Regulation of hospital medicines based on costs and effects. Experiences from Germany, the Netherlands, Switzerland, the United Kingdom, Norway and Sweden

Summary

Rising pharmaceutical costs and the pricing of new hospital medicines pose a regulatory challenge to the Danish healthcare system. To inform discussions on pharmaceutical regulation, the Danish Ministry of Health commissioned the Danish Institute for Local and Regional Government Research (KORA) to conduct a comparative analysis of pharmaceutical regulation in Germany, the Netherlands, Switzerland, the United Kingdom, Norway and Sweden.

The present report describes and compares the regulation of pharmaceuticals in the six countries mentioned above. It focuses on pharmaceuticals that are categorised as hospital medicines in Denmark, i.e. pharmaceuticals bought by hospitals and used for the treatment of patients during hospitalization or in ambulatory care. The analytical focus is, in particular, on the models used for setting priorities for the adoption of new medication in the six countries. This means that the focus is on the assessment of the added value of new pharmaceuticals and on related decisions about whether or not to finance their use within the health care systems. The report comprises seven chapters. The first chapter presents a comparative analysis of the regulation in the six countries. The comparative analysis builds on more detailed descriptions of the regulation in each of the countries that are presented in the following six chapters.

The report is based on publicly available reports on pharmaceutical regulation and interviews with key stakeholders in the six countries. Moreover, case studies of the adoption and use of five treatments were undertaken. The five treatments included Infliximab (e.g. used in the treatment of rheumatoid arthritis), Abiraterone (used in the treatment of prostate cancer), Aflibercept (used in the treatment of impaired vision caused by, for example, macular edema), Ipilimumab (used in the treatment of advanced melanoma) and Daclatasvir and other products used in the treatment of chronic hepatitis C. The treatments were chosen based on the challenges they are likely to present for cost control in the countries in question. The case studies allowed for comparison of specific decisions made regarding new pharmaceuticals. Hence, they provided insight to the practical functioning of the regulatory systems.

The general tendency is that the countries include value-based price setting in their decisions on whether to finance new pharmaceuticals. The model for how the prioritisation decisions are made, however, varies among the countries.

The main conclusions of the report are summarised below, organised according to the following questions:

- How is the adoption of new pharmaceuticals organised?
- How is the 'value' and 'added value' assessed in the evaluation of new medicines?

Danish Institute for
Local and Regional Government Research

Købmagergade 22
DK-1150 København K

E-mail: kora@kora.dk
Phone: +45 444 555 00

- What are the consequences of including costs and effects in the regulation of pharmaceuticals?
- Which resources are used for the assessment of added value?
- How are assessments of added value integrated with other elements in the regulation of pharmaceuticals?

How is the adoption of new pharmaceuticals organised?

The conditions for obtaining marketing authorisation are similar across the countries. For the EU member states, the approval of new medicines is increasingly handled by the European Medicines Agency (EMA) and the marketing authorisation by the EU Commission. The approval procedures in Norway follow those of EMA. Even though Switzerland has an independent approval procedure and an independent approval institution (SWISSMEDIC), their criteria and decisions are usually in line with those of EMA. In contrast, the countries differ considerably with regard to the regulation *after* marketing authorisation has been obtained. This regulation usually has profound impact on patients' *actual* access to new pharmaceuticals, as approval by EMA does not automatically lead to national adoption.

Basically, the countries differ with regard to whether or not decisions regarding financing of new pharmaceuticals are made at the national level. The Norwegian, Swedish and the UK health care systems are characterised by general tax financing, public ownership and hierarchical organisation (Beveridge style). In line with this organisation, decisions about financing and use of new medicines are made centrally – either by a national evaluation institution like the British NICE (National Institute for Health and Care Excellence), by means of collaborative models on "new methods", as in Norway, or through a model of regional collaboration, as in the Swedish system of "Ordnat Införande". These countries all include the treatment costs, when making decision about financing new medicines through the public health care budgets. Moreover, assessments of cost-effectiveness are actively used by the public health authorities in price negotiations with pharmaceutical companies. This approach can be understood as attempts to obtain 'value-based pricing'.

In Germany and Switzerland, the healthcare services are mainly financed through statutory health insurance (Bismarck style). Hence, the role of public authorities in the regulation is more indirect. While the authorities establish and monitor the adherence to regulatory frameworks, decisions about adoption and financing of new pharmaceuticals are typically decentralised to the suppliers and the health insurers or sickness funds. In Switzerland, the role of the health care authorities (Federal Office of Public Health, FOPH) is limited to the setting of maximum prices. The existence of a maximum price is here a precondition for reimbursement of medicine costs by health insurers. Below the maximum prices levels, the suppliers and the purchasers in the hospitals negotiate additional discounts. In Germany, the Federal Joint Committee (Gemeinsamer Bundesausschuss, G-BA) has been established as a joint organisation for the suppliers and the sickness funds. Based on federal legislation, G-BA is authorised to exclude certain types of pharmaceuticals from the statutory health insurance (*ineffective* pharmaceuticals, medicines for *minor conditions*, *life-style medication* and *non-prescription* drugs for patients above the age of 12). Typically, these pharmaceuticals do not comprise the medicines that drive the costs in the Danish hospital sector. The main regulatory task of the G-BA is to provide information about the added value of new pharmaceuticals. This information is used by the um-

brella organisation of sickness funds (GKV Spitzenverband) in price negotiations with the pharmaceutical companies. In Germany, the assessment of added value is made solely for pharmaceuticals used in out-patient care (including ambulatory care led by hospital specialists). For in-patient care, individual hospitals are responsible for price negotiations and procurement of pharmaceuticals. In Germany, new pharmaceuticals must be reimbursed by the sickness funds from the time of marketing approval. In Switzerland, the health insurers must reimburse new pharmaceuticals from the moment a maximum price has been set. Unlike in the British, Swedish and Norwegian system, limitations in the use of new pharmaceuticals are not the result of decisions made by public authorities. Rather, limitations in the use of pharmaceuticals depend on financial incentives built into the reimbursement systems.

The Dutch pharmaceutical regulation follows principles of managed competition. It comprises elements from both the Beveridge style and the Bismarck style health care systems. Formally, the authority to make decisions on reimbursement of new pharmaceuticals in the statutory health insurance resides with the Minister of Health, Welfare and Sports. The minister makes her decisions based on recommendations of the Dutch National Health Care Institute (Zorginstituut Nederland, ZiN), which undertakes health technology assessments of new pharmaceuticals. For pharmaceuticals used in out-patient care, a positive decision by the minister is required to *include* new pharmaceuticals in the statutory health insurance. In contrast, pharmaceuticals used in in-patient care are automatically included in the statutory health insurance. Therefore, an active decision is required to *exclude* new pharmaceuticals. The assessment of in-patient medicines is typically conducted after the products have been put on the market and used by hospital specialists. Moreover, decisions to exclude pharmaceuticals from the statutory health insurance are very rare. Therefore, in practice it is left to the individual hospitals in negotiation with the health insurers to find ways to limit the use of pharmaceuticals for in-patient care, if the expenses exceed the budgets. This carries a risk of implicit patient selection or other forms of treatment rationing. After the data were collected for this report, a reform of the Dutch regulation of pharmaceuticals for in-patient care was announced by the Dutch Minister of Health, Welfare and Sports. The Dutch informants expected the reform to address, among others, the challenges related to the timing of the assessments of in-patient medicine.

Generally, the pharmaceutical market is characterised by a lack of transparency regarding prices. Furthermore, data on the actual use of pharmaceuticals are sparse. Due to these conditions, it has not been possible to compare the effectiveness of the regulatory systems in terms of pricing and access to new treatments. In the insurance-based systems (Bismarck style), the adoption of new pharmaceuticals usually occurs immediately after marketing. In these countries, price negotiation in combination with financial incentives appears to be the most important instrument in relation to cost control. Because of the decentralisation of financing, procurement and decisions regarding use, no centralised setting of priorities for the adoption of new medicines is undertaken. Case studies of the adoption and use of five pharmaceuticals across the countries indicate that the use of new pharmaceuticals is rarely limited in the insurance-based health care systems and that it is difficult to stimulate the uptake of biosimilar products.

Of the Beveridge style health care systems, Norway and the UK have the longest experience with centralised decisions on the adoption of new medication. In both these countries, it is a state responsibility to run and finance the health care systems. Accordingly, there is a clear

connection between the political and financial responsibility for decisions on the adoption of new medication. In Sweden, the operation and financing of health care services is decentralised to regional level governments. This decentralisation of responsibility is also reflected in the regulation targeted at the adoption of new pharmaceuticals. The Swedish model of 'Ordnat Införande' is based on shared decision-making among the regional governments. However, no means are in place to enforce individual regional governments' commitment to their shared decisions. The model of 'Ordnat Införande' has been in force since January 2015. So far, relatively few decisions not to finance new pharmaceuticals have been made. Therefore, the political robustness of the system remains to be seen. As an indication of the pressure that can be expected in relation to future decisions to reject the financing of new treatments, the Swedish patient organisations withdrew from the board of decision makers already at an early stage in the preparation of the 'Ordnat Införande' model. Presumably, the patient organisations wished to avoid being held partly responsible in the case of negative evaluations of new medicines. In the UK, citizens are included in decisions to adopt new medication. They are recruited directly by NICE to serve on appraisal committees, rather than as representatives of advocacy groups. In Norway, patient or citizen representatives are not involved in the making of prioritisation decisions. Crucial for the opportunity of centralised priority setting to ensure cost control is full political commitment to the decisions made. Without a clear political mandate to reject public financing of a new treatment, the regulatory systems have no bargaining power.

Overall, the organising principles of the health care systems are reflected in the regulation targeted at the adoption of new pharmaceuticals. With the exception of Switzerland and Germany, decisions to adopt and finance new pharmaceuticals are based on explicit assessments of cost-effectiveness. In Norway, Sweden, the UK (and partly in the Netherlands), there is a clear political responsibility for decisions to adopt or reject new pharmaceuticals. In Germany and Switzerland, the uptake of new pharmaceuticals is largely under the control of health care suppliers, with some influence from health insurers/sickness funds.

How are the concepts of 'value' and 'added value' operationalised in the assessment of new pharmaceuticals?

There is considerable variation among the six countries in the assessment of added value and in the threshold value applied to decide on acceptability. In the UK and Norway, the most important aspect in the assessment of added value is the costs per quality-adjusted life year (QALY). Rather than a fixed threshold, the political willingness to pay is influenced by additional factors, such as the availability of other treatment options or the innovativeness of a new medicine. Of the six countries, the British health care system has the least resources available. The Gross Domestic Product (GDP) per inhabitant and the total health care expenditures as a share of GDP are considerably lower in the UK than in the other countries. In the UK, the political willingness to pay for new pharmaceuticals is stated to be about GBP 20,000-30,000 (about EUR 25,000-38,000) per QALY. Measured by the GDP per inhabitant, Norway is the most prosperous country in the analysis. The political willingness to pay for new pharmaceuticals appears to be higher in Norway than in the UK. No official threshold is stated in Norway, and according

to Norwegian informants no official threshold is wanted. However, mentioning has been made by Norwegian health care authorities of a threshold range up to NOK 700,000-800,000 (about EUR 75,000-85,000) per QALY. In Sweden QALYs are also part of the assessment of the added value of new pharmaceuticals, though their impact on decisions to adopt new medicines is less direct. In the model of 'Ordnat Införande', a multitude of criteria are included in the assessment of 'added value'. However, the relative weighting given to the criteria are unclear, which makes the assessment of new treatments less transparent than in Norway and the UK. In Sweden, empirical examples indicate that for very rare serious diseases the political willingness to pay exceeds SEK 1,000,000 (>EUR 100,000) per QALY. However, there are other examples of new pharmaceuticals that have been rejected in Sweden but accepted in the UK, where the threshold values are relatively low. In the Netherlands, no formal threshold values exist for the political willingness to pay for new pharmaceuticals, but informants mentioned an informal threshold value around EUR 80,000 per QALY. Like in the other countries, the threshold value would be adjusted upwards or downwards dependent on other criteria, such as the seriousness of the condition.

The criteria for adoption of new pharmaceuticals are most explicitly linked to cost-effectiveness in the Netherlands, Norway and the UK. In these countries, any price reductions will therefore impact the assessment of added value in a direct way. This can make price negotiations with pharmaceutical companies more straightforward. However, it also creates an incentive for pharmaceutical companies to price their products just below the threshold value. In Sweden, the evaluation institutions are allowed greater flexibility in relation to interpreting the assessment criteria. Over time, the decisions made to adopt or reject new treatments will make the relative weighting of the assessment criteria more explicit.

QALYs play an important role as an indicator of added value in the Netherlands, Norway and the UK. In Switzerland, costs of new pharmaceuticals are also taken into account – but not as part of formal cost-effectiveness analyses. Instead, cost consequence assessments are made. In Germany, on the other hand, costs are not included in the assessment of added value. Rather, added value is understood as relative clinical efficacy. A distinct feature of the Swedish model of 'Ordnat Införande' appears to be that more importance is ascribed to the rarity and seriousness of the disease and less to the treatment effects than in the other countries.

The use of QALYs as the primary indicator of added value provides an opportunity for greater transparency in decisions to adopt new pharmaceuticals. Other criteria may be just as valid, but in practice they are often more difficult to formalise. Different groups in society have different stakes in new medicines. The use of transparent criteria in the assessment of new pharmaceuticals can be seen as a basic condition for the democratic legitimacy of decisions to reject or adopt new treatments in public health care systems. However, the explicit inclusion of costs in the assessment of added value also allows pharmaceutical companies to price their products precisely to meet the accepted threshold value.

What are the consequences of including costs and effects in the regulation of pharmaceuticals?

Basically, value-based pricing concerns the relationship between costs and effects for a single product. If this relationship is favourable relative to the political willingness to pay in a given country, the recommendation will generally be to adopt a new treatment, even if the budget impact is high. Value-based pricing is therefore likely to influence the consumption and resource use on pharmaceuticals. The use of value-based pricing does not necessarily reduce the overall consumption of pharmaceuticals or diminish the pharmaceutical expenses. Longitudinal, cross-national data on pharmaceutical consumption are sparse and difficult to interpret (e.g. due to clinical variation). Therefore, we have not been able to estimate the effect of value-based pricing on consumption or total pharmaceutical expenses. However, in the UK, which has the longest experience with value-based pricing, there is no indication that the consumption of medicines has diminished relative to other countries since the establishment of NICE. It may be argued, instead, that the use of pharmaceuticals in the British health care system has become more *focused* on products with a certain cost-effectiveness ratio. When rising pharmaceutical expenses put pressure on hospital budgets, the alternative to centralised priority setting will often be treatment-rationing locally at the hospitals. In effect, this means less transparent decisions about the use of new pharmaceuticals for the treatment of individual patients. Centralised priority setting involves both adoption and rejection of new pharmaceuticals. Hence, it clarifies for patients, providers and funders which pharmaceuticals that should be financed.

When decisions to adopt new pharmaceuticals rest on assessments of cost-effectiveness, this implies that pharmaceuticals that are not considered sufficiently cost-effective compared to alternative treatment options will not be funded. As a consequence, patients must pay out-of-pocket if they want a treatment that is not included in the reimbursement scheme (e.g. through supplementary health insurance) – unless it is possible to apply for individual access and coverage of treatment expenses. In the UK it is possible (until 1st of July 2016), for physicians to apply on behalf of individual cancer patients for funding of a treatment that has not (yet) been assessed by NICE or has been rejected. In Norway, no such opportunity exists. If patients wish to receive a treatment not included in the reimbursement scheme due to unfavourable cost-effectiveness, they rely on private funding. Moreover, they also rely on private health care providers, because the treatment cannot be offered within the publicly funded healthcare system. In Sweden, patients may, in theory, access treatments that have been rejected under the 'Ordnat Införande' model, if a regional government decides to pay for the treatment. Whether this will happen in practice remains to be seen.

In Norway, Sweden and the UK, cost-effectiveness assessments are seen as providing a useful framework for price negotiation. Often, rebates are obtained because companies seek to ensure that new products are priced according to the political willingness to pay. However, this opportunity is dependent on the timing of the assessments. In the Netherlands, where the assessment of new out-patient medicines has typically been conducted one to two years after marketing, the possibility of obtaining price reductions has been limited. At this point in time, the products have often already been integrated in clinical practice, because they are automatically covered by the statutory health insurance. In this case, it is very difficult for political decision-makers to put pressure on pharmaceutical companies (e.g. by threatening to exclude a product from the reimbursement scheme), because health professionals and patient organisations are

likely to support continued use of a new medicine. In contrast, new medicines will typically not be funded in Norway, Sweden and the UK, until their reimbursement status has been clarified. In these countries there is a continuous dialogue between the health authorities and pharmaceutical companies about pricing during the assessment of a new pharmaceutical. The experience from these countries is that a considerable proportion of the pharmaceuticals that were initially excluded from public reimbursement could be included following additional price negotiations.

Another outcome of the negotiations with pharmaceutical companies can be risk-sharing agreements. These have been obtained in the Netherlands, in particular, but also in the UK and Sweden. Risk-sharing agreements may imply, for example, that pricing is conditional on the outcomes of additional studies. However, the general experience from these countries is that risk-sharing agreements are resource demanding and difficult to administer. As a consequence, they are rarely used or are limited to simple price-volume agreements.

A consequence of basing decisions to adopt new treatments on assessments of added value is a delay in the availability of new pharmaceuticals. In the countries examined, the delay that can be directly attributed to the preparation of health economic evaluations is estimated to be about three months. In cases where it is difficult to reach agreement on the price or obtain relevant data, the delay will be longer.

The experience, especially from Norway and the UK, is that a readiness to reject the adoption of new treatments based on cost-effectiveness assessment provides the opportunity to negotiate lower prices than would otherwise be possible. This opportunity implies that some pharmaceuticals might not become available for the patients, if price agreements between the health authorities and pharmaceutical companies cannot be reached. The lower the political willingness to pay for new pharmaceuticals, the greater the pressure for lower prices will be, and the greater will be the risk of pharmaceutical companies withdrawing products from the national market. In the UK, where the political willingness to pay for new pharmaceuticals is lower than in the other countries, the list of non-reimbursed medicines is rather comprehensive.

It is difficult to draw any firm conclusions about pharmaceutical prices across the countries. Because rebates are usually confidential, official information on pharmaceutical prices do not reflect the real prices. Previous studies indicate that the price level in Norway and the UK might be lower than in the other countries. German and Swiss informants mentioned that they consider their countries to be high price countries comparable to Denmark, for example.

Which resources are used for the assessment of added value?

The assessment of added value comprises different elements and is organised differently in the six countries. Therefore, a direct comparison of the resources spent on the assessment of new pharmaceuticals is not meaningful. In Norway, informants estimated that the Norwegian Medicines Agency (Statens Legemiddelverk) spends 10-12 full-time equivalents (FTEs) on health eco-

nomic evaluations of hospital medicines a year. The regional governments use about two FTEs, while a joint organisation for the procurement of pharmaceuticals (Legemiddelinnkjøpssamarbeid, LIS) spends around 6.5 FTEs. It is estimated that, altogether, about 20 FTEs are used to undertake assessments of hospital medicines and engage in price negotiations with pharmaceutical companies. In addition to the 20 FTEs, resources are drawn, among others, from human resource (HR) units. Moreover, additional resources are used for analyses performed by the Norwegian evaluation institute (Nasjonalt kunnskapssenter for helsetjenesten). In the UK, about 120 NICE employees undertake assessments of new (in and out-patient) pharmaceuticals. Like in Norway, resources are also drawn from units that are external to the evaluation institution. In Germany, about 40 FTEs are allocated to the evaluation of new (outpatient) pharmaceuticals by the Institute for Quality and Efficiency in Health Care (IQWiG). In addition, resources for price negotiation, procurement and reimbursement, among others, are drawn from the G-BA, GKV Spitzenverband, local sickness funds and health care providers. In the Netherlands, 17 ZiN employees undertake assessments of new (in and out-patient) pharmaceuticals. In addition, resources for price negotiation, among others, are drawn from the Ministry of Health, Welfare and Sport. Moreover, resources are drawn from health care providers and insurance companies for price negotiation, procurement and reimbursement. In Sweden, approximately SEK 9 million (about EUR 970,000) have been earmarked for the operation of "Ordnat Införande". In addition, resources are used for health economic assessments undertaken by the Swedish Dental and Pharmaceutical Benefits Institute (Tandvårds- och Läkemedelsförmånsverket, TLV), (7-8 employees). In Switzerland, 12 FTEs are employed by the FOPH to evaluate pharmaceuticals in relation to the maximum price system.

A necessary condition for value-based pricing is the allocation of resources to undertake assessments of pharmaceuticals. In the countries examined, the size of the health care systems and the availability of resources present different frameworks for the assessment of new medicines. For example, there are differences in how large a share of the new medicines undergo assessment, how comprehensive the assessment is and whether it involves a health economic evaluation. Generally, the health economic evaluations undertaken in the UK are more comprehensive than those undertaken in the other countries.

How are assessments of added value integrated with other elements in the regulation of pharmaceuticals?

Until now, the focus has been on assessments of and decisions to adopt new pharmaceuticals. Sensible use of pharmaceuticals – both clinically and financially – requires several other regulatory elements. However, it is outside the scope of the present report to provide a comprehensive overview of the wider regulatory frameworks. Instead, we mention a few elements with direct relevance to the organisation of pharmaceutical assessments and the setting of priorities for the adoption of new treatments.

When assessing new medicines, most evaluation institutions assess one pharmaceutical at a time and evaluate its value compared to an existing treatment. In some instances, a broader approach is warranted, however. For example, it can be necessary to undertake an overall assessment of an entire group of therapies for a patient group to ensure the use of cost-effective

treatment when patents expire. The adoption of the biosimilar TNF-alpha inhibitor Remsima® may serve as an illustration of this issue. It varies considerably among the countries whether and when Remsima® has been adopted and to what extent it is used as a substitute for the more expensive biological product, Remicade®. In the British health care system, which is generally known for its focus on cost-effectiveness, the adoption of Remsima® has been surprisingly slow. To stimulate the use of Remsima®, NICE was required to undertake a broad and rather time demanding assessment of the therapy area as a whole (rheumatoid arthritis). The broad assessment was necessary for NICE to issue a recommendation on the use of Remsima® as the preferred product. Without this formal recommendation, the hospitals had little incentive to start using the less costly product, because, as a rule, they are entitled to reimbursement of all treatments recommended by NICE. In the insurance-based health care systems, the incentives for health care providers to change their treatment behaviour are also limited. Unless pharmaceuticals are explicitly excluded from coverage under the statutory health insurance, sickness funds and health insurers are typically required to reimburse the treatment expenses. Therefore, the incentive structure will depend on the specific configuration of the reimbursement system in combination with local agreements between health care providers and insurers.

To stimulate clinically and financially sensible use of pharmaceuticals, it is important that regulatory structures support rather than counteract each other. For example, processes of procurement should be aligned with the assessment of new pharmaceuticals (e.g. via timely purchase of therapeutically comparable products undertaken by a shared procurement organisation), and reimbursement systems should stimulate the use of pharmaceuticals found to have added value. Moreover, monitoring and timely assessments of entire therapy areas (in contrast to individual assessments of single pharmaceuticals) is important to stimulate competition among comparable treatments.