



BREVE 11

VALUE BASED DRUG REIMBURSEMENT: INTRODUCTION TO THE MAIN FEATURES OF THE GERMAN PHARMACEUTICAL POLICY

Based on a presentation at Red Criteria by Dr. Wolfgang Greiner, September 2015

A series on policies and methods based on presentations for experts. Prepared by CRITERIA, a knowledge network on prioritization and health benefit plans from the Inter-American Development Bank.



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VALUE BASED DRUG REIMBURSEMENT: INTRODUCTION TO THE MAIN FEATURES OF THE GERMAN PHARMA- CEUTICAL POLICY

INTRODUCTION

This *Breve* is based on a webinar presented by Dr. Wolfgang Greiner, professor at the University of Bielefeld, member of the scientific Advisory group of the German Institute for Quality and Efficiency in Health Care (“IQWiG”)¹ and the EuroQol² group. The presentation was delivered on September 29, 2015, to the members of CRITERIA, the Knowledge Network on Health

1 IQWiG is an independent scientific institute, which examines the benefits and harms of medical interventions for patients. It provides information about the advantages and disadvantages of examination and treatment methods in the form of scientific reports and easily understandable health information. (<https://www.iqwig.de>)

2 The EuroQol Group Association (“The EuroQol Group”) comprises a network of international, multilingual, multidisciplinary researchers focusing on health and health care topics, originally from seven centers in England, Finland, the Netherlands, Norway and Sweden.

Benefits Packages and Priority Setting in Health the Inter-American Development Bank³.

Health care budgets around the world are hit by the increasing costs of medicines, especially new, innovative drugs, which tend to be very expensive. Germany, which is the most important market for pharmaceuticals in Europe, has also been facing exploding costs due to increasing drug prices. In 2011, Germany introduced the new drug regulation law AMNOG (Gesetz zur Neuordnung des Arzneimittelmarktes) with the aim to reduce the rising costs of pharmaceutical expenditure of the sickness funds, and to provide fair competition on the market. The idea was to create a balance between innovation and containing the costs of drugs.

The following *Breve* looks at the German experience with regards to its policies meant to reduce the pharmaceutical expenditure. It provides an overview of the different ways of regulating the pharmaceutical market, and of controlling access to reimbursement.

3 The audio, PowerPoint presentation and transcript can be accessed on the website of CRITERIA at: [http:// www. redcriteria.org/webinars](http://www.redcriteria.org/webinars)

PHARMA- CEUTICAL EXPENDITURE REGULATION: WHY CARE?

Pharmaceutical expenditure has increased steeply over the past years in many countries around the world. Policy makers face the challenge of regulating the pharmaceutical market in a context of tension between scarce resources to finance health care systems and high costs of innovation. The pharmaceutical industry is interested in achieving a high price, yet other interest groups like doctors, patients and policy makers struggle with increasing expenses.

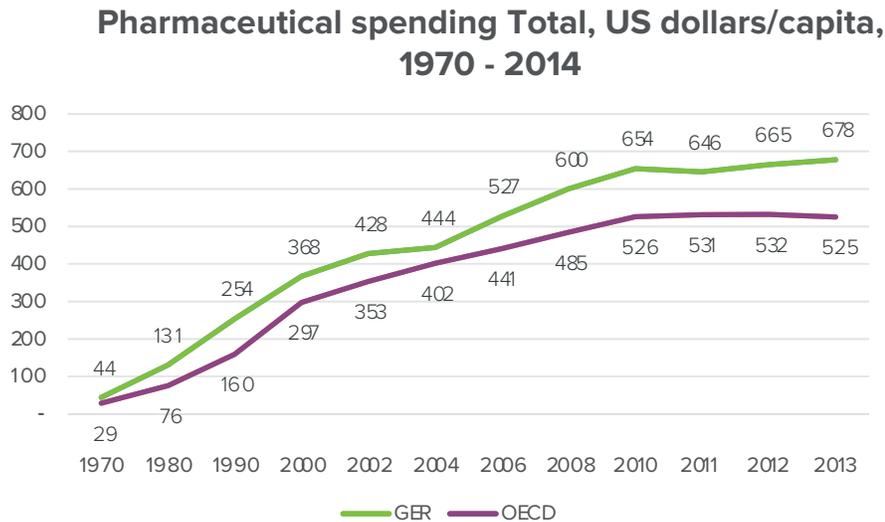
Pharmaceutical expenditure regulation implies two important aspects: regulation of generic drugs and regulation of innovative drugs. Regulation of generic drugs is crucial because of its potential to save important resources. Innovative drug pricing is complex and challenging yet, also crucial since prices for innovative treatments can be very high. As a recent Breve on the “Cancer Industry and the Pharmaceutical Policy in Germany”⁴ illustrates, in the U.S., prices for cancer drugs, for one year of therapy, have ten folded from around \$10.000 to \$100.000 from 2000 to 2012. At the same time household income has decreased⁵.

Prices for pharmaceutical products vary and depend on a countries economic wealth, regulatory policies and control mechanisms in place. Depending on the context, different criteria should be taken into consideration to design drug pricing and drug reimbursement policies. High drug prices can have a considerable impact on pharmaceutical expenditure. Drug prices in Germany have been higher than the average price of all OECD countries but they are now about the same as the average in these countries. Pharmaceutical expenditure in Germany has experienced significant growth during the last decades.

⁴ The Breve “Cancer Industry and the Pharmaceutical Policy in Germany” is based on a presentation by Dr. Karl Lauterbach. He recently published a book on the “Cancer Industry” in Germany.

⁵ Mayo Clinic Proc. 2015, 90(4): 500-504

Figure 1. Development of expenses for drugs per capita



Source: OECD, health expenditure indicators

Figure 1 clearly shows how expenditure increased considerably in all OECD countries between 1970 and 2010. Since 2010, OECD countries, including Germany, have taken stricter measures to control expenditure. The development of expenses shown in the graph demonstrates that countries have been successful in slowing down pharmaceutical expenditure growth. In addition, the amount of generic drugs has incremented. This has also contributed to a decrease in expenses in some countries like Germany.

The next section provides an overview of the main regulatory measures that were taken in Germany. It explains different control mechanisms and incentives to influence supply and demand of pharmaceuticals, and how the different parties involved in this process can shape it.

In Germany growing expenditure and high prices were the main drivers for the decision to strengthen the pharmaceutical policy through different means, focusing on legal regulations and policy revisions rather than simple price cuts.

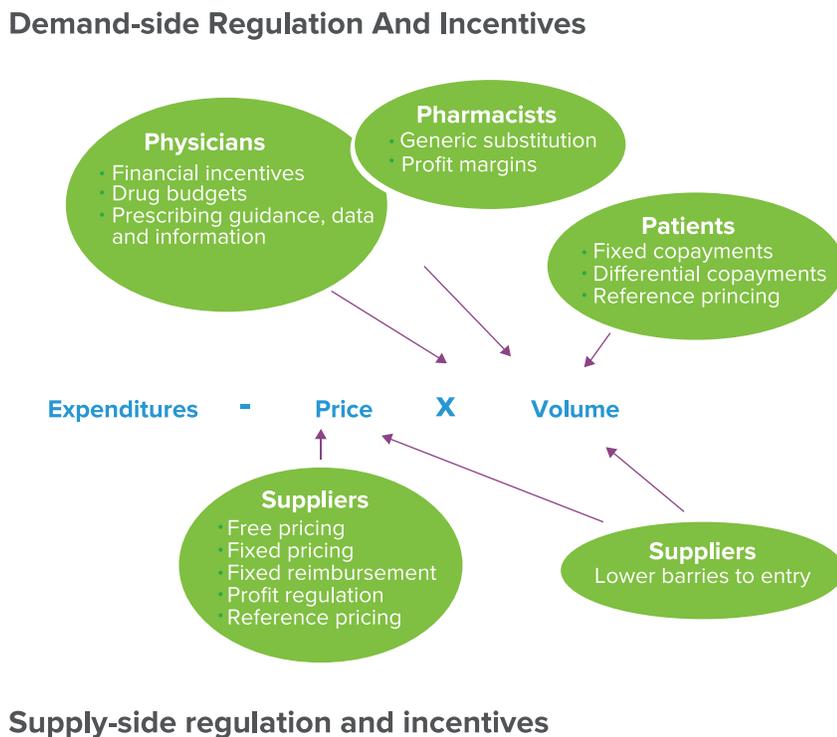
OVERVIEW OF REGULATORY MEASURES REGARDING PHARMACEUTICAL EXPENDITURE

Policies to regulate prices and reimbursements can be targeted at different actors and can focus on the demand side as well as on the supply side. Some national governments prioritize supply side measures and others focus more on the demand side.

As a starting point, it is important to understand that the pharmaceutical expenditure of a country equals the price multiplied by the volume of drugs dispensed. Therefore both the price and the volume are important variables to be considered by pharmaceutical policy regulations.

Figure 2 illustrates the influence of the different stakeholders on the volume and the price of pharmaceutical products. These stakeholders are physicians, pharmacists and patients on the demand side, and suppliers on the supply side. Players on the demand side mainly influence volume, while supply side players affect both the price and the volume of drugs.

Figure 2. Measures to regulate prices and reimbursement



DEMAND-SIDE PHYSICIANS

Physicians are the most important group influencing the demand of pharmaceuticals since they issue the prescriptions. There are three main policy measures focused on physicians:

1. Financial Incentives

Financial incentives can encourage doctors to prescribe more generic drugs. In Germany “integrated care” initiatives have been implemented in some parts of the country. One element of this initiative is a system of premiums for doctors who achieve a higher generic quota in their prescriptions, compared to the average percentage of generics prescribed across the country. Currently about 75 percent of all prescriptions in Germany are for generics. This might lead to quality problems if the doctors feel pressured to receive the financial incentive and as a consequence don't prescribe new innovative drugs, which are very costly. There is however no evidence to show that this is currently a problem in Germany.

2. Drug budgets

Germany moved from regional budgets to physician-level drug budgets. The size of the budget per physician depends on the type of practice and the number of patients. For example a dermatologist has a lower drug budget per person than an oncologist. If a doctor surpasses the established quarterly budget, a consulting session is held to advise the doctor on how to save money. If doctors surpass their individual medicine budget by

25 percent they have to refund the difference between the actual budget and the target budget in case they cannot justify the higher expenses. This has only occurred in a few cases and this regulation has had a considerable impact on the prescription behavior of physicians. It is unclear how these drug budgets impact quality since there is currently no control mechanism in place.

3. Prescribing guidance

Prescribing guidelines not only set a framework which mandates doctors to prescribe rationally and consistently according to the medicine's indications and therapeutic needs of their patients, but they also favor the choice of the cheaper alternatives among those that are medically interchangeable⁶.

In Germany the General Assembly Board (G-BA – Gemeinsamer Bundesausschuss⁷) issues a prescribing guideline⁸, which establishes the kind and the quantity of a drug that can be prescribed for each indication. The decision on what is being paid for and what is included in the prescribing guidance is therefore taken between the sickness fund and the physicians.

⁶ Panos Kanavos (2011), Overview Of Pharmaceutical Pricing And Reimbursement Regulation In Europe

⁷ The G-BA The Federal Joint Committee (G-BA) is the highest decision-making body of the joint self-government of physicians, dentists, hospitals and health insurance funds in Germany.

⁸ Heilmittel Richtlinie

DEMAND-SIDE PHARMACIST

Pharmacists play an important role in influencing the demand of pharmaceutical products, mainly because they are in part responsible for generic substitution. Since 2002, pharmacists in Germany must substitute and dispense equivalent lower cost, generic medicines, unless the physician explicitly rules this out by ticking a box on the prescription ('Aut-idem-Regelung')⁹.

Pharmacists receive a fixed margin per service of 3% of the price of the drug and an additional allowance per prescription, as well as 0.16 Euro as a compensation for ensuring an emergency service. Before the German health system reform in 2004¹⁰, compensation of pharmacists was calculated exclusively as a percentage of the price of the drugs sold. Therefore, pharmacists received high premiums for expensive drugs and had an incentive to sell them.

DEMAND-SIDE PATIENTS

Patients have an impact on the demand of pharmaceuticals through copayments. If copayments are too high patients cannot afford the drugs and if they are too low they won't influence the demand of drugs and there is no impact on the saving of health care costs. In the German health system, copayments are low compared to other countries. Patient copayments are 10% of the pharmacy retail price, with a minimum fee of 5 Euros and a maximum of 10 Euros per prescription. In addition the regulation includes a social clause, which limits the copayment to a maximum of 2% of gross income per year.

In other countries, such as the US or Canada, copayments are much higher. In France, for example, a system of differential copayment is in place. In a differential copayment system patients pay a certain percentage rate depending on certain factors for example how essential the drug is. For example, patients suffering from a cold pay a higher copayment for the drugs they need than patients with serious illnesses.

⁹ Gabi – Generics and Biosimilars Initiative (2014): German Policies and Legislation

¹⁰ Gesetz zur Modernisierung der gesetzlichen Krankenversicherung

SUPPLY-SIDE POLICY MEASURES INFLUENCING THE PRICE

On the supply side, policy measures to control costs can either influence the price or the quantity of pharmaceuticals. With regards to prices, countries can resort to different policies such as profit regulation, free pricing, fixed prices, fixed reimbursement, or reference pricing. Most European countries directly exert control over drug prices.

Some countries use free pricing. This was the case in Germany before the recent reforms, and it involved substantial increases in the expenditure for pharmaceuticals. In other countries policies of fixed reimbursements can be found. This means prices have to be fixed and value for money may come into play, an issue that will be discussed later. In the U.K. a profit regulation is in place, which implies that the prices of all branded drugs must be set so as to ensure that the overall rate of return on capital is within the authorized boundaries negotiated between the authorities and the pharmaceutical companies¹¹. Finally many countries resort to reference pricing a policy under which the prices charged for drugs within the country (internal reference pricing) or in other countries are taken into consideration when establishing prices.

¹¹ Panos Kanavos (2011): Overview Of Pharmaceutical Pricing And Reimbursement Regulation In Europe

SUPPLY-SIDE POLICY MEASURES INFLUENCING THE VOLUME

Entry barriers are a policy measure taken by many countries to influence the volume of pharmaceuticals on the market. Australia, for example, has high entry barriers. If a product is not on the list of drugs that can be subscribed it cannot enter the market. The manufacturer has to contact the regulators and apply for market entry for the new drug. In Germany, on the contrary, any approved drug can enter the market. Once a certain price for the drug is set, manufacturers can decide if they want to stay on the market or opt out. Lower barriers to market entry may improve competition and provide more options to patients and doctors.

PRICING OF PHARMA- CEUTICALS IN GERMANY

The German regulatory instruments for the pharmaceutical sector are applied at several levels: industry, physician, pharmacy and patient levels.

At industry level, several regulatory measures have been taken and pricing regulations are a crucial instrument for policy makers in this

context. In Germany, the main regulations at the industry level include:

· **AMNOG**

One of the main changes has been a central benefit assessment and price regulation of innovative drugs through the new drug regulation law AMNOG (Arzneimittelneuordnungsgesetz), which was introduced in 2011. This aspect will be discussed in more detail below.

· **Price Moratorium**

A price moratorium was in place in Germany, which meant that the price of drugs could not be raised. When the moratorium was lifted, pharmaceutical expenditure increased by more than 10 percent.

· **Compulsory discounts**

Pharmaceutical manufacturers also have to grant some compulsory discounts to the public health insurance funds with the aim of reducing costs for drugs

· **Reference prices**

Germany uses an internal reference pricing system for generics and for drugs that have a generic alternative. For new, innovative drugs a different mechanism is used to regulate pricing which is defined in the new drug regulation law (AMNOG). The following sections look at these differential processes for generics and innovative drugs in more detail.

REFERENCE PRICING

A reference pricing system is a system that establishes a reimbursement level or reference price for a group of interchangeable medicines. If a medicine is priced above the reference price, the patient pays the difference between the price of the medicine and the reference price (Dylst et al., 2012).

Reference pricing was introduced in Germany in 1988 in the context of the reform of the health sector (Gesundheitsreformgesetz - GRG), and as a measure to confront the rising prices of medicines. It was gradually extended over the years to different groups of medicines.

Reference pricing in Germany refers to the existence of an internal reference price. The process is divided in two steps. First, pharmaceutical products are categorized in three groups. This is done by the Federal Joint Committee (G-BA)¹². As a second step the reference prices are determined by the sickness funds.

12 The Federal Joint Committee is the supreme decision-making body in statutory health care in Germany. Physicians, dentists, hospitals, sickness funds and patients are represented in the committee.

Figure 3. Grouping of pharmaceuticals in Germany

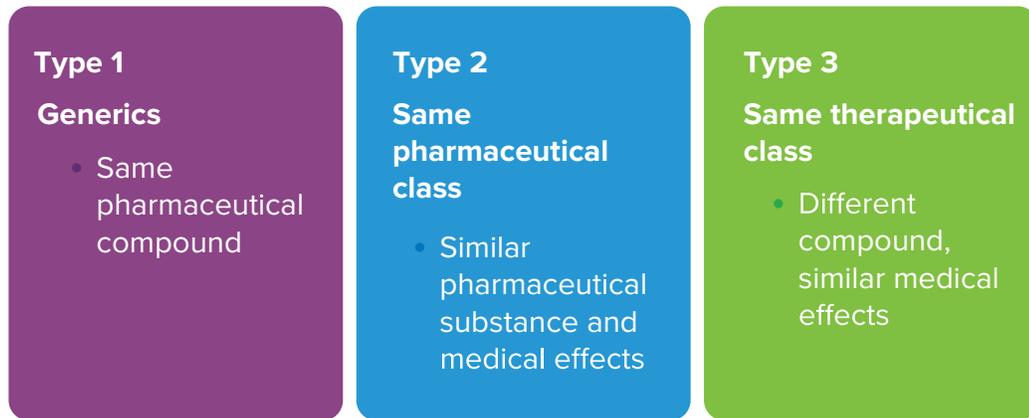


Figure 3 summarizes the different groups of pharmaceuticals determined by the G-BA. Type 1 includes medicines with the same compound, type 2 are pharmaceuticals with a comparable pharmaceutical substance, and type 3 medicines with different compounds but the same therapeutic effect. This classification allows doctors to choose alternatives within the groups. For each reference price group the G-BA determines the average daily dose and standard package size, which is then the basis for the calculation of the price. The (quite complex) determination process of the reference price does not differ by reference price group type (type 1, 2 or 3).

Reference prices are determined based on the prices of the whole market for each product. To determine the reference prices, products are ranked according to their price and reference prices are set at the level of the highest price in the lower 30% of the price range for each product.

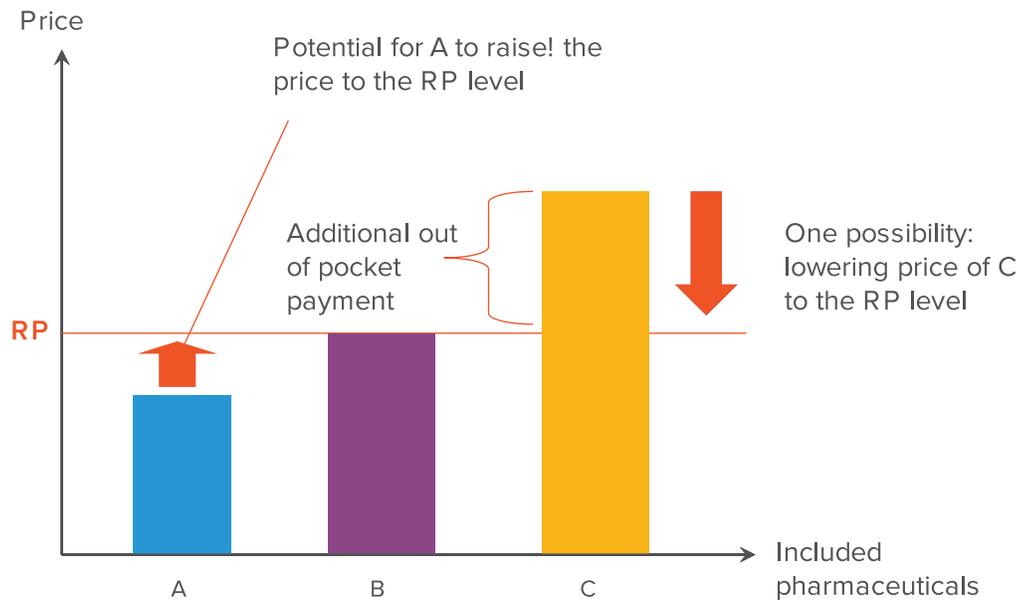
In the case that the physicians prescribe a medicine with a price that is above the reference price, they have to inform the patient that the difference will have to be paid by the patient himself and that a cheaper alternative exists. This is always the case since the reference price is usually set for products for which generic substitutes exist¹³¹⁴.

Figure 4 shows how prices are adjusted in relation to the reference price. If the price for a product is higher than the reference price, the drug manufacturer has the option to lower the price to the reference price level, or to keep the higher price. In that case, the insured has to pay out of pocket for the difference. If the price is set below the RP the manufacturer can raise it. Yet in the

13 Gemeinsamer Bundesausschuss (2016): Festbetragsgruppenbildung (grouping of pharmaceuticals) <https://www.g-ba.de/institution/themenschwerpunkte/arzneimittel/festbetrag/>

14 In principle, reference price groups are also possible for drugs still under patent, but this is not very likely as these kinds of drugs are usually very similar in price (and then no discount is possible).

Figure 4. Internal Reference Price Groups



case that the price is 30 percent below the RP level it can be convenient for the manufacturer to keep the lower price, since copayments for the patient are lifted in these cases. This provision was introduced based on requests by patients to have a zero copayment option.

PRICING FOR INNOVATIVE OR PATENT DRUGS VIA AMNOG

Innovative drug pricing is more challenging and more complex than the internal reference pricing system, yet it is crucial since innovative drugs are very expensive and constitute the lion’s share of the increase in pharmaceutical expenses.

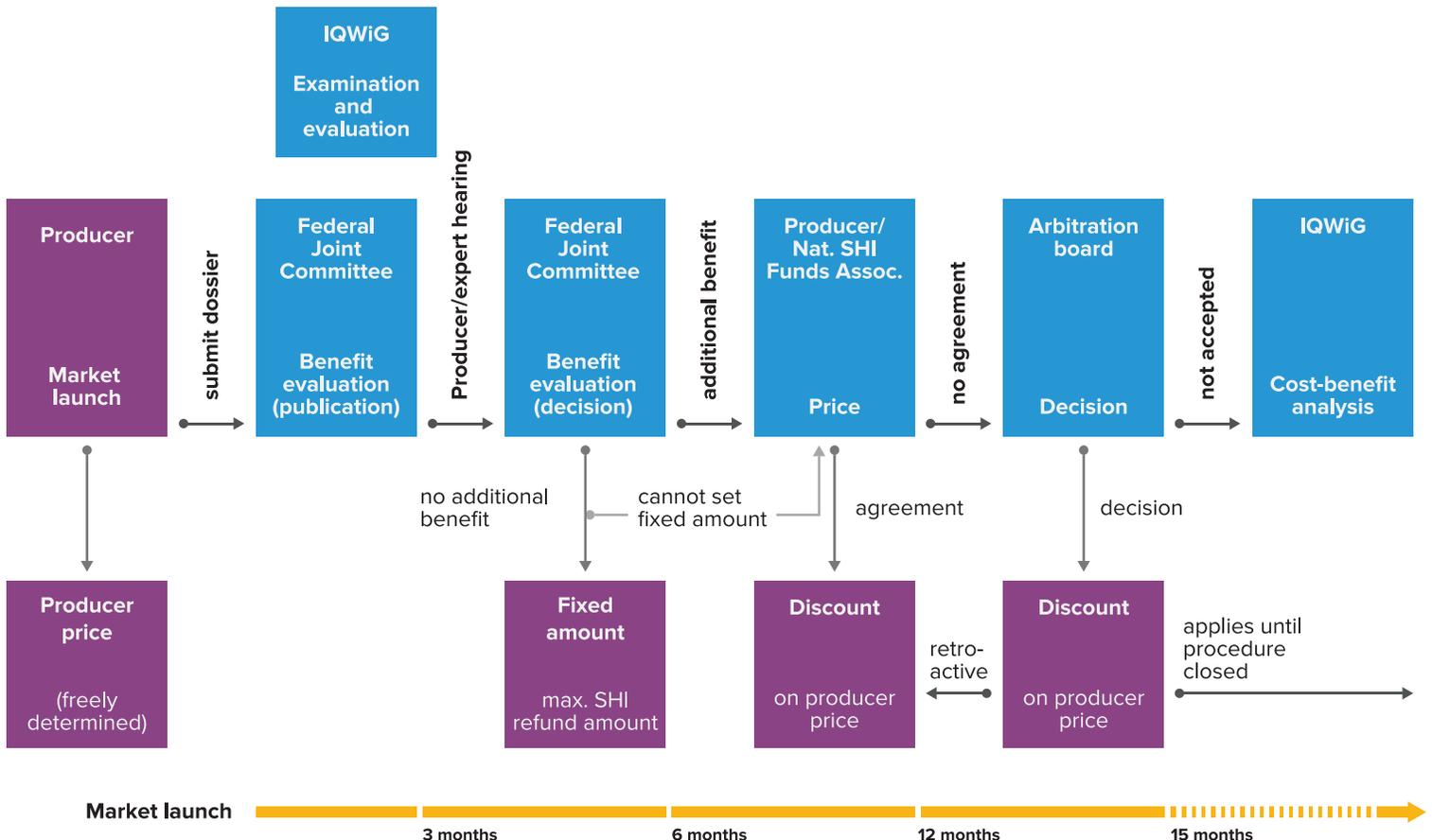
As analyzed in a recent *Breve* on the “Cancer Industry”¹⁵, in many countries around the world, providing extremely high drug prices for new innovative drugs are affecting the financial sustainability of health care systems. Especially for cancer new treatments are very important. Dr. Lauterbach estimates that within the next 15 years expenditure for drugs in Germany will increase from 6 billion Euros per year to 40 billion Euros per year. In many countries with a less strong solidarity system than the German system, patients are struggling to pay for their treatment.

¹⁵ This *Breve* was based on a presentation by Dr. Karl Lauterbach. He recently published a book on the “Cancer Industry” and Pharmaceutical Policy in Germany.

Germany tried to mitigate this increase in expenses by introducing a new mechanism to define pricing for innovative drugs. The process, which was established in 2011 by the “Law on the Reorganization of the Pharmaceutical Market” (AMNOG), is meant to ensure better cost-efficiency. In addition this new law aims at making sure that only the most effective drugs, which can prove their additional value for patients, are on the market. The Federal Joint Committee (G-BA - “Gemeinsamer Bundesausschuss”), along with the Institute for Quality and Efficiency in Health Care (“IQWiG”) are in charge of assessing newly authorized pharmaceuticals.

Before AMNOG, Germany was one of the few European countries where pharmaceutical companies could set drugs prices freely. Since 2011 manufacturers have to prove the additional benefit of a medicine for new innovative drugs immediately at market entry. The process is described in Figure 5 and summarized in the box that follows.

Figure 5. German benefit evaluation and remuneration process according to AMNOG



Source: Federal Ministry of Health (Bundesministerium für Gesundheit), 2016

Box: The AMNOG policy process in a nutshell

Under AMNOG, pharmaceutical companies can set the initial list price when they bring a new drug to market. Upon launch, however, they have to submit a cost-benefit dossier to G-BA, the self-governance body that makes reimbursement decisions. On the basis of the dossier, and views from other stakeholders, G-BA assesses the drug's benefits over recognized, standard therapies, taking into account conversations with the Institute for Quality and Efficiency in Healthcare (IQWiG) to consider patient-related benefits.

G-BA has six months to make this assessment and award the drug a final rating between one and six – Level 1 denotes “extensive benefit” over a chosen comparator, while Level 6 means “less benefit” than the comparator. The same product can receive different ratings based on patient subpopulations within the product's licensed indication. Based on these ratings, the company then enters negotiations with the National Association of Statutory Health Insurances, which represents all the SHI funds, to set the reimbursement price. One year after market launch, this reimbursement price replaces the initial list price of the drug.

Source: Sieler et al. (2015)

Directly after approval of a drug by the European Medicines Agency, the manufacturer can enter the German market and set a price freely. This price is valid during the process of pricing assessment through the AMNOG, which takes one year. Figure 6 shows the different steps during the 12 months until the price is decided on. Generally, the volume of drugs is not very high during the first year since the producer has to promote the new drug among the doctors. Therefore the first year of free pricing has not led to many problems so far. Nevertheless, this first year of free pricing has caused some controversy especially since, in a few isolated cases, the expenditure during the first year has been very high. The most prominent example

was the introduction of a new Hepatitis C drug on the German market. These very costly drugs are much more effective than previous treatments that were already available. The first year of free pricing for these treatments led to an explosion in costs for the German health care system.

Figure 6: Timeline for price setting decision



Source: DGHO (2015): Frühe Nutzenbewertung neuer Arzneimittel in Deutschland 2011-2014

Although the manufacturer is allowed to set a free price at market entry, the pharmaceutical company is obliged to present a dossier to the G-BA. This dossier includes a compilation of all studies that have been carried out regarding the new drug. Specific rules have to be followed by the producer. This dossier has to be complete and provide an unbiased overview. The manufacturer has to include all available studies, not only the ones that are favorable to the manufacturer. In the event that not all documents are properly included, manufacturers are accountable and can be taken to court. Therefore, generally manufacturers prepare these documents very carefully. The preparation of these dossiers can be very costly. An agency charges approximately 300.000 to 400.000 Euros to prepare a dossier. Once the document has been delivered to the Federal Joint Committee (G-BA) they analyze it. The Institute for Quality and Efficiency in Health Care ("IQWiG"¹⁶)

carries out the scientific part of the analysis. They look into the studies and determine if the drug provides an additional benefit.

ADDITIONAL BENEFIT CATEGORIZATION

Figure 7 shows the additional benefit categories established by AMNOG. If the medicine is assigned to a category with a higher additional benefit, the price can be higher. In case that there is no additional benefit, the drug falls directly into the reference price group and gets assigned a fixed amount. The findings are presented at a public expert hearing.

In Germany, a discussion to define who should participate in the assessment and the decision making process has taken place, including subjects like the ways in which doctors should be involved. In other countries, the participation of different stakeholders in the decision making process is organized

¹⁶ IQWiG is an independent scientific institute, which examines the benefits and harms of medical interventions for patients. It provides information about the advantages and disadvantages of examination and treatment methods in the form of scientific reports and easily understandable health information. (<https://www.iqwig.de>)

differently. In the UK, for example, anybody who is in some way involved in the health care system can participate and present their opinion, which will then be included in the decision making process.

Figure 7: Additional Benefit Categories according to AMNOG

Significant additional benefit: Healing, significant prolongation of life time, long-term absence of severe symptom or avoidance of severe adverse events.

Considerable additional benefit: Dilution of severe symptoms, moderate prolongation of life time. For patients, noticeable relief of illness.

Marginal additional benefit: Reduction of not severe symptoms of illness.

Not quantifiable additional benefit.

No additional benefit: No proven higher efficiency of the new drug (compared to the comparison therapy).

Source: Adapted from DGHO (2015): Frühe Nutzenbewertung neuer Arzneimittel in Deutschland 2011-2014

Between 2011 and 2014 the majority of the innovative drugs were categorized with “no additional benefit” or “marginal additional benefit”. Only once in 150 cases assessed by the IQWiG, an innovative drug was classified as having a “significant additional benefit”¹⁷.

¹⁷ DGHO (2015): Frühe Nutzenbewertung neuer Arzneimittel in Deutschland 2011-2014

In this case the drug has to lead to healing, lead to a long-term prolongation of life of about five or ten years, demonstrate long-term absence of severe symptoms and extensive prevention of severe side effects.

In some cases benefits are not quantifiable. This is often understood as if the drug does not have any additional benefit. Yet, this is not the case. If the additional benefit is not quantifiable the studies are not thorough enough. Oftentimes this happens when orphan drugs are assessed¹⁸.

PRICING

The Federal Joint Committee (G-BA) judges the additional benefit yet, it does not decide on the price. Prices are negotiated on the basis of the benefit assessment. Yet, the actual influence of the additional benefits categorization on prices is not exactly known. Oftentimes those innovative drugs with a more considerable benefit achieve a higher price. Nevertheless, this is not an automatic process. The price is negotiated between the manufacturer and the sickness fund association. Therefore, there is a separation between the decision on the benefit and the price. If there is no agreement between the producer and the sickness funds an arbitration board takes the final decision.

The price is negotiated on the basis of three factors: 1) the magnitude of the additional benefit,

¹⁸ DGHO (2015): Frühe Nutzenbewertung neuer Arzneimittel in Deutschland 2011-2014

2) the price of appropriate comparison treatment and 3) the average European price. If a cheap comparison treatment is available it might be difficult for the manufacturer to achieve a high price.

COST BENEFIT ANALYSIS

In contrast to other countries, such as the UK or Australia, where cost benefit analysis play a mayor role in determining the prices of drugs, Germany does not use cost-benefit analysis as a basis for pricing. In the past, some universities carried out cost-benefit analysis. Nevertheless, research money has recently rather been spent on medical research and on compiling the required dossiers, which are rather costly, even though minor when compared with the study costs.

In theory, the manufacturer can ask IQWiG for a cost-benefit analysis in case that the arbitration board sets a price which the producer does not accept. This is the only step in this process where a cost benefit analysis can come into play. Nevertheless, it has not been carried out in practice. Manufacturers prefer not to ask for it since they don't perceive the IQWiG as a partner but rather as a controlling instance, which examines them thoroughly.

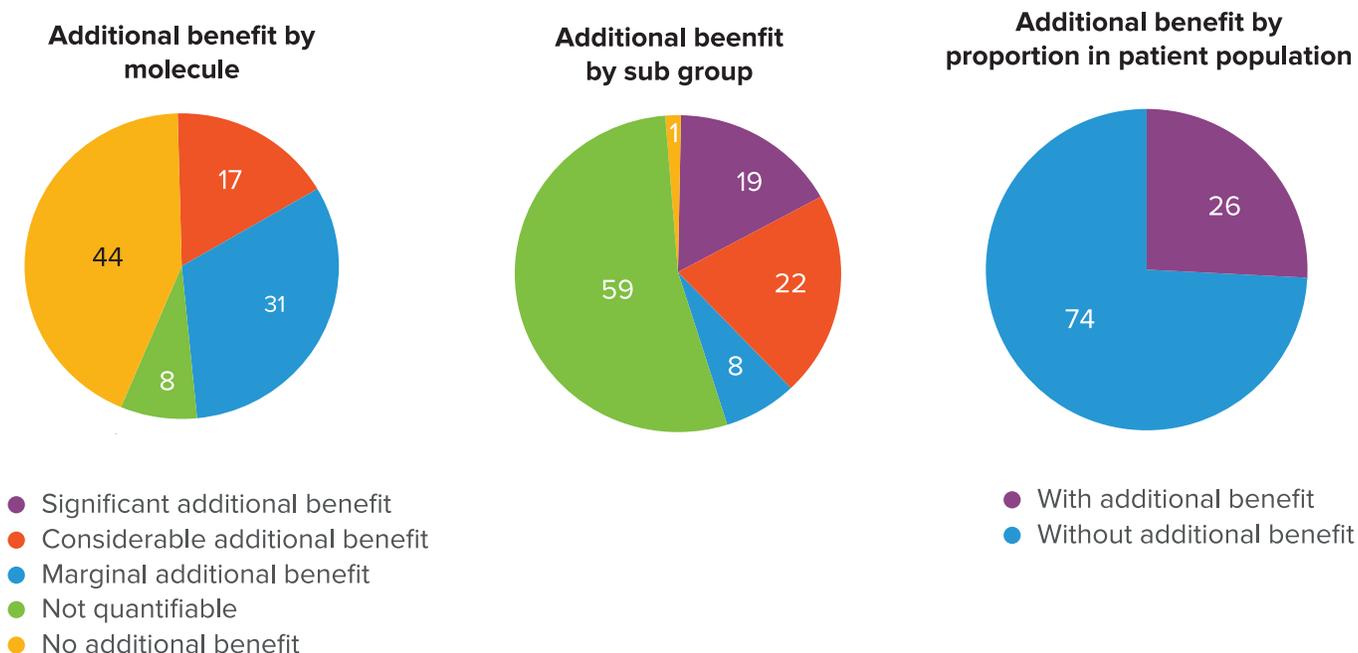
RESULTS

The results of the analysis of additional benefits by the AMNOG process depend on which group is taken into consideration. Figure 8 shows

the additional benefit by molecule, by patient sub group, and by proportion in the patient population. The number of cases where an additional benefit was found is higher when looking at the molecule than at the sub group. Especially the number of cases qualified as having no additional benefit is much higher by subgroups (59%) than by molecules (44%).

As far as the proportion of the patient population is concerned, 74% of the cases are classified without an additional benefit. If there are several patient sub groups, the additional benefit might just apply to a small sub group and, as a result, the number of cases without an additional benefit is elevated. In these cases, it is difficult for the manufacturer to prove that there is an additional benefit at least in the subgroup.

Figure 8: Experiences with AMNOG: Additional benefit



Source: Greiner/Witte: AMNOG-Report 2015

CHALLENGES REGARDING THE AMNOG PROCESS

Over the years, several challenges have emerged regarding the AMNOG process, including the following:

· Lack of long term benefit assessment

Germany, there is no benefit assessment foreseen to assess if drugs meet their expectations after a certain period of time. This type of analysis is complex. It can be based on sickness fund data but then it does not achieve the same quality as a real study since, for example, it lacks the control group.

· Bypassing of benefit assessment

In some instances, the benefit assessment process can be evaded. This is the case,

for example, for orphan drugs, which are needed by a limited number of patients (if sales are less than 50 million Euros p.a.). For these drugs for the treatment of rare diseases, IQWiG only assesses the cost of therapies and patient numbers.¹⁹

· Quality of life

Quality of life, as reported directly by patients, is considered to be an important aspect under German law. Recently, more studies take this important factor into account than before. Formerly, the only aspects considered were related to mortality, complications and safety of the treatment.

¹⁹ DGHO (2015): Frühe Nutzenbewertung neuer Arzneimittel in Deutschland 2011-2014

An analysis of the AMNOG process shows that 80 percent of the dossiers include some information regarding quality of life. In half of these cases the manufacturer suggested that an additional benefit could be derived from the quality of life data. As of the end of 2015, only in eight cases the G-BA decided for an additional benefit based on quality of life. In many countries, including Germany, quality of life research is considered too soft.

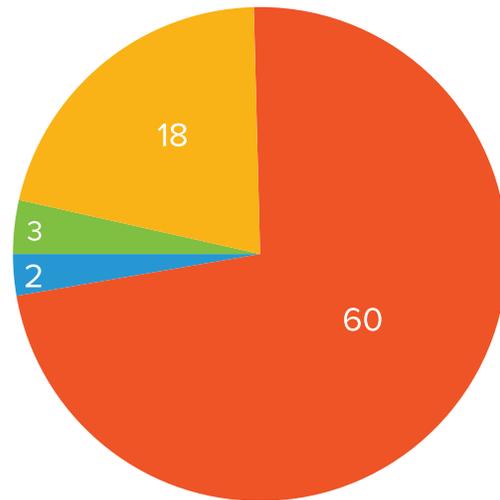
There is still a lot of improvement required in this area, in order to better incorporate patient reported assessments of quality of life into determining the added value of a treatment.

Market exit

In some cases manufacturers decide that the price set for their product is too low. They might decide to opt-out and take their product off the market. Figure 9 shows, that as of the end of 2014, 80 cases were registered out of which 18 decided to leave the market. Those who accept are assigned to a reference price group. The positive effect of this regulation is that manufacturers that know that their product does not have an additional benefit agree to be assigned to a reference price group and do not negotiate to achieve a higher price.

Figure 9: Market exit (“Opt-Out”)

Reimbursement status of all compounds which have been assessed until the end of 2014 (n=83) per 08.06.2015



- price was successfully negotiated
- price has been fixed by arbitration board
- reference price group
- opt-out

Source: Greiner/Witte: AMNOG-Report 2015

Choice of appropriate comparison treatment

There is an ongoing discussion in Germany on how to identify the adequate comparison treatment. Producers claim that their product is compared to very cheap generic alternatives. Choosing the right comparator is not only important from a point of view of pricing but also from a medical point of view.

· Subgroup based pricing

Patient subgroups are sometimes used in market admission studies and in the dossiers presented by the manufacturer, because some compounds have different effects according to the patient group, the stage of the disease or previous therapy. In the event that additional benefits might only apply to certain subgroups within the patient groups. This can be scientifically challenging because evidence is generally not defined for these smaller sub groups. For the manufacturer it can therefore be difficult to prove that there is an additional benefit.

· Temporary free pricing in the first year after market launch

As analyzed in a previous section, the fact that the manufacturer can establish a free price until the AMNOG process determines a price has caused some controversy. New, innovative drugs are very costly and treatment costs can be a big burden for the health care system. On the other hand, sales in the first year are usually not very high, as prescribers are not yet used to the new drug.

· No cost-benefit analysis

As discussed before, cost-benefit analysis is not used as a tool to determine prices of drugs in Germany. Cost-benefit analysis could be a valuable and useful addition to show the value of a new drug. Even though it is foreseen as a last step in the AMNOG process, it is not applied in practice.

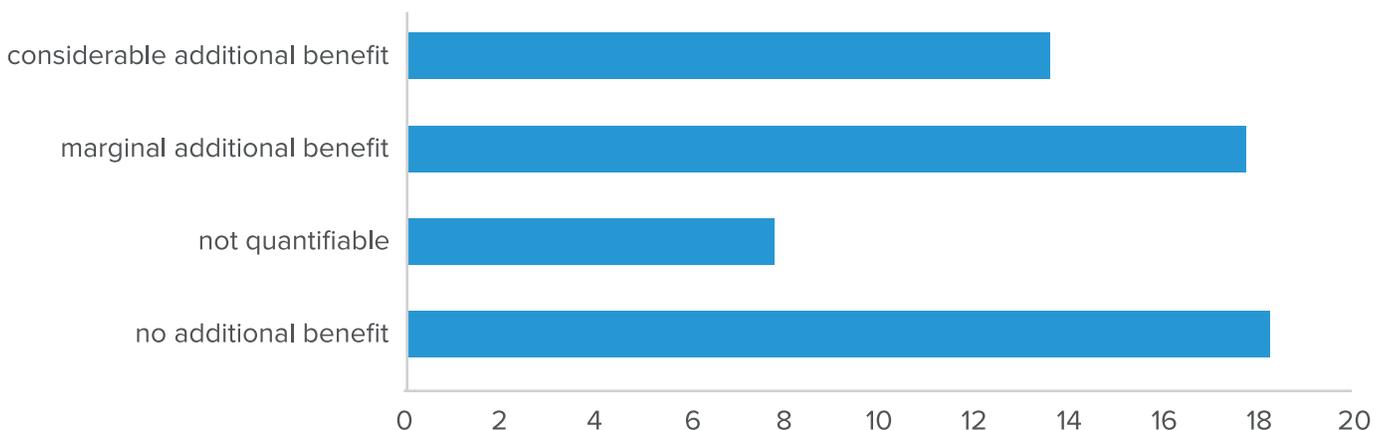
· Benefit assessment of drugs which were launched before AMNOG

Innovative treatments, which have been launched before 2011, are not subject to the AMNOG procedure and can therefore have higher prices without an assessment.

· Influence of additional benefit on prescription behavior

Figure 10 shows that there is an increase in the number of prescriptions, even for drugs qualified as having no additional benefit. This occurs because of a lack of communication of the assessment results to the doctors. Information systems are in place to improve access to these results.

Figure 10: Influence of additional benefit on the prescription behavior



Source: Greiner/Witte: AMNOG-Report 2015

CONCLUSIONS AND POLICY OUTLOOK

Germany expected to achieve 2.2 billion Euros of savings per year due to the newly introduced drug regulation law AMNOG. Nevertheless so far the savings have only reached about 250 million Euros per year. But this is mainly due to the fact that AMNOG has been introduced just 5 years ago. The savings increase year by year, as the average discount is about 15 % as expected.

In addition, the AMNOG has some other positive impacts. One of the positive effects has been an increase in the quality of studies. Manufacturers are under pressure to present a successful dossier to IQWiG. Another positive consequence is that value based pricing contributes to improving patient care. It is not just an instrument to contain costs. If the outcomes of the assessment of added value are communicated successfully to the prescriber, this can have a positive result for the patient.

Price regulation for drugs is a complex topic, which causes controversy. Different groups including, governments, insurance funds, manufacturers, patients, physicians, pharmacists, policy makers, have vested and sometimes divergent interests when it comes to pricing decisions. Also there is an ongoing discussion in Germany, and other countries, on what the best methodologies are to define how a price should be determined (e.g. economic

aspects vs. medical aspects). In addition, price regulations for generics are very different from innovative drugs.

Policy makers in Germany face important questions and discussions regarding topics such as the better integration of quality of life values, which will provide new perspectives of the value of drugs, the introduction of cost-benefit analysis which is currently not foreseen, and the choice of the comparator. Manufacturers complain often times that they are compared with very cheap generic drugs.

The AMNOG has now been in place for five years and has been modified slightly over the years. It is an evolving system and there are still a lot of discussions regarding the methods used and the positive and negative impacts of this new law.

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