INTERDISCIPLINARY PLATFORM ON BENEFIT ASSESSMENT

Vol. 4
April 2017

AMNOG 2.0 – Information Problems

Springer Medizin

Publications of the Interdisciplinary Platform on Benefit Assessment

VOLUME 1
Four years of AMNOG – discourse and impulses

VOLUME 2
Clinical studies – which endpoints count?

VOLUME 3
Adaptive pathways – opportunities and risks

All volumes are available at any time here:
http://www.aerztezeitung.de/politik_gesellschaft/gp_specials/plattform_zur_nutzenbewertung/ or https://tinyurl.com/zgfeflk

Volume 4
April 2017

Contents

Goals of the platform

In 2011, the legislator initiated a paradigm shift in the field of pharmaceutical supply in Germany, with far-reaching consequences. The principle, based on the AMNOG, provides that: for new active substances brought on the German market, the pharmaceutical company must prove an additional patient-relevant benefit compared to the available standard of treatment – the appropriate comparative therapy (ACT) – if a higher reimbursement price is sought than for the ACT.

The additional benefit is evaluated and determined by the Federal Joint Committee (Gemeinsamer Bundesausschuss), generally on the basis of proposals from the IQWiG. The pricing is determined largely by the result of this additional benefit assessment. In Germany the price is for the first time negotiated between the National Association of Health insurance Funds and the pharmaceutical company.

The assessment of the additional benefit by the G-BA is the result of expert work based on a law (AMNOG) and on procedural and methodical regulations (e.g. IQWiG methods). The active players on the side of the G-BA and the health insurance funds are classified as scientists, hospital physicians and office-based statutory health insurance physicians, the Medical Service of the Health Funds (Medizinischer Dienst der Krankenkassen, MDK) and employees of the insurance fund administration, but also as patient representatives, however, they act on the basis of their own interests. Value dossiers for new drugs, likewise classified and interest-based, are submitted by the pharmaceutical companies to the G-BA, which serve as the basis for the assessment of the additional benefit.

Because the supply of pharmaceuticals to the population is significantly influenced by the assessment of the additional benefit, it makes sense to provide critical and careful support for the assessment process with a focus on identifying possible faults and counteracting imbalances. The Interdisciplinary Platform on benefit assessment set itself the task of supporting the benefit assessment within a small group of experts with the following objectives:

- Discussing the procedures for the assessment of the additional benefit, including in relation to drug approval,
- Working towards international standards of evidence-based medicine and of health economy being adhered to and applied,
- Determining whether and to what extent actual patient-relevant additional benefits, in particular in the areas of mortality, morbidity and quality of life, are identified and which methodological problems occur during the process,
- Identifying possible undesirable developments, in particular with regard to supplying patients with new active substances,
- Enabling and holding a constructive dialogue with all players involved in the benefit assessment procedure.

The Interdisciplinary Platform would like to make a contribution to ensuring that new active substances are transparently and fairly assessed. The Advisory Council considers an interdisciplinary discussion regarding the results of the assessment and the applied benefit assessment methods to be essential. Furthermore, in the benefit assessment process it sees a good opportunity to inform the prescribing physicians of the expected additional benefits of new drugs for patients earlier than it was previously the case.

The interdisciplinary platform resulted from the discussion process between clinicians and experts. The mutual desire to pool specialist knowledge in the form of interdisciplinary seminars is supported by an open consortium of sponsors. These include Roche Pharma AG, DAK Gesundheit, Xcenda GmbH and Springer Medizin.

The Advisory Council of the Interdisciplinary Platform on Benefit Assessment

Getting the information about benefits of drugs using practice IT systems

By Dr. Pamela Aidelsburger and Dr. Jürgen Bausch

In the year 2016, no statutory health insurance physician in Germany still uses a patient file card to document the services provided, prescriptions, consultation reports of specialist colleagues and, if applicable, doctor's letters from the hospital – as commonly practised in the past. Nothing runs without a practice IT system today. The fact that the practice IT system enables the targeted control of the doctor's prescriptions has long been recognised and is utilised by all players in the system. In some contracts for family doctors, the contractual partners generate the additional honorarium through savings on drug prescriptions .

Since five years the Federal Joint Committee (G-BA), applying the principles of evidence-based medicine, has been striving to assess all new active substances that come to market regarding their additional benefit that is relevant for patients. A considerable number of early benefit assessments has been completed. The information density from the early benefit assessments that can be subsequently used in science and practice is substantial.

Unfortunately however, the G-BA decisions regarding the additional benefit of a new medication, which are binding for all players in the system, are written by lawyers for lawyers. This does not make them easier to read. Not to mention interpreting them correctly. Many roads lead to a G-BA decision. Identifying the right road, detours or meanders takes a lot of practice. This is one of the reasons why G-BA decisions are not exactly favourite reading for doctors, even though they should be especially well informed of the benefits and risks of new pharmaceutical products when they want to prescribe them.

Some new pharmaceutical products are successful in the market despite a negative benefit assessment. Other pharmaceutical products fall far short of expected sales even though a considerable additional benefit has been confirmed. That means patients are receiving a treatment with no proven additional benefit, which insurers say is unefficient. In the opposite case, doctors withhold an effective treatment from their patients even though the result of the early benefit assessment confirmed an additional benefit compared to the standard of care.

Both cases however reduce the complex decision making process to prescribe the „right" pharmaceutical product for solving patient problems to a simple model. No one will dispute the view that the prescription decision for or against a pharmaceutical product depends on the individual patient, and that information about effects, benefits and risks is a basic prerequisite. Since the physician in the statutory health insurance system also has to observe the efficiency principle, information is required about what the prescription costs and whether there are lower-cost alternatives that allow the treatment objective to be achieved to the same degree..

The planned Pharmaceutical Products Supply Strengthening Act calls for the early benefit assessment decisions of the G-BA to be arranged so they are suitable for the software of practice management systems and therefore become available to doctors more quickly. Ideally so that, when a medication with an available benefit assessment is prescribed, information appears automatically in the practice IT system that briefly and concisely reflects the current G-BA result and also includes notes regarding the efficiency of the prescription.

It is highly likely that just about everyone will welcome this approach by lawmakers. In principle the availability of information about a new active substance from a neutral scientific source at the time of prescribing by the doctor is desirable. A note that a medication is not efficient should also be welcomed by all doctors who want to avoid an efficiency audit of their prescriptions.

„Most problems arise in their solution“ (Leonardo da Vinci): It is foreseeable that redrafting the G-BA decisions to create electronically readable versions will in many cases reach a volume that is actually going to prove unsuitable as a short version for the practice software. Most of the G-BA decisions are based on an assessment of subgroup results. These differ significantly in part – anything from a significant additional benefit to no benefit for different subgroups is conceivable - even though the pharmaceutical product is approved for treatment in a uniform indication.

The statement that a substance approved in Germany and for which a benefit assessment has been completed is not efficient is even more problematic. After the benefit assessment process by the G-BA, the National Association of Statutory Health Insurance Funds negotiates a discount on the list price for the new active substance that is determined by the pharmaceutical product manufacturer at the launch and is valid in the first market year. If the G-BA does not recognise an additional benefit (or if the dossier is missing), the price cannot be higher than that of the appropriate comparative treatment. A lack of efficiency would therefore not even be possible in this case.

If an additional benefit was recognised for the new medication by the G-BA, the reimbursement price is set in the course of negotiations or by arbitration. Things get complicated with inhomogeneous G-BA decisions. In some cases, an additional benefit has been recognised for some subgroups but not for others. Usually this is because no studies are on hand for those subgroups or the data were insufficient for proof of an additional benefit. This leads to a mixed price in the price negotiations at the end of the process.

Doctors believe that every prescription is also efficient in this case (assuming it is prescribed in accordance with the indications / label). Insurers do not unanimously agree with this view. They believe that a prescription for patients in a subgroup for which no additional benefit was recognised is not an efficient prescription. Things would be simple if the National Association of Statutory Health Insurance Funds were to stand by its negotiated mixed price. But that is not the case. Which means that in case of doubt, the doctor may have to medically justify the prescription when the practice software indicates that insurers do not consider it efficient .

These few examples show: many obstacles will have to be overcome before all doctor information systems in Germany can be equipped with the required software. Especially since the doctor’s treatment decision is not based solely on the G-BA decision, but voices are starting to be heard that the knowledge of the scientific societies and recommendations of high-ranking guidelines should also be depicted in the software.

Level-headed parliamentarians are already speaking out in favour of assigning this complex and complicated issue to the self-administration body that has implemented the legal efficiency audits for decades. But before going live with this new information system for all of the more than 130,000 statutory health insurance physicians, any serious faults should be identified and if applicable rectified in an adequate trial phase.

Contact:
Springer Medizin Verlag GmbH
gp@springer.com

Benefit-oriented pharmaceutical product information for doctors – AMNOG 2.0

Michael Hennrich | Member of the German Parliament

This article explores central issues in the context of the parliamentary debate on the Pharmaceutical Products Supply Strengthening Act. It discusses where in relation to the early benefit assessment of new pharmaceutical products there is a current need for regulation Deliberations are focusing on the planned provisions regarding confidentiality of the reimbursement amount and the issue of the extent to which the AMNOG can make a contribution to improving the quality of the pharmaceutical supply. Here aspirations are tied to the planned doctor information system. Three different levels for the design of such a doctor information system can be identified. The question of whether all three components can be integrated into a doctor information system without overloading it has not yet been answered at this time..

We are currently at the end of the legislative period and are now – after concluding the dialogue with the drug industry – putting pharmaceutical product topics on the law-making agenda.

We will make some adjustments to the cabinet draft of the Pharmaceutical Products Supply Strengthening Act (AM-VSG) that may cause recurring irritation and displeasure in the industry, but for which there really are no reasonable alternatives if one does not want to entirely lose sight of a moderate spending trend. In concrete terms, we are talking about extending the price moratorium and manufacturer discount.

Incredibly many and in part also highly emotional reactions are seen when we pursue the assessment of new active substances in the AMNOG procedure or the development of the AMNOG procedure in general. Awaiting developments and examining day-to-day problems that actually occur could be a very meaningful tool to minimise concerns here. From my perspective, many points that were considered problematic at the outset have developed favourably in recent years, especially under the auspices of the Federal Joint Committee (G-BA), and numerous problems have been amicably resolved. Thus the crucial question is where a certain need for regulation still remains at this time for us as lawmakers.

Upon taking a closer look at the AMNOG, five levels we as lawmakers have to consider can be identified. These levels are: 1.) consulting, 2.) assessment by the Institute for Quality and efficiency in Healthcare (IQWiG) and the G-BA, 3.) pricing, 4.) handling of a price that is found, in particular regarding the issues of confidentiality and sales volume thresholds, and 5.) ensuring that the benefit and innovation are actually realised in healthcare.

The matter of a consultation caused concern among industry representatives at the outset since it was unclear for a long time what that would look like. Today however I have the impression that the consultations are working well. Certainly the joint paper of the G-BA, Federal Institute for Medications and Medical Devices (BfArM) and Paul-Ehrlich Institute (PEI) was an important cornerstone for this. The provisions agreed here regarding the structure and process for the consultations and the way results are obtained established clarity for the industry.

Benefit assessment: it was right to wait and see

There is currently no further need for regulation in this area from our perspective. The participation of the IQWiG is certainly a question that still remains open. Institutionalising is excluded here due to the existing provisions as well as the relationship between the IQWiG and G-BA. We will have to discuss adopting a provision allowing the IQWiG to be included in the consultations by application of the pharmaceutical companies, even though I would prefer to avoid major interventions in the institutional structure.

The benefit assessment is the second area. It turned out that awaiting actual developments was the right approach. There were numerous debates on this stage of the AMNOG – especially in the area of chronic diseases such as diabetes, epilepsy and Parkinson's. No additional benefit was attested for many of these products due to a lack of corresponding evidence, even though they are of significant importance in day-to-day healthcare. This is repeatedly causing tension between all participants.

Here the two key questions have always been: Can the problem be solved at the assessment level? And how do we handle new evidence?

In the end I believe it is probably better for us to solve the problem at the price level. Although we have already made major progress here in some areas, the handling of new evidence in a procedure for example still remains largely open.

Whether the current rule that an assessment procedure will be carried out again if there are new insights within twelve months should be amended or softened also needs to be clarified. New solutions may be of interest here as well. Professor Hecken from the G-BA for example suggests attempting to tighten up the procedure overall but retaining the one-year term.

Another matter that needs to be resolved in the law-making process is what to do with active substances for which there are no dossiers. I am in favour of a clear and simple solution: no dossiers also means no reimbursement.

I found a surprise in the AM-VSG draft regarding the transfer of evidence. Section 5 of the Pharmaceutical Prod-

Michael Hennrich, *studied law in Passau and Bonn. From 1991 to 1995, he worked as scientific assistant for member of the Bundestag Elmar Müller in Bonn. He has been a freelance lawyer since 1995. From 1998 to 2003, he was Regional Managing Director of the CDU Baden-Württemberg Economic Council. Since 2002 he has been the representative for the Nürtingen constituency, since 2013 correspondent for the pharmaceutical supply and pharmacies. He has also been Chairman of the Health Committee since 2015.*

uct Benefits Ordinance calls for provisions leaving this up to the discretion of the G-BA. Allow me to remind you: the starting point for this was a debate on medicines for children. It has always been my view regarding this topic that we need a special provision on medicines for children. I am therefore surprised that the draft legislation now calls for even more sweeping and extensive regulation. I believe there is still a need for discussion here.

No broad assessment of products in the existing market planned

Regarding the issue of an assessment of products in the existing market, the paper by the Union and SPD in particular caused some irritation since we had intended an expanded assessment of products in the existing market here. I would like to point out that joint papers by coalition partners, especially in a grand coalition, naturally have to contain compromises. However, it is also clear to all participants that we do not want a broad assessment of products in the existing market. When it came to the volume of savings related to the assessment of products in the existing market three years ago, the National Association of Statutory Health Insurance Funds calculated an amount of around EUR 280 million. This figure has not gotten larger in the last three years and may have shrunk somewhat.

Based on that the Union has no interest in a very broad assessment of products in the existing market. We also made this position very clear in the course of the AM-VSG hearing at the Federal Ministry of Health. What we are interested in here is the assessment of known active substances for new indications. How the provision will then look in concrete terms remains open however. Various models using the pharmaceutical registration number, ATC code or document protection are conceivable here. A new ATC code should be sufficient in my view.

Dealing with prices is the next question. The relationship between centralised and decentralised price negotiation may also gain importance in this context. Is it possible to make advance options available for concluding discount agreements according to Section 130a, Paragraph 8 of the Social Security Code (SGB) V? How does this relate to what are known as added value contracts that are expressly regulated in the AMNOG? It is certainly conceivable to me that it would be good to get a bit of leeway in the system for greater flexibility. Regardless however it is also clear that centralised price negotiation has to be decisive.

On the topic of pricing/price determination, especially in view of European referencing and the publication of the reimbursement amount, suggestions for optimising the procedure were submitted to us by both the industry and the health insurers. We all agree that this is the main focus of the AM-VSG.

At the core there are three points here that are important in this context:

a) **Exclusion of reimbursement:** For PCSK9 inhibitors, the practice has already been adopted that the active substance is now only being reimbursed for such – extremely small – populations that obtain a benefit from it. This however has not resulted in no additional benefit being attested for the active substance overall. Therefore the lowest cost comparator would be decisive. What we achieve with the reimbursement exclusion however is that the pharmaceutical company can obtain a higher price for the small group with the additional benefit.

Here too the question is how to regulate the procedure. Is a sole application right of the manufacturer reasonable? Or does it have to take place by agreement between the participants? I believe it is mandatory that this form of prescription exclusion cannot be implemented against the will of the pharmaceuticals manufacturer.

b) **Price-volume agreements:** I was surprised that a provision for this was to be explicitly included in the law. So far it could be assumed that price-volume agreements are already possible. Yet this is now being clarified in the wording of the law. Furthermore, the medical profession is proposing to tighten up the former „can" wording into a binding rule. There is however very little enthusiasm for this proposal among politicians.

c) **Response to chronic illnesses:** This is mainly about pricing and solving a problem, namely that the reimbursement amount must not lead to higher annual treatment costs than the most efficient alternative. Especially in the field of chronic diseases where generic alternatives are available, this provision makes research relatively unattractive since the company is at risk of not obtaining a positive benefit assessment. A possible solution would be to replace the „may" in the wording of the law with a „shall" in order to increase the investment attractiveness. It is astounding to me that this aspect is highly disputed. Such a change is criticised in particular by the health insurers and National Association of Statutory Health Insurance Funds, and some members of the SPD. For me as a lawyer this change does not constitute a softening of the provision. „Shall" means that the most efficient treatment sets the standard „as a rule" and deviations are only permitted in exceptional cases.

Such a „shall provision" is hardly litigable and thus I also do not see any new danger for the pricing mechanism.

One hears in regards to an epilepsy product currently undergoing pricing that other options probably exist. I am curious how this is going to develop. If there is a good and smart solution on the self-administration side that we as lawmakers would not have to touch, this would be satisfactory for all sides.

Questions related to the European reference price also belong to the topic of pricing. Here we were surprised that the reference to European prices was suddenly eliminated. Uncertainty regarding the handling of this rule was relatively great among all participants. It is important to note in regards to this topic that the arbitration board also needs this anchor for pricing. Insofar I believe this reference will also be found again in the law.

Regulation can form a good basis

Now I want to explore the issues that – aside from the doctor information system – have been discussed by the general public. For one, there is the topic of the confidentiality of the reimbursement amount and what is known as the sales volume threshold. To be entirely open, I was pleased when reading the first draft that a clever solution had been found to remove the topic from parliamentary debate by means of regulations. An openly conducted dispute with the coalition partner SPD surely would not be very conducive here.

Even though there are still open questions regarding this solution, the regulation, insofar as it can be defined more precisely, may form a basis for confidentiality or a non-public listing.

I deliberately say „may" since I am not sure whether we are still going to reach a solution together with our coalition partner in this legislative period.

I remain open regarding the retroactive reimbursement amount and the sales volume threshold: I would not have a problem with a retroactive reimbursement amount at the time of the G-BA decision, especially for products with no additional benefit. It is not clear to me why unrestricted pricing should continue for products with no additional benefit. The AMNOG was conceived to reward innovations. But when it has been established that a new product has no additional benefit, I see no reason to maintain the privi-

lege of the higher price for a longer period of time. Especially against the background that retroactive effect is in part agreed for products with an additional benefit. This would lead to the paradox result that products with an additional benefit could potentially be in a worse position than products with no additional benefit.

Recently the SPD has also indicated that it accepts the retroactive reimbursement amount. Thus I am confident that a solution to this will be found. Currently the turnover threshold for the application of the reimbursement amount is set at EUR 250 million. I cannot imagine that this will be accepted that way by everyone concerned.

Quality of care rarely raised as an issue

However, most of the tension and dynamics revolve around the question of how the products are used in the health care . What has always bothered me about this debate is the fact that we have consistently talked only about efficiency when it comes to this topic. The quality of care was rarely or even never raised as an issue. The traffic light is synonymous for efficiency: red, yellow, green.

But this does not indicate whether it offers an additional benefit for the individual patient or not. We as lawmakers in part contributed to this by transferring the responsibility for reviewing efficiency to the regional contractual partners in the Statutory Health Insurance Care Strengthening Act (GKV-VSG). The spirit and purpose of this provision is still not entirely clear to me. With the concept of „consultation before financial panelties" of the AMNOG, we made an important contribution to address the doctors' fear of penalties and I continue to believe that we will refine this accordingly.

Regional provisions bear risks

The regional solution standardised in the GKV-VSG does however bear the risk of uncertainty. Thus I am not sure whether a regional approach that is meaningful in other areas such as medical care will lead to the desired results here. From the perspective of patients, I do not believe that a regional solution is a sensible approach to the question of care, especially if this will then also be based on quotas. Here it is not clear how to ensure that the product with an additional benefit reaches those who need it. The focus on efficiency when it comes to the question of care leads to a highly heterogeneous care landscape.

So the question is whether we cannot design something better here. This question is also raised especially in reference to the results of the 2016 AMNOG Report by DAK-Gesundheit that describes how new active substances arrive in day-to-day healthcare. The study led to the conclusion that it plays virtually no role whether it is a product with or without an additional benefit. This cannot have been the spirit and purpose of the AMNOG. If one wants to focus on quality going forward, setting up a doctor information system is the right approach.

One learns something new every day as a parliamentarian. I want to describe for you from my perspective what issues we need to examine and what potential solutions I see. The first question that needs to be resolved is whether there should be a centrally managed and centrally implemented system, or whether we can maintain plurality and decentralisation. I have long been a supporter of a very centralised system when it comes to this issue, but the question is whether such a system can be established in compliance with cartel law.

The second issue that needs to be resolved is the question of jurisdiction. The law says that the G-BA has to prepare the information accordingly in machine readable form. We also discussed whether the German Institute for Medical Documentation and Information (DIMDI) can play a greater role in this process. Naturally this raises the ques-

tion of whether strict government regulation is needed here, or whether models that can be implemented by self-administration can be chosen as well.

Of course one also needs to clarify what possible solutions already exist here that can be further developed and optimised. The issue of governance and participation rights then comes up quickly as well. Who has to be included when the information is prepared? Of course it is clear to us as well that the information is not passed on 1:1 but has to be presented in a certain context. Here the fascinating question is who wants to be involved in what form, and who must be included. This is the only way a good solution can be found in terms of Section 70 SGB V. The core issue with the doctor information system is therefore how deep such a system should go. Once again I want to identify three levels that play a central role.

- **The first level** is about the information regarding the assessment of AMNOG products. Here it is clear to all of us that we definitely want this.
- **The second level** is about control, the price signal and efficiency. How does this have to be implemented in a doctor information system and how do we deal with confidentiality? If confidentiality needs to be considered, the implementation of such a system is far more difficult compared to open prices.
- **The third level** is about subsequent studies/post-approval studies, and therefore an aspect that has been more in the background so far.

Finally the question arises whether the three aforementioned components can be part of one system, or if levels 1 and 2, being the assessment and price signal, have to be addressed separately from the topic of new evidence on level 3.

This remains to be clarified in the subsequent process. So far regulation is primarily through Sections 73 and 35a – but the depth of regulation in these standards will not be sufficient.

Therapeutic freedom must be protected

General requirements for the doctor information system: our expectation is that doctors will receive information of sufficiently good quality to make the right treatment decision. It is important to maintain therapeutic freedom and not anticipate the doctor's decision. The presentation of the AMNOG decisions must be broken down in great detail – what populations are affected and where is there an additional benefit? Dealing with the genotypes in such a system will also be an issue for us.

The fascinating question is what criteria for a treatment decision will actually become part of a doctor information system. Technical information in the form of external evidence is indispensable.

Dealing with the topic of „guidelines" will be exciting, a field that plays a correspondingly subordinate role in the parliamentary debate. How to deal with the pharmaceutical guidelines and corresponding appendices also remains open – even though I believe this point should definitely be covered by a doctor information system. A reasonable balance needs to be found for all of this.

On the second level – control of the price signal – a lot depends on the fundamental choice between public reimbursement amounts and confidentiality. There is also additional potential for a doctor information system on this level. Tiered pricing according to the degree of the additional benefit is a possibility. Naturally this leads to additional issues such as the efficiency review in the future.

I am leaving the topic of the third level for such a doctor information system aside for the time being, since it would go too far in the current legislative procedure and we must not overload such a doctor information system.

Overall these are the areas we are currently dealing with, and also the topics that make the AM-VSG so fascinating. If we make progress here, we can legitimately speak of AMNOG 2.0 – if not, it will be more of an AMNOG 0.5.

Information for doctors regarding G-BA decisions on benefit-oriented reimbursement

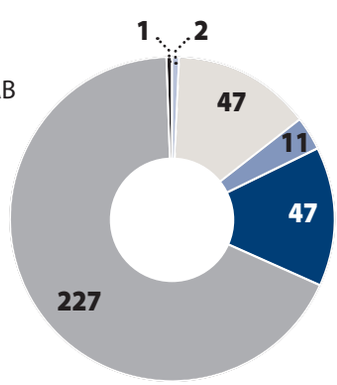
Jana Muriel Kleinert and Dr. Antje Haas | National Association of Statutory Health Insurance Funds

A lot has been accomplished in regards to increasing competition and improving quality while simultaneously slowing the cost increase for pharmaceuticals since the introduction of the AMNOG five years ago. Unfortunately the detailed and complex results of the early benefit assessment in the G-BA are not yet adequately reflected in care. That has to change. This is why the National Association of Statutory Health Insurance Funds is proposing its concept of benefit-oriented reimbursement. The concept includes simple and targeted information for the medical profession regarding the extent and likelihood of the additional benefit of new pharmaceutical products as well as differentiated prices in order to better represent the detailed additional benefit decisions in the reimbursement amounts.

Five years of AMNOG: The early benefit assessment was introduced on 1 January 2011 with the German Pharmaceutical Market Reorganisation Act (AMNOG). On the one hand, the goal of the AMNOG was to control the rapidly increasing spending on pharmaceutical products, strengthen fair competition and introduce a greater focus on patient welfare. Since then the price of new pharmaceutical products is supposed to be guided by the additional benefit. On the other hand, the bureaucratic load on doctors was to be reduced and citizens were to be better informed by providing independent information[1].

Results of the early benefit assessment in the G-BA

- Benefit assessment for 151 active substances
  - 47 with AB
  - 57 without AB
  - 47 with mixed AB
- 335 patient groups
  - 2 with significant AB
  - 47 with considerable AB
  - 11 with not quantifiable AB
  - 47 with minor AB
  - 227 without AB
  - 1 with minor AB



Source: own representation according to G-BA assessment
Last update: 15 October 2016

Figure 1: The indications of the 151 active substances are allocated to 335 patient groups.

A lot has already been accomplished in the first five years since the introduction. 151 active substances[2] (as of September 2016) have gone through the process in the Federal Joint Committee (G-BA) since the introduction of the early benefit assessment. The extent and likelihood of their additional benefit was evaluated in a transparent and elaborate Health Technology Assessment (HTA) procedure. In the course of the benefit assessment, the G-BA in accordance with the approval – as also frequently practised previously by the Institute for Quality and Efficiency in Healthcare (IQWIG) – breaks down the approved indications for the active substances into sub-indications and/or patient groups, and attests different additional benefit levels for these patient groups when this appears meaningful in terms of content. The breakdown into sub-indications depends on medical factors, different comparative treatments or the study design of the manufacturers.

47 decisions were made up to 15 September 2016 encompassing an additional benefit for the overall approved indication of an active substance, in 57 decisions no additional benefit was attested for the overall indication compared to the appropriate comparative treatment, and for 47 other active substances a decision with multiple patient groups was reached where some of the patient groups had an additional benefit and some did not. Overall the indications of the 151 active substances were allocated to 335 patient groups. This means a G-BA decision encompasses more than two patient groups on average (see Figure 1).

In the AMNOG process, the early benefit assessment is followed by the reimbursement amount negotiations between the pharmaceutical company and the National Association of Statutory Health Insurance Funds. 119 reimbursement amounts were agreed on the basis of the G-BA decisions by September of 2016. Negotiations for 34 active substances were in progress at that time, an agreement could not (yet) be reached for three pharmaceutical products and these are or were therefore decided by the arbitration board according to Section 130b, Paragraph 5 SGB

Dr. Antje Haas *is a specialist for internal medicine, haematology, internal oncology and haemostaseology. She has been heading the Medicine and Drug Division of the National Association of Statutory Health Insurance Funds since 2012. From 2008 to 2012 she managed the Hospitals Department of the National Association of Statutory Health Insurance Funds. Previously she was engaged in clinical and scientific work for inpatient and ambulatory healthcare for many years.*

Jana Muriel Kleinert *is a graduate economist. She has been a consultant in the AMNOG unit of the National Association of Statutory Health Insurance Funds Medicine and Drug Division since 2014. Previously she worked in the Quality Assurance unit within the Hospitals Department of the National Association of Statutory Health Insurance Funds starting in 2010.*

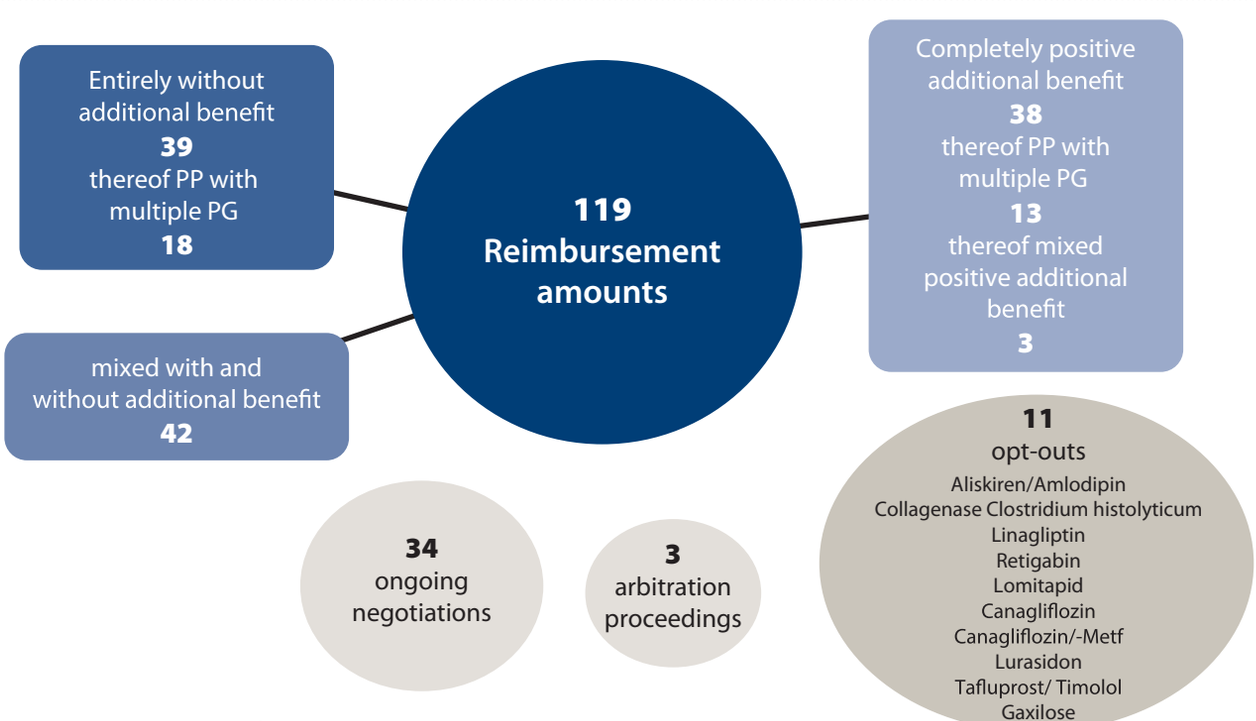
V, and for eleven pharmaceutical products the manufacturer chose to opt out, which means no reimbursement amount was agreed with the National Association of Statutory Health Insurance Funds but the product was taken off the German market directly after the G-BA decision (see Figure 2).

Strengthening the relationship between the G-BA benefit assessment and the reimbursement amount

According to Section 130b, Paragraph 3 SGB V, a reimbursement amount needs to be agreed for pharmaceutical products with no additional benefit that does not lead to higher annual treatment costs than the appropriate comparative treatment.

For pharmaceutical products with an additional benefit, the reimbursement amount is agreed with a surcharge on the annual treatment costs of the appropriate comparative treatment according to the framework agreement between the relevant umbrella organisation of the pharmaceutical companies and the National Association of Statutory Health Insurance Funds. The surcharge is based on the extent of the additional benefit established according to

Stronger link between prices and additional benefits



Source: National Association of Statutory Health Insurance Funds

Figure 2: In eleven cases the manufacturer chose the opt-out after the end of reimbursement amount negotiations.

the G-BA decision and additional criteria defined in the framework agreement, such as the actual selling prices for the pharmaceutical product in other European countries and the cost of comparable pharmaceutical products.

Of the 119 valid reimbursement amounts in September, 42 pharmaceutical products have a mixed additional benefit with patient groups with and without an additional benefit. The 39 pharmaceutical products without an additional benefit encompass 18 active substances with different patient groups. However, all of these patient groups cannot expect an additional benefit. The situation is similar for the 38 reimbursement amounts for active substances with an additional benefit. These encompass 13 pharmaceutical products with several patient groups, of which three active substances have a different but positive additional benefit.

Mixed prices are established for these active substances as well, since the different patient groups in part have different appropriate comparative treatments and therefore different anchor prices. However, the situation is more problematic for the 42 pharmaceutical products where some patient groups have an additional benefit but others do not. By law a uniform reimbursement amount has to be agreed here as well (see Figure 3).

For pharmaceutical products with several patient groups, some of which have an additional benefit and others not, both aforementioned criteria must be met in principle which is why an „overall mixed price" is formed. This mixed price that is formed across all patient groups is therefore not qualitatively equivalent and efficient for all patients. The reimbursement amounts are distorted by mixed price formation because an average price is formed that is too low for the patient group with an additional benefit and too high for the patient group without an additional benefit or with a lesser benefit.

Here the formation of the mixed price is based on an assumed distribution of the patients between the patient groups with and without an additional benefit. These assumptions however, for example based on studies or epidemiological data, by no means necessarily correspond to the actual prescription reality. When actual prescriptions correspond to the ratio predicted in the negotiations, the mixed price correctly reflects reality, at least in the arithmetical average.

If on the other hand most prescriptions are in the pa-

G-BA additional benefit assessment and reimbursement amount

- **1. Pharmaceutical product completely without additional benefit:**
  - Reimbursement amount capped by the annual treatment costs of the most efficient appropriate comparative treatment.
- **2. Pharmaceutical product completely with additional benefit, but possibly mixed extent of additional benefit:**
  - Reimbursement amount per surcharge on appropriate comparative treatment.
- **3. Pharmaceutical product partly with additional benefit:**
  - G-BA attests different additional benefit for different patient groups in a decision.
  - According to Section 130b SGB V, a reimbursement amount has to be negotiated per active substance (mixed price).
  - Reimbursement for all patient groups – with and without additional benefit.

Source: National Association of Statutory Health Insurance Funds

Figure 3: An „overall mixed price" has to be formed for preparations that partly have an additional benefit.

tient group with an additional benefit, the price for this patient group is „reduced" by the patient group with no additional benefit and therefore actually too low on average.

When prescriptions are mainly in the patient group with no additional benefit on the other hand, the price is excessive since it should not actually be higher than the cost of the appropriate comparative treatment.

This problem can be illustrated for instance using the treatment of chronic obstructive pulmonary disease (COPD) as an example. As shown in Figure 4, the active substance combination Indacaterol/Glycopyrronium in the early benefit assessment of the G-BA exhibited an additional benefit over Tiotropium/Formoterol for patient groups 1 and 2.

According to the provisions of the framework agreement for determining the reimbursement amount, a surcharge is applied here to the annual treatment cost of EUR 1074.89 for the appropriate comparative treatment.

At the same time however, the combination did not show an additional benefit compared to the comparative

Required information using COPD as an example

Aclidinium/Formoterol		Indacaterol/Glycopyrronium	
829.08 €*	PG a) COPD stage II	PG a) COPD stage II	958.00 €*
	Indication of minor AB vs. Formoterol EUR 349.51*	Hint of minor AB vs. Tiotropium/Formoterol EUR 1,074.89*	
829.08 €*	PG b) COPD stage III < 2 exacerbations/year	PG b) COPD stage III < 2 exacerbations/year	958.00 €*
	Indication of considerable AB vs. Formoterol EUR 349.51*	Indication of minor AB vs. Tiotropium/Formoterol EUR 1,074.89	
829.08 €*	PG c) COPD stage IV < 2 exacerbations/year	PG c) COPD stage IV < 2 exacerbations/year	958.00 €*
	No additional benefit efficient appropriate comparative	No additional benefit efficient appropriate comparative	
829.08 €*	PG d) COPD stage III + IV ≥ 2 exacerbations/year	PG d) COPD stage III + IV ≥ 2 exacerbations/year	958.00 €*
	No additional benefit efficient appropriate comparative	No additional benefit efficient appropriate comparative	

*Annual treatment costs as pharmacy selling prices

Source: own representation according to G-BA decision of 5 August 2014

Figure 4: The mixed price formation system does not lead to a satisfactory result for anyone.

treatment Formoterol in the other two patient groups 3 and 4. Here the reimbursement amount according to Section 130b, Paragraph 3 SGB V is not permitted to lead to higher annual treatment costs than the appropriate comparative treatment, which means the annual treatment costs must not exceed EUR 349.51.

As the example shows, the contractual partners through formation of a mixed price had to agree on a reimbursement amount that, in the patient groups with an additional benefit (1 and 2), does not represent a surcharge on the comparative treatment but is actually below its cost. At the same time however, the costs of the comparative treatment in the patient groups with no additional benefit (3 and 4) exceed the upper price limit according to law. This result does not constitute a satisfactory situation for any of the parties.

The problem is aggravated when another treatment option is considered in addition. For Aclidinium/Formoterol, an additional benefit was also attested for two patient groups and no additional benefit for two patient groups in the G-BA decision (see right side of Figure 3). The difference is that the appropriate comparative treatments are not the same. Unlike Indacaterol/Glycopyrronium that was compared to another combination, Tiotropium/Formoterol, the additional benefit for Aclidinium/Formoterol was determined compared to Formoterol alone. This means the results of the two early benefit assessments by the G-BA are not readily comparable.

Making comprehensive information accessible to doctors

While the different comparative treatments are also reflected by the reimbursement amount, the reimbursement amount is not the only criterion that has to be considered for prescribing. As shown by the COPD example, a lot of information is required for doctors to make a substantiated decision about an efficient prescription of high quality. The price alone is not sufficient as a criterion.

A variety of detailed information about new pharmaceutical products is in theory available to the medical profession since the introduction of the AMNOG.

When a new pharmaceutical product is released in the German market, the pharmaceutical company's dossier provides important information about it. The assessment of the Institute for Quality and efficiency in Healthcare (IQWIG) is available after three months with what is known as the early benefit assessment.

According to a judgement of the Federal Social Court, the IQWIG assessment can be presumed to be accurate even though it is not binding like the G-BA decision. It in turn is available after another three months, that is six months after the new active substance is brought to market, and is binding for doctors as part of the G-BA's pharmaceutical products guideline.

Reality however shows that this offered information is not adequately taken into account by doctors. According to a survey from the 2015 Innovation Report, only 15 percent of surveyed doctors use the G-BA decisions as a source[3]. This deficiency is highly problematic. In order to address this information deficit, the information from the G-BA decisions must be prepared in user-friendly form and made available to the medical profession in the practice management software, directly in the prescription process.

Currently the practice software provides information on the active substance, pharmaceutical form, and dosage, as well as pricing with identification of the reimbursement amount or reference price. Information is also provided from the pharmaceutical products directive according to Section 92, Paragraph 1, Sentence 2, No. 6 SGB V (AM-RL) such as prescription exclusions and prescription limitations

from Annex III, indication exceptions according to the OTC exception list (Attachment I), or the prescribability of medical devices according to Attachment V, as well as notices from the pharmaceutical product agreements according to Section 84, Paragraph 1 SGB V.

Information from Attachment XII of the AM-RL, that is the results of the early benefit assessment, is however lacking. This information from the G-BA decisions regarding the field of application, patient groups, appropriate comparative treatment and additional benefit of new pharmaceutical products should also be provided in the software going forward, making it quickly and easily available to doctors. That means the practice software has to evolve from administrative software into prescription support software for doctors.

The update cycle also has to be adapted in order to ensure adequate timeliness. Currently the information in the practice management software is only updated quarterly. Since the pricing information is updated every 14 days and the G-BA decisions are also made with a 14-day frequency, the information in the practice software should be updated on the same cycle. Such an update cycle was already introduced legally with the law for secure digital communication and applications in healthcare and the amendment of other laws as of 21 December 2015 (E-Health Act) but has not been implemented in practice to date.

In order to be usable for doctors in the prescription process, the information has to be provided in a clear, comprehensible and easy to grasp form. The information should be presented to the doctor uniformly and in easily recognisable form, always in the same location in the user interface, without additional user interaction and without interrupting the workflow. For cases where there are multiple notes, the display sequence has to be defined in advance.

Here one also has to consider that not all information can be displayed on the first level. Differentiation is therefore required so as not to overload the software and therefore the prescription process.

Providing the entire pharmaceutical products directive of the G-BA in machine readable form and making it available in the doctor information system would be sensible. This allows the doctor to make a „vertically" substantiated prescription decision. What additional information is required beyond that for a „horizontal" comparison should be the object of further discussion. Here one has to decide what the doctor needs to see at first glance and what information should be available only on demand.

Simplifying and improving quality and the efficiency of prescriptions

As illustrated by the COPD example above, doctors can only make a substantiated decision about the quality and efficiency of the prescription with the help of information about the field of application, patient group, appropriate comparative treatment and additional benefit. The reimbursement amount is no carte blanche for efficiency. Since a prescription requires knowledge and an assessment of additional benefit differences, efficiency always has to be decided on a case by case basis.

In the example shown in Figure 4, both Indacaterol/Glycopyrronium and Aclidinium/Formoterol have an additional benefit in groups a) and b), but to a different extent (considerable/minor) and respectively compared to other appropriate comparative treatments. The information about the additional benefit alone is therefore useless for the doctor. Clear information is required at the current, generally recognised level of medical knowledge in order to decide what pharmaceutical product to prefer over another and when.

Furthermore, a reimbursement amount does not guar-

antee a price that is „reasonable for the benefit". The low reimbursement amount for Aclidinium/Formoterol in group c) is not efficient since no additional benefit compared to the appropriate comparative treatment was found here, which means the comparative treatment should be prescribed unless medical reasons speak against that. Performing a thought experiment on efficiency clearly shows the extent of distortion caused by the mixed price. As shown in Figure 3, Aclidinium/Formoterolin has an additional benefit in two patient groups (a and b) and no additional benefit in the other two patient groups (c and d). The difference between the reimbursement amount for Aclidinium/Formoterol at EUR 829.08 per year and the more efficient appropriate comparative treatment with a cost of EUR 349.51 per year is therefore EUR 479.57 per patient and year. This means that every prescription for Aclidinium/Formoterol instead of the most efficient comparative treatment in groups c and d with no additional benefit costs statutory health insurance EUR 479.57 per patient and year. It means more costs with no additional benefit. If every patient in groups c and d (total of 230,000 patients) would receive Aclidinium/Formoterol instead of the comparative treatment, the additional spending caused by the mixed price with no additional benefit would be in excess of EUR 100 million.

These additional costs with no additional benefit must be avoided from the perspective of the National Association of Statutory Health Insurance Funds. Aside from the additional costs for statutory health insurance, there is legal uncertainty and a financial penalty risk for doctors when they prescribe new, costly preparations without adequately taking into account information about the differentiated additional benefit from the G-BA.

Due to the information deficit in the practice software and the uniform mixed price for the entire indication area, it is not readily apparent to doctors without extensive effort for which patient groups a prescription is efficient or not.

Represent differentiated benefit decisions with differentiated reimbursement amounts

The concept of benefit-oriented reimbursement is based on both the insufficient awareness among doctors of the G-BA decisions and the mixed price that intensifies the phenomenon.

On the one hand as previously described, all information from the pharmaceutical products directive of the G-BA must be available to the medical profession in machine readable form, directly usable in the practice software. On the other hand, prices for new pharmaceutical products should reflect their additional benefit and there should not be a need to form a mixed price across different patient groups with different additional benefit levels. Since a mixed price is not equally efficient for all patient groups because it is too high for the patient groups where the pharmaceutical product has no additional benefit while it is proportionally too low for the patient groups with an additional benefit, differentiated reimbursement amounts should be introduced (see Figure 5).

In cases where the G-BA in its early benefit assessment according to Section 35a SGB V determines an additional benefit for an active substance with some patient groups but not others, the settlement price should be differentiated by the patient groups with and the patient groups without an additional benefit. The settlement price for patients with an additional benefit (additional benefit price) could be agreed based on the additional benefit, while the settlement price for patient groups with no additional benefit (base price) would not be allowed to lead to higher annual treatment costs than the most cost effective appropriate comparative treatment.

This would result in differentiated prices and ensure that manufacturers receive a price that is reasonable for the benefit, but without causing unjustified additional costs for patients with no additional benefit. For patient groups with a minor additional benefit or no information about the additional benefit (no dossier), it should be possible to consistently exclude the patient groups in question from care.

For benefit-oriented reimbursement, the information about the patient groups would have to be transferred from the G-BA to the doctor's practice and also from the practice to the health insurer. This should be automated in machine readable form to reduce sources of errors, and is possible by encoding the patient groups in the practice software without causing additional effort for the doctor. At the same time, the transfer of information about the patient group from the doctor's practice to the health insurer can prevent audits. When health insurers receive the patient group-specific prescription, no audit would for instance not have to be initiated for the prescription of Aclidinium/Formoterol in group a) and b) (see the example in Figure 3). Currently however, it is generally not known in what sub-indication a pharmaceutical product was prescribed.

Stronger link between prices and additional benefits

Problem:
Mixed prices fall short of G-BA decision
Solution:
Differentiated pricing depending on additional benefit.
Information about sub-indications to health insurers.

- ▸ Patients/premium payers
  - Better care
  - Value the precise use of resources
- ▸ Doctors
  - Quality and efficiency of the prescription
- ▸ Pharmaceutical companies
  - Price follows the additional benefit
- ▸ Health insurers
  - Ex-ante management of care in the direction of quality and efficiency

Source: National Association of Statutory Health Insurance Funds

Figure 5: Mixed prices are not equally efficient for all patient groups.

Improving efficiency through benefit-oriented reimbursement

Mixed prices are not uneconomical per se, it depends on the proportions of the groups in the prescription reality. When most prescriptions are in the patient group with an additional benefit, this is favourable from the health insurer perspective since the price for this patient group is „reduced" by the group with no additional benefit. If on the other hand prescriptions are mainly in the patient group with no additional benefit, the price is excessive from the health insurer perspective since it should not actually be higher than the cost of the appropriate comparative treatment. With benefit-oriented prices, the price would be reasonable for the benefit in all sub-indications. The reimbursement amount could reflect the additional benefit correctly, and additional costs with no additional benefit would be avoided.

Differentiated prices could be presented in the form of a base price (with no additional benefit) and a calculated surcharge (additional benefit surcharge) representing the difference between the base price and the additional benefit price. Both prices would have to be available to all participants in the statutory health insurance system in order

to maintain the controlling function.

To avoid excessive burdens on the players at the different trade levels, the base price should be used as the basis for calculating the profit margins of wholesalers and pharmacies (according to the pharmaceutical price regulation). Then the inventory costs of wholesalers and pharmacies for the patient groups with no additional benefit would not be excessive, and would not have to be compensated with great administrative effort after the fact.

A reversed transaction would be particularly laborious if all trade levels had to be taken into account. If the base prices were used as the allocation base for mark-ups, the manufacturer through the pharmacy or pharmacy data centre would receive a surcharge when the pharmaceutical product is sold in the sub-indication with an additional benefit. This could be realised similar to the manufacturer discounts or even offset against the same by the pharmacy data centre. Transferring the patient groups to the health insurers is required here. This approach would result in the least administrative effort for all participants, and would ensure the low-cost and adequate implementation of differentiated prices.

Additional benefit-based prices, greater transparency and less effort

For manufacturers, benefit-oriented reimbursement would lead to higher additional benefit-based prices with an improved reference effect in other EU countries for patient groups with an additional benefit, even though there would also be a lower price for patient groups with no additional benefit.

An efficient prescription would be simpler to realise for doctors and the risk and effort of efficiency audits would be reduced. By providing the information about the additional benefit per patient group directly in the practice software, the selection of prescriptions can be improved in advance and costly subsequent audits can be avoided. The effort and conflict potential of subsequent efficiency audits could be considerably reduced as a result. Prescribing new preparations at an additional benefit-adjusted price would be assured. This improves patient care and saves resources that can be sensibly used elsewhere.

Transparency in the healthcare system would be improved at the same time. Transferring the patient groups in the routine data would enable the analysis of prescriptions and target group-specific monitoring. The quality of care would also be improved through better access by doctors to the results of the G-BA benefit assessment, especially in reference to the respective patient groups, and patients would be assured of receiving the treatment best suited to them.

Literature:

[1] See Federal Ministry of Health: Glossar Begriffe von a z: Arzneimittelmarktneuordnungsgesetz(AMNOG): http://www.bundesgesundheitsministerium.de/service/begriffe-von-a-z/a/ arzneimittelmarktneuordnungsgesetz-amnog.html(abgerufen20.11.2016).
[2]Own analysis according to G-BA; last update 15 September 2016.
[3]See Glaeske, Ludwig, Thürmann (publishers): „Innovationsreport 2015", scientific study on the supply of innovative pharmaceutical products.

The doctor information system from an industry's perspective

Dr. Markus Frick | Association of Research-Based Pharmaceutical Companies

The aim of the planned doctor information system to provide doctors with a better basis of information is worthy of support. How such a system is implemented is crucial in order to avoid sending the wrong messages and consecutively worsening the treatment quality. A doctor information system must not lead to the management of prescriptions and control of doctors by health insurers.

The perspectives of the scientific societies, clinical practitioners and patients are of special importance for the preparation of information. It is necessary in particular to ensure that nationwide information and downstream regional regulations do not contradict each other, and that the often complex decisions of the Federal Joint Committee are communicated free of contradictions. The misconception that pharmaceutical products with no proven additional benefit are inferior to the prescription standard or even „useless" or not prescribable must be avoided. The doctor information system has to support the presentation of the G-BA decisions, supplemented by the evidence-based guidelines. Only then can the system serve as a decision-making aid for doctors in the concrete prescription situation, making it possible to improve treatment.

The federal government wants to set up a doctor information system that provides the prescribing doctors with relevant information about pharmaceutical products for prescriptions through their practice software. Discussion is focusing in particular on the G-BA decisions on the additional benefit of pharmaceutical products, but also high quality guidelines of the medical societies. Doctors are already making their treatment decisions on the basis of various information sources, in particular based on guidelines of the scientific and medical societies (see Figure 1).

Further improving their basis of information is fundamentally a good idea. However, a doctor information system must not allow health insurers to control prescriptions and manage costs, nor restrict the treatment freedom of doctors. Otherwise the good intentions would have the opposite effect and patient care would deteriorate.

The drug manufacturers support the approach of providing doctors with even better information than before regarding the benefit and therapeutic value of pharmaceutical products, so that they can make justified treatment decisions for every patient from a medical-therapeutic perspective. In order to assess the specific information needs of doctors, it is important to know that most innovative pharmaceutical products by far are „specialist preparations" so that the target audience consists primarily of medical specialists. Figure 2 shows the proportion of pharmaceutical products that, according to their approval and/or G-BA decision, may only be prescribed by medical specialists with special qualifications.

One has to reject a doctor information system that serves to monitor or control doctors, as propagandised by the health insurers, that is to say an information system that serves as a lever for health insurers to selectively limit

the prescription of pharmaceutical products to those patient groups for which an additional benefit is considered proven. This would severely restrict patient access to important treatment alternatives. Observing the following principles for the further realisation of this project is therefore essential:

Provide doctors with a broad basis of information: Guidelines are tailored to the treatment and decision making situation in the practice and evaluate new medications in comparison to all alternatives available in the indication area. They represent the state of medical science that also has to be considered for prescriptions according to the SGB V.

The benefit assessment decisions of the G-BA on the other hand are not aimed at the doctor's concrete treatment situations, but primarily at price regulation for the respective medication. While they can surely constitute valuable additional information for the doctor, they cannot define the state of medical knowledge by themselves, let alone replace guidelines.

Such a guideline-supported doctor information system with information prepared in a user-friendly format is not trivial and, in case of improper implementation, can lead to inappropriate care and declining quality. The perspectives of the scientific societies, clinical practitioners and patients are of special importance for preparing this information. A central role is played by the scientific medical societies that prepare the evidence-based guidelines in a structured consensus building process under the umbrella of the AWMF (Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften e.V.).

A doctor information system that serves to control rather than inform the doctor and incorrectly suggests that pharmaceutical products with no proven additional benefit are „inferior" or not prescribable would reduce the quality of care and violate a fundamental principle of evidence-based medicine that was named already by David Sackett: „Good doctors use both individual clinical expertise and the best available external evidence, and neither alone is enough. Without clinical expertise, practice risks becoming tyrannised by evidence, for even excellent external evidence may be inapplicable to or inappropriate for an individual patient."[1]

correct information transfer design:

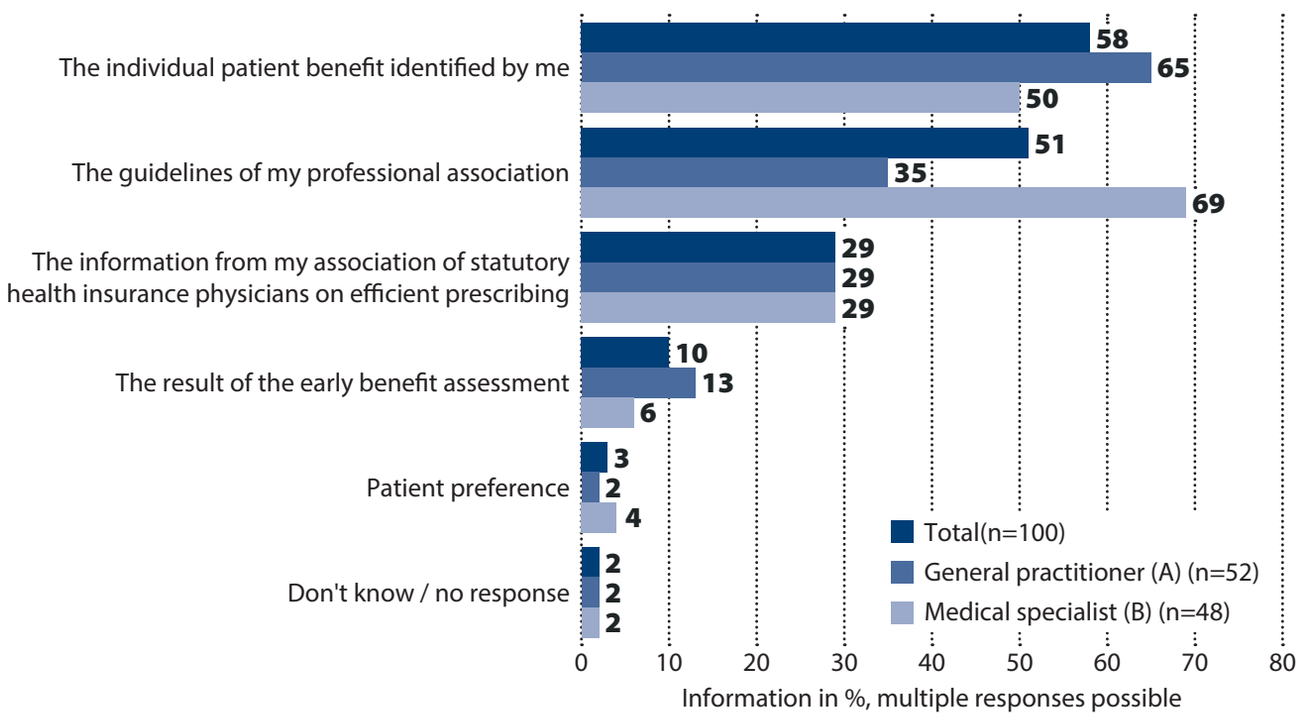
The additional benefit assessment according to Section 35a SGB V generates added information about innovative pharmaceutical products:

The G-BA evaluates whether an additional benefit has been proven for a pharmaceutical product compared to a

Dr. Markus Frick *MPH, has been with the vfa as Market and Reimbursement Director since September of 2012. The internist and health scientist worked at the universities of Bonn and Düsseldorf for twelve years, mainly in haematology/oncology. In 2001 he moved to Westdeutsche Brust-Centrum GmbH as Medical Department Manager. He was employed by Aventis Pharma Deutschland from 2003 to 2012. Since 2012 he has been responsible for HTA & benefit assessment, pricing and market access as Market and Reimbursement Director of the vfa.*

What do doctors have to say about prescription behaviour?

What factors actually determine their prescription behaviour?



Source: YouGov 2016 – report for the VfA, survey of established APIs and medical specialists

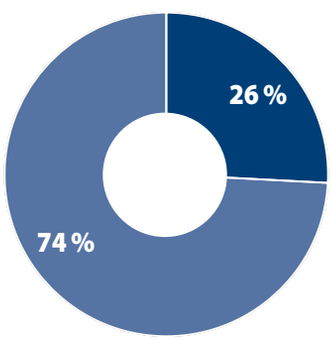
Figure 1: Doctors are already making their treatment decisions on the basis of various information sources, in particular based on guidelines.

comparative treatment established by it. Only when a pharmaceutical product has proven its superiority over the comparative medication, so the underlying rationale, is it also permitted to cost more. At the same time the AMNOG process ensures that treatment alternatives in cases where clear superiority cannot be demonstrated yet by the early studies are available for medical care at comparable prices.

It consciously does not restrict the doctor's treatment options. If no superiority over the comparative treatment chosen by the G-BA can be proven for a medication, the law says that it may not be more expensive than the comparative treatment. efficiency is therefore ensured by price regulations. The medications should however remain available as treatment options since their benefit is equivalent to that of the comparative treatment established by the G-BA.

This basic principle of the AMNOG is aimed primarily at the quality of patient care. Thus the specific information

Mostly specialist preparations in AMNOG



The G-BA has established requirements for **quality-assured administration** specifying that only "qualified doctors (or specialists) with sufficient experience in the indication area (or with similar pharmaceutical products)" or certain groups of medical specialist shall use the AMNOG medications.

Data basis: 160 proceedings; own representation;
data as of 19 July 2016

Figure 2: Special preparations in AMNOG: pharmaceutical products that are only prescribed by specialists.

from the AMNOG procedure must not be shortened or misinterpreted. Accordingly the minimum implementation requirement has to be that the information gained in the course of the benefit assessment is transferred to the doctor in objectively correct form. As a rule the G-BA decisions are complex and differentiated (example: evidence of a considerable additional benefit compared to comparative treatment A was determined for patient group 1; evidence of a minor additional benefit compared to comparative treatment B was noted for patient group 2; an additional benefit compared to comparative treatment C was not proven for patient group 3).

Naturally these decisions cannot be summarised into a simple message for the doctor. However, the information on the additional benefit of the pharmaceutical product (part 1 of the G-BA decision) could be published verbatim in a text field or as a document in the practice software.

One must also ensure that the doctor is able to correctly interpret the assessment result that the additional benefit has been proven, or „additional benefit not proven". The latter means that the G-BA classifies the additional benefit of the medication as not proven to be greater than that of the comparative treatment – but also not less. This must be communicated unequivocally to the doctor.

Efficient prescribing given as the result of the reimbursement amount negotiations:

The statutory health insurance physician should also know that a reimbursement amount was agreed. This information is already contained in the records according to Section 131 SGB V today and can be transferred to the doctor by means of a flag in the practice software for all pharmaceutical products with a regulated reimbursement amount (for example with a cross, as in the discount agreements according to Section 130a, Paragraph 8 SGB V). For the doctor, „regulated reimbursement amount" then means that the National Association of Statutory Health Insurance Funds and pharmaceutical company have assumed responsibility for efficient prescribing of the pharmaceutical product at the federal level. Based on the economic control exerted by the AMNOG on the reimbursement amounts, the doctor can then focus on selecting the most suitable pharmaceutical product for medical treatment.

The issue of a prescription's efficiency is already regulated conclusively by the AMNOG system. In cases with mixed prices (sub-groups with different assessments), it is also possible to ensure that, even in case of deviations

from the quantity structure underlying the mixed price, no additional costs are incurred by the insured community. From the perspective of the drug manufacturers, it would therefore not be economically constructive as well as medically misleading for the G-BA to establish efficiency signals differentiated by patient groups for the doctor following the reimbursement amount negotiations. Instead the information for doctors can focus on medical information.

Establishing unambiguous communication about the added therapeutic value:

As noted in the in the report on the results of the dialogue with the pharmaceutical industry, it is essential to ensure that regional agreements of health insurers and associations of statutory health insurance physicians regarding information for doctors do not contradict the nationwide information. In fact Germany currently has a patchwork quilt of collective and selective, specific contract provisions regarding prescription management at the doctor level, encompassing AMNOG medications. Such regional measures along with the warnings and financial penalty decisions connected to them cause massive uncertainty for doctors, so they hesitate to prescribe pharmaceutical products that have gone through the AMNOG procedure. It is foreseeable even now that this problem will keep worsening the more pharmaceutical products are centrally regulated by the AMNOG.

Clear rules are therefore required stating that regional measures and results communicated nationwide are not allowed to contradict each other. The regional players are not permitted to reinterpret nor shorten these, for example by classifying pharmaceutical products with no proven additional benefit as „useless" or flagging their prescription as „not efficient".

A highly simplified system for AMNOG products would also be misleading for the doctor at the regional level and should be excluded by corresponding specifications for a doctor information system and the providers of practice software.

The drug manufacturers are emphatically speaking out in favour of binding implementation specifications according to the principles for the G-BA and all other participants in the regulation.

Evidence-based guidelines and G-BA decisions: the doctor requires both types of information:

Consideration of high quality guidelines by the doctor is key for good prescription quality. According to the AWMF, „guidelines [are] systematically developed, scientifically justified and practice-oriented decision making aids for appropriate medical approaches to special health problems."[2]

The guidelines of high methodology quality (levels 2 and 3) are based on systematic evidence research and follow uniform qualitative standards. In the implementation of a doctor information system, the doctor has to be provided with the information from the corresponding evidence-based guideline, especially since it complements the content of the G-BA decisions.

Guidelines are also much more likely to solve the doctor's decision making problem of making the best choice for the prescription of the specific patient. This is because the guideline starts with the patient's clinical situation and, on this basis, identifies the best treatment option, while the G-BA decisions follow the approach of starting with the pharmaceutical product and asking whether there is a proven better, equivalent or inferior alternative for it.

Furthermore, the AMNOG by limiting itself to consideration of the studies examining the „appropriate comparative treatment" chosen by the G-BA follows a strictly vertical approach (comparison exclusively with the appropriate

Synoptic comparison of evidence-based guidelines (S2 & S3) and G-BA decisions (Section 35a SGB V)

	EbM guideline (S2, S3, NVL)	G-BA decision
Responsibility for content	Professional associations (scientific community)	Self-governance
Conflict of interest	Addressed in the procedure [1)]	Representation of interests[1)]: insurers, KBV, DKG
Decision making	Formal consensus building (Delphi process)	Weighted majority decision[1)]
Scope	Patient/indication logic	Active substance logic
Comparator	All therapeutic alternatives ("A vs. B vs. C…vs. n")	ACT only ("A vs B")[2)]
EbM approach	EbM[3)]	EbHC[4)]
Evidence-based	Systematic full research	"Shifting the burden of proof": Pharmaceutical co. dossier, no examination obligation
Dealing with uncertainty (error minimisation)	Optimisation approach (of alpha & beta error)	Alpha error minimisation, beta error disregarded
Decision level	Patient	System

[1)] As the top self-administration body, voting rights in the G-BA are held by the party representatives of the GKV-VS (50 percent of the votes), the KBV (25 percent) and the DKG (25 percent). The three votes of the non-partisan members decide when there is no majority.

[2)] Multiple responses possible [3)] Evidence-based medicine [4)] Evidence-based healthcare

Quelle: [1] F Osterloh: Leitlinien: Neuer Umgang mit Interessenskonflikten. Deutsches Ärzteblatt 2016; 113(51–52): A 2360

Table 1: Guidelines and G-BA decisions are fundamentally different and simultaneously complement each other in terms of content.

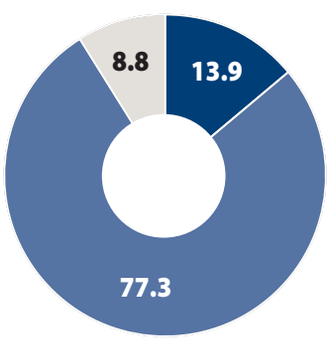
comparative treatment), while guidelines follow a two-dimensional approach (vertical and horizontal) under consideration of all meaningful alternatives.

A synoptic comparison shows that guidelines and G-BA decisions are fundamentally different and complement each other in terms of content (see Table 1). This illustrates why guidelines are the central source of information for the doctor: Guidelines are aimed at providing the doctor (and patient) with decision making support in the concrete prescription situation, while decisions according to Section 35a SGB V primarily serve to establish a uniform reimbursement amount.

Instead of the classic individual medical approach of evidence-based medicine, the concept of evidence-based

"Additional benefit not proven" usually due to formal reasons

Additional benefit not proven (N=274 sub-populations)



Data basis: main grounds for G-BA decisions of concluded procedures (with no additional benefit assessed: 274 sub-populations, excluding initial procedure in case of repeat procedure); last update: 11 January 2017

Figure 3: For about three quarters of the prescription constellations, the AMNOG assessment is „additional benefit not proven".

healthcare that addresses decisions at the system level takes effect here. This difference between the individual medical and collective perspective would become an actual contradiction if the lack of evidence of an additional benefit would lead to a decision of non-prescribability at the system level (and thus for all patients). Of the three central EbM pillars (external evidence, internal evidence of the doctor and preference of the patient), only the external evidence as the basis of the G-BA decision would be left, while shared decision making[4] at the individual level between patient and doctor would become irrelevant if central definition makes a decentralised decision between alternatives impossible.

In concrete terms this would for example mean that a new active substance for which the additional benefit is classified as not proven but that has a different side effect profile would not be available, even to patients who do not tolerate the old active substance.

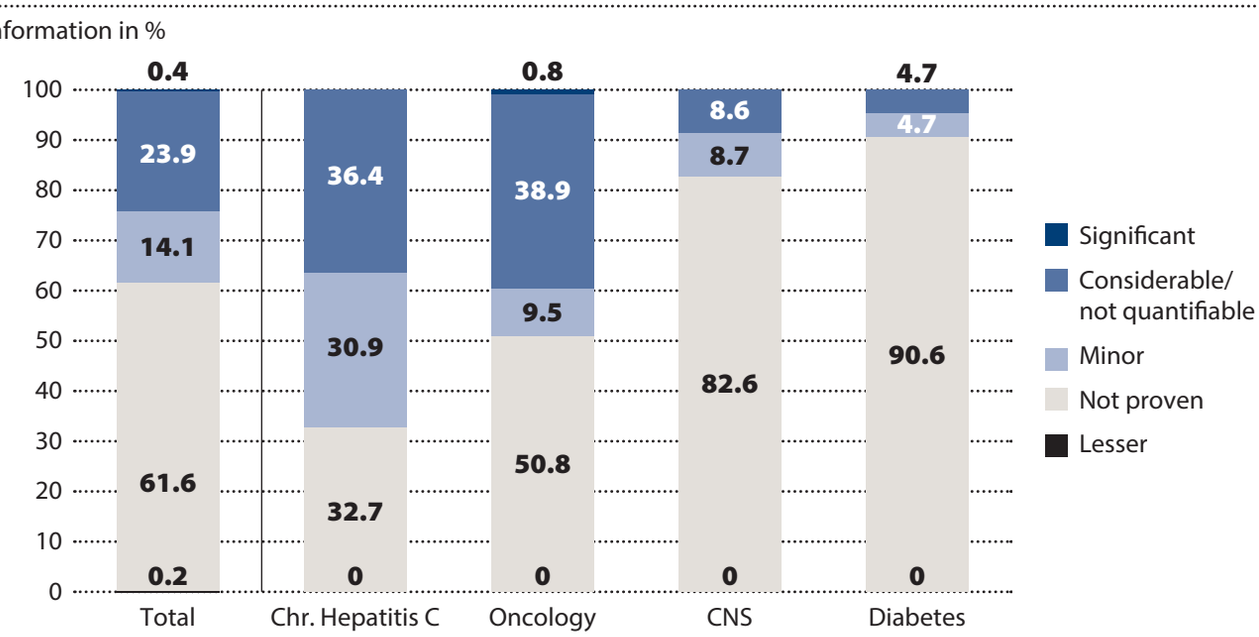
For all of these reasons, it is essential to ensure that the doctor information system actually serves to provide the doctor with information, but not to dictate, monitor, or subtly control the doctor. Another key difference between decisions according to Section 35a SGB V and guidelines is due to epistemology and methodology reasons: for around three quarters of the prescription constellations, the AMNOG assessment is „additional benefit not proven" and therefore does not specify an evidence-based preference (Figure 3). This may be suited for deriving a reimbursement price from this assumption of non-superiority, but leads to a care problem when options with no proven additional benefit are no longer available (Figure 4).

Guidelines on the other hand must be able to provide recommendations for the common therapeutic constellations. The reason that guidelines are generally able to make evidence-based recommendations while Section 35a decisions in fact make no preference statement for the majority of cases lies in the narrowed focus of the AMNOG and the corresponding G-BA decisions: Only those studies that precisely meet the G-BA requirements are considered, so that even the smallest deviation from these leads to the statement „additional benefit not proven" while guidelines follow the principle of the best available evidence.

This can be illustrated using the endpoint of „progression-free survival" (PFS) as an example, which is generally considered not relevant by the G-BA.

When a study proves a PFS benefit, this does not lead to

Proportion of the assigned additional benefit highly dependent on the type of illness



Source: vfa AMNOG procedure database; last update 7 February 2017; 453 patient groups in 214 concluded procedures

Figure 4: Proven additional benefit for assessed pharmaceutical products: The proportion of the recognised additional benefit fluctuates greatly depending on the type of illness.

the recognition of a proven additional benefit in the G-BA decision as a rule, even though specialists and oncology guidelines do in fact classify this as a therapeutic benefit. Ultimately a different approach to decision uncertainty is behind this: the IQWiG and G-BA with their approach of the virtually sole consideration of the best possible evidence follow the concept of minimising the risk of incorrectly attesting an additional benefit for a product that does not deserve it; biostatisticians call this the alpha error.

Here the AMNOG has to accept that products with an additional benefit are incorrectly assessed as „additional benefit not proven".

Considering all evidence (principle of the best available evidence) in guidelines and also by the approval authorities[5] on the other hand attempts to limit both types of errors, thereby promoting neither excessive nor insufficient care. This is illustrated in concrete terms when one considers that the narrow requirements of the AMNOG assessment lead to the conclusion that the additional benefit is not proven in two thirds of all cases.

While that may work for pricing, it would be just as unsuitable for prescription management as a guideline that cannot make a recommendation for two thirds of all patients.

Strengthen therapeutic freedom for doctors – no prescription management:

The health insurers are promoting an own software solution (for instance from the ARMIN model project) as the model for the planned doctor information system. These systems work with vivid colour codes and automated simplifying functions that subtly control the doctor's prescription behaviour in the treatment situation with the patient. Such IT solutions would be entirely unsuitable here. Pronounced simplification is unable to represent the differentiated additional benefit assessment of the G-BA. The doctor has to know for example what treatments were included in the comparison and which ones were not, and what the clinical background is behind an assessment such as „evidence of a considerable additional benefit" or also „additional benefit not proven". For instance there have recently been several assessments of cancer medications where the assessment was „additional benefit not proven" due to offsetting with side effects or a lack of data on quality of life. In the concrete prescribing situation on the other hand, it does in fact appear highly relevant for the patient and oncologist to know whether a possible treatment option has been proven to extend survival or not.

Furthermore, the differentiation by patient groups and the respective comparison standards chosen by the G-BA in the benefit assessment do not necessarily correspond to the situation in the doctor's practice as it is reflected in the applicable guidelines of the medical societies. Any reduction of information for doctors to a simplified statement as in the (possibly semi-quantified) recognition of an additional benefit versus „additional benefit not proven" generally falls short, since essential information for the doctor's treatment decision is missing.

This applies in particular to the statement „additional benefit not proven" that, contrary to a widespread misconception of the AMNOG, does not mean the pharmaceutical product is inferior or prescribing it is not Efficient. Rather what this G-BA decision says is that the pharmaceutical product is at least equivalent to the comparative treatment (otherwise the G-BA would have assigned it to the category „lesser benefit") and the reimbursement amount is not higher than the cost of the most efficient comparative treatment.

For good quality of care reasons it is also mandatory that these pharmaceutical products remain available to the doctor as equivalent prescription options, since the lack of proof of an additional benefit does not mean that an additional benefit for the concrete patient is lacking. The result „additional benefit not proven" is due to formal reasons in over two thirds of all cases, whenever studies coordinated with the approval authorities do not meet the study design requirements of the G-BA (usually comparative treatment, endpoints or subgroups).

There is neither a medical nor an economic reason to discriminate against prescribing pharmaceutical products with a proven benefit, but for which an additional benefit is not (yet) proven. To the contrary, there are good reasons to make them available to patients and doctors without discrimination:

- **Equality of care must be maintained**

The AMNOG results differ significantly by the type of illness. With chronic illnesses in particular, proving an additional benefit succeeds only rarely, simply because of the dynamics of the disease.

An incorrectly understood doctor information system would permanently cut off entire illness groups such as CNS diseases from progress in medications.

- **Quality of care must not be allowed to suffer**

Active substances that are classified as having no proven additional benefit for formal reasons may be the evi-

dence-based preferred choice of medical specialists, for example because the assessment of the correct comparative treatment differentiates between the G-BA and the professional association. The latter is the case in 31 percent of the oncology assessments according to the DGHO evaluation.[6] With renal cell carcinoma for example, the result of this is that the sole preferred active substance according to the guideline[7] (evidence level 1+, recommendation level A) receives the assessment „additional benefit not proven" for 99 percent of patients in the G-BA procedure. A doctor information system must be designed so that the recognised state of medical knowledge and therefore decision making by the doctor supported by guidelines is promoted and not impeded.

- **Patient preference must continue to count**

The preferences of patients and doctors are not consistently taken into account at the system level. MS therapy is an example that clearly shows many patients and doctors prefer the new active substances that no longer have to be injected, even though they are categorised as „additional benefit not proven". Discrimination against these valuable prescription alternatives by a misleading doctor information system must not be permitted, especially since they do not cause additional costs according to the AMNOG logic.

A uniform doctor information system integrated into the practice software harbours both opportunities and risks for the quality of care.

Thus the question of „how" to implement this is by no means trivial and requires a detailed examination of the strengths and weaknesses of the assessment systems that are to be integrated, the types of incentives that are created, and the accuracy and comprehensibility of its messages.

It is crucial not to implement any simplifying mechanisms or intransparent prescription management tools that translate the additional benefit assessments of the G-BA into therapy specifications for established patient groups, compelling corresponding encoding and documentation by the doctor, and in the end exposing the doctor to direct control by the health insurers, circumventing the associations of statutory health insurance physicians. In particular, the common misinterpretation of the AMNOG that pharmaceutical products with no proven additional benefit are worse than the standard of care, not efficient, downright „useless" or not prescribable must not be promoted. This has to be prevented through clear requirements for a doctor information system and the providers of practice software. Otherwise the G-BA decisions would be misinterpreted, the treatment quality reduced, and important treatment options for patients cut off.

Literature:

[1]Ärztliches Zentrum für Qualität in der Medizin (date of access: 6 January 2017): glossary on „Leitlinien" (guidelines). Internet: http://www.leitlinien.de/glossar?search_letter=l

[2]Osterloh F (2016): Leitlinien: Neuer Umgang mit Interessenskonflikten. (Guidelines: a new way to handle conflicts of interest). Deutsches Ärzteblatt 113(51-52): A 2360

[3]Frosch DL, Kaplan RM (1999): Shared decision making in clinical medicine: past research and future directions. American Journal of Preventive Medicine Volume 17, Issue 4: 285 294

[4]Eichler HG et al (2013): The risk of risk aversion in drug regulations. Nature Reviews Drug Discovery: 1 10

[5]Wörmann B (2015): Frühe Nutzenbewertung neuer Arzneimittel in Deutschland (Early benefit assessment of new pharmaceutical products in Germany). DGHO health policy publication series, volume 6: 33

[6]Oncology guideline program (Deutsche Krebsgesellschaft, Deutsche Krebshilfe, AWMF) (date of access:
12 January 2017): Diagnostik, Therapie und Nachsorge des Nierenzellkarzinoms (Diagnostics, treatment and follow-up of renal cell carcinoma), long version 1.0, 2015, AWMF register number: 043/01

[7]OL. Internet: http://leitlinienprogrammonkologie.de/Leitlinien.7.0.html: 82

The position of the KBV: benefit-oriented and cost effective pharmaceutical supply

Dipl.-Med. Regina Feldmann | Deputy Chairperson of the KBV (National Association of Statutory Health Insurance Physicians) (until 31 December 2016)

It is and was the objective and method of the early benefit assessment to establish the additional benefit of a new pharmaceutical product for the purpose of pricing. Especially because the G-BA decisions are sometimes highly complex and difficult to comprehend in practice, providing compact information about them that is usable in practice constitutes a challenge. Having such information available to doctors in their practice software during the prescription process is however essential. The better this information is, the greater the resulting transparency regarding the additional benefit. This has to go hand in hand with binding price-volume agreements so that statutory health insurance physicians get prescription security. Furthermore, doctor information systems have to be dedicated solely to information for doctors. Efficiency information that factually leads to prescription exclusions or applications for other damages, or individual audits by health insurers and therefore recourse against statutory health insurance physicians, is not acceptable.

When it comes to the early benefit assessment, the doctor information systems and their design are of special importance for statutory health insurance physicians – especially in regards to how the decisions of the Federal Joint Committee (G-BA) on the early benefit assessment are presented in the practice software. It has been my opinion for years that information about the G-BA decisions has to be available to doctors in their practice software during the prescription process. I consider it positive that we are meanwhile able to examine this in more concrete and surely also more controversial terms.

A look back at six years of AMNOG

Where do we stand after nearly six years of AMNOG? Subsequently I want to discuss the draft of the Pharmaceutical Products Supply Strengthening Act (AM-VSG) and the planned provisions for doctor information systems it contains. We as the KBV not only have a lot of experience with doctor information systems, we also have a very concrete concept of the purpose that is to be served by these doctor information systems in the context of the early benefit assessment procedure. And we have a clear concept of what this information should look like. I therefore want to also present our thoughts about this at the end of my article.

Let us begin with a quantitative examination of the early benefit assessment:

To date the G-BA has completed 207 early benefit assessment procedures up to mid-September 2016. An additional benefit was recognised for about 60 percent of the pharmaceutical products assessed in the procedure. In 207 procedures, 433 subgroups were in turn formed, with the proportion of subgroups with no additional benefit being significantly higher.

However, 433 subgroups also mean that two subgroups were formed on average per procedure. This is not always easy to implement in practice.

Following this quantitative examination, I want to draw a qualitative interim conclusion and therefore a balance.

What is going well, and what needs to be improved?

How complex the process of dividing the fields of application for new pharmaceutical products into subgroups can get is illustrated by the procedure for Empagliflozin, an antidiabetic assessed by the G-BA for the second time on 1 September 2016. Empagliflozin is approved for the treatment of diabetes mellitus type 2 as monotherapy in patients for whom diet and exercise alone are not adequate for blood sugar management and the administration of Metformin is considered unsuitable due to intolerance or contraindications, or as combination therapy with other pharmaceutical products that lower blood sugar, including insulin, when these are not adequate for blood sugar management together with diet and exercise. The G-BA formed ten subgroups to assess the additional benefit (see Figure 1).

Dipl.-Med. Regina Feldmann *was licensed as a physician in 1976 and was subsequently recognised as a general medicine specialist in 1982. She has been established as a general practitioner in Meiningen (Thuringia) since 1991. From 2001 to 2004 she was a member of the board for the KV (Association of Statutory Health Insurance Physicians). Then she was 1st chair of the KV board from 2005 to 2012. She was a KBV board member from May of 2012 to December of 2016, responsible for GP care. Currently she is a delegate of KV Thuringia.*

Based on the randomised, controlled endpoint study, the EMPA-REG outcome study (Zinman et. al. 2015) in which the included patients had a manifest cardiovascular disease such as myocardial infarction, stroke, unstable angina pectoris, coronary heart disease or peripheral arterial occlusive disease, subgroup formation differentiated between patients with and without manifest cardiovascular disease in addition to the treatment form (monotherapy/combination therapy). Six subgroups were formed to assess the fixed combination of Empagliflozin/Metformin that is approved for the treatment of diabetes mellitus type 2 in addition to diet and exercise for improved blood sugar management.

Here too the patient population was divided into patients with and without manifest cardiovascular disease.

The G-BA confirmed evidence of a minor additional benefit for Empagliflozin in the combination therapy of Empagliflozin plus Metformin for patients without a pre-existing cardiovascular condition. In the overall view, a benefit of Empagliflozin (prevention of non-fatal cardiac infarction and hypoglycaemia) was seen notwithstanding disadvantages in the occurrence of side effects in the area of the kidneys and urinary tract as well as the genitals and breasts.

In a combination therapy of Empagliflozin with other medications for patients with manifest cardiovascular disease, evidence of a considerable additional benefit was noted on the basis of largely positive results of the EMPA-

REG outcome study (benefits were found in overall and cardiovascular mortality, heart failure and kidney failure)

However, the manufacturer did not present any suitable data for the fixed combination. Therefore the G-BA classified the data submitted for determining an additional benefit as not suitable for deriving an additional benefit. Consequently the additional benefit for the fixed combination of Empagliflozin/Metformin is not proven.

This is difficult to explain to my practising colleagues. In practice one would assume that a patient taking the fixed combination would get the same benefit as that obtained from having to take two medications separately.

In fact one could even assume that the patient would be better off since the risk of forgetting a tablet is reduced. Here it is essential for us as doctors that we can rely on knowing that prescribing the free or the fixed combination is equally efficient. The reimbursement amount negotiations between manufacturers and the National Association of Statutory Health Insurance Funds must accomplish this from our perspective.

Case study: Empagliflozin and fixed combination Empagliflozin/Metformin

The G-BA formed 6 and 10 subgroups respectively

a) Monotherapy
a1) Patients *without* manifest cardiovascular disease
a2) Patients *with* manifest cardiovascular disease
b) Combination with a blood sugar reducing pharmaceutical product other than insulin
b1) Double combination with Metformin
b1.1) Patients *without* manifest cardiovascular disease
b1.2) Patients *with* manifest cardiovascular disease
b2) Double combination with a blood sugar reducing pharmaceutical product other than Metformin and Insulin
b2.1) Patients *without* manifest cardiovascular disease
b2.2) Patients *with* manifest cardiovascular disease
c) Combination with at least two other blood sugar reducing pharmaceutical product
c1) Patients *without* manifest cardiovascular disease
c2) Patients *with* manifest cardiovascular disease
d) Combination with insulin (with or without oral antidiabetic)
d1) Patients *without* manifest cardiovascular disease
d2) Patients *with* manifest cardiovascular disease

Empagliflozin/Metformin

Figure 1: The G-BA formed ten subgroups to assess the additional benefit.

Editing of G-BA decisions suitable for use in practice

Especially because the G-BA decisions are sometimes highly complex and difficult to comprehend in practice, providing compact information about them that is usable in practice constitutes a challenge.

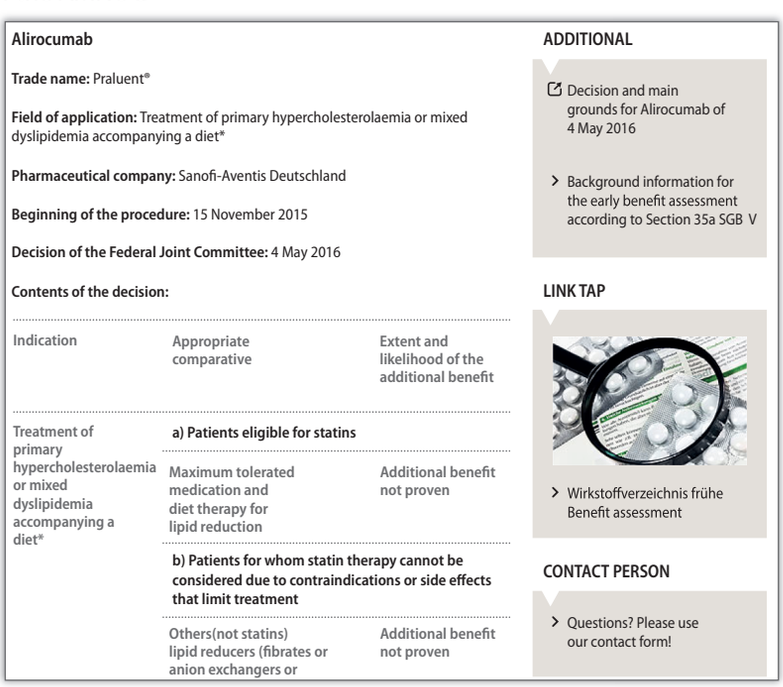
The associations of statutory health insurance physicians and the KBV are already informing statutory health insurance physicians regularly about every early benefit assessment decision of the G-BA. This has been done by the KBV since the beginning of the AMNOG procedure on its website – for every active substance regarding its assessment in the form of a „profile".

It contains information about the approved and assessed field of application, appropriate comparative treatment, study situation, additional benefit and quality assurance requirements for administration (see Figure 2). We have however noted as well that this information has to be made available more directly in the doctor's practice. Insofar we are very pleased and consider it sensible that this issue was also discussed in the course of the dialogue with

KBV early benefit assessment information for statutory health insurance physicians

KBV has been providing this since the beginning of the AMNOG

- "Profiles" for all assessed pharmaceutical products:
  - Field of application
  - G-BA decision
  - Summary of the study situation
  - Practice notes
- The decisions are also published in the "Deutsches Ärzteblatt"



Source: KBV – www.kbv.de/ais

Example: Alirocumab

Figure 2: The KBV informs statutory health insurance physicians about the content of benefit assessment decisions in summarised form.

the pharmaceutical industry that the medical profession was not involved in. Improving access to information about the decisions of the G-BA on the early benefit assessment of pharmaceutical products is no doubt necessary. Anyone who has examined the G-BA early benefit assessment decisions and their comprehensibility and readability more closely knows why that is so. We consider it very positive that providing this information is intended to improve the treatment freedom of doctors. This however is an aspect we are no longer able to discern in the draft of the AM-VSG and the regulation it contains.

Doctor information system: requirements in the AM-VSG

The draft law is kept very brief regarding the design of the doctor information systems. It mainly contains technical specifications – like the transfer of the G-BA decisions to a machine readable form. There are also implementation specifications in the form of deadlines for the delivery of data to be transferred to the practice management systems. The details are to be defined in a regulation. Specifications regarding notes on the efficiency of prescriptions compared to other pharmaceutical products are to be included in that as well. From our perspective, this bears significant risks for statutory health insurance physicians in regards to prescription security. We fear that health insurers will use the absence of an additional benefit as a test criterion for individual audits. This would factually have the effect of a prescription exclusion.

We also believe that such efficiency notes, if they are tied to the criterion of „additional benefit yes“ or „additional benefit no“, do not adequately represent medical progress. In the G-BA we for instance have the case that a new pharmaceutical product for the treatment of malignant melanoma has not exhibited an additional benefit because no study data for a comparison with the current standard treatment are on hand, but in the meantime the product itself is being used as the appropriate comparative treatment for subsequent new pharmaceutical products.

When discussing efficiency notes in the doctor information systems, one has to recall what the purpose of the early benefit assessment by the G-BA is. It is primarily a tool for the adequate pricing of new pharmaceutical products. Especially regarding this point however, the draft law is not consistent and far-reaching enough as it stands. The proposal to establish quantities and sales volumes in the reimbursement amount agreements does take the right direction. However, concluding such agreements has to be binding. This provides both statutory health insurers and pharmaceutical companies with the required planning reliability. The risk of additional spending that goes beyond the agreements is borne by the pharmaceutical company.

Binding price-volume agreements would significantly improve the prescription security of statutory health insurance physicians as well. This applies in particular for the indication-appropriate and medically justified prescription of pharmaceutical products in subgroups for which the G-BA has not determined an additional benefit. Statutory health insurance physicians must be able to rely on agreed reimbursement amounts establishing efficiency across the entire field of application for the pharmaceutical product.

It is and was the objective and method of the early benefit assessment to establish the additional benefit of a new pharmaceutical product for the purpose of pricing. Improving information about these decisions for statutory health insurance physicians to enhance transparency about the additional benefit is a good and correct step. This means the information has to be made available directly in the doctor's practice in the future – that is in the practice management systems. However, the G-BA deci-

sions have to be prepared so they are practical and actually add value in the practice. Then they can be better considered in the treatment decision and have an effect in terms of evidence-based prescription management.

Requirements for practical regulation

A note is required in the prescription process indicating that there is an early benefit assessment for this pharmaceutical product and when the G-BA decision was made. The presentation of the result has to include the approved indication, the subgroups formed by the G-BA, the appropriate comparative treatment, and the extent and likelihood of the additional benefit. Notes for the practice and requirements for quality-assured administration can serve as additional information available on demand. For anyone interested in the details, the G-BA decision should be accessible as well.

From our perspective, what are the requirements and conditions for a consistent implementation of the early benefit assessment, from the G-BA decision to representation in the practice management software?

1. We need binding price-volume agreements and the associated prescription security for statutory health insurance physicians.

2. Doctor information systems have to be dedicated solely to information for doctors. What we reject in this context is efficiency information that factually leads to prescription exclusions or financial penalties, or individual audits by health insurers and therefore recourse against statutory health insurance physicians.

We view the delivery of early benefit assessment decisions as a further development of the delivery of information about evidence in the prescription process through the practice software. This is a route we have already taken with the KBV medication catalogue that has been used successfully for more than two years already in the Saxony and Thuringia regional pharmaceutical products initiative, and that will also be used by some KVs in the future instead of budgets for pharmaceutical products management.

But there are also other prerequisites for the introduction of doctor information systems that we are pushing for. Clinicians for example also require access to the corresponding information through the software used in the hospital. This is relevant as well because the provisions for care by statutory health insurance physicians apply with the introduction of provisions for discharge management according to Section 39, Paragraph 1a SGB V in case of a corresponding prescription of pharmaceutical products. Furthermore, hospitals even now are supposed to use pharmaceutical products upon discharge that are appropriate and efficient for prescribing in care by statutory health insurance physicians as well (Section 115c SGB V). Software providers also have to be obligated by law to implement the representation of the G-BA early benefit assessment decisions without placing additional financial burdens on statutory health insurance physicians. Using the introduction of a uniform nationwide medication plan as an example, we see that the costs for the implementation of new legal regulations are passed on directly to statutory health insurance physicians. Such an approach must be prevented for the implementation of the early benefit assessment.

Literature:

Zinman B, Wanner C, Lachin JM, Fitchett D, Bluhmki E, Hantel S, Mattheus M, Devins T, Johansen OE, Woerle HJ, Broedl UC, Inzucchi SE; EMPA-REG OUTCOME Investigators (2015): Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. N Engl J Med 373: 2117-2128

Is „no additional benefit“ sufficient information?

Dr. Thomas Kaiser | Institute for Quality and Efficiency in Healthcare

The intended goal of the doctor information system to assist with the prescription of pharmaceutical products represents a major challenge, especially when the assessment is „additional benefit not proven“. This is because a new pharmaceutical product may be considered a meaningful additional treatment option even without a proven additional benefit – depending on the data situation for a new pharmaceutical product on the one hand and the appropriate comparative treatment on the other hand. For other cases, one can deduce that the appropriate comparative treatment should generally be chosen. A simple algorithm that exclusively accesses information already available in the AMNOG procedure could considerably improve the intended support of the doctor information system in the treatment decision for pharmaceutical products with no proven additional benefit.

The draft of the Pharmaceutical Products Supply Strengthening Act (AM-VSG) states that the decisions of the Federal Joint Committee (G-BA) on the early benefit assessment of pharmaceutical products will also be published in a machine readable form in the future, which will then be integrated into the practice software for doctors1. The goal is to „provide doctors with better information about additional benefit matters through an information system, thereby supporting them in their treatment decisions“1.

The discussion of this point mentioned in the AM-VSG shows that, especially when the assessment result is „additional benefit not proven“, very different views exist about what this result means for the treatment decision. While some participants believe that the new pharmaceutical product generally should not be prescribed in these cases, others consider a new pharmaceutical product a regular, meaningful additional treatment option notwithstanding this assessment. Clearly both cannot be accurate at the same time.

How a differentiated treatment decision can be supported even for pharmaceutical products with no proven additional benefit is described in the following. Only information already available in the AMNOG procedure is used here. The explanations that follow consider content-related criteria only (data volume and quality). Additional efficiency considerations in general or in specific cases are outside the scope of this article.

Additional benefit not proven – one result, several reasons

When the result of the early benefit assessment is that the additional benefit for a new active substance is not proven, this can have various reasons.

After more than 150 assessments since the AMNOG came into force, the following reasons in particular can be identified:

1. The pharmaceutical company submits at least one relevant study. In the overall view, the assessment does not indicate an advantage or disadvantage for the new active substance compared to the appropriate comparative treatment. Here the confidence level of the relevant study or studies can be

a. high or

b. low.

To put it differently: the assessment can be the result of a good or limited data situation.

2. Although the pharmaceutical company identifies at least one relevant study, it does not present a proper evaluation of the study or studies in the dossier, or its information search is incomplete

(which means it does not submit all relevant data).

Dr. Thomas Kaiser *is a doctor and system developer. He studied medicine in Cologne after working as a programmer, and was active in the internal medicine field for several years. In 2002 he co-founded the Institute for Evidence-Based Medicine in Cologne. He has been working there as Head of Pharmaceutical Product Assessment since 2004, the year the IQWiG was founded, co-managing this department since 2011 with Dr. Beate Wieseler.*

3. The pharmaceutical company submits a proper dossier, but the dossier contains no relevant study.

4. The pharmaceutical company does not submit a dossier, or it only addresses some of the issues related to the benefit assessment (for example, is only submits studies for previously treated patients but not for patients that were never treated before).

Only in case 1a is the statement „additional benefit not proven" based on a complete and comprehensive data situation. Relevant data are also available in case 1b, and these are fully known as well, but the data situation is limited and the confidence level of the statement „additional benefit not proven" is therefore low.

In all other cases, the assessment „additional benefit not proven" is the result of missing data: either the data situation is incomplete (cases 2 and 4) or no relevant data are available at all (case 3). The fact is that it remains open in all of these cases whether, if all relevant data were submitted and/or adequate studies were conducted, this would result in an additional benefit, no additional benefit, or a minor benefit for the new active substance compared to the appropriate comparative treatment. As a result, the following 3 categories can be derived for the quality of data underlying the statement „additional benefit not proven":

- **Category 1:** Data fully known, good data situation (case 1a)
- **Category 2:** Data fully known, limited data situation (case 1b)
- **Category 3:** No data available or data situation not known (cases 2 through 4).

Data situation for the appropriate comparative treatment – good, moderate or poor?

According to the Pharmaceutical Products Benefit Assessment Ordinance (AM-NutzenV), the appropriate compara-

tive treatment generally has to be determined according to benchmarks derived from the international standards of evidence-based medicine. In concrete terms, the appropriate comparative treatment should preferably be a treatment for which endpoint studies are available and that has proven itself in practical application[2]. The evidence research underlying the selection of the appropriate comparative treatment is published by the G-BA on its website (e.g. for Alirocumab[3]). Experience to date shows that, even for existing and broadly used treatment options that can be considered as an appropriate comparative treatment, the quantity and quality of data is going to vary. For the treatment of hypercholesterolaemia with statins for example, extensive data on morbidity and mortality are available from several randomised studies. Such data are lacking for treatment with lipid apharesis.

The data quantity and quality for the appropriate comparative treatment can also be described using different categories. Without describing these in further detail, one could for instance differentiate between the three categories „good", „moderate" and „poor".

Does the data quality influence the treatment decision?

The decision whether and in what cases a pharmaceutical product, notwithstanding the assessment „additional benefit not proven", constitutes a meaningful or possible treatment option can be effectively supported with the information described above regarding the data situation for the assessment of the new active substance and the data situation for the appropriate comparative treatment.

Here the starting point is the general assessment principle that no additional benefit is recognised without positive data. This also corresponds to the approval principle: approval is not issued without positive data regarding effectiveness. One also has to consider that one knows less about new pharmaceutical products prima vista then about treatments that have existed for years.

Based on this information, the following algorithm could be helpful for the treatment decision:

- In cases where comprehensive data from the early benefit assessment are available and these lead to „additional benefit not proven" for the new active substance, the new active substance can be considered a meaningful additional treatment option next to the appropriate comparative treatment.
- In cases where the assessment „additional benefit not proven" is based on a complete but limited data situation, the data situation for the appropriate comparative treatment constitutes a meaningful additional decision criterion:

a) If the data situation for the appropriate comparative treatment is good (meaning these data are of better quality than the assessment data from the early benefit assessment), it appears reasonable to generally prefer the appropriate comparative treatment based on this good data situation.

b) If the data situation for the appropriate comparative treatment is moderate or poor (meaning the quality of these data is similar to that of the assessment data from the early benefit assessment, but also not sufficient), the new active substance could be considered as a possible treatment (with justification).

- In cases where no data are available from the early benefit assessment or the data situation is not known (for example because incomplete data were submitted in the dossier), it seems reasonable to generally prefer the appropriate comparative treatment, even if the data situation for it is poor.

In this situation in particular, one has to consider that

Decision aid for the scenario "additional benefit not proven"

Data situation to establish the appr. comparative treatment	Data situation from the early benefit assessment to compare the new active substance to the appropriate comparative treatment (Assessment result: additional benefit not proven)		
	Data situation known, comprehensive	Data situation known, limited	No data, or data situation not known
Good	A	C	C
Moderate	A	B	C
Poor	A	B	C

Figure 1: Scenarios for supporting the treatment decision according to the data situation. See the preceding text for an explanation of categories A through C.

the new active substance may even have a lesser benefit than the appropriate comparative treatment.

Overall one can therefore differentiate between three scenarios for the question whether a pharmaceutical product assessed as „additional benefit not proven" generally constitutes a treatment option:

A: The new pharmaceutical product is a regular, meaningful additional treatment option.

B: The new pharmaceutical product is a possible treatment option (with justification).

C: The new pharmaceutical product is generally not a meaningful additional treatment option.

This is illustrated in Figure 1 with the help of a traffic light system. Differentiating between the categories in the practice software could also be realised in other ways (with text only for example).

Literature:

[1] Deutscher Bundestag (2016). Draft of a law to strengthen the pharmaceutical supply in statutory health insurance (Pharmaceutical Products Supply Strengthening Act – AM-VSG); printed matter 18/10208 of 7 November 2016. URL: http://dip21. bundestag.de/dip21/btd/18/102/1810208.pdf.

[2] Federal Ministry of Health (2014). Regulation on the benefit assessment of pharmaceutical products according to Section 35a, Paragraph 1 SGB V for reimbursement agreements according to Section 130b SGB V (Pharmaceutical Products Benefit Assessment Ordinance – AM-NutzenV); last update: 27 March 2014. URL: http://www.gesetze-im-internet.de/ bundesrecht/am-nutzenv/gesamt.pdf.

[3] Federal Joint Committee (2016). Research and synopsis of the evidence to determine the appropriate comparative treatment according to Section 35a SGB V; procedure: Alirocumab; last update: September 2015. URL: https://www.g-ba.de/ downloads/92-975-1219/2016-02-15_ Informationen-zVT_Alirocumab.pdf.

Information for doctors about G-BA decisions: Is it that simple?

Dr. Antje Behring | Early Benefit Assessment Procedure Coordinator, Pharmaceutical Products Department, G-BA

The doctor information system defined in the AM-VSG draft law is intended to better inform the medical profession about the contents and results of the early benefit assessment by the G-BA in the course of the individual treatment decision through the practice software. Treatment-related information about the additional benefit, available standard treatments, results of patient groups and quality requirements is to be made directly and immediately available to doctors. In order to effectively achieve the objective of practice-oriented and meaningful use however, one must consider prior to the implementation what information, prepared how, with what metadata and in what context should be provided. Examining the available data and information as well as the needs of doctors in day-to-day clinical practice is therefore essential. Furthermore, a corresponding information system should be implemented in hospitals as well in order to avoid interface problems.

Even before the draft legislation „Law to strengthen the pharmaceutical supply in statutory health insurance" (Pharmaceutical Products Supply Strengthening Act – AM-VSG), Section 73, Paragraph 8 SGB V stated that:

„To ensure efficient prescription practices [...] inform the associations of statutory health insurance physicians and national associations of statutory health insurance physicians as well as the health insurers and their associations, and the statutory health insurance physicians, also on a comparative basis, about efficient, prescribable products and sources of supply, including the respective prices and fees, and to provide notes about indications and therapeutic benefits according to the generally recognised state of medical knowledge [...]. [...] The information and notes shall include the trade name, indications and prices as well as other information that is relevant for prescribing pharmaceutical products, in particular based on the guidelines according to Section 92, Paragraph 1, Sentence 2, No. 6 in a manner that makes a direct comparison possible; [...]".

The AM-VSG draft legislation[1] now explicitly states that delivering the information from the benefit assessment decisions according to Section 35a SGB V to the doctor information systems in the practice software programs is mandatory going forward.

This is because the results of the decisions according to

Section 35a SGB V are largely unknown in the medical profession, and there is also uncertainty about how to handle the results of the benefit assessment in the context of prescribing pharmaceutical products.

How the transfer of information will be implemented has not yet been defined in concrete terms. Interpretations range from a simple presentation of basic information to complex networking of the information from guidelines and concrete study results. Whether the legal mandate is to represent the normative requirements of the G-BA decision and pharmaceutical products guideline or to link this information with scientific/clinical recommendations has to be defined. Currently the main focus of the public discussion is on the notes for efficient prescription practices addressed in the draft law that are supposed to be incorporated in the doctor information system.

In addition to the aspect of efficiency notes however, an overview is first required of the information currently contained in the decisions according to Section 35a SGB V, and what information from these decisions can be reasonably provided in the form of a machine readable version. These questions together with the issue of what additional information may have to be delivered from other sources have to be answered in a regulated process. Here one also needs to consider what information could be relevant for which group of doctors at what point in the prescription process.

Dr. Antje Behring *has been a consultant in the Pharmaceutical Products department of the G-BA office since 2011 and Team Leader for AMNOG since 2015. From 2009 to 2011, she worked for Barmer GEK in Bavaria as a consulting pharmacists. Before studying pharmacy and earning her doctorate, she worked as an outpatient and inpatient physiotherapist.*

Contents of the decision according to Section 35a SGB V

In addition to information about the active substance and indication, a decision according to Section 35a SGB V includes information that can differ depending on the patient group being considered:

- Appropriate comparative treatment
- Extent and likelihood of the additional benefit in comparison to the appropriate comparative treatment against which the additional benefit was proven
- Patient numbers, if quantifiable
- Study results by endpoints
- Information about the quality assured administration of the pharmaceutical product
- Costs of the pharmaceutical product being assessed and all selected appropriate comparative treatments
- Costs for additional statutory health insurance services required
- Validity period of the decision, if applicable

Even if only the core information from the decisions is incorporated in the doctor information system, the concrete information content of the individual aspects of a benefit assessment decision must be examined prior to the implementation. Aggregated or shortened representation bears the risk of the circumstances not been correctly imparted, but with excessively detailed representation on the other

hand there is a risk of missing the goal of direct and fast access to information.

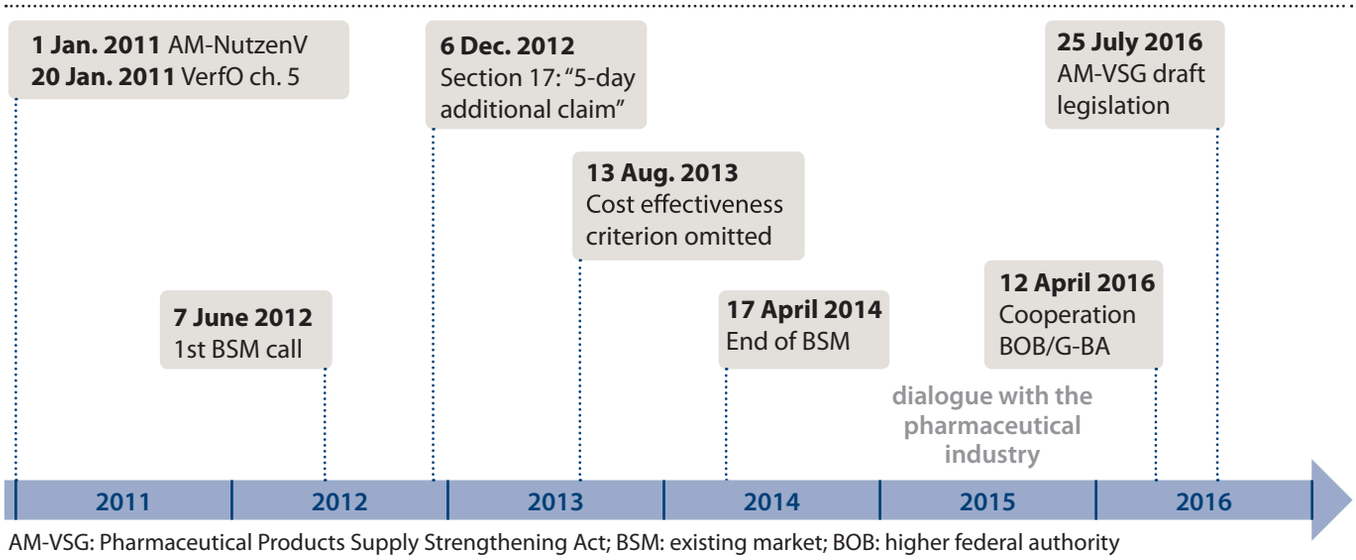
Core information in a decision Active substance:
The G-BA assessments are listed on the G-BA website under the name of the active substance, contrary to the approach of the European regulatory authority that lists the pharmaceutical products under their trade name. Therefore, the trade name of the assessed pharmaceutical product is generally not part of the decisions according to Section 35a SGB V. Unique assignment to the pharmaceutical product is nevertheless possible via the combination of the active substance and field of application.

A few exceptions aside, only pharmaceutical products brought to market in Germany after 1 January 2011 containing a new active substance/new active substance combination are currently assessed in the course of the benefit assessment.

This means no benefit assessment is available for active substances brought to market before 1 January 2011 (see Figure 1).

But since some of these active substances, insofar as they are approved and evidence-based, are considered as possible appropriate comparative treatments for certain indications, information may be available on these active substances regarding their positioning in the treatment cascade compared to the newly assessed active substance in the indication in question. To what extent information for active substances considered as appropriate comparative treatments in a decision according to Section 35a SGB V should be explicitly provided in the doctor information system remains to be discussed.

Changes in the AMNOG procedure since 2011



AM-VSG: Pharmaceutical Products Supply Strengthening Act; BSM: existing market; BOB: higher federal authority

Figure 1: Several points of the AMNOG have been changed since 2011.

Field of application/indication:
The decision contains the phrasing of the field of application according to technical information section 4.1 for the indication in question. A field of application can be added for an active substance that has already been approved, either through a separate approval or a type 2 major change according to Appendix 2, No. 2, Letter a of Regulation (EC) No. 1234/2008[2]. It is therefore possible to have different pharmaceutical products respectively with different fields of application on the market (for example the active substance Aflibercept: as Eylea® indicated for eye diseases and as Zaltrap® indicated for treatment of metastic colorectal carcinoma). The other and more common case is that a pharmaceutical product is indicated for different, distinct fields of application. When a new (sub-)field of application is assessed, the decision only contains the phrasing of this (sub-)field of application, even if the pharmaceutical product itself is approved for other fields of application.

To relate the benefit assessment decision to the doctor information system, it may be meaningful to assign a corresponding ICD 10 diagnosis code to the field of application in the decision in order to tag the information in the decision as relevant for the specific indication. Without a link to the technical information for a pharmaceutical product, even presenting the field of application however remains incomplete in its wording since contraindications, that is to say conditions under which the pharmaceutical product explicitly may not be administered, are not shown. Further information from the approval is therefore indispensable for the overall view of the field of application being assessed.

Patient populations:
Statements regarding the extent of the additional benefit are often differentiated for the individual patient populations. This is due to various causes: Either specific patient groups are explicitly named in the field of application for the pharmaceutical product in question, or the field of application is so broadly defined that various treatment situations are included. As a result, different appropriate comparative treatments may have to be established for the active substance per patient group. Separate patient groups may also be formed due to an effect modification, where the extent of the additional benefit for the pharmaceutical product compared to the appropriate comparative treatment differs.

Thus the significance of the new active substance in the treatment concept for the indication in question very often cannot be summarised in a single statement about the additional benefit, but differentiated findings regarding what additional benefit is proven to what extent for which patient groups can be noted in the field of application. In day-to-day clinical practice the individual situation of the patient is also influenced by various factors that affect the suitability of a treatment. These may include a previous treatment, the patient's general condition, or also certain co-morbidities that have to be taken into account in selecting the treatment. Not all of these situations can be examined and represented since the assessment becomes confusing at a certain level of detail. Nevertheless, patient groups that benefit from a treatment to a greater or lesser extent should be presented in the doctor information system, including the criteria used to define the individual patient groups.

Extent and likelihood of the additional benefit, study results:
The extent of the additional benefit and the therapeutic meaning of the additional benefit compared to the benefit of the appropriate comparative treatment is assigned to

the categories „significant", „considerable", „minor", „not quantifiable" and „no" additional benefit. It can also be determined that the benefit of the pharmaceutical product being assessed is less than the benefit of the appropriate comparative treatment. As a rule, an additional benefit is made more concrete by statements regarding the likelihood of the additional benefit, that is to say whether an indication, hint or proof can be derived from the submitted data.

Only presenting the extent and likelihood of the additional benefit does not make it apparent what endpoints and aspects formed the basis for demonstrating superiority over the comparative treatment. But even presenting study results could not fully interpret the qualitative statement regarding the additional benefit, so that this information could not be adequately presented in a doctor information system but would lead to misunderstandings due to the necessary aggregation of the information. Incorporating other sources of information such as the main reasons for the decision is therefore essential.

When there is no proven additional benefit on the other hand, a rapid interpretation of the statement in reference to considering a prescription for such a pharmaceutical products is by all means needed. This is because the statement „an additional benefit has not been proven" does not mean that the assessed pharmaceutical product cannot be equally considered for the treatment of the indication in question.

These considerations could for example be clarified with notes regarding efficiency, which incorporate the assessment criteria for the additional benefit.

Costs of the pharmaceutical products and notes regarding efficient prescribing:

Regardless of whether the pharmaceutical product prices and reimbursement amount results remain transparent, is seems important to include the prescribing doctors in decisions regarding efficient prescription practices. Even if the results of the reimbursement amount negotiations remain public in some form, notes regarding efficient prescription practices help prescribing doctors determine how the information and statements of a decision according to Section 35a SGB V could or should be taken into account in prescribing.

It would therefore be conceivable in a two-stage process (see Figure 1) that, in addition to the objective information from the decision according to Section 35a SGB V that is provided in machine readable form in a timely manner after the decision is made, the information from the reimbursement amount negotiations or arbitration board is supplied to the doctor information system in a commented, descriptive form. This means the information has to be submitted to the G-BA directly after the corresponding negotiations or arbitration proceedings are concluded.

Within three months after agreeing on or setting a reimbursement amount, the G-BA would make a decision, where applicable differentiated by individual patient groups, whether prescribing the pharmaceutical product in the patient group is fundamentally efficient, in what cases a prescription requires special justification, and in what treatment situations efficiency is only given when unusual circumstances apply.

These circumstances also have to be described in the notes regarding efficient prescribing. Before a decision is made, the affected pharmaceutical companies and the science and practice representatives (Section 92, Paragraph 3a, Sentence 2 SGB B applies correspondingly) should be given the opportunity to comment on the form of the notes according to Section 73, Paragraph 9, No. 5.

This ensures that the participants have exchanged argu-

ments regarding the effects of these notes and have been heard in this regard.

Conclusion

According to the draft law, the information contained in the decision according to Section 35a SGB V must be made available in machine readable form so it can be delivered to the doctor information system. In the course of discussions regarding the procedure, it is necessary to clarify and regulate to what extent the duties for providing the infor-

Information delivery challenges – efficiency notes

- Combination of treatment note and information from the decisions according to Section 35a
- Meaningful even if reimbursement amounts remain public

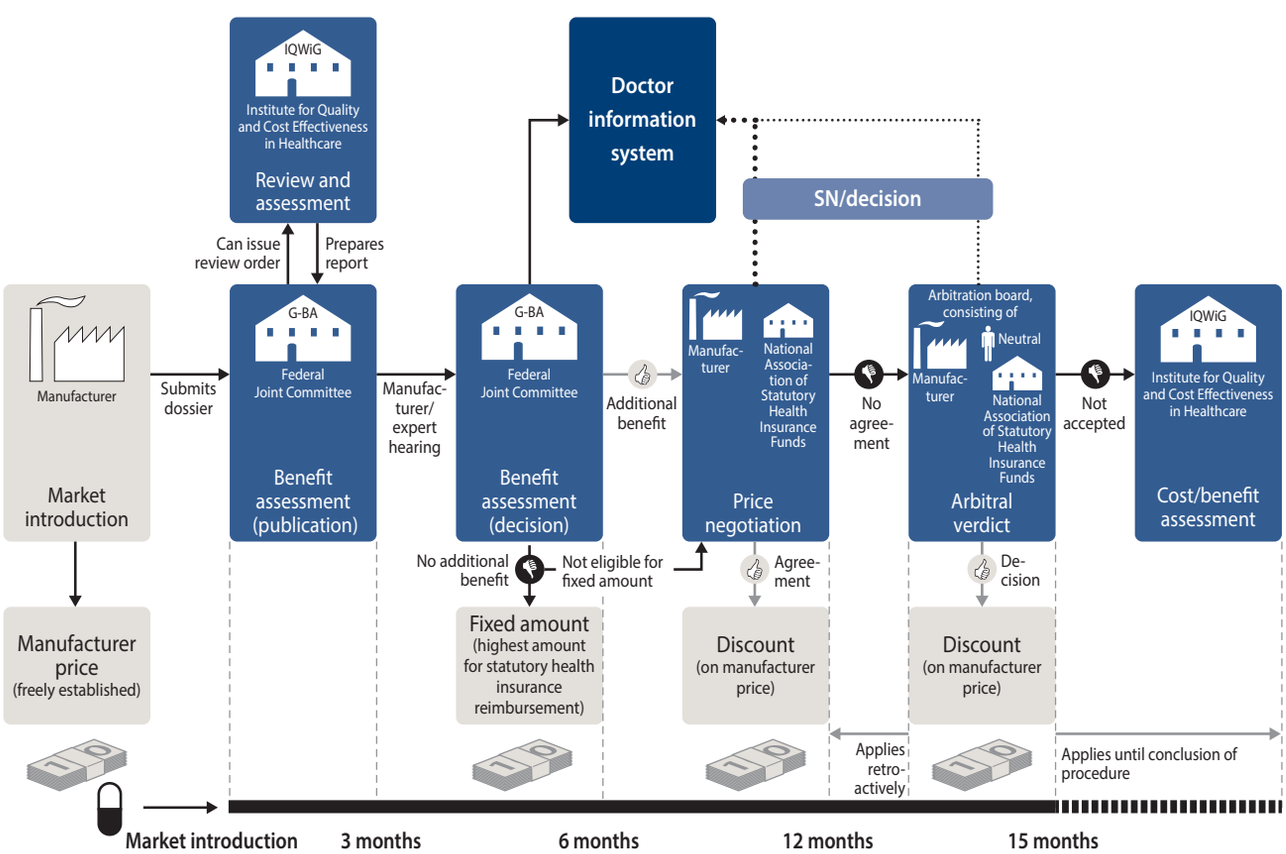


Figure 2: Flow of information in the doctor information system (modified according to BMG: „Faire Preise für Arzneimittel“ (Fair Prices for Pharmaceutical Products)

mation by the G-BA and the responsibility of the software providers can be defined. It is however worthwhile to take a closer look at the available information, and to review to what extent all aspects of the decision have to be presented. In addition to key information such as the active substance, indication, patient groups, and extent and likelihood of the additional benefit compared to the appropriate comparative treatment, other contents of the decision could possibly be omitted, for instance data regarding the size of the patient population or some of the information on quality assured administration. The latter is usually covered by the technical information. Additional information such as the study situation, guidelines or study results could be linked through other providers.

For all information supplied to the doctor information systems, ongoing maintenance will be essential in regards to timeliness so that the doctor information system creates genuine added value for patients and system users. The notes regarding the efficiency of a pharmaceutical product do not constitute a general prescription exclusion nor a limitation of treatment freedom. The notes offer information in descriptive form to the effect whether additional treatment options may require more careful consideration in the applicable patient group. This also provides certainty regarding the interpretation of the decisions in reference to the prescription.

Even today a doctor has to prepare an information synthesis from various sources. However, accessing the different sources is currently laborious and could be simplified by such an information system. The multi-factorial decision processes in the selection of treatments for individual patients remain in the hands of the doctor and cannot be replaced by information from the benefit assessment decisions or the notes regarding efficient prescribing. Whether the more targeted and appropriately priced prescribing of pharmaceutical products can be realised in the foreseeable future remains to be seen. However, the prerequisites for providing information directly to doctors would be established.

Reverence list:

[1]BMG; draft legislation of the BMG for a law to strengthen the pharmaceutical supply in statutory health insurance (Pharmaceutical Products Supply Strengthening Act – AM-VSG), see proposed amendment to Section 73, Paragraph 9 SGB V

[2]Regulation (EC) No. 1234/2008 of the Commission of 24 November 2008 on the review and amendment of approvals for human and veterinary pharmaceutical products (ABl. L 334 of 12 December 2008, page 7)

Doctor information system: an undertaking with unclear consequences

Dr. Florian Staeck

The AMNOG was originally intended as a law for the assessment of the additional benefit and for centrally establishing the price. In the meantime however, the consequences of the AMNOG are revealed in day-to-day healthcare. Transferring the results of the early benefit assessment to practising doctors has in particular proven to be a bottleneck here. According to respondents, the website of the Federal Joint Committee for example is not considered a primary source of information by practising doctors. Insurer representatives also criticise that, so far, there is usually no correlation between the diffusion of new active substances in healthcare and the degree of the additional benefit established by the G-BA.

Against this background, the draft of the Pharmaceutical Products Supply Strengthening Act submitted in October of 2016 contains provisions for improving the information provided to doctors. It intends for the decisions of the G-BA to be edited in machine readable form and provided to doctors through their practice software. The doctor information system is also intended to contain notes regarding the efficiency of the treatment with pharmaceutical products.

Numerous unresolved problems that are disputed between the self- governance partners arise from this project. Implementing the doctor information system is associated with content-related, legal, financial and methodology issues and, as of October 2016, there are few solutions suitable for reaching a consensus among the participants. This became clear at the 4th Convention of the Interdisciplinary Platform on Benefit Assessment on 7/8 October 2016 in Kelkheim.

The aim is to assist doctors with making decisions on treatments with pharmaceutical products while maintaining their treatment freedom and accountability.

It is hoped that preparing the G-BA decisions for the practice software of practising doctors will also make a contribution to improving the quality of treatment with pharmaceutical products. Prior to the implementation however, one is urged to take into account national and international experience regarding what information even reaches doctors as a rule. Accordingly reproducing the full text of HTA body decisions has proven not to be helpful abroad. This applies correspondingly to price information for pharmaceutical products. Alternative prescription suggestions on the other hand were well received by the doctors. Especially when the identified alternatives could lead to better results.

Warning against a comprehensive roll-out

In view of the many unanswered questions, voices were raised requesting that a doctor information system should either be implemented subject to strict requirements, or first be tested only on a regional basis as opposed to an immediate comprehensive roll-out. Otherwise the planned doctor information system could very quickly overload itself. A „clearing house“ could also be advisable, with the responsibility of avoiding possible misunderstandings in the interpretation of G-BA decisions in the doctor information system. Establishing a comparable tool for patient information, if possible in parallel, was also suggested. In the interest of joint decision making by the doctor and patient, the data generated in the AMNOG process should be prepared so that they are also comprehensible for the patient.

Another focus of the discussions was the fear of doctors that an additional efficiency audit of prescription practices would also be installed through the information system.

This is based on the concept of „benefit-oriented reimbursement“ launched by the National Association of Statutory Health Insurance Funds in the summer of 2016, which

calls for agreeing on different prices for the same active substance for differently assessed patient groups. A price no higher than that of the appropriate comparative treatment is to apply in subgroups for which the G-BA did not determine a proven additional benefit in its assessment. For subgroups with an additional benefit, an appropriate reimbursement amount is to be agreed between the drug manufacturer and the National Association of Statutory Health Insurance Funds, as is currently the case.

Benefit-oriented reimbursement instead of a mixed price?

From the perspective of insurers, this „ benefit-oriented reimbursement" will replace the current mixed price model underlying every negotiated reimbursement amount. What practising doctors criticise about the current pricing model is that the reimbursement amount does not establish clarity regarding the efficiency of prescriptions, especially in subgroups with no additional benefit.

However, doctors associate a benefit-oriented reimbursement model with the fear that every prescription in subgroups with no additional benefit will be automatically considered „not efficient" in the future and could potentially bear the risk of recourse. Individual audits have already been initiated in the past by the health insurers for prescriptions of high-priced pharmaceutical products when they were prescribed in subgroups with no established additional benefit. The extent of the individual audits initiated to date was viewed differently. While some discussion participants reported that audit applications are at most observed sporadically with few health insurers, other warned of the – intentional – deterrent effect of recourse applications up to six-figure amounts.

The benefit-oriented reimbursement concept was also opposed with the argument that the early benefit assessment and the AMNOG procedure would be overloaded by attempting to redesign them as a quality tool regulating patient access to new treatments. In the end patients would be „held captive" by the dossier submitted by the manufacturer to the G-BA. This is because, depending on the price level of the appropriate comparative treatment, the required degree of the additional benefit of a new active substance would vary in order to reach a price level that is adequate from the manufacturer's perspective in the subsequent negotiations. The existing contradictions between the benefit assessment decisions of the G-BA and existing S3 guidelines would also be exacerbated because deviating prescriptions would then be in particular need of justification.

Furthermore, the concept of the National Association of Statutory Health Insurance Funds would reveal a methodology problem of the assessment process even more clearly – the fact that no additional benefit has been proven for a medication must not be equated to the lack of an additional benefit. Insofar it would be fatal if the lack of a proven additional benefit would have such a severe impact on prescribing options.

The possible obligation for practising doctors to also disclose the patient subgroup on the prescription was the subject of especially controversial discussion. Aside from violating medical confidentiality, the associated additional encoding would impose a new bureaucratic burden on practising doctors. This applies in particular to general practitioners who issue 75 to 80 percent of all prescriptions. Furthermore, around 50 percent of prescriptions by general practitioners are said to be recurring prescriptions for products originally prescribed by medical specialists or hospitals.

How to proceed here with a lack of diagnosis codes is unclear. Enforced encoding and precise assignment of the

patients to subgroups would also require excessive diagnostics by general practitioners to the detriment of speaking medicine. The opposing argument was that encoding could be realised through the practice software „with little effort". However, warnings were heard that this approach would be contrary to medical secrecy. That is because the prescription is intended solely as a preparation and dispensing order for the pharmacist. This could be counteracted with suitable encryption algorithms so the pharmacist would not receive access to any information about the diagnosis, so the counter-argument.

The benefit-oriented reimbursement model was also met with scepticism regarding a warning that administering multiple prices through one pharmaceutical registration number is not possible. Participants responded that technical solutions to this problem exist as well, for example a patient group code generated by the G-BA.

Price-volume agreements as an alternative?

A fundamentally different approach to dealing with the mixed price problem was also the subject of controversial discussion by the participants: (excessively) complex information systems could be avoided with price-volume agreements between the pharmaceuticals manufacturer and the National Association of Statutory Health Insurance Funds. This model was for example practised successfully in France, where the average price level for pharmaceutical products is also said to be lower compared to Germany. Representatives of the statutory health insurance physicians in particular prefer this model – especially since they expect it would make the efficiency audits obsolete.

Critics of price-volume agreements on the other hand pointed out that it would lead to the formation of undifferentiated prices that are unrelated to the additional benefit. Insofar the benefit-oriented reimbursement model should therefore be preferred.

The volume-related agreements were questioned regarding their potential manipulative use by manufacturers. For instance, one would have to clarify in advance what happens when the originally agreed price-volume structure is not realised in practice – for example because doctors prescribe a medication more often than originally expected. Participants responded that clear agreements in this regard would have to be reached in advance. It would for example be conceivable when exceeding the agreed volume to lower the price to the level of the appropriate comparative treatment, so that paying parties would not be exposed to efficiency risk. The advantage of the price-volume agreements would be that efficiency is established at an aggregate level. However, the problem of how to break down price-volume agreements at the national level to individual insurers remained open.

The possibility of a manufacturer threatening health insurers to take a medication off the market because the price is too low after it has been broadly introduced only exists in theory. Market withdrawal has always been possible. However, all previous cases of market withdrawals have occurred under unfavourable conditions for the manufacturer (no recognition of an additional benefit, generic comparative treatment).

It was argued that a „can" provision for the formation of price-volume agreements in the AMNOG amendment is too weak. Phrasing this regulation as a „shall" provision would be better.

The plenum of the interdisciplinary platform also discussed other aspects of a doctor information system:

- **Dealing with the information „additional benefit not proven":** A doctor information system could help supplement the information that the additional benefit of a medication could not be proven and state it in more con-

crete terms. Very different constellations are behind the statement „no proven additional benefit" in the current assessment scheme: possible causes include the lack of a manufacturer dossier, the lack of relevant studies, or improper methodology in the evaluation of studies that are actually relevant. For the appropriate comparative treatment chosen in an assessment procedure, usable data are not always available either even though the evidence situation is convincing overall. Against this background the differentiated presentation of this information in the doctor information system is meaningful, so the proposal.

- **Problem of product and comparator-based assessment and its implementation in the doctor information system:** Participants warned that a solely product-specific preparation of information from the G-BA decisions would not be well received by doctors. This is because two products are always compared to each other in the AMNOG procedure. Doctors however require an overview of the entire spectrum of active substances for an indication for their prescription decisions. Prescription guidelines are always based on indications as well, not on specific active substances. The numerous new active substances for hepatitis C treatment in recent years were referred to as an example. An information system based solely on the context of the G-BA decisions would hardly be helpful for doctors here. That would also be the case for instance if the appropriate comparative treatment is changed compared to earlier G-BA decisions. This problem too speaks in favour of creating a doctor information system with an information function only, but no control characteristics.
- **Distorted information in the doctor information system due to privileged treatment of orphan drugs:** An additional benefit for orphan drugs is automatically assumed in the AMNOG system due to a legal fiction. In a doctor information system, the appropriate comparative treatment would be automatically in a worse position compared to orphan drugs going forward. It was therefore suggested to exclude the privileged position of these medications from the benefit assessment. Instead an advantage for orphan drugs desired by lawmakers in price negotiations between the manufacturer and National Association of Statutory Health Insurance Funds could be considered.
- **Liability law aspects in the doctor information system:** The question whether a doctor information system would be for information delivery only or could also be used for prescription management was the subject of intense and controversial discussion. On the other hand, there was agreement that any future doctor information system would have to guarantee the timeliness of information. Otherwise liability problems could arise, for example if doctors issue prescriptions in reliance on a data situation that is actually obsolete.

Even converting the G-BA decisions into a more easily readable form will be a major challenge for the doctor information system – the participants at the 4th Convention of the Interdisciplinary Platform on Benefit Assessment agreed on that. This planned system generates many new challenges in and of itself, so that it might be wise to launch a doctor information system with a „caveat".

DISCUSSION PARTICIPANTS

Dr. Pamela Aidelsburger
Silke Baumann
Dr. Jürgen Bausch
Dr. Antje Behring
Claus Burgardt
Prof. Dr. Eva Susanne Dietrich
Regina Feldmann
Dr. Markus Frick
Isabel Henkel
Michael Hennrich, MdB
Dr. Harald Herholz
Dr. Rainer Hess
Dr. Thomas Kaiser
Jana M. Kleinert
Dr. Klaus Koch
Lothar Kuntz
Helmut Laschet
Thomas Mayer
Dr. Ulf Maywald
Dr. Thomas Mittendorf
Prof. Dr. Jörg Ruof
Prof. Dr. Ulrich Schwabe
Prof. Dr. Friedrich Wilhelm Schwartz
Dr. Florian Staeck
Dr. Sibylle Steiner
Wolfgang van den Bergh
Frank Wallbrecht
Julian Witte
Prof. Dr. Bernhard Wörmann

ADVISORY BOARD OF THE INTERDISCIPLINARY PLATFORM ON BENEFIT ASSESSMENT

Dr. Pamela Aidelsburger
Dr. Jürgen Bausch
Wolfgang van den Bergh
Dr. Harald Herholz
Dr. Rainer Hess
Helmut Laschet
Dr. Ulf Maywald
Prof. Dr. Jörg Ruof
Prof. Dr. Ulrich Schwabe
Prof. Dr. Friedrich Wilhelm Schwartz
Dr. Florian Staeck

IMPRINT

PUBLISHER
Editorial Advisory Board for the interdisciplinary platform:
Prof. Dr. Ulrich Schwabe, Pharmakologisches Institut der Universität Heidelberg
Im Neuenheimer Feld 366 69120 Heidelberg
Dr. Harald Herholz
Kassenärztliche Vereinigung Hessen
Georg-Voigt-Straße 15
60325 Frankfurt / Main

PUBLISHING COMPANY
Springer Medizin Verlag GmbH Wolfgang van den Bergh, Chief Editor
Am Forsthaus Gravenbruch 5 63263 Neu-Isenburg
Commercial register: Berlin Charlottenburg District Court
German Commercial Register (HRB): 167094 B
VAT ID: DE 230026696

Telephone: +49 6102 5060
E-mail address: info@aerztezeitung.de

PUBLISHING COMPANY
Springer Medizin Verlag GmbH
Am Forsthaus Gravenbruch 5
63263 Neu-Isenburg

EDITORIAL WORK
Dr. Florian Staeck
Wolfgang van den Bergh,
Helmut Laschet

AUTHORS
Dr. Antje Behring
Regina Feldmann
Dr. Markus Frick
Dr. Antje Haas
Michael Hennrich
Jana Muriel Kleinert
Dr. Thomas Kaiser
Dr. Florian Staeck

PICTURE CREDITS
Cover picture: Stillfx / fotolia.com

LAYOUT / GRAFICS
Sandra Bahr
Oliver Hippmann

PRINTING
F&W Druck und Mediencenter GmbH
Holzhauser Feld 2, 83361 Kienberg

Springer Medizin

In cooperation with and with the friendly support of Roche Pharma AG, DAK Gesundheit, Xcenda GmbH and SpringerMedizin

INTERDISCIPLINARY PLATFORM ON BENEFIT ASSESSMENT

AMNOG 2.0 – Information Problems

Volume 4
April 2017