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Pharmaceutical policies

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INNOVATIVE PAYMENT SYSTEMS FOR MEDICINES IN EUROPE



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An important policy objective for health care in most European countries is to obtain value for money from new pharmaceuticals. The authors consider policies regarding reimbursement and scan the horizon to identify new payment systems that may become more important.

An important policy objective for health care in most European countries is to obtain value for money from new pharmaceuticals when deciding on access and reimbursement. However, there should be sufficient reward for innovation in the pharmaceutical sector in order to sustain research and development of new products. Economists describe this as a subtle balance between static efficiency (getting value for money now) and dynamic efficiency (securing value for money in the future). A range of policies exist, including various forms of restrictions on the reimbursement of pharmaceuticals, price controls (sometimes involving cross referencing of prices in foreign countries), and policies regarding the delivery of pharmaceuticals like generic substitution or the use of prescription guidelines.

CURRENT POLICIES

Two policies have become popular in recent years: reference pricing and value-based reimbursement. Germany, The Netherlands and Sweden, for example, have introduced reference pricing. In this system pharmaceuticals judged to be similar are 'clustered' in a group. In The Netherlands medicines are clustered which have a similar area of application and a comparable method of administration, no clinically relevant differences in their properties and which are intended for a group of patients regarded as similar [1]. In other countries the definition of a cluster may be slightly different. Each cluster has a reimbursement limit, which is set using different criteria. Upon introduction in The Netherlands the arithmetic mean of the original prices of the drugs in the cluster determined this limit. Adding a new medicine to the cluster should not increase costs, since it is used in the

same target group as the existing drugs and cannot be reimbursed at a higher level. If the drug is priced above this limit, the difference between the limit-price and the actual-price needs to be paid out of pocket by the patient (co-payment). As manufacturers do not want patients to be deterred by co-payment, most of them choose to set prices at or close to the reimbursement limit. So when these systems were introduced there was a convergence of prices to the reimbursement limit producing initial savings, but in the long run the system appears to restrict a healthy price competition.

The second system, value-based reimbursement (using health technology assessment), considers the incremental cost-effectiveness ratio (ICER), comparing a new medicine with already existing alternatives, and grants reimbursement when this ratio is within an acceptable range. This system is now in place in Belgium, Germany, The Netherlands, Portugal and the Scandinavian countries. In the UK the National Institute for Health and Clinical Excellence (NICE) provides recommendations on the use of pharmaceuticals for the National Health Service (NHS) on this basis. In this system the manufacturer is stimulated to set a price which results in an acceptable cost-effectiveness ratio [2]. Pharmaceuticals that do not pass this test are excluded from reimbursement. However, this is not observed very often as in most cases the system leads to a narrowing of the indication of the drug to those subgroups for which it is most cost-effective. This in turn leads to restrictions on reimbursement for smaller patient groups.

Some countries, like The Netherlands, use both systems simultaneously. If a manufacturer in The Netherlands claims that a product is not thera-

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apeutically interchangeable but in fact more effective than current medication the manufacturer may request a premium price. In this case the company has to apply for admission to the list of non-cluster drugs, for which no reimbursement limit exists. They then have to demonstrate the superiority of the product in terms of cost-effectiveness. If approved, similar drugs may request to be treated likewise with reimbursement at the same level, and a new cluster starts. So value-based reimbursement is used to set the reimbursement limit of a new cluster [1].

In these systems a one-time decision about reimbursement is made shortly after licensing of the drug, when there is still rather limited information on what the effectiveness (and actual costs) will be when prescribed in everyday practice. The evidence available at registration is very much driven by regulatory requirements. In the case of pharmaceuticals the endpoints in trials, which have limited observation periods, will often be of an intermediate nature (surrogate endpoints like reduction in cholesterol levels rather than cardiovascular events such as myocardial infarction, cerebrovascular accident or death), which adds to the uncertainty. The chances of making a decision which is a false positive (allowing a drug which in the end appears to be not cost-effective or safe, e.g. rofecoxib) or false negative (disapproval of a medicine that may demonstrate value for money in actual practice or may be an important intermediate step toward real innovation) are significant. Furthermore, manufacturers will try to maximise sales after approval and have little or no incentive to stimulate cost-effective use of their drugs. Finally, many pharmaceuticals in the pipeline will have difficulty in getting approval under value-based reimbursement as they often have to compete against cheaper generic drugs while requiring a much higher price to at least pay back R & D. If reimbursement of new medicines is denied repeatedly due to this mechanism, dynamic efficiency in the market will be jeopardised.

INNOVATIVE PAYMENT SYSTEMS

After regular use in practice more information becomes available about the actual performance of a pharmaceutical, especially when it is subject to outcomes research.

Outcomes research is the analysis of outcomes and costs of technologies as they perform in daily practice, where compliance is less than perfect, where patients often have comorbidity (no exclusion criteria as in a phase III trial) and an average quality of care. Often these studies are based on observational designs in contrast to the experimental designs used in phase II and III trials. They pose specific methodological problems as biases have to be accounted for when analysing observational data. Such biases may relate to selection (more difficult and possibly risky cases get the new medicine) or information (incomplete or inaccurate data). So the uncertainty regarding the performance of new medicines will gradually decrease when more (clinical) experience is gained.



This triggered the development of so-called 'coverage with evidence development (CED)' meaning that the reimbursement decision is conditional upon the evidence which becomes available in a pre-specified period of time [3]. An example of such conditional reimbursement is the system of paying for expensive hospital drugs in The Netherlands [4]. After a preliminary assessment of cost-effectiveness a new, expensive hospital drug may be placed on a specific list. Health insurers will then reimburse 80% of the costs, leaving only 20% to be paid out of the hospital budget. The reimbursement is, however, condition-

al on the monitoring of the performance, i.e. cost-effectiveness, of the drug in practice. Continuation of this financing regimen depends on the results of an outcomes research analysis after three years. So for continued reimbursement the evidence about the performance in daily practice is emphasised.

These CED-systems may also be combined with sharing responsibility between stakeholders in so-called risk sharing agreements. A risk sharing agreement can be seen as: 'a contract between two parties who agree to engage in a transaction in which there are uncertainties regarding its final value'. Nevertheless, one party, the pharmaceutical company, has sufficient confidence in its claims of either effectiveness or efficiency that it is ready to accept a reward or a penalty depending on the observed performance of its product [5]. Risk may be shared between: government/insurer and manufacturer, government/insurer and prescriber

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(bonus/malus systems depending on prescribing performance), and government/insurer and patient (penalty on poor compliance). Here we concentrate on risk sharing involving government/insurer and manufacturer. Schemes may differ according to built-in incentives and indicators of success and may have different levels of sophistication. A rather simple measure of success is the limitation of total volume or total sales to a pre-specified maximum level. One example is the pay back schemes enforced by the *Commission de la Transparence* in France. These schemes involve the government and the manufacturer but the latter can be held responsible only to a certain degree given the global nature of the indicator for success and the lack of built in incentives to all stakeholders involved. In Germany, Novartis has offered to limit the maximum costs for ranibizumab (to treat wet age-related macular degeneration) at Euros 315 million per year. The arrangement was criticised, as the run time was relatively short, and then most doctors may have become familiar with the drug, perpetuating prescribing without a price arrangement. Pharmaceutical companies

will make every effort to maintain official list prices, as they may play a role in international reference pricing.

More sophisticated are risk sharing schemes where there is an indicator of success representing (cost-)effectiveness. This may be process related, e.g. appropriate use within the indication and penalties for prescribing outside the indication, or outcome related. In the UK, NICE has used cost-effectiveness as a performance indicator in the case of recommending multiple sclerosis drugs (cost-effectiveness in practice may not exceed GBP 36,000 (Euros 40,000)). In another case the NHS pays for bortezomib when used to treat multiple myeloma only when patients show a full or partial response to treatment after four cycles. If the patient does not respond sufficiently, the manufacturer must rebate the full cost of bortezomib treatment. Recently it was decided that ranibizumab will be paid for by the NHS up to a maximum of 14 injections (at a cost of more than GBP 10,000 (Euros 11,400)), with the manufacturer picking up the bill for any further treatment. In Germany, Novartis will refund the costs of using their osteoporosis drug, zoledronic acid, if a fracture due to osteoporosis occurs within a year after infusion [6]. Bayer offered patients in Denmark a refund if they were not satisfied with the erectile dysfunction drug vardenafil. Since 2006, the National Health Service of Italy has been using risk sharing, e.g. erlotinib when used for advanced non-small-cell lung cancer. The company is paid 50% of the usual price for two months, thereby refunding costs for about the 50% of patients that will see disease progression at or before eight weeks treatment. Similar arrangements have been made for other cancer drugs like dasatinib, sorafenib or sunitinib. So, if treatment is continued after response assessment, it is paid for at the full price [7].

There are obvious advantages of these schemes over a one-time decision on reimbursement just after registration if they comply with a number of conditions [3]:

- it must be possible to demonstrate the drug's contribution to efficiency (outcomes research)
- additional data collection should have the potential to reduce the uncertainty in a reasonable time frame
- the benefit of the scheme should justify the cost
- the risk taker must be able to significantly impact results
- no manipulation of the result indicator must be possible
- the flexibility of the arrangement should ensure the opportunity to have adequate study designs and reduce uncertainty about cost-effectiveness and safety.

The potential of these schemes is to reduce the chances of mistakes in terms of false positive and negative reimburse-



ment decisions. There is not much experience yet, however, with stopping reimbursement or limiting the use of pharmaceuticals when providers and patients have grown accustomed to using them.

CONCLUSION

Since the uncertainty about the performance of a pharmaceutical decreases later in its life cycle, there is an argument for deciding on reimbursement in steps and thus limiting the chance of a wrong decision at the start of the life cycle. The question is whether the transaction costs of step-wise decision-making (additional data collection, contracting and regulation) weigh up against the benefits (CED, risk sharing), i.e. a reduction in the chance of making a wrong decision and the associated costs of health improvement. The latter will be higher when the drug is expected to offer significant benefits but there is uncertainty around the clinical effectiveness or cost-effectiveness which can be overcome by evidence generated in an appropriate time frame [3]. Furthermore, conditional reimbursement may help to balance the arguments for static and dynamic efficiency and be more lenient toward those pharmaceuticals that hold a promise for real innovation. It is expected that in a number of cases the benefits of these schemes will outweigh their costs and that we will observe more in the future.

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