

The Speaker of the Lower House of Parliament

The States-General

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Date January 29, 2016

Regarding Medicines Policy Plan: New drugs available to patients fast at an acceptable cost

Dear Speaker,

Medicines play an important role in the quality of life for many Dutch people. Diseases which were once terminal are now treatable thanks to medicines. People recover more quickly, can continue to work even though they are ill, or can continue to live on their own. Think of the roughly one million people with diabetes who thanks to medicines can play an active role in society, or of the 100,000 children with asthma who thanks to inhaled medication can take part at school, or of the roughly 4 million Dutch people who reduce their risk of heart and cardiovascular disease with blood pressure medication and cholesterol-lowering drugs. Or think of people with cancer, with complicated or rare diseases, who enjoy a better quality of life thanks to ever improving drugs.

Medicines are thus inseparably tied to the quality of healthcare in The Netherlands. In recent years, together with insurance companies, pharmacists, doctors, hospitals, patients and pharmaceutical companies, we have been able to offer patients a broad range of pharmaceutical care while at the same time controlling the cost of medicines, thanks in part to an attractive climate for innovation.

Responsibility for controlling the costs of healthcare rests for a large part with healthcare providers and insurers. They have managed to keep costs down due to a regulatory mix: first and foremost because insurers use selective drugs procurement through the so-called preference policy, in which patients are prescribed equivalent generic drugs. Hospitals' procurement of medicines has also played a part. These hospitals purchase drugs using funds from their own budgets and thus have an interest in price negotiations and cooperative procurement. That is why various medicines in the Health Care Insurance Act not paid for by hospitals have now been brought under the hospital's financial responsibility. We are also continuously looking into the proven efficacy of medicines in the basic insurance package in order to determine whether they still meet the criteria for reimbursement. Finally, for the last three years we have negotiated with drugs manufacturers regarding the price of expensive medicines. This was done primarily with drugs supplied outside the hospital and only in the rare situation that a medicine comes on the market for which no alternatives exist and which threaten to eat up a large percentage of healthcare spending. Thanks to this mix of regulations, in the last few years the cost of drugs has remained limited to approximately 9 percent of the total healthcare budget. This in part explains why healthcare costs, instead of going over budget as they have for years, are in fact now coming in under budget.

This success notwithstanding, it is time to set a new course. The field of medicines is undergoing a period of rapid development. For years, advances in the improvement of drugs took place gradually. Now developments are occurring in a rush, partly thanks to new technologies. New drugs are offering new prospects for many people with serious diseases which had been nearly untreatable, such as lung cancer, cystic fibrosis and hepatitis C. They are cured, or live longer, but even more importantly: they have a better *quality* of life. This has happened, for instance, for people with rheumatism and MS and rare diseases. And this does not just concern the elderly, but also affects young people in their prime of life. This is fantastic news.

At the same time, it presents us with major dilemmas. This is because the costs of these new drugs are extraordinarily high, in some cases 500,000 euros per patient for one year.

The instruments which we have successfully used to date to assure accessibility of new drugs and limit costs are no longer sufficient. The reasons are as follows:

- Patients want accelerated access to innovative drugs, particularly when they have no alternative and it is a question of life and death. The current system of market authorization offers insufficient possibilities for this.
- More and more innovative drugs are being developed for very small numbers of patients, drugs which are ineffective for other patients with the same disease. In the current market authorization system, these drugs are not given enough chance, due to which they do not reach the patient, or reach them too late.
- Cheaper, generic alternatives are not yet available for new drugs that involve high costs.
- With a global market share of about 2 percent, The Netherlands has little leverage to influence the behaviour of pharmaceutical companies operating globally or the price of their products.
- In a market where medicines are largely paid for through insurance premiums, the profit-oriented industry does not make drugs pricing very transparent. This makes a sensible discussion regarding socially acceptable drugs prices that much more difficult. It does not help that numerous countries in Europe make confidential price agreements.
- A price can be determined based on the costs of developing and producing a drug (development costs, developments that fail, etc.), based on the added value of the drug in the treatment of the patient, or based on the estimate of what society is prepared to pay.
- Undesirable use is made of instruments meant to promote innovation. Pharmaceutical companies are protected at various levels by patent laws and supplementary protection mechanisms such as market protection for orphan drugs. These protective mechanisms were, at the time they were adopted, meant to encourage innovation and are partly responsible for the birth of new effective drugs. In this context the instrument worked well. However, as the Consumer and Market Authority (ACM) noted in a report¹ last year, the industry now sometimes makes undesirable use of the available protection in order to maximize profit from a product.
- With the newest generation of biological drugs in particular, the relationship between innovation and a reasonable, socially acceptable price is absent.
- The amount of money for new products is extremely large, which threatens other healthcare spending.

¹ "Pharmacy Under Scrutiny", Consumer and Market Authority (ACM), February 2015

In short, due to various regulations important drugs have come on the market, but the growth of increasingly expensive drugs is putting more and more pressure on the affordability, and with that the sustainability, of the healthcare system. The current system of development and commercialization of drugs is tough to maintain. One way or another, the bill has to be paid: by an increase in the insurance premium, through a higher deductible or higher income-dependent premium, by denying patients access to certain new drugs (by not reimbursing for them) or by removing other types of care from the basic insurance package.

In my plan, therefore, keeping innovative drugs *accessible* for *acceptable prices* is central. I want to achieve a stronger negotiating position for the purchaser in order to compel that the price of a drug comes into a better balance with its actual cost and added value. In addition, I want our system to offer sufficient room for new developments and innovations. At the same time, the costs should remain acceptable for the premium payer in the long term and the patient must be assured that he is receiving the care he needs.

This corresponds with the cabinet's goal to continue giving renewal a chance, even with the fast pace of innovation, while at the same time guaranteeing public interests such as safety, quality, reliable care and affordability².

It starts with making clear choices: what drugs do we really need? And how do we deal with drugs which come on the market? If the government is prepared to assume the risks of getting new products to the patient in a timely manner by accelerating market authorization or conditional reimbursement, then the government also need to clarify under what conditions we are prepared to do so and what costs we find acceptable. When drugs have a limited added value for our healthcare, we also should make clear that our willingness to continue to pay high prices is limited.

This is only possible if we know what patients and doctors need when it comes to the development of new drugs. We need to look at the sector much more strategically and consciously. In order to be an equal partner in the global pharmaceutical industry, governments (national and at the EU level) need to share expertise and information and cooperate wherever possible.

With all of this in mind, we seek to initiate a sustainable change in the pharmaceutical sector. We will push for a different approach to drugs development and the way drugs are brought to market. Traditionally, the pharmaceutical industry's revenue model is based on optimal use of market exclusivity. Therefore, we need to be open for *alternative business models*.

In this way we can enable researchers, entrepreneurs and healthcare organizations to work on valuable products for suitable prices. These are also products which in the current revenue model are not always seen as attractive commercially.

The cabinet is a proponent of healthy entrepreneurship and recognizes the contribution the pharmaceutical industry has made to patient care. That's why we want to conduct a discussion with the industry on how they can actively contribute to the sustainability of healthcare and innovation in the long term. We owe this to patients who are acutely dependent on the products the industry brings to market.

Our funding system needs to continue to provide sufficient space for innovation, but should also be geared toward controlling costs. In addition to adjustments aimed at generating pressure on prices such as can be expected in a free market, parties such as healthcare providers and insurers have a

² Also see the recent cabinet letter to the House of Representatives 'Room for innovation and renewal through future-proof laws and regulations' (session 2014-2015, 33 009, no. 10).

substantial role to play. They need to contribute to the solution to this collective problem of drugs prices. As the government, we need to enable these parties to the greatest extent possible to procure medicines efficiently. However, providers and insurers also have the crucial task in the coming years to do their utmost to ensure the responsible use of drugs. This will lead not only to improved quality of care but also to controlling costs.

European cooperation is an important condition for a system of sustainable drugs provision. Member states, through voluntary cooperation, can take a stand to bring about the necessary changes in market authorization, regulations governing supplementary market protection in addition to patent law, and reimbursement. If we are successful, we will ensure an attractive drugs market and the right care for patients for the long term.

The complexity of this subject and the international landscape we find ourselves in requires a multifaceted approach. Both for the short and long term, domestically as well as internationally. We are convinced that it is possible to achieve national and international results if we focus on the common interest of all parties involved: patients want access to innovative medicines, doctors want to proscribe these medicines, governments want to guarantee quality care for a fair price and the industry wants to sell new medicines and hence receive reimbursement from insured care.

In this letter, I am setting out the cabinet's plan and how we will implement it. Towards this end we have solicited the advice of the Dutch Healthcare Authority (NZa) and the Dutch Cancer Society (KWF)³ on expensive drugs, as well as the recent the Consumer and Market Authority (ACM) report 'Pharmacy Under Scrutiny'. At the same time, we are looking into the division between intramural and extramural drugs provision and the structural application of the sluice for intramural drugs, including the criteria employed for the sluice. In addition, through this letter we are following through on the motion of MP Leijten (SP) (Proceedings of the lower house 29477, n 301), the motion of MP Van Dijk (Labour Party) (Proceedings of the lower house 29477, n 339) and the motion of MPs Van Dijk (Labour Party) and Bruins Slot (CDA) (Proceedings of the lower house 29477, n 337). In addition, in this letter we provide follow-up to the reaction to the report 'Insurance package management of orphan drugs' from the National Health Care Institute (ZiNL) and we react to the advice from The Dutch Advisory Board on Regulatory Burden's (Actal) about regulatory burden related to authorization of drugs to the reimbursement system.

Regarding the recent motion by MPs Voortman and Bouwmeester, in which the cabinet, upon forwarding the medicines policy plan, is requested to inform parliament as to which interested parties influenced the realization and content of this medicines plan, I can report to you the following. During the process of developing the plan, a number of meetings were organized with government parties and external parties in order to discuss the plan's goal. The *government parties* included organizations which are part of the 'medicines chain' (Central Committee on Research Involving Human Subjects (CCMO), Netherlands Pharmacovigilance Centre Lareb, Medicines Evaluation Board (CBG), The Health Care Inspectorate (IGZ), the Central Information Unit on Health Care Professions (CIBG) and the National Institute for Public Health and the Environment (RIVM)) as well as the National Health Care Institute (ZiNL) and the Dutch Healthcare Authority (NZa). External parties included the pharmaceutical branch organization KNMP; Dutch Generic and Biosimilar Medicines Association (Bogin); healthcare insurers Achmea, Menzis, CZ and VGZ; the Association for

³ Investigative report – 'Accessibility and affordability of medicines in specialist medical care', the Dutch Healthcare Authority (NZa) (29 June 2015) and advice – 'Effective new anti-cancer drugs, but the financing system is creaking at the seams', Dutch Cancer Society (KWF) (2 June 2015).

Innovative Medicines in The Netherlands (Nefarma); the Dutch biotech industry interest group HollandBio; the Federation of Patients and Consumer Organizations in the Netherlands (NPCF); Dutch Hospital Association (NVZ); the Netherlands Federation of University Medical Centres (NFU); the Dutch Association of Medical Specialists (FMS); and the branch interest groups for hospital pharmacists and policlinic pharmacists, the NVZA en NVPF). In addition, individual representatives of healthcare institutions, professional groups, academic institutions, top sector firms and patients were approached⁴.

⁴ Given that the MPs' request was not made in advance, there is no guarantee that the list is exhaustive.

1. New business models and innovative products

The importance of innovation

Policy, whether current or future, must continue to stimulate innovation. In addition to a favourable research climate, The Netherlands should also make it possible to experiment with business models which contribute to a more sustainable development model for drugs: The Netherlands can be a breeding ground for new business models.

Many diseases are impossible to treat at the moment. There are high hopes for breakthrough therapies, especially for those diseases associated with a high level of suffering or with rapid deterioration. We actively support basic research, in particular into rare diseases with little prospect for innovative remedies. I explained this in the innovation letter sent on 5 October 2015, and I described our plans for the role of the VWS in the top sector *Life Sciences and Health* (LSH)⁵.

Top Sector Life Sciences and Health

The Dutch top sector Life Sciences and Health (LSH) is doing extremely well. Experts agree that the ingredients for recent, as well as future, success include the following: excellent scientific research, increasing attention for converting new scientific insights into valuable products, an ever increasing number of entrepreneurial scientists, and the availability of venture capital investment.

The measures necessary to achieve acceptable prices should not, as far as we are concerned, needlessly interfere with the successful Dutch business climate in the life sciences.

Attach conditions to collective financing of research

The Netherlands enjoys a high level of quality when it comes to researchers and scientific disciplines: top level research is done in a wide array of fields. The prominent place the theme 'Disease and Health' (including research into drugs and diagnostics) holds in the Dutch National Research Agenda⁶ demonstrates that there is broad support and appreciation in the Netherlands for university research and so-called spin-offs from universities.

This often involves public money. At some point, successful initiatives are taken over by pharmaceutical companies. This says a lot about the quality of our institutions. However, at the moment that such successful initiatives lead to new products which are brought to market at high prices, we need to **prevent the Dutch taxpayer from paying double for the same drug**.

So far, research has been financed through subsidies which do not need to be paid back, even when commercial success is a direct result of the research. Plus, no conditions exist regarding how the price structure of the developed product is set. **From now on, I will set conditions on collective financing for drugs development and innovation (for instance, from a Netherlands Organisation for Health Research and Development (ZonMw) programme).** The cabinet will look into how best to set these conditions.

⁵ <https://www.rijksoverheid.nl/actueel/nieuws/2015/10/05/schippers-gaat-innovatieve-nederlandse-zorgbedrijvigheid-inter-nationaal-stimuleren>, in Dutch.

⁶ Cabinet Reaction to the Dutch National Research Agenda, Ministry of Education, Culture and Science, reference number 852987 (27 November 2015).

In certain sectors, some are calling for Open Access to publications and optimal access to research data as the best option to encourage innovation. This can be true for drugs as well. In addition, we can set a condition that in the event of a commercial success, the public investment is either paid back into the subsidized research programme or that the profit is shared. It is our position that conditions can also be tied to the price structure of the developed product. We are considering professional Technology Transfer Offices at research institutions which would ensure that research gets put into practice in producing affordable products and which would oversee profit sharing with public institutions.

Case study – Public investments lead to commercial successes

Various examples demonstrate that thanks to Dutch subsidies, drugs have been developed and brought to market by private parties for sky high prices. Recent examples are Myozyme and Glybera. Glybera was developed with the assistance of a Netherlands Organisation for Health Research and Development (ZonMw) subsidy in the programme 'Transnational Gene Therapy Research'. It is the first gene therapy product granted authorization for the European market. Certainly, this is a splendid success for this ZonMw programme. But the flip side is that Glybera's manufacturer charges € 1.1 million per treatment and the money from the relevant ZonMw programme has been disbursed⁷. Myozyme has been developed, thanks to publically funded basic research at Erasmus University, to treat Pompe disease. Although the Erasmus University Medical Center received compensation thanks to the transfer of technology, the drug earns tens of millions of euros annually, in the Netherlands alone € 50 million. These examples beg the question: are we paying double?

Promoting alternative business models

For some diseases or product clusters, the earnings model for traditional companies is not auspicious. This concerns diseases for which, even under the current patent protection regime, development and production of new products is not viable, nor is developing certain orphan drug alternatives. The most obvious of these is antibiotics. There is a great demand for new drugs due to increasing resistance to existing antibiotics. However, these new antibiotics must be used as selectively as possible. At the same time, it is crucially important to keep older, still effective antibiotics on the market as long as possible. The current business model for the development of new antibiotics therefore is widely seen as a model which fails to generate an adequate return on investment. In turn, the existing medicines earn very little. With this in mind, in an international context we argue for offering sufficient impetus for companies to keep developing these essential medicines in addition to producing existing drugs. This corresponds with European and global initiatives aimed at developing new business models, bundling funds and collaborating with the pharmaceutical industry which aims to develop new antibiotics or their alternatives.

Our ambition concerning new models extends further. The current model in which companies occupy their market position by means of intellectual property law and patent protection, and in which earnings are high, appears to be reaching its limit. **We seek to create space for new ideas,**

⁷ Manufacturer Chiesi has set the price for treatment of one patient in Germany at € 1.1 million.

cooperative associations and models for developing drugs and bringing them on the market at a socially acceptable price. We are eager to discuss this with the pharmaceutical industry. We will also support initiatives that make use of innovative business models in order to develop and produce (orphan) drugs, as the National Health Care Institute (ZiNL) has advised me⁸. An example of this type of initiative is Fair Medicine⁹, where this is occurring in cooperation with various interested parties including prescribers, insurers, patients, researchers and producers. These types of initiatives make it clear that transparency in justifying costs is possible. These types of initiatives and creative ideas deserve the chance to prove themselves. We will look into ways to encourage good proposals so they can contribute to a sustainable turn around in the sector.

2. Tackle the problem of undesirable high prices

General

Pharmaceutical care needs to remain affordable in the long term. The prices we pay for medicines need to continue to reflect the costs of development and production on the one hand, and the value to society on the other. Therefore, we will take measures to better control the price of drugs so that in the long term we continue to have room for new, innovative drugs. Domestically, I will improve parties' negotiating positions and, where necessary, I will introduce more price pressure in our financing system. Internationally, I am looking for partners to negotiate prices and to conduct a fundamental discussion regarding the sustainability of the current system.

The current system is unsustainable

The pharmaceutical sector is capital intensive. It has developed countless valuable drugs. In part thanks to private investments in Research and Development, it is possible to develop drugs and administer them to patients who otherwise would have had no hope for a good treatment.

That being said, the importance of shareholder value has led to tension between corporations' commercial interests and the interests of patients dependent on these drugs in getting access to them. It is not the patient's need or sustainable innovation, but the highest possible profit that seems to drive the industry.

We are seeing more and more examples of this: drugs with high costs per patient¹⁰, even though the added value is uncertain, or medicines with a high total cost projection that puts pressure on the affordability of care¹¹, while this is not in relation to the estimated cost of development, market registration and production. Examples also abound of unexplainable price rises for products already on the market for some time¹².

⁸ Advice insurance package manager orphan drugs, National Health Care Institute (ZiNL) (26 October 2015)

⁹ <http://fairmedicine.eu/> This involves a cooperative association with among others universities, prescribers, patients and companies with the goal to develop diverse medicines deemed commercially uninteresting.

¹⁰ See the case study 'Nivolumab' elsewhere in this letter

¹¹ See the case study 'Sovaldi' elsewhere in this letter

¹² The manufacturer Amco, which makes the drug 'Parnate', recently raised the price by more than €1000 'in order to bring the price more in line with the British': <http://www.skipt.nl/actueel/id23453-fabrikant-draait-prijsverhoging-parbate-terug.html>, in Dutch

This leads to a burdensome problem for patient access to these drugs¹³. The anticipated success of many new drugs in the manufacturing pipeline will only serve to exacerbate this problem¹⁴. In the end, it is not in the interest of the industry if its products are no longer reimbursed due to their high cost.

Case Study -- Sovaldi

In 2014 Sovaldi was the first of a series of new drugs for the treatment of patients with chronic hepatitis C virus (HCV). The drug was considered an important breakthrough in treating this disease. The National Health Care Institute (ZINL) advised that the drug be included in insurance reimbursement packages, but warned of the high costs. Based on the supplier's price, the average healthcare practitioner budgeted between € 48,000 and € 96,000 per patient for one treatment.

Sovaldi's high price structure led to criticism from governments and other healthcare payers around the world. Sovaldi became a symbol for the growing unease regarding the ever increasing prices of new drugs.

This case study is an example of the principle of value-based pricing which the industry often uses to legitimize prices of innovative drugs. According to the supplier, the price of Sovaldi was a reflection of the value for the patient (recovery, added quality-adjusted life-years, or QALY), and the economic value of avoiding HCV related medical costs in the long term.

In a value approach such as this, the price is justified based on what society is willing to pay for an added year of life or reduction of problems associated with a disease. This value approach differs fundamentally from an approach in which prices are justified based on a reasonable relationship between investment costs and development costs, reward for innovation and a reasonable profit.

In the case of Sovaldi, in which the provider used a value-based rationale to set the price between €48,000 and € 96,000 per treatment, volume appears to be subordinate. Spending on Sovaldi in Germany and France amounted in just the first year to hundreds of millions of euros. In a country such as Italy, with more than 70,000 known HCV patients, the total costs would come to about 4 billion euros. Keep in mind, we are talking about the cost of just one drug which has an enormous impact on pharmaceutical expenditure.

The Netherlands has an estimated 20,000 HCV patients. If the entire population of these patients were to be treated, the total cost would amount to 1.3 billion euros. This calls into question the provider's earnings model as well as the development costs and the price structure of the drug. If the price is justified based on the value of the treatment for the individual patient (who does not carry the cost him or herself, but has the drug paid for by an insurance collective), when brought out to include the whole population of patients, this type of price structure can lead to disproportionately high macro-economic costs. As a consequence, patients have limited access to drugs and/or other care is displaced.

¹³ See for instance chapter 2.2 ('Trends in pharmaceutical expenditure in the context of new medicines') pp. 28-29 of the WHO-report 'Access to new medicines in Europe' (2015), regarding rising drugs expenditures in OSCE countries in the period 2000 – 2009.

¹⁴ Moody's outlook for global pharmaceutical industry (September 2015).

In the end, in The Netherlands, as well as in other countries, payers get reimbursed for Sovaldi only once the provider has made price concessions through a financial agreement based on a price-volume ratio.

I feel it is important to work together with all interested parties to make sure drug prices are socially acceptable. I consider it my responsibility to enable all those concerned to make a contribution. Where necessary, I am taking measures myself to control prices and expenditures.

These measures extend over three levels: expanding purchasing power in the current system, nationwide measures, and international cooperation.

Facilitating cooperation in drugs procurement

At the national level I will better equip healthcare insurers and providers in the drugs procurement process. As the Dutch Healthcare Authority (NZA) report¹⁵, among others, shows, there are opportunities to improve cooperation among these parties.

Therefore, this past summer I took the initiative to reach administrative agreements, together with the relevant parties in the administrative consultation specialist medical care, to ensure affordability and accessibility of expensive drugs for the long term. The agreements are geared toward, among other things, improving the purchasing power within the system.

The starting point is better market information. A horizon scan should provide structural insight into what new expensive drugs are in the pipeline, about their indication expansion and about the expiration of the patent. The Ministry of Health, Welfare and Sport (VWS) has already drawn up such a summary. I am taking the initiative to further develop this horizon scan, together with healthcare insurers and providers, and to take it further so that this information can be useful to everyone: by healthcare providers and insurers to prepare for drugs procurement, by those involved with procurement in prioritizing which drugs should come under special price deals, and by practitioners and providers to organize care regarding new products. The procurement successes should result in a price decrease when indications are expanded and volume increases, in order to keep pharmaceutical care available to patients in the long term.

I seek to support healthcare insurers and providers by increasing the clout and expertise needed to negotiate effectively with the pharmaceutical industry. **To achieve this, I am establishing a platform for sharing expertise and information concerning the procurement of drugs.** Through this platform, parties can share their knowledge and experience and explore the possibilities for joint procurement allowed under the Dutch Competition Act. New and successful initiatives can be shared and evaluated.

In practice, we see various examples in which therapeutic preference policy is used. For instance, in hospitals where practitioners in conjunction with administrators and pharmacists choose which medicines they purchase. Medical factors take a leading role in these decisions, but price is also considered. This is already happening in, among others, the Sint Maartenskliniek. In addition, a new

¹⁵ Investigative report – ‘Accessibility and affordability of medicines in specialist medical care’, the Dutch Healthcare Authority (NZA) (29 June 2015).

initiative launched by healthcare insurer VGZ in South Limburg is a form of therapeutic preference policy. I applaud these initiatives because practitioners and other professionals are in the driver's seat.

Collaborative procurement

Hospitals and other parties can combine forces in the procurement phase. Group purchasing organizations are responsible for the procurement of multiple products and consumer articles. This is happening with increasing frequency with drugs procurement.

Case Study – Cooperation in procurement of drugs

The group purchasing organization Hospital Pharmacy Academic Hospitals (IZAAZ) was established in 2012. They attempt to bring about lower prices through collaboration. The number of pharmacies which participate differs depending on the drug. Each hospital maintains its own contracts.

In 2014 healthcare insurer Achmea announced, together with twelve hospitals, they would collectively purchase certain medicines (the so-called TNF alpha inhibitors), with an eye on keeping expensive drugs affordable. The approach survived assessment by a judge who ruled that the way this purchase was done did not violate doctors' freedom of choice.

Another example is the cooperation of six hospitals in the Santeon group. These hospitals have developed their own guidelines for care of patients who use so-called biologicals. On this basis, the hospitals jointly purchase these expensive drugs.

It was recently revealed that insurer VGZ in the Maastricht region had joined up with doctors and pharmacists in a project to procure medicine to treat lung disease for the entire region. Doctors and pharmacists have compiled a list of their preferred drugs. VGZ will ask the manufacturers for their bids. Since a number of equivalent products are on the market, it is expected that savings can be made without sacrificing the quality of care.

Healthcare insurer Achmea has launched a resolution for 2016 to jointly purchase expensive drugs with a number of healthcare providers through the 'Impact Collective Pharmacy'. This will yield both financial and qualitative benefits. Achmea wants to pursue the initiative for three to five years and expand it step by step.

Expertise regarding procurement cooperation and financial agreements legally allowed by the Dutch Competition Act is an important factor for these groups. **I have requested the Authority for Consumers and Markets (ACM) to establish guidelines** so parties can make better use of the possibilities afforded under the law.

I remain in intensive consultation with parties in the field to ensure that the administrative agreements achieve the desired results. In Appendix 2 you will find all the agreements and joint measures which emerged from the administrative consultation specialist medical care. With these measures I, together with the signatories, am carrying out a number of the recommendations in the

Dutch Healthcare Authority (NZa) and the Dutch Cancer Society (KWF) reports published in the summer of 2015 as a means of ensuring the accessibility and affordability of expensive drugs.

For an up-to-date overview of the expenditures for expensive drugs in hospitals and in order to examine the agreements made by healthcare insurers and providers and how they have implemented these agreements, I am setting up the Expensive Medications Monitor. The Dutch Healthcare Authority (NZa) will play an important role (see Appendix 2). This monitor should provide insight into prescription behaviour and variation among medical practices regarding expensive intramural drugs. To the greatest extent possible, I will include patients' experiences in this process.

Controlling the price of expensive drugs in the intramural setting is a joint responsibility for which we need to take advantage of all options. We also need to prevent differences arising among hospitals in the care they offer (differences that the patient may not always detect) due to the price of a drug. This is unacceptable; doctors should be able to provide the treatment necessary according to the latest scientific and professional norms, or else make clear that they are not in a position to provide this treatment. Since this involves the legal obligation known as 'the duty of care', the Dutch Healthcare Authority (NZa) therefore also needs to monitor these situations. This is an important responsibility for the institutions themselves and deserves close attention.

With this in mind, I am encouraging every hospital to establish a **medicines commission** in which administrators, practitioners, pharmacists and procurement managers can jointly discuss and determine their institution's policy regarding expensive drugs. There are already positive examples of this in practice, including the fact that healthcare professionals are actively implementing policy on responsible use and reducing waste of expensive drugs. Insurers can consider this in the procurement process as well. The comparison information available from insurers is therefore essential. I will also make agreements on how this comparison information can be put to better use.

Needed changes in the reimbursement system and insurance package management

I will work on our insurance package authorization and reimbursement system in order to achieve more effective price pressure. This applies to **both intramural and extramural** drugs in the Drug Reimbursement System (GVS).

Insurers play a valuable role in the efficacy of pharmaceutical care. The selective procurement of drugs, the so-called preference policy, has created the financial manoeuvring room to get new, expensive types of care to the patient. However, in the current system there are two groups of drugs for which price reduction is not happening in and of itself.

First of all, this involves new drugs which have as yet no competition (the price does not fall even as volume increases). Secondly, there are drugs whose price does not necessarily fall even when competition increases. In a free market, one would expect the price to fall in both these cases (as did occur in the case of TNF alpha inhibitors).

In order to achieve price pressure in the Drug Reimbursement System (GVS) and better account for truly innovative drugs, we are introducing a reimbursement discount. This is a discount on the reimbursement limit of a GVS cluster when an increasing number of mutually interchangeable products are in that cluster. Enough freedom of choice will remain for doctors to continue prescribing the right medicines, but if manufacturers do not lower their price, a supplementary co-payment can be introduced for the patient.

I have decided, first of all, to implement a thorough reassessment of GVS clusters which will include an upkeep of the current system. This offers a good foundation for introducing a reimbursement discount as a new impetus in the system. First, I will flush out more of the technical details. In doing so, I will keep in mind that healthcare insurers must continue to fulfil their role in procurement.

In addition to the existing medications reimbursement system, The Netherlands is implementing the Drugs Prices Law (WGP) for intramural and extramural drugs. The maximum price of a drug in the Netherlands is determined based on prices in four surrounding reference countries. Partly due to the confidential price agreements made by neighbouring countries, the effect of the price reference system has deteriorated significantly. After all, the actual negotiated prices are currently under the price level included in the WGP. Any gain from a potential change in the WGP would be quite limited and is not my priority. **Therefore, I will not modify the WGP in the short term.** During the Dutch EU presidency in 2016, in the EU context, I will take active leadership in the discussion about price transparency and European cooperation. It is worthwhile to know one another's negotiated prices. A recent study published in the Lancet¹⁶, under the leadership of the Antonie van Leeuwenhoek hospital, clearly demonstrated this. We need to take a good look at what role the price reference system in Europe can play in the long run. If we want to use the price reference system, it needs to provide added value.

At the moment we have two different systems of insurance package management in The Netherlands: a *closed system* for extramural medicines (pharmaceutical care) and an *open system* for intramural medicines (specialized medical care). An intramural drug flows into the basic insurance package automatically if it satisfies professional and scientific standards. This automatic system does not exist for extramural drugs. The existence of these two systems developed historically because cost control was particularly necessary for drugs used in extramural care. At this moment, I do not **see any advantage in having one system** for both markets. Transition costs are substantial and it is only of interest for the patient if the drug is included in the basic insurance package. Since more and more expensive intramural drugs are flowing into the basic package, my efforts at the moment are geared toward adaptation of the intramural system. The goal is to limit the principle of open inflow for certain expensive drugs, based on an assessment of risk.

Case Study -- NIVOLUMAB

The total expenditure on intramural (hospital) drugs amounts to about 1.5 billion euros annually. In June 2015 a drug was allowed on the market with a potential annual cost projection of more than 200 million euros for just one indication. Until that point, the most expensive drug had cost approximately 70 million euros. In order to guarantee patient accessibility and affordability of care for the long term, in July 2015 a so-called sluice was introduced for this medicine, Nivolumab. This meant the drug was moved out of the basic insurance package in order to enable price negotiations and to take care of appropriate use, by among other things setting up a register. In the wake of adequate agreements regarding appropriate use and positive negotiations, the sluice was opened and the medicine has been returned to the basic insurance package as of 1 March 2016.

¹⁶ 'Cancer drugs in 16 European countries, Australia, and New Zealand: a cross-country price comparison study', The Lancet Oncology Online (3 December 2015).

In the last few years I have gained experience in improving and closing financial agreements at the national level. This policy has proven a success in providing patients access to new drugs by controlling expenditures. Therefore, following the completed pilot phase, **I will provide a structural role for the Drug Price Negotiation Unit.** I will further expand the manner in which I use financial agreements to guarantee affordability. The unit's capacity will be enlarged to its budgeted size. Cooperation of the Drug Price Negotiation Unit with interested parties is being intensified. This involves cooperation *prior* to negotiations (for instance through setting priorities and estimating patient volume) and *after* negotiations (estimating the total cost projection).

The openly defined system for intramural drugs ensures a flexible insurance package and encourages innovation. Because of this, patients have the fastest possible access to the right care. At the same time, it is important that expenditures remain manageable. I see a risk primarily when it comes to expensive intramural drugs which potentially displace other necessary care. I will more frequently apply agreements, which are mostly used in extramural care, for intramural drugs. In 2015, to this end I introduced an instrument in the case of the drug Nivolumab (see case study elsewhere in this letter) in the form of the so-called sluice¹⁷. With this instrument, an intramural drug with a high financial risk is removed from the open inflow into the insurance package. In the period that the drug is put in the sluice, the Healthcare Authority (NZa) can make an assessment and agreements can be made regarding a financial agreement, responsible use, and further research. Only when there is an acceptable price and cost projection, and if there are sufficient guarantees for responsible use and good registration of efficacy, can this drug become accessible as insured care in the long term.

In 2016 I will further define the financial agreement instrument. This includes the legal basis for the possibility of temporarily placing a drug which falls under the Health Care Insurance Act formulation for performance medical care outside the basic insurance package. Moreover, besides the goal of the sluice, criteria and considerations will be established which determine in which cases a drug can be placed in the sluice.

In addition, in 2016 I will work out the technical details for how the **sluice construction** can be expanded through using the instrument to support decentralized (collaborative) procurement and price negotiations by healthcare insurers and/or providers. The medicine would wait in the sluice – just as with central price agreements – so that an adequate price can be negotiated. After which a decision about the insurance package can be made.

Finally, the National Health Care Institute (ZiNL) recently made recommendations for improvements in insurance package management of orphan drugs and at the same time described how the institute would further set up the assessment framework and process for orphan drugs.¹⁸ The advice provided a useful analysis of the context in which orphan drugs are developed, priced and administered. Many of the recommendations are in line with the policy measures I mentioned above. This includes the advice to expand international cooperation in guaranteeing the affordability of orphan drugs, to set up a horizon scan with prescribers and insurers and to place more emphasis on setting up registers, particularly for orphan drugs.

One subject in particular deserves more attention. This is the possibility to come to so-called '**orphan drugs agreements**' with professional groups regarding the administering of certain orphan drugs. These agreements can be made if the Health Care Institute (ZiNL) is of the opinion that extra attention is needed before an effective orphan drug can be authorized for the insurance package in a responsible manner.

¹⁷ Letter to parliament regarding a sluice for intramural medicines, reference number 794299-139107-GMT

¹⁸ Advice Package Management Orphan Drugs, The National Health Care Institute (ZiNL) (26 October 2015)

A still to be established indication commission, mandated with advising about the starting or stopping of a treatment with an orphan drug for an individual patient, will be included in this process.

I endorse the method of working described above, while recognizing the potential risks of unnecessary delay in patients' access to an orphan drug or disproportionate increase in administrative costs. I will consult with the Health Care Institute (ZiNL) about this in the near future.

Tackle unnecessary measures in the reimbursement system

We should remain focused on removing unnecessary obstacles in authorizing drugs for the *reimbursement system*. The Dutch Advisory Board on Regulatory Burden's (Actal) recently published investigation includes relevant recommendations¹⁹. The main conclusion of the research is that bottlenecks occur primarily in the practical implementation and in the regulation of procedures. These lead to unnecessary regulatory burden in the pharmaceutical companies. Based on Actal's recommendations, I will, together with the Health Care Institute (ZiNL), look for opportunities to remove unnecessary regulation and to provide more clarity regarding procedures. I will also make the assessment criteria for intramural and extramural medicines less ambiguous. The obstacles specifically highlighted in the research regarding conditional authorization of drugs to the insurance package will be dealt with in the evaluation of the pilot we are currently carrying out with this tool. For the rest, it will remain necessary to justify authorization, due to its conditional nature, so that the assessment process for authorization can take place within the allotted timeframe.

International cooperation is needed

Due to the limited size of the Dutch market, prices are determined primarily at an international level. Given The Netherlands' positive attitude when it comes to innovative drugs, but also in the realization that The Netherlands makes up just a small portion of the global market, I actively seek international cooperation. Therefore, I am looking within Europe for **cooperation in areas which can promote fast access to drugs and innovation, but also guarantee affordability and increase transparency among member countries.**

I would like to put an end to the current situation in which companies benefit from fragmented procurement and budgeting of medicines in Europe. The premium payers and patients, in The Netherlands and throughout the European Union, are the victims. This situation has led to major differences among the member states in patients' access to medicines. Some countries can no longer afford new expensive drugs. Even in The Netherlands, new expensive drugs threaten to displace other care.

I envision cooperation with other member states in various fields. For instance, in sharing information about drugs, markets and prices, starting with performing a joint horizon scan. Better cooperation in the area of Health Technology Assessment (HTA) as the basis for reimbursement decisions is also fruitful. The Netherlands is actively working on this through the Dutch Health Care Institute (ZiNL). Indeed, ZiNL enjoys a prominent position in Europe in this area, and our contribution

¹⁹ Investigation into regulatory pressure in authorization of drugs to the reimbursement system, Actal (December 2015)

is therefore well integrated. In the period 2016-2019, ZiNL will take over as coordinator for the European Network on HTA (EUnetHTA), contributing to our efforts.

Furthermore, I see ample opportunity for cooperation regarding the prices of specific medicines. I have already made a start with Belgium and Luxemburg. We have begun an association in which we share information and are implementing a pilot involving price negotiations for one drug. Plus, we have agreed to be more transparent with one another about our prices. In the next few months it will become clear whether or not this cooperation has led to any concrete results.

During the European presidency I will invite my colleagues to discuss these topics and, where possible, make additional voluntary agreements. In this way I aim, step by step, to bring more countries together so that together we can make a difference on issues where separately it has proven to be difficult.

3. Responsible use of medicines

General

Responsible use of medicines means that the patient receives the medicine necessary for his treatment. Nothing more and nothing less. Unnecessary use of medicines, which have no effect or can even cause unnecessary side effects and damage health, must be prevented. In addition, responsible use contributes to cost control.

Due to various parties' efforts, much has already been accomplished when it comes to responsible use, but rapid developments in pharmaceutical care necessitate continuous vigilance in this area. The **correct 'start and stop criteria'** for a treatment must be known, as well as the proper dosage, regardless of the patient's characteristics or situation. Only then does it become possible to develop and update quality standards. Both the registering authorities, as well as the insurance package authorities, healthcare practitioners, pharmacists and patients would like to have more insight into what new drugs can do in practice.

I plan to encourage the development of this field of expertise. Therefore, I am promoting **the facilitation of diagnostic development** and research through the Netherlands Organisation for Health Research and Development (ZonMw) programme Rational Pharmacotherapy.

Facilitate diagnostic developments

The trend toward more '*targeted and personalized medicines*' (also called Precision Medicine in the United States) enables practitioners to more accurately select the right medicine for the right patient. Greater interest in biomarkers in diagnostics has meant that doctors are better at predicting if and how treatment will work on the patient. Investing now in good infrastructure and new methods will in time produce better quality and cost control. It is important to me that new methods which can make the administration of '*personalized medicine*' successful should be developed and put into practice. When it comes to diagnostics, it is important to push just as hard as with other developments in the area of personalized medicine.

Case Study – Diagnostics in support of treatment

There are several examples in The Netherlands of targeted development and administration of diagnostics in support of treatment with drugs.

For instance, Professor Hans Clevers, at the Hubrecht Institute, has developed **organoid technology**. With this technology, a drug's efficacy for an individual patient can be tested on living tissue that is cultivated in the lab. Another way to predict a drug's efficacy is through the **DNA sequencing** of tissue from a tumour, as is being done at the Antoine van Leeuwenhoek cancer institute in Amsterdam.

Another relevant example is an initiative by professor of pharmacogenetics Ron van Schaik of the Erasmus University Medical Center in which a preventive test is conducted to measure the activity of five enzymes in the liver which together metabolize 80% of all medicines in the body. Patients can then take this information to doctors and pharmacists. In this way major side effects can be prevented in patients who take longer to metabolize a medicine. Patients with a fast metabolic rate are given a higher dosage for the medicine to remain effective.

The willingness among doctors, insurers and the industry to further develop and more frequently apply these methods is high. Diverse parties (including practitioners, the pharmaceutical industry and insurers) want to cooperate on this with the government. The Netherlands has a good infrastructure to make progress with these methods.

For these types and other new methods, I am creating a multi-year stimulus plan. I am making 10 million euros available for implementation over a five-year period.

Continuation of the Netherlands Organisation for Health Research and Development (ZonMw) programme Rational Pharmacotherapy

In order to further encourage the responsible use of medicines I continue to invest in the ZonMw programme Rational Pharmacotherapy. I initiated this programme in 2012 in order to further investigate more effective, safer and efficient uses of the current arsenal of medicines and to broadly communicate and apply the findings from this research. I have made 91 million euros available for expanding subsidies in the period 2016-2019. The projects which have been granted subsidies in open tender rounds to date received 15% of their financing from the pharmaceutical industry, healthcare insurers and other organizations.

Community Pharmacy

The community pharmacist is pre-eminently the healthcare provider best placed to improve patients' responsible use of medicines. The moment the pharmacist hands over a medicine is the moment to inform a patient regarding the benefit and necessity of a prescribed medicine, the manner of use and the importance of adherence to the treatment. The pharmacist is above all well positioned to track how the drug is used in practice, and its potential interaction with other medications. If necessary, he can intervene (for instance by making a medication assessment for patients with polypharmacy), and maintain contact about the intervention with other healthcare providers. Good pharmaceutical care

as an integral part of primary care and specialist medical care is at the vanguard of our policy. Both the dispensing pharmacist as well as the pharmaceutical care giver who work with other professional groups in primary and secondary care play important roles. Recently, the Community Pharmacist was recognized as a specialty.

The agenda I drafted with the sector in 2013 as a result of the Rinnooy Kan and Reibestein survey of the pharmaceutical sector remains current. I will continue to work with the relevant parties to complete this agenda. Among other things, this means I will continue encouraging medical file transfers between primary and secondary health care providers by modifying the current guideline **medication file transfer**. In addition, work is being done to improve the exchange of **laboratory tests** between doctors and pharmacists, to specify the **indications on the prescription**, and promoting **adherence to the treatment**. In accordance with the agreements made in the administrative consultation on pharmacy, The Health Care Inspectorate (IGZ) will intensify its supervision of medication file transfer and medication assessment.

Encouraging the use of biosimilars

I will focus particular attention on the responsible use of biosimilars²⁰. With the availability of biosimilars, the original patented drug now has competition. This can lead to significant savings. Particularly in the next few years when a number of important biologicals in oncology and rheumatism (TNF alpha inhibitors) come out of patent protection.

Both the Medicines Evaluation Board (CBG) and the Dutch Association of Medical Specialists (FMS) indicate that biosimilars must be administered with care. Both maintain that a patient starting a treatment can be treated with a biosimilar. But the organisations also write that in switching a patient from an original product to a biosimilar, the prescriber must use the necessary caution.

Neighbouring countries are also acquiring experience in the use of biosimilars. Soon more data will become available regarding practical experience in the transfer of patients from original products to biosimilars. I will actively share this information and experience in The Netherlands.

I seek to **encourage the use of biosimilars**. I see all the necessary steps moving in the right direction: patients, practitioners, healthcare providers and insurers jointly taking the initiative to expand the use of biosimilars. I applaud the fact that practitioners are taking the initiative and I will support them so this can be expedited. That is why I am in contact with those involved on how we can make this acceleration happen. If this does not lead to the desired results, I will consider limiting the reimbursement of original products.

Case Study – biosimilars

Two examples of countries which have made a clear choice to use biosimilars based on cost are Norway and Denmark.

²⁰ A biosimilar is a medicine that is designed to be equivalent with an existing biological drug (the 'reference drug'). Biosimilars are not the same as generic drugs, which have a simpler chemical structure. Biosimilars are considered to be identical to the reference drug.

Norway and Denmark have publically financed healthcare systems, in which tenders are put out each year for medicines based on the active ingredient. Given that biosimilars are considered an equivalent alternative for the original TNF alpha inhibitors, the product that wins the tender gets preference for new patients and patients who, for medical reasons, must switch to another TNF alpha inhibitor. This has resulted in remarkable savings.

Doctors can deviate from the preferred drug if it is medically necessary, but by now even many existing patients have been transferred from, for instance, the original product Remicade (a rheumatism inhibitor) to the biosimilar. With savings sometimes reaching 70%, doctors in these countries point out that they can no longer justify prescribing the original product.

4. Introduce balance in the pharmaceutical market structure

General

Provisions in the field of intellectual property (patent law) have created an innovated climate in the pharmaceutical sector and created opportunity for the industry to develop valuable products for patients. Nevertheless, when drugs are authorized for the market the question arises more and more often as to whether the current (supplementary) European provisions in the form of supplementary protection certificates, data protection and market exclusivity, have not overshot the mark. Since new drugs enjoy a strong monopoly for individual indication classes, we need to make sure this dominant market position does not disadvantage the patient and the premium payer. Therefore, I am pursuing a better balance between rewarding innovation (availability of the right products) and the future affordability of our healthcare.

In order to keep the drugs market in a healthy balance, two things are necessary. Protection of intellectual property and the interest of investors must be proportionate to the goal, namely, encouraging innovation. In addition, corporate *behaviour* and abiding by the rules are of utmost importance. On both points, due to international law, I can exercise only modest influence. But I will use to the greatest extent possible the instruments I do have at my disposal.

Protection constructions supplemental to patent law

We need to take a good look at the balance between the availability of new drugs and the asking price of such drugs. In the international context I have initiated a discussion about the effects of protection constructions which are built into the market authorization regulations of the EU, in addition to the general patent provisions, such as **supplementary protection certificates** in the area of medicines. Given that other EU member countries recognize this issue, during the Dutch EU presidency I will seek to highlight the undesired effects these protection constructions have on medicines.

Market protection of orphan drugs leads to unwanted effects

I will spotlight in particular a group of drugs which for some time now has enjoyed special incentives, namely orphan drugs²¹. In addition to the usual patent protection, manufacturers also receive protection of their data exclusivity and receive ten years of market exclusivity for the disease for which their drug was developed.

That means the first medicine to come on the market for a disease has a monopoly, regardless of whether or not it is the best medicine for the patient. In recent years this EU policy has resulted in a hefty increase in products with an 'orphan indication'. For patients with rare disease, for whom specific drugs were developed, this is indeed a good development.²²

But the surge of these new products for specific European market authorization appears to be thanks in part to the broad definition of the concept 'orphan drug' and the length of market exclusivity that is offered. Plus, manufacturers more often register a drug for all sorts of sub-indications of the disease. By means of this 'cutting up' of indications, the manufacturer comes into consideration for orphan drug status for the product, which results in monopolies and the associated prices. This is not what was intended by the EU regulations.

I believe that these special incentives have missed their target. The industry's strategic behaviour is no longer defensible given the threat to the accessibility and affordability of care, and the high price of orphan drugs necessitates a critical analysis of the current instrument. This problem has been acknowledged by a number of EU member states. Therefore, I will work toward a clearer delineation of the 'unmet medical need' which defines which indications fall under the EU orphan drugs regulation. I also plan to table a discussion on whether the balance between orphan drugs' market exclusivity and the supply of new products, which in practice meet these unmet medical needs, indeed still makes sense. After all, the regulation should continue to ensure that drugs are developed which best serve patients with rare diseases, rather than that drugs are developed with the most chance for market exclusivity. In this regard we are reinforcing the European Commission's ongoing consultancy process for 2016 concerning the functioning of the current EU legislation in the field of orphan drugs.

Manufacturers' improper behaviour

It is illegal for companies to make deals limiting competition, just as they cannot abuse their dominant market position. The pharmaceutical sector in The Netherlands and Europe are also obliged to abide by these rules pertaining to competition.

I therefore read with interest the recent Authority for Consumers and Markets (ACM) paper on the pharmaceutical sector. This paper divulges that certain manufacturers of chemical brand name drugs obstructed the acceptance and use of less expensive (generic) drugs²³. This was done in part through the maintenance and extension of brand name drugs' market exclusivity. The ACM observed, however, that not all behaviour could be contested using competition law. At times it appears that the European competition constructions in the area of intellectual property interfere with the application of competition law. Some behaviour can also result in obstructing the development of generic drugs. From the perspective of social cost to the consumer, this is not desirable.

²¹ See also <http://www.nationaalkompas.nl/gezondheid-en-ziekte/ziekten-en-aandoeningen/zeldzame-ziekten/watzijn/> (in Dutch).

²² See for example chapter 3.3 ('Effectiveness of the Orphan Regulation') of the Ecorys report 'How well does regulation work? The cases of pediatric medicines, orphan drugs and advanced therapies' (November 2015).

²³ See for example p. 3 of the aforementioned ACM paper (in Dutch).

Manufacturers are operating in a grey area of European competition law. Future rulings by the Court of Justice of the European Union should clarify when an abuse of a position of economic power has occurred, not to mention cartel forming, and when it has not.

As far as I am concerned, it is the industry's important social responsibility to use its influence in the market prudently. The market structure, through the current patent law and supplemental protection certificates, has made the aforementioned behaviour possible. But from the perspective of corporate social responsibility, in other words, taking into account the interests of the patient and the premium payer, these kinds of practices which minimize competition and maximize profits are unwelcome.

At the national level, my ability to tackle such behaviour is, as I mentioned above, limited in the short term. That having been said, I did request the ACM to continue to closely monitor this behaviour, and where possible, to take action to combat unauthorized behaviour. The ACM has decided to free up supplemental capacity in order to continue to closely monitor the market.

It is my understanding that the European Commission is also closely following these practices in order to step in, based on European competition law, when they feel it is appropriate.

5. Accessibility of innovative products

General

Market authorization regulations are there for a purpose: they provide assurances that the products that enter the market are safe and effective. However, we are seeing more and more changes in this type of product on the drugs market. Consider personalized medicine, or orphan drugs for smaller and smaller groups of patients. For this reason, I would like to look at which types of product are falling through the cracks, and how we can nevertheless facilitate and accelerate market authorization. In addition, the various requirements imposed on the market authorization and reimbursement of a product must be brought in line with each other so that the *time-to-patient* is reduced. Shifting between the authorization procedures and reimbursement procedures as much as possible will save valuable time.

Therefore, I am taking the initiative in the question of how flexible forms of market authorization (conditional authorization, adaptive pathways) can be improved in order to get certain products to the patient faster, but also affordably. In the area of accessibility, I will spotlight better concurrence between market authorization and reimbursement requirements, with the intention of scraping superfluous rules and accelerate authorization.

Establishing European market authorization rules

In 2015, we looked back on 50 years of European regulation concerning market authorization of medicines. This regulation was spawned by incidents involving unsafe products. To this day, EU regulation aims to ensure that safe and effective products, which meet agreed-upon quality criteria, enter the market. This is still an important starting point in our drugs legislation. A new medicine can come on the market in The Netherlands only after it is registered by the Medicines Evaluation Board (CBG) and in Europe by the European Medicines Agency (EMA).

These rules remain sufficient for most products. However, new developments require further consideration. Patients more frequently demand accelerated access to new drugs which are not yet registered in The Netherlands, or which have yet to prove their added value in relation to an existing drug. This desire is particularly acute in cases of severe illness, given that market authorization procedure is often lengthy.

Special product categories

Developments are also taking place in the case of special categories of drugs, such as orphan drugs and personalized medicine. Drugs are being developed for ever smaller groups, or even sub-groups, of patients. This begs the question as to whether or not the current market authorization rules are sufficiently tailored to the needs of small groups of patients. Besides, drugs are being developed to intervene in a specific bodily mechanism or to work only for people with a particular genetic profile. What then is the most effective manner to evaluate and register medicines?

These developments call into question whether the current EU market authorization system is sufficiently equipped for the future. As far as I am concerned, we need to orient our efforts toward faster but careful market authorization for the certain promising drugs. That requires discussion in Europe and adapting current processes and procedures. With an eye toward the future, Europe needs to take on this challenge. The first step is engaging our experts in European consultative bodies to bring the discussion forward.

Linking market authorization and insurance package management

In the first place, we need to speed things up wherever possible. We will need to keep the spotlight on removing unnecessary roadblocks in the market authorization requirements. The recent report by the Dutch Advisory Board on Regulatory Burden (Actal) has offered some relief. We need to ensure that dossier requirements in the field of market authorization (EU) and insurance package authorization (national) as much as possible are in line with one another, so that administrative costs and the time needed to get a product to the patient are both reduced.

I have agreed with the National Health Care Institute (ZiNL) and the Medicines Evaluation Board (CBG) to make this streamlining happen. Cooperation and coordination between CBG and ZiNL procedures play an important role. What we have agreed in The Netherlands, we will also have to agree at the European level. The decision whether or not to allow a drug into the basic insurance package will remain a national matter, but the collection of data needs to be streamlined. This simplification will be an important step forward in getting promising drugs to the patient more quickly.

Market authorization for promising products

There is not as much data regarding drugs developed for indications in small numbers of patients as there is regarding drugs for larger groups. This makes it difficult, in the current system of market authorization, to come to a well-considered assessment about the efficacy and safety of a product before it is dispensed to a patient. For groups of patients whereby a new drug can be an important breakthrough in their disease, or can mean the difference between life and death, the question is if the original, more rigid market authorization requirements are still relevant. In these cases, policy

needs to be geared toward determining, together with the manufacturer and the doctors, how such products can prove their value to the patient.

I will seize the opportunity provided by the Dutch EU presidency to work with my European colleagues on a more flexible market authorization system for special categories of products for 'unmet medical needs' (the treatment of diseases where patients are eagerly awaiting new developments). This includes more flexible mechanisms such as conditional authorization and 'adaptive pathways', which the European Medicines Agency (EMA) is currently trying out²⁴. By opening a dialogue in advance with the manufacturer, it can be determined ahead of time what criteria the product must meet. It can be agreed under what conditions a product can be conditionally authorized for the market and under what conditions the product can be considered for reimbursement. In the case of reimbursement, conditions in the current Conditional Authorization to the basic insurance package also play a role. At the least, these would include the following: required supplemental research (for instance regarding supplemental data and cost effectiveness), agreements regarding financial consequences, and agreements regarding the procedure in the event of expulsion from the insurance package ('the exit strategy'). This accelerates the process of authorization, although safety must always remain the first priority.

For drugs which are authorized by such conditional market authorization or pathway, there may be insufficient data available to determine the efficacy according to the legal criteria 'the current state of science and practice'. Therefore, such a medicine will not be allowed to directly flow into the standard insurance package. When accelerated acceptance of a promising, innovative and socially relevant drug is requested, the drug may be considered for acceptance for a defined period through a Conditional Authorization. During the Conditional Authorization, data is collected regarding the efficacy of the care. At the end of the process of Conditional Authorization, it is determined if the drug meets the current state of science and practice. If that is not the case, it is established that the drug is not effective and thus it is not authorized for the package. Of course, other insurance package criteria also play a role.

Pharmacy preparation

The starting point of our policy is the use of registered drugs. After all, registered drugs are tested for safety and efficacy, and a good system for pharmacovigilance is in place. In The Netherlands, medicines are also produced in special compounding pharmacies for the supply of local pharmacies. Compared to magistral compounding (compounding in the local pharmacy), such second-tier supplied preparations have the advantage that the compounding quality is better safeguarded.

These unregistered pharmacy compounds are reimbursed in the event there is rational pharmacotherapy. I consider this option important from the perspective of personalized medicine. For instance, for children who receive certain medicines in drops instead of the difficult to swallow

²⁴ To be considered for conditional authorization, the product's risk-reward balance must be positive, supplemental clinical data must still be provided, and the product needs to meet an unmet medical need, among other criteria. During the test with adaptive pathways, European market authorization authorities are looking into how drugs can be made available to the patient earlier through a customized procedure, and they advise the manufacturer about, for instance, the design of the trials. Both mechanisms are thus customized or abbreviated forms of market authorization in an effort to comply with the growing patient demand for timely access to products which meet an unmet medical need.

tablets or for the elderly who receive adapted medicine. In the interest of the patients, this personalized medicine needs to remain possible under strict conditions. With this approach – personalized medicine must remain possible – I would like to re-assess the recent Court of Justice of the EU ruling regarding re-delivery from compounding pharmacies (cases C544/13 and C545/13, 16 July 2015). In this case it was ruled that pharmacists are allowed to prepare medicines exclusively for their own patients (and not on a commercial scale).

In the last few years, we have also seen cases in which the price of medicines after registration increased exponentially compared to the price for an already recognized available compound. Since only a portion of this price rise can be explained by the cost of extra research necessary for registration, I consider this a very unwanted development. It is also socially unjustifiable. The medicine regulatory system is, as a matter of principle, geared toward registration. This is the preferred manner, but not at any price. Classification of a drug as a so-called ‘new active substance’, according to the European guideline for medicines, also plays a role in registration and price determination. By regarding a drug as a new active substance, protective mechanisms kick in and it becomes more difficult for producers of generic drugs to enter the market. Price competition is thus delayed. In consultation with the Medicines Evaluation Board, I am looking into how this can be accommodated in the European context.

6. Better information services

General

I see that there is a growing need to monitor the practical efficacy, functioning and (side) effects of (new) drugs. This information can be collected using *patient or hospital registrations*. This results in better start and stop criteria for the treatment, provides information as to when and by what type of patient the drug can best be used and offers information for reimbursement decisions.

Registries

We see that many parties are actively working on registries, both national and international. But not everyone is pursuing the same goal. In practice, developments regarding registries are taking place in a fractured manner, and a structural approach does not happen by itself. Therefore, in 2016, together with various parties, I will draft an information services plan of action. This plan should clarify achievable goals, the manner of working, roles, tasks and responsibilities, and the financing of registries. I will ensure that this does not lead to a large amount of new administrative burdens. We should only encourage those registries which matter.

Furthermore, it is important that doctors register the indication for which they prescribe an expensive drug and that more information comes to light about prescription behaviour and variation among doctors’ practices. To facilitate this, I have instructed the Central Information Unit on Health Care Professions (CIBG) to create and maintain a databank with all add-on drugs and the indications for which they can be prescribed.

Disclose information

I am also moving forward with the process initiated last year by the Healthcare Authority (NZa), the Medicines Evaluation Board (CBG), the Netherlands Pharmacovigilance Centre Lareb, the Dutch Institute for Rational Use of Medicine (IVM), and the Dutch Drug Bulletin to improve independent information service regarding drugs for healthcare providers and to disclose more information. But in addition to providers, patients also need access to good information. In the coming year, I will proceed with making accessible independent information services on drugs for patients. In The Netherlands, there is a lot of information on medicines available. However, it is not sufficiently tailored to the needs of the patient, not to mention difficult to find. Together with the aforementioned organizations, which have access to this information, I will ensure that this is taken care of for patients in the not too distant future.

7. In conclusion

Healthcare in The Netherlands is facing a major challenge in the coming years. The cycle of innovation, market access, reimbursement and the best use of medicines requires an increasingly integrated approach.

Controlling costs in order to continue to provide high-level care in the future is of crucial importance. We want to work with the industry, healthcare insurers, healthcare providers and patients to make this happen. This requires clear roles and distinct choices in the way we set up our pharmaceutical sector. Nationally, when it is feasible, and in Europe, when it is necessary. This is the only way we can work toward a system which, based on patients' needs, safeguards access to valuable medicines. With the introduction of new, valuable medicines, we need to be willing to determine jointly under what conditions they can be (temporarily) reimbursed in our current system.

The measures I have set out in this letter offer a solid basis for good pharmaceutical care: now and in the future.

Yours sincerely,

The Minister of Health, Welfare and Sport

mw. drs. E.I. Schippers