccines by public authorities.
- Evaluate a possible immunisation programme for adults, similar to the Child Immunisation Programme.

Box 24.1 To facilitate research and innovation, the government will:

- Establish a joint research programme for national clinical multicentre studies in the regional health authorities.
- Strengthen the research infrastructure for clinical trials through NorCRIN, expand the capacity of clinical trial units at university hospitals, and establish a separate point of contact for early phase clinical trials.
- Improve national research cooperation on clinical trials through research networks.
- Develop the helsenorge.no website to inform patients about clinical trials.
- Assess whether patient participation in clinical trials should become part of the results-based financing system for research in the regional health authorities.
- Continue and carry forward Nordic and international cooperation on clinical trials.
- Assist the pharmaceutical industry and research community with regulatory advice through the Norwegian Medicines Agency's advisory service Viril. The Norwegian Medicines Agency will cooperate with NorCRIN.