



INTERDISCIPLINARY PLATFORM ON BENEFIT ASSESSMENT

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Physician information via software: Ways and goals

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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 In-

terdisciplinary 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

Summarised G-BA decisions – a longer learning process

By Dr Pamela Aidelsburger and Dr Jürgen Bausch

Refreshing knowledge and being curious about new developments are constant companions of physicians throughout their entire professional life. Daily medical care is characterised by finding solutions for individual patient problems. Physicians, who want to exercise their profession conscientiously and make therapeutic improvements available to their patients, must engage in ongoing continuing training. As a logical consequence, mandatory continuing medical education (CME) has been stipulated in the Professional Code for Physicians in Germany and physicians must furnish proof of their participation in appropriate educational measures on a regular basis.

However, there are justifiable complaints that many physicians do not sufficiently make use of official benefit assessments of pharmaceutical products in their decision-making process. During early benefit assessments, a significant amount of knowledge and information on the additional benefit and potential harm of a new substance, care landscape, epidemiology, costs, and therapeutic need is gathered in a concise and transparent manner. This information is discussed and evaluated during the benefit assessment procedure by experts of the Institute for Quality and Efficiency in Healthcare (IQWiG) and Federal Joint Committee (G-BA).

One could assume that practising physicians eagerly use this information. However, in the past we have seen that only a small percentage of physicians take note of the G-BA decisions on the benefit assessment in a timely manner. According to the German Act on Strengthening Pharmaceutical Supply in Statutory Health Insurance (AM-VSG) passed in summer 2017, all statutory health insurance physicians shall be informed about G-BA decisions via their practice IT system.

Whether this new information channel for early benefit assessments necessarily covers the physicians' informational needs is yet to be determined. Physicians focus on medical care of their patients and questions around economic efficiency. But can these needs be fulfilled with G-BA decisions on the benefit assessment for a certain pharmaceutical product? In the decision making, the physician has to take a therapeutic decision for every individual patient. If therapy A is not suitable, therapy B or C might be and also watchful waiting would be a conscious therapy decision.

During the benefit assessment, the new pharmaceutical is compared to the appropriate comparative treatment (ACT) that has been established by the G-BA, but not against all other eligible comparative treatments. The physician might therefore derive from the decisions that therapy A has no additional benefit for a certain patient as compared to therapy B, but he still does not know whether therapy C might be more advantageous.

An allocation of various comparative treatments to certain sub-populations or classification into several subgroups often does not solve the problem, but creates new gaps in the decision-making process. Due to their fragmentary nature, G-BA decisions cannot be the only decision algorithm for physicians. This would only be possible, if ALL „either/or“ situations were illustrated.

However, G-BA decisions can provide useful information regarding the efficiency of a certain prescription which becomes increasingly relevant for physicians. Early benefit assessment more and more frequently reveals a mixed subgroup result, i.e. an additional benefit is proven for some of the patients only as compared to the ACT, whereas an additional benefit is not established for certain patient groups despite the same diagnosis.

The G-BA and the National Association of Statutory Health Insurance Physicians (KBV) are now trying to find a

solution for the technical implementation of a physician information system (PIS). It became apparent that the specific interests of all stakeholders will result in different approaches. Only a few approaches are restricted to the mere provision of information about G-BA decisions, while the majority aims at including therapeutic recommendations.

Indeed, it should not be forgotten that the purpose of the early benefit assessment in the German Drug Market Restructuring Act (AMNOG) was only to serve as a basis for price negotiations with health insurance providers and not to guide medical treatment decisions. It is thus not surprising that physicians were quite reluctant to inform themselves about the G-BA decisions so far. They do not provide much information about all therapeutic options, but might be relevant in the context of economic efficiency issues.

However, the regulation as required in the AMVSG that will serve as a basis for the physician information system from the Federal Ministry for Health (BMG) is still missing. Experts of all professions know that a successful conversion of G-BA decisions into an electronic summary for the physicians' practice management systems is a challenging task. Practicable results will probably involve a longer learning curve. The BMG would thus be well advised to give self-administration the possibility to test the physician information system in some health insurance (KV) regions before rolling the system out across Germany.

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Physician information system – a vision in detail

Dr Antje Haas and Maximilian Kuhn | National Association of Statutory Health Insurance Funds (GKV-Spitzenverband)

The purpose of the physician information system (PIS) is to inform statutory health insurance physicians about the results of early benefit assessment in a timely and well-structured manner. From a technical point of view, timeliness and interoperability of the PIS are mandatory. For the transcription of the decisions of the Federal Joint Committee (G-BA) into machine-readable form, data fields for patient groups must be defined and stratified at the semantic level. For instance, the description in the justification and differentiation of patient groups based on the field of application should be more structured and consistent than it is now. Due to semantic structuring on patient group level and technical encoding, all treatment options can be allocated to the respective therapeutic area with a horizontal comparison of several pharmaceutical products which is essential for a fair and correct representation of all decisions. In addition to the decision documents pursuant to Section 35a, further annexes of the German Drug Prescription Directive (AM-RL) and efficiency notes should be integrated into the PIS in a context-sensitive manner. It is apparent that major challenges remain regarding the integration of guidelines into the PIS.

Introduction

Since 2011, a comprehensive and differentiated evaluation of the effect of a pharmaceutical product on the patient-specific endpoint categories mortality, morbidity, quality of life, and adverse events as compared to the current treatment standard is performed and published within the scope of the early benefit assessment directly after a pharmaceutical product is placed on the market. This process does not only involve systematic processing and independent assessment of the existing evidence, but patient representatives, professional associations, individual physicians and pharmaceutical companies are given the opportunity to submit their comments. However, the decision documents published by the G-BA are caught between the conflicting priorities of two different target groups: On the one hand, they serve as a legal basis for the negotiation of a price that is reasonable for both contractual parties based on the respectively benefit in accordance with Section 130b of the 5th German Social Codebook (Sozialgesetzbuch V, SGB V). On the other hand, they serve as information for practising physicians, expert groups, and the interested public about a certain pharmaceutical product – aimed at improving the quality of the prescription of pharmaceuticals.

Against this background it becomes apparent why only limited attention has been given to these decisions by the attending physicians so far. In a joint analysis of the sick-fund DAK-Gesundheit and the German journal „Der Hausarzt“ in 2015, only 12 percent of the participating physicians stated to obtain information about new pharmaceutical products from the G-BA or IQWiG website (Greiner W., 2016). Thus, the acquired knowledge of the early benefit assessment is only marginally used by medical practices. In particular, the decisions must be prepared in such a way to meet the requirements of medical-scientific target groups – especially for the office-based statutory health insurance

physicians for prescription – providing all prescription-relevant information in a well-structured way and at a low threshold.

With the revised version of Sections 35a (3a) and 73 (9) SGB V, authorities set up the legal framework for the further development of practice management systems (PMS) within the scope of the German Act on Strengthening Pharmaceutical Supply in Statutory Health Insurance (AMVSG). The task now is to formulate clear specifications for the further development of PIS pursuant to Section 73 (9) Paragraph 2 SGB V. The aim of the PIS is to communicate the results of the early benefit assessment to medical practices to ensure a rapid and at the same time the best possible horizontal and vertical information of physicians across Germany about potential patient-relevant benefit of specific treatment options thus enabling informed decisions for each patient. Moreover, informed and differentiated decisions prior to prescription as well as documentati-

on of the prescription decisions including the justification, if appropriate, help reduce the risk of a potential recourse.

The authors would like to present the necessary steps to establish the technical requirements for the transcription of the decisions pursuant to Section 35a and integration of further information into the PIS from the viewpoint of the National Association of Statutory Health Insurance Funds.

Conflict of recommendatory character and binding effect

Structuring of the PIS will inevitably lead to a conflict of interests regarding its level of legal obligation. The legal framework should be weighed and taken into consideration by regulators. At present, the following poles can be defined:

If the PIS is intended as a recommendation for action only, both therapeutic freedom and responsibility for the effi-

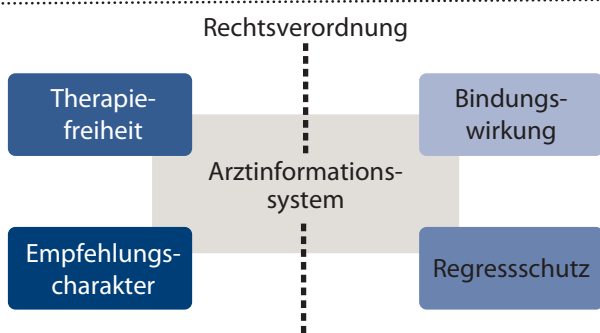


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Gestaltungsvarianten eines Arztinformationssystems



Quelle: Eigene Darstellung

Abbildung 1: Bei Ausgestaltung des AIS muss eine Abwägung zwischen reiner Handlungsempfehlung und „Regressschutz“ getroffen werden.

ciency of a certain prescription remain with the practising physician. But if protection against a potential recourse is the ultimate goal, information in the PIS must have a higher binding effect (see Figure 1).

In return for an improved ex ante information, the question then arises to what extent the unpopular ex post prescription control by means of efficiency audits pursuant to Section 106b SGB V can be reduced.

However, from the viewpoint of the National Association of Statutory Health Insurance Funds, the extreme type of a prohibitive effect of the PIS is not an option; a therapy decision must still be possible on an individual basis even against the recommendation of the PIS. Especially in this case, the practising physician benefits from the ex-ante information, as he can evaluate in which cases comprehensive documentation of the individual treatment decision is feasible and in which cases it can be omitted.

Technical requirements

According to the regulation pursuant Section 73 (9) Paragraph 2 SGB V, any known technical deficiency of PMS systems must be resolved in order to set up an information system that fully meets the requirements of the medical profession. Only with a smooth exchange of current data and easy data linking the requirements of an increasingly digital healthcare can be fulfilled.

Timeliness of information

Although price and product information according to Section 131 (4) SGB V and pharmacy software are updated bi-weekly and G-BA decisions are also taken bi-weekly, most PMS systems have considerably longer update periods – at present usually quarterly. In spite of an existing legal basis in the Act on Secure Digital Communication and Applications in the Healthcare System (eHealthG), legally binding update intervals were set up by arbitration from 1 April 2018 at monthly and as of 2020 at bi-weekly intervals.

In medical practice, the discrepancy of these update periods has led to problems that could have been avoided: In 2014, an adjustment of the reference price for AT1 receptor antagonists (sartane) caused some annoyance among patients, as prescription of the original pharmaceutical product olmesartan – supposedly without co-payment – turned out to be a pharmaceutical product requiring co-payment in the pharmacy (according to current data status). However, with the implementation of the physician information system, a timely communication to physicians will be required on a bi-weekly basis.

Interoperability and modular design

Although authorities have suggested the integration of open and standardised interfaces for patient data into management software for statutory health insurance physi-

ans/dentists and hospitals with the eHealthG in 2015, which was called for again in 2017 with the Act on Modernisation of the Epidemiological Surveillance of Infectious Diseases (EÜMoG) especially in programmes pursuant to Section 73 (9) SGB V, such interfaces have neither been defined nor implemented to date.

These delays are detrimental for statutory health insurance physicians: Due to the lack of standardised interfaces, the physician cannot change from one module of the practice management systems to another (e.g. patient module, prescription module), but has to change the entire PMS leading to increased costs and loss of certification. This situation does not only lead to a dominant position of the software manufacturer, as a change of the PMS is associated with additions costs, time, and frequently a loss of data without a standardised interface, but also affects the price and performance competition between the individual manufacturers.

Linking modules

Different PMS modules, especially patient and prescription modules, must be linked via consistent interfaces. Pharmacy software systems include an automatic verification of warnings, contraindications, and drug interactions. In the medium term and with the implementation of PIS at the latest, this should also be possible with all PMS systems to support the practising physician and further improve the safety of pharmacotherapy. For this purpose, an individual adjustment of the display sensitivity is required.

Preparation of information according to Section 35a (3a)

From a linked PDF file to context-sensitive and interactive information about a pharmaceutical product more than just technical barriers must be overcome. The question,

then, is which level is suitable for a semantic preparation of the decision documents. Stratification of prescription-relevant information must be defined and mandatory differentiated from optional information. Last but not least, prerequisites must be defined to also enable horizontal adjustment within the range of indication, if required.

Preparation by patient group

In general, a semantic preparation of a G-BA decision in machine-readable form can be performed by pharmaceutical product, indication, or patient group. In order to limit information to what is essential, the respective patient group seems to be appropriate for the presentation in the PIS; it is the lowest level on which all prescription-relevant decision information is available, the level on which the G-BA grants the additional benefit and the intuitive level of orientation for the perception of the individual findings of the patient. Upon reading a decision, the reader follows the same path.

With the transcription of the decision documents into machine-readable form, data field-oriented thinking will find its way into the early benefit assessment requiring a more structured approach to grouping patients. For a smooth representation and improved comparability of the decisions and decision generations, the G-BA should further improve the consistency of the patient group segmentation by indication.

Definition and stratification of data fields

If patient groups are used as a level of preparation and comparison, the entire G-BA decision including parts of the justification must be converted to a machine-readable form with a mark-up language. For this purpose, both G-BA decision and justification do not only have to clearly differentiate between patient groups, but also need a clear

structuring of the underlying information in data fields (name of the patient group, extent and probability of the additional benefit, appropriate comparative treatment (ACT), selected comparator, conclusions of the justification, conclusions per endpoint category, quality-assured application notes, etc.). On the basis of the defined data fields, a decision is taken at which hierarchy levels they will be presented in the PMS and what information or hierarchy levels, respectively, must be considered for the prescription and what information is only provided optionally for further research.

Linking of individual decisions

Especially if several innovative treatment options are approved for a certain therapeutic field within a short time, considering only one G-BA decision might be misleading, as this is only a vertical distinction between the evaluated pharmaceutical product and the treatment standard at the time of the decision-making. However, any changes of the

ACT can limit comparability of different treatment options, e.g. treatment options affecting mitogen-activated protein kinases in BRAF-V600 positive advanced malignant melanoma (see Table 1): In 2012, a significant additional benefit was indicated for vemurafenib against the treatment standard dacarbazine due to its advantages in terms of overall survival and adverse events. Due to the extent of the demonstrated benefit of vemurafenib, the ACT also had to be adapted accordingly so that dabrafenib which was compared to the now obsolete treatment standard dacarbazine within the scope of the Phase-III trial, did not demonstrate an additional benefit against the ACT vemurafenib during the benefit assessment procedure 18 months later. Comparing the additional benefit of both BRAF inhibitors on the basis of the individual decisions without knowing the modified object of comparison, dabrafenib would falsely be considered inferior to vemurafenib.

Another two years later, a comparison of the respective combinations of BRAF and MEK inhibitors versus a vemura-

Therapieoptionen beim BRAF-V600-positiven fortgeschrittenen malignen Melanom

| Vemurafenib | Dabrafenib | Dabrafenib + Trametinib | Vemurafenib + Cobimetinib |
|---|------------------------------------|--|--|
| (Beschluss vom 06.09.2012) | (Beschluss vom 03.04.2014) | (Beschluss vom 17.03.2016) | (Beschluss vom 02.06.2016) |
| Hinweis auf einen beträchtlichen Zusatznutzen. | Ein Zusatznutzen ist nicht belegt. | Hinweis auf einen beträchtlichen Zusatznutzen. | Hinweis auf einen beträchtlichen Zusatznutzen. |
| Die zweckmäßige Vergleichstherapie für die Behandlung von Patienten mit BRAF-V600 Mutation-positivem nicht resezierbarem oder metastasiertem Melanom ist: | | | |
| Dacarbazin | Vemurafenib | Vemurafenib | Vemurafenib |

Quelle: Eigene Darstellung

Tabelle 1: Änderungen in der zweckmäßigen Vergleichstherapie können die Vergleichbarkeit des Zusatznutzens verschiedener Therapieoptionen einschränken.

fenib monotherapy revealed advantages in all four endpoint categories presenting an indication for a significant additional benefit; both decisions were taken within a short period of time so that the later decision was not associated with any disadvantages as in the first example and therapeutic comparability was demonstrated in the decisions at first glance. Nevertheless, comparing the decisions on vemurafenib and the combination of vemurafenib + cobimetinib or dabrafenib + trametinib, respectively, without knowing the modified object of comparison would create a wrong impression, i.e. therapeutic comparability of a vemurafenib monotherapy against the combinations.

Only if the physician reviews several decisions including their additional benefit and the respective ACT in a horizontal comparison, a fair comparison of various decision generations can be made. Decisions on a potential inclusion of the existing market, which is not part of the ACT, should certainly be taken at a later stage.

In order to avoid misinterpretation and provide practising physicians with a user-friendly and quick overview of existing treatment options, evaluating indications or recommendations might be integrated into the horizontal comparison, e.g. in graphic form. As mentioned above, these notes are not always associated with the existence or lack of an additional benefit, respectively.

A horizontal comparison in the relevant treatment area is only possible, if the individual pharmaceutical products are technically linked by indication. In order to ensure precise and quick information of the physician, it must be fine-tuned beyond the ICD-10 code, as many ICD-10 codes cover various treatment situations (example C50.- malignant neoplasms of breast – does not distinguish between neo-adjuvant/adjuvant vs advanced or receptor status). At a technical level, encoding must ensure representation of the patient groups of the G-BA. The practising physician,

however, has no encoding obligation using new catalogues etc., he only selects a text on the interface that corresponds to the patient's treatment situation.

Additional information

In addition, Section 73 (9) Paragraph 4 SGB V also specifies that the PIS should also outline the provisions for ambulatory statutory healthcare on the effectiveness and efficiency of the prescription of pharmaceuticals as compared to other treatment options. Accordingly, the contents of the AM-RL and efficiency notes for prescriptions by physicians in the statutory health insurance system should be integrated into the PIS in a user-friendly form to provide the physician with comprehensive information on the efficiency of the prescription as quickly as possible.

German Drug Prescription Directive (AM-RL)

According to the results of the early benefit assessment (Annex XII of the AM-RL) any information provided in the annexes of the AM-RL must be provided in machine-readable form to make it available at a low threshold and context-sensitive in accordance with the directive.

Efficiency notes

Besides the result of the benefit assessment, regulations on the efficiency of ambulatory statutory healthcare also include national (exempt from efficiency audits according to Section 130b SGB V, agreement on medical aids according to Section 84 (7) SGB V), regional (agreement on physiotherapy and regional target agreements according to Section 84 (1) SGB V, regional exempts from efficiency audits), and sick-fund specific rebate agreements according to 130c SGB V or Section 130a (8), respectively) measures. This information is important for prescription and should thus be incorporated into the PIS on a binding and intuiti-

ve basis. Like common pharmacy software, icons and mandatory filter functions, e.g. by reimbursement amount, rebate agreement, special characteristics, or target agreement, help to integrate this information into daily prescription without user interaction.

Guidelines

Recently, an expert assessment on behalf of the Association of Research-based Pharmaceutical Companies (vfa) suggested that the G-BA decisions and S1 treatment recommendations (onkopedia.de) and position statements by the German Society for Haematology and Medical Oncology (DGHO), respectively, draw different conclusions in some cases regarding the importance of a pharmaceutical for a certain indication (Ruof J, 2017). Although this fact is not very surprising, knowing that even within evidence and consensus-based S3 guidelines several medical-scientific professional associations evaluate the importance of treatment options differently (BÄK, KBV, AWMF, 2013), the question is how additional information of guidelines can be integrated into the PIS in a clearly arranged form.

In this context, some barriers must be overcome. For most diseases, several guidelines are available with different methodological quality (S1, S2k, S2e, S3), different timeliness, from different countries and with a focus on different medical care situations and approval requirements, different transparency requirements, different extent and handling of conflicts of interest, different extent of participation of both external professional public and patients, as well as incoherent design. In order to avoid leaving the practising physician with an abundance of – in some cases conflicting – information recommendations in PDF format behind, the National Association of Statutory Health Insurance Funds recommends to only include guidelines after

one „lead guideline“ has been specified by an independent institute (e.g. IQWiG) which is graphically processed and converted into machine-readable form to ensure a context-sensitive representation. However, as inconsistencies with the AM-RL should be considered, guidelines should not be included in the first implementation stage of the PIS.

Outlook

The implementation of the PIS provides an opportunity to set the course for an international example for the provision of evidence-based information on pharmaceuticals. Against this background, it becomes apparent that not all stakeholders can be satisfied with a scaled-down version of a physician information system and that it is time to lay a solid foundation for physician information in the digital age. Some time ago, a specialist book provided current information for medical decisions over a period of several years. Due to the rapid progress of medical and pharmaceutical research, up-to-date information which is required for clinical decisions can nowadays only be provided with a software-based solution adapted to the physician's individual prescription practice.

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Can G-BA benefit assessment decisions be summarised?

Professor Josef Hecken | Impartial chair of the Federal Joint Committee (G-BA)

With the Act on Remedies and Aids (HHVG) the prerequisites for the use of electronic programmes for the prescription of pharmaceuticals in ambulatory statutory healthcare were readjusted. It defines the contents of electronic programmes in ambulatory statutory healthcare and stipulates that decisions of the Federal Joint Committee (G-BA) on the benefit assessment must be clearly stated according to Section 35a. The intention of this physician information system (PIS) is to ensure that benefit assessment decisions are made available to a large number of physicians in the ambulatory statutory health insurance system taking effect in the prescription behaviour.

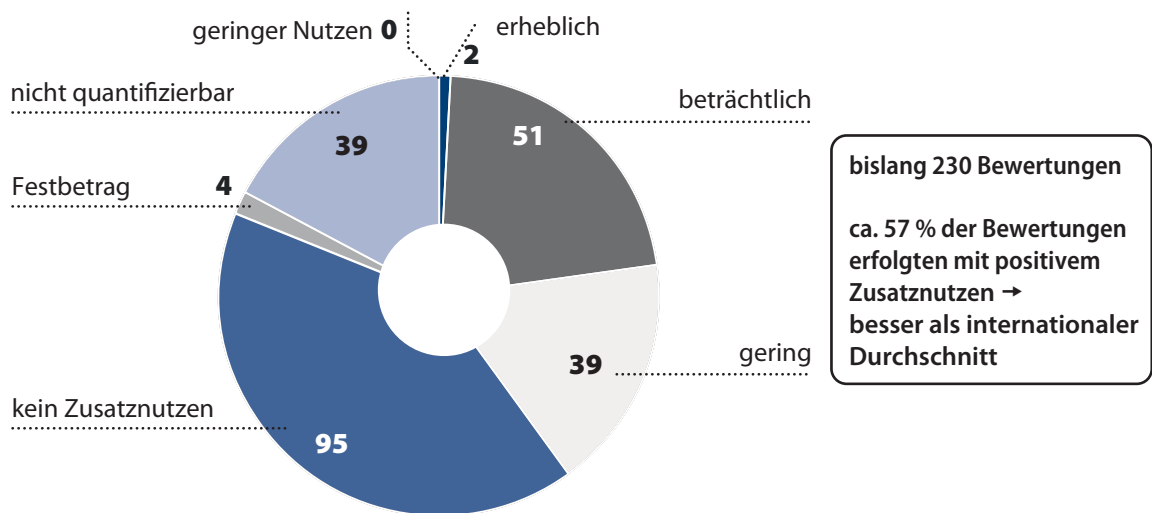
With the HHVG, the new Paragraphs 9 and 10 in Section 73 of the 5th German Social Codebook (Sozialgesetzbuch V, SGB V) were implemented. Section 73 Paragraph 9 stipulates the prerequisites for the use of electronic programmes for the prescription of pharmaceuticals in ambulatory statutory healthcare. It defines the contents of electronic programmes in ambulatory statutory healthcare and stipulates that decisions of the G-BA on the benefit assessment must be clearly stated according to Section 35a. With this regulation, the Federal Minister for Health gets the power to issue ambulatory statutory instruments enabling him to regulate the details about the representation of the benefit assessment, promote its further development (where appropriate), and define in which form efficiency notes for the prescription of pharmaceuticals must be issued as compared to other treatment options.

The intention of this physician information system (PIS) is to ensure that benefit assessment decisions are made available to a large number of physicians in the ambulatory statutory health insurance system pursuant to Section 35a SGB V very quickly to take effect in the prescription behaviour. Even five years after the German Drug Market Restructuring Act (AMNOG) came into force, there are still significant information deficits – partly due to the large number of decisions – especially among physicians without specialisation who are not involved in scientific discussions about new active substances as intensively as medical specialists (see Figure 1). Moreover, G-BA benefit assessment decisions including justification are often quite extensive. This is necessary in order to increase legal certainty of the decisions, as jurisdiction requires reviewing of all relevant facts presented within the scope of the hearing procedure.

Thus, a short and schematic representation of the G-BA

Das AMNOG erfüllt seinen Zweck

Höchste Zusatznutzenkategorie je Verfahren nach § 35a SGB V



Quelle: Eigene Darstellung, eigene Berechnung

Abbildung 1: 57 Prozent der Bewertungen haben einen positiven Zusatznutzen der Medikamente ergeben.



Since July 2012, **Professor Josef Hecken** has been Impartial Chairman of the Federal Joint Committee (G-BA). Between 2009 and 2012, he was engaged as State Secretary at the Federal Ministry for Family Affairs, Senior Citizens, Women and Youth. Further positions in his career include: President of the Federal Insurance Office (2008-2009), Minister of Justice, Health and Social Affairs and, from 2008, also Labour of the Saarland.

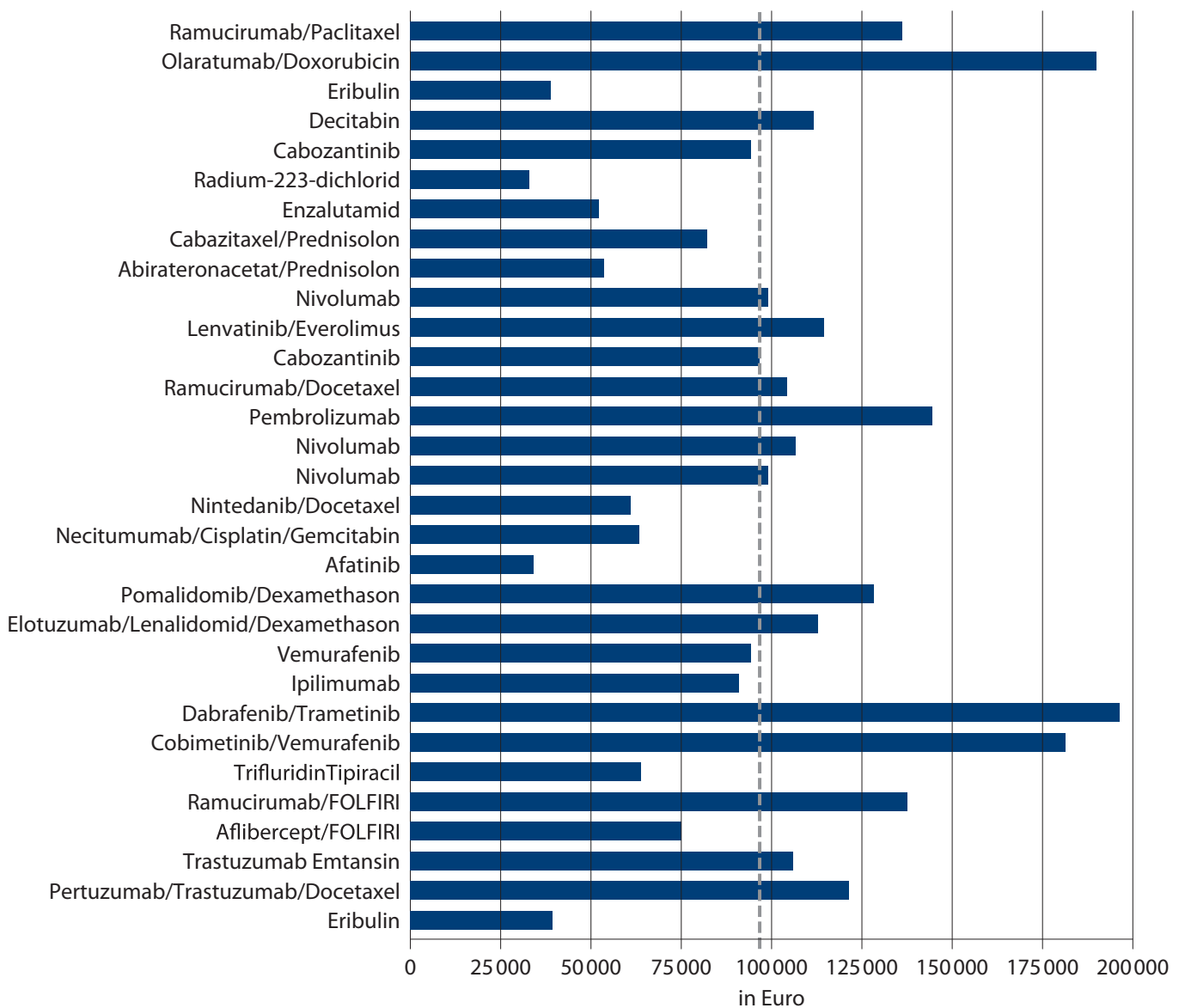
decisions in the PIS presents several challenges, as text reductions bear the risk that differentiated and important data are left out or modified. Nevertheless, this appears to be feasible and the approach will be discussed below.

II. Key question: Nature of efficiency notes

The central question regarding the PIS and its design must be clarified and defined in detail in the regulation by the Minister for Health. This regulation is not yet available, as the legal provision only stipulates that the Federal Ministry is authorised to specify the presentation of the regulation on the appropriateness and efficiency of the prescription of pharmaceuticals compared to other treatment options.

It is not yet clear to what extent Federal Ministry will set its own provisions in the regulation.

Jahrestherapiekosten neuer onkologischer Wirkstoffe



Quelle: Eigene Darstellung

Abbildung 2: Hinweise zur Wirtschaftlichkeit hätten wegen der Kostenentwicklung eine hohe Relevanz.

If efficiency notes shall be regulated, the essential question is whether the PIS shall only provide detailed information so that the physician can take his own decision about the appropriateness and efficiency of a certain prescription or whether the PIS shall set up binding specifications, in which cases and for which patients the prescription of a certain active substance would be appropriate and economical.

If the information in the PIS shall be binding for ambulatory statutory health insurance physicians, different legal regulations will apply and questions arise that go far beyond the problems of the mere provision of information. In this case, it should be determined whether the PIS acts in fact as a non-prescription regulation for the sub-groups for which it is not considered efficient on the basis of the precise efficiency notes that are binding for physicians.

If such a factual effect is confirmed, the decision about the efficiency notes would have to be taken in a formalised procedure to ensure involvement of all potentially affected pharmaceutical companies, professional associations, and other stakeholders.

Regardless of their legal nature, efficiency notes are not only highly relevant in the field of oncology with regard to the cost development (see Figures 2 and 3).

III. Representation of benefit assessment decisions in pharmaceutical software according to § 35 a Paragraph 3a SGB V

a) Information about significant benefit assessment decisions

At present, decisions on the benefit assessment pursuant to Section 35 a SGB V include any information as defined in Chapter 5 of Section 20 of the G-BA Rule of Procedures (VerfO), i.e.:

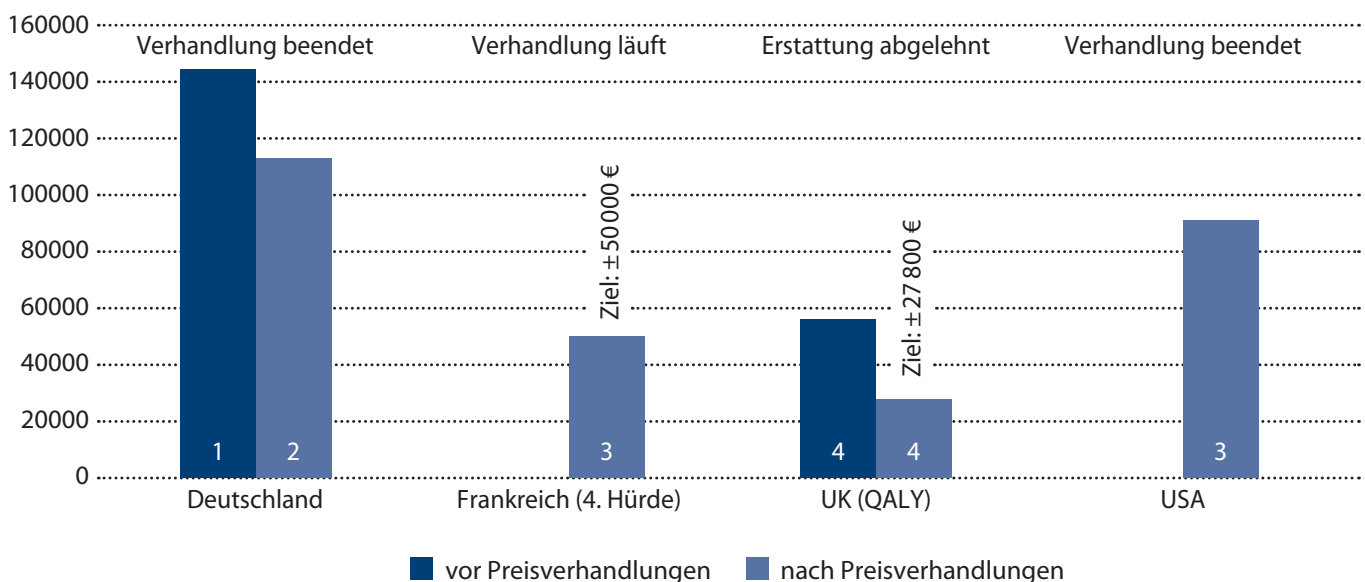
- active substance/active substance combination and evaluated indication relating to the decision,
- evaluated patient populations, including information on the appropriate comparative treatment (ACT) as defined by the G-BA,
 - extent and probability of the additional benefit as compared to the ACT selected by the pharmaceutical company,
 - information about the study results, where applicable,
 - information about a quality-assured application for the pharmaceutical,
 - information about the number of patients,
 - information about the annual treatment costs of both the respective pharmaceutical and ACT,
 - information about the date and validity period of the decision.

At present, this information is not quickly and easily accessible in clinical practice and has to be compiled and represented appropriately. In order to integrate essential content of the decisions on the early (additional) benefit assessment, represent it in pharmaceutical information systems of the medical practice and provide highly-informative data, existing information of the decision documents (decision and justification) must be extracted, processed and provided in electronic form. Besides a clear allocation of an active substance/active substance combination and the respective indication of a pharmaceutical, the following information of the benefit assessment decisions must be provided for every definable and evaluated patient group in machine-readable form for the use of electronic programmes:

- appropriate comparative treatment as defined by the G-BA,
- specific appropriate comparative treatment the state-

Preisniveau für onkologische Wirkstoffe in Deutschland trotz AMNOG weiterhin hoch im internationalen Vergleich (Beispiel Pembrolizumab (Melanom))

Jahrestherapiekosten in Euro



¹ Beschluss vom 4. Februar 2016; Anhaltspunkt für einen beträchtlichen Zusatznutzen gegenüber Ipilimumab und Hinweis auf einen beträchtlichen Zusatznutzen gegenüber einer patientenindividuellen Therapie nach Maßgabe des behandelnden Arztes (Ipilimumab)

² Auf Basis der Angaben der Lauer-Taxe zum Erstattungsbetrag (gemäß § 78 Abs. 3a AMG; rechnerisch auf ein Jahr standardisiert)

³ <http://www.apmhealthurope.com>; Merck & Co aiming to make Keytruda available in France 'as soon as possible'; 13. Oktober 2016

⁴ <http://www.apmhealthurope.com>; UK's NICE rejects MSD's Keytruda in advanced lung cancer; 4. Oktober 2016

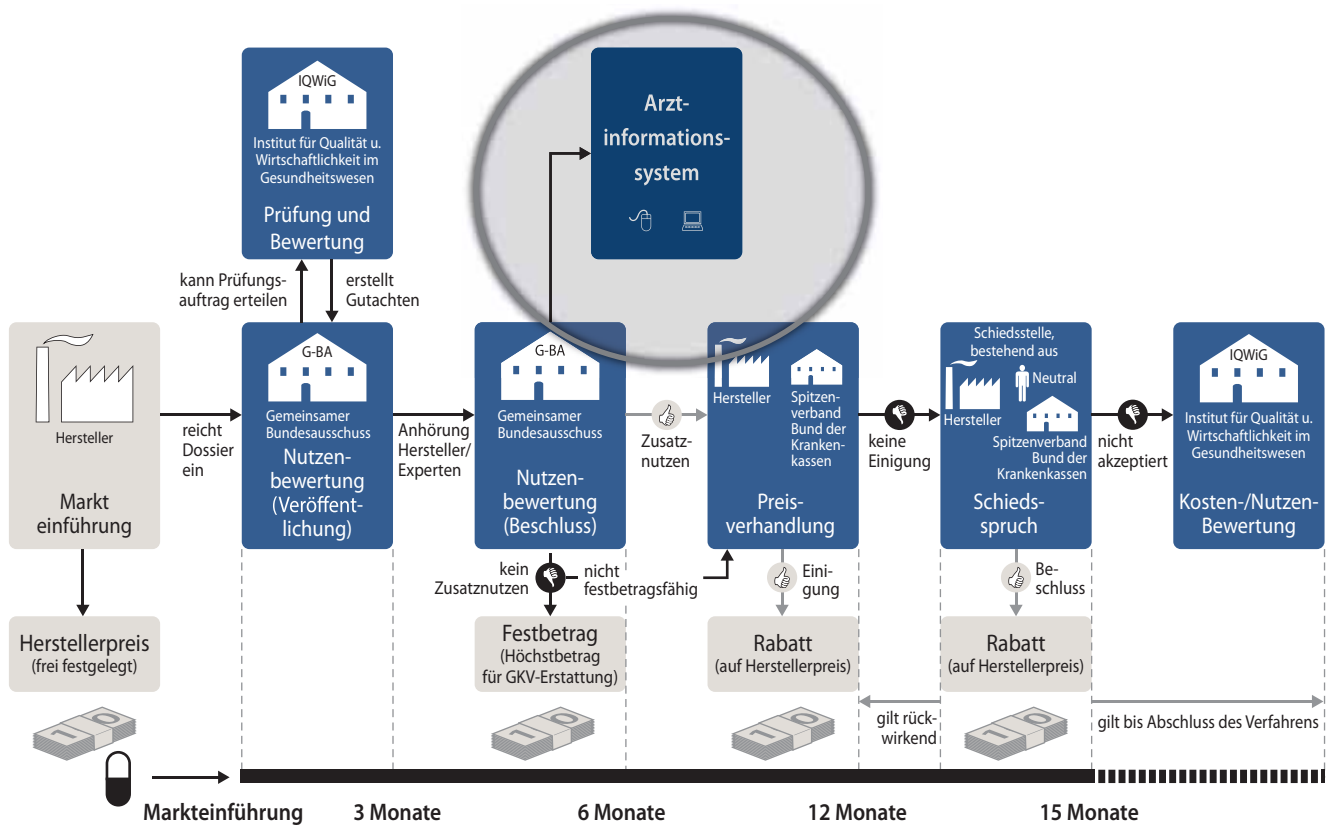
Abbildung 3: Auch nach den Erstattungsbetrags-Verhandlungen liegt der Preis im internationalen Vergleich noch hoch.

- ment on the additional benefit is based on,
- category of extent and probability of the additional benefit,
- short description of the evidence base and major aspects of the decision for the evaluation in consideration of the therapeutic effects in endpoint categories mortality, morbidity, quality of life, and side effects, • requirements for a quality-assured application,

- annual treatment costs of the evaluated active substance and appropriate comparative treatments,
- references to any other decisions relating to this indication,
- state of the information (date of the decision for the patient group; validity period of the decision, where applicable).

Making the decision available in such a form gives the phy-

Einführung Arztinformationssystem



Quelle: BMG, ergänzt um eigene Darstellung

Abbildung 4: Ablaufschema nach der Einführung eines Arztinformationssystems.

sician all relevant information enabling him to account for the efficiency principle during the prescription of the new active substance/new active substance combination as compared to the appropriate comparative treatment (see Figure 4).

However, the interpretation of both efficiency and significance of a new active substance/new active substance combination as compared to the other treatment options

lies within the responsibility of the respective physician. This interpretation goes far beyond a mere comparison of the evaluated active substance and the actual appropriate comparative treatment.

If the G-BA should be obliged to provide efficiency notes for active substances that are evaluated according to Section 35a SGB V against other pharmaceuticals for the respective indication, it recognises the necessity to take a se-

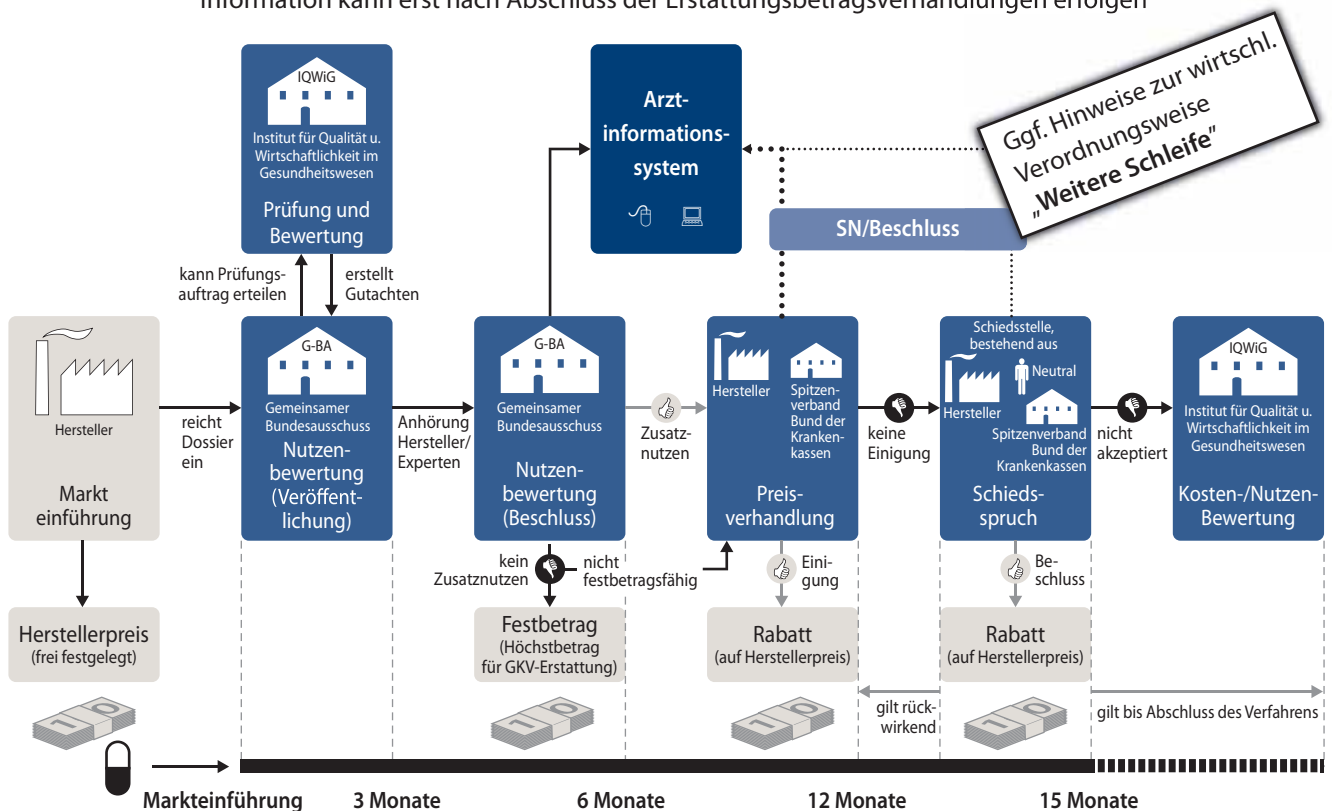
parate decision with prior hearing procedure directly after the negotiation or determination of the reimbursement amount due to the significance and control effect of these notes for the prescriptions and potential involvement of other pharmaceutical companies (see Figure 5).

Any notes about an economic prescription and conclusions about the significance of the pharmaceutical as com-

pared to other treatment options are an important input for the prescribing physician. The representation in physician information systems might not be implemented for all procedures in a first step, but can be supplemented later on the basis of minimum requirements.

Herausforderungen der Informationsbereitstellung: Hinweise zur Wirtschaftlichkeit

Kombination aus Therapiehinweis und Information aus den Beschlüssen nach §35 a
 Information kann erst nach Abschluss der Erstattungsbetragsverhandlungen erfolgen



Quelle: BMG, ergänzt um eigene Darstellung

Abbildung 5: Bei Hinweisen zur Wirtschaftlichkeit wäre ein vorgeschaltetes Stellungnahmeverfahren nötig.

b) Other requirements relating to the content-related representation

The presentation of the contents of the benefit assessment decisions should provide a clear and neutral visualisation of essential information for the physician in his practice workflow/prescription process. Essential information could be provided at a first level and further information of the decision upon request at subordinate levels.

If several decisions are available for one active substance and multiple indications, only details that are relevant for the respective indication should be presented. The following core data should be presented during the prescription process:

- If multiple benefit assessment decisions are available for one active substance and different indications, the respective indication must be selected first. The representation of all evaluated patient groups for an active substance would be confusing.
- Moreover, for every evaluated patient group/treatment situation in the indication,
- the appropriate comparative treatment as defined by the G-BA,
- the appropriate comparative treatment selected by the pharmaceutical company in contrast to the statements made on the additional benefit,
- the extent and probability of the additional benefit of the respective pharmaceutical,
- the annual treatment costs of the evaluated active substance and appropriate comparative treatments should be presented in accordance with the state of the information.
- If the G-BA will be obliged to provide efficiency notes for the evaluated active substance as compared to other pharmaceuticals in the indication, these should also be displayed.

As required, the following optional data fields should be added for every patient group:

- short description of the evidence base and major aspects of the decision for the evaluation in consideration of the therapeutic effects in endpoint categories mortality, morbidity, quality of life and side effects.

Requirements for a quality-assured application:

- references to other decisions relating to this indication/patient group,
- where appropriate, notes on the significance of the evaluated active substance for the respective patient population as compared to other treatment options,
- where appropriate, relevant companion diagnostics, medical services that are mandatory for the application of the pharmaceutical.

c) Requirements for a hierarchical representation

At the first hierarchy level, the following information should be provided:

1. Trade name, active substance, / active substance combination,
2. Therapeutic area, indication according to the approval,
3. Patient group(s) with
 - a. appropriate comparative treatment,
 - b. extent and probability of the additional benefit as compared to the ACT selected by the pharmaceutical company,
 - c. annual treatment costs of the evaluated active substance and appropriate comparative treatments,
 - d. efficiency notes on the evaluated active substance in the treatment situation as compared to other treatment options (where compulsory for the G-BA),

- e. state of the information.

At further levels, the following information should be provided::

4. Evidence base for the assessment,
5. Major aspects of the decision for the evaluation in consideration of the therapeutic effects in endpoint categories mortality, morbidity, quality of life, and side effects,
6. Requirements for a quality- assured application,
7. Annual treatment costs of the evaluated active substance and appropriate comparative treatments,
8. References to other decisions relating to this indication/patient group.

specifications to regional agreements for active substances between health insurance provider and Regional Association of SHI-Accredited Physicians (KV) should also be regulated.

IV. Other minimum contents and requirements according to Section 73 Paragraph 9 Sentence 1 SGB V

Due to the fact that existing pharmaceutical information systems contain references to the drug prescription directive for the individual active substance (e.g. on non-prescription, OTC-exception list, fixed payments), further comments are not required.

It is, however, important that the decisions of the pharmaceutical guideline are communicated promptly after they have come into force. If efficiency notes are specified in such a way that e.g. statements on comparing various pharmaceuticals with new or existing active substances for an indication shall be provided beyond a mere comparison of a certain pharmaceutical with a new active substance against the relevant appropriate comparative treatment, a separate procedure will be necessary.

V. Conclusions

It remains to be seen what the regulation will look like and whether specifications on the efficiency notes will be decisive. If they are strictly binding, the relationship of these

Physician information system: Provision of information or control mechanism?

Dr Markus Frick | Dr Ulrike Götting, Association of Research-Based Pharmaceutical Companies (vfa)

So far, the political background for the design of the content of the physician information system (PIS) is not clear. Suggestions made by health insurance providers seem to indicate a highly-complex prescription control based on the decisions of the Federal Joint Committee (G-BA). The fact that German Drug Market Restructuring Act (AMNOG) decisions are not intended as guidance for physicians as to whether a pharmaceutical is best suited for a certain patient from a medical-therapeutic viewpoint is neglected. They cannot replace evidence-based guidelines. Thus, there are many reasons for a lean implementation of the specifications provided in the Act on Strengthening Pharmaceutical Supply in Statutory Health Insurance (AMVSG) with a practical orientation initially, focussing on a correct and complete representation of G-BA decisions and guidelines in the practice software.

In March 2017, the introduction of a „Physician information system“ (PIS) was approved by the German Bundestag within the scope of the AMVSG. However, it is still unclear what this name stands for: A new kind of information supply about G-BA decisions for physicians? Or a new software module for the prescription of pharmaceuticals?

In the AMVSG, only a few general specifications are given on the physician information system (new Sections 35 Para. 3a and 73 Para. 9 SGB V). The specific design will be specified by a regulation by the Federal Ministry of Health. To date, the Ministry has not yet indicated how this is to be put into practice, but only gathered feedback from a number of stakeholders in May/June 2017 within the scope of a consultation procedure.

The discussion about the implementation of the AMVSG specifications has only just begun and will probably remain an issue for some time to come. It is therefore all the more important at this stage to realise the essential aspects and carefully consider into which direction the political course should be set.

From our point of view, there are two major topics to be discussed:

- Do we want to create a solid basis for the prescription behaviour of physicians with a physician information system or do we want to (remote) control prescription of physicians? In other words: How much treatment responsibility should the physician have in clinical practice and how many pharmaceutical treatment alternatives should he or his patients be given, respectively?
- The first question is: Do G-BA additional benefit assessments provide an adequate basis for a responsible prescription control – if this is the goal? And, if not, how should an appropriate database for day-to-day healthcare

look like and how could it be set up?

Implementation alternative „physician control“

Health insurance providers and physicians have very different opinions on this question. Until now, health insurance providers, above all the National Association of Statutory Health Insurance Funds (GKV-Spitzenverband) and the Federal Association of Local Health Insurance Funds (AOK-Bundesverband), propagate a controlling physician information system (see also Kleinert/Haas 2017, GKV-Spitzenverband 2017, gid 2017, Beckmann/Maiwald 2017, AOK-Bundesverband 2017). G-BA decisions shall be edited for every patient group as selected by the G-BA and displayed in the practice software on a context-sensitive basis during the prescription procedure. Visual highlights, such as co-

lor codes or other visual signs, shall facilitate orientation. Moreover, the results of the additional benefit assessment shall be linked to the information on the efficiency of a certain pharmaceutical. On this basis, the software indicates in which cases the physician should prescribe a certain pharmaceutical and in which cases a prescription might lead to a recourse.

The AOK affiliate gevko GmbH has presented such a software module to make this alternative politically attractive. They refer to IT solutions from selective agreements (S3C interface) that virtually enable health insurance providers to remote control the medical prescription process – provided both physicians and patients gave their written consent. Obviously, this IT approach shall now be transferred to standard care and rolled out across Germany.



Since September 2012, **Dr Markus Frick MPH** has been head of the Market and Reimbursement division of the vfa. The internist and health scientist worked at the universities of Bonn and Düsseldorf for twelve years, mainly in the field of haematology/oncology. In 2001, he joined the 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.



Dr Ulrike Götting is responsible for the coordination of physician information system at the vfa. Since 2001, she has been working for the vfa and took care of a broad range of topics regarding drug regulation. She is a graduated social scientist and previously worked for an association of statutory health insurance providers and a private health insurance company.

The fact that regional IT systems – that are used as a role model – focus on the prescription of general practitioners and selection of pharmaceuticals of various manufacturers with the same active substance does not seem to play a role. They „help“ the physician to select the product with the best discount conditions. On the contrary, AMNOG regulated pharmaceuticals involve pharmaceuticals with different active substances in predominantly complex treatment situations, e.g. oncology or virology patients.

About one fifth of all AMNOG pharmaceuticals may only be prescribed by appropriately qualified physicians pursuant to their approval. Especially for this target group and the complex treatment decisions, the approach of providing information to physicians with „simple visual signals“ is not at all suitable. A traffic light system for prescriptions or similar reductionistic approaches would at best be ignored by physicians; in a worse case, they would act as therapeutic limitations and thus impair medical care.

Implementation alternative „supply of information“

In contrast, physicians made various suggestions for the implementation of a practical information system providing valuable support without monitoring or controlling them more than before (e.g. BÄK/AKdÄ 2017, KBV 2017, Winnat 2016, Wörmann 2016, AWMF 2017). G-BA additional benefit decisions should be communicated to physician via the PIS without any reductionistic misinterpretation or simplifications. Physicians are strictly against any technical linking of individual decisions with various pharmaceuticals and diagnoses. In addition to the G-BA decisions, physicians should also be granted access to the entire evidence on the diagnostics and treatment options for the respective indication. The physician information system must not be used for prescription control on the basis of a threatening recourse.

Implementation proposals by physicians are based on the findings that although the AMNOG decisions by the G-BA present valuable individual information on new pharmaceuticals, they are not intended as guidance for physicians whether a certain drug is most suitable for a certain patient from a medical-therapeutic point of view. The therapeutic significance of the evaluated pharmaceutical as compared to other treatment options cannot simply be derived from G-BA decisions. By the way, that's also the G-BA's understanding (e.g. Behring 2017). Equating the phrases „additional benefit not proven“ and “the pharmaceutical should not be prescribed“ would be misleading and irresponsible from a medical point of view.

In practical terms, that means: Despite a clearly proven prolongation of life of new cancer medications, the G-BA's assessed it repeatedly as „additional benefit not proven“. The reason for this was a „miscalculation“ of the prolongation of life with side-effects or missing data on the disease-specific quality of life. However, the basic principle of evidence-based medicine is that physician and patient jointly decide about the best treatment depending on the patient's individual preference. For a patient for whom the prolongation of his life is paramount, this new therapy would be the best option and any „ban“ of the pharmaceutical without proven additional benefit by the physician information system would in fact result in mistreatment.

AMNOG decisions are not therapeutic advices

What does the G-BA do during the AMNOG benefit assessment? The G-BA evaluates the additional benefit of a certain pharmaceutical against a comparator. A potential additional benefit always depends on the comparison. Thus, this is a relative and not an absolute statement.

For example, the G-BA's assessment on the melanoma drug dabrafenib was „additional benefit not proven“ after

changing to vemurafenib as comparative treatment during the procedure. According to the medical guideline, vemurafenib is an equivalent treatment option to dabrafenib. This would in fact be the correct interpretation of the G-BA decision: The unproven additional benefit does not constitute a therapeutic inferiority of a certain drug, but only a lack of proof of its superiority. The example shows: The G-BA decision on the additional benefit should not be interpreted as a treatment recommendation leading to prescription exclusion. It is just a statement for the price finding process for the product.

Another example from another indication is the elbasvir/grazoprevir drug combination for the treatment of chronic hepatitis C. In the approval study, it was compared to an older standard treatment. For the AMNOG benefit assessment, the G-BA determined the new combinations „ledipasvir/sofosbuvir or ombitasvir/paritaprevir/ritonavir plus dasabuvir“ as comparative treatment which had previously been assessed positively and came to the conclusion that the additional benefit is „not proven“. However, according to the guideline, elbasvir/grazoprevir is an equivalent option to the comparative treatments. The different G-BA decisions can be attributed to the fact that comparator was changed by the G-BA. It does not allow any conclusions on the prescription relevance of the active substance.

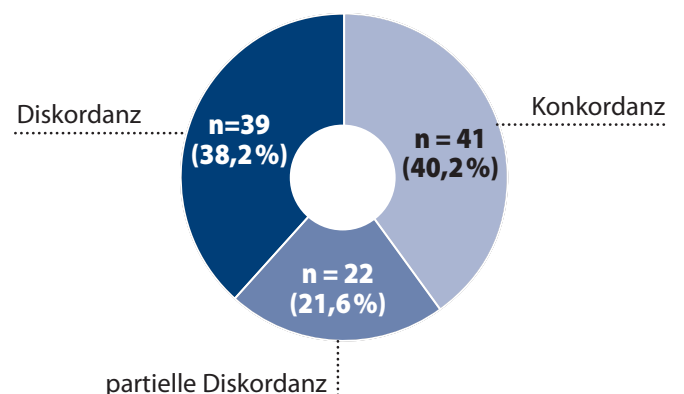
AMNOG decisions do not replace guidelines

Are pharmaceuticals without proven additional benefit dispensable for prescription? Certainly not. According to the scientific societies, many pharmaceuticals for which the G-BA has not determined an additional benefit, play a significant role in the healthcare landscape. Hence, treatment guidelines recommend these drugs as a valuable therapeutic alternative or even as treatment without alternative.

For example, the guideline recommends the anti-cancer drug crizotinib as therapy without alternative for patients with ROS1-positive advanced non-small cell lung cancer. Due to the study design, the G-BA assessed the additional benefit as „not proven“. Therefore, it would be fatal if the drug was not available for the treatment of these cancer patients as a consequence of this assessment.

And these are not isolated cases. A systematic comparison of the G-BA decisions in the field of oncology with current guidelines of the German Society for Haematology and Medical Oncology (DGHO) revealed a high level of un-conformity (Ruof et al. 2017). In some 60 percent of all patient groups, the G-BA additional benefit decision differs from the prescription recommendations of evidence-based guidelines (cf. Figures 1 and 2). The G-BA determined that an additional benefit of the respective drugs cannot be proven – in the majority of the cases for formal reasons,

Konkordanz zwischen G-BA-Beschluss und Empfehlung in Leitlinien – Gesamtbild Onkologie

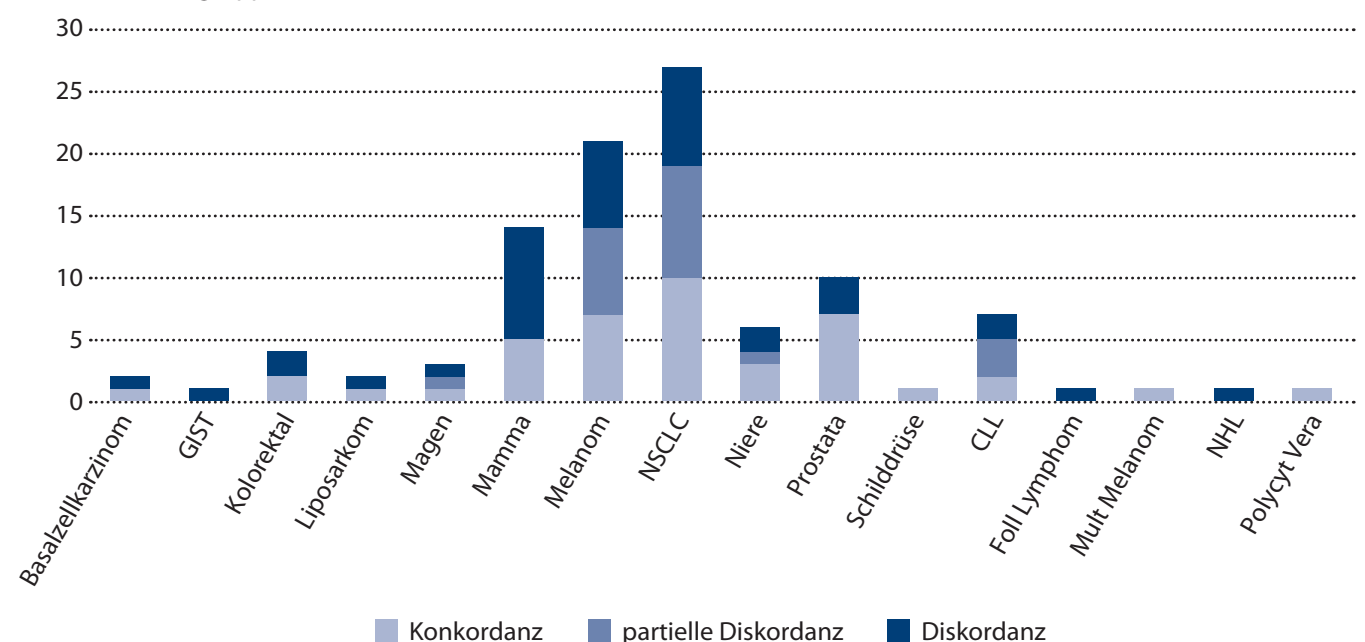


Quelle: HealthEcon

Abbildung 1: In rund 60 Prozent der Fälle weicht der G-BA-Beschluss von Leitlinien-Empfehlungen ab.

Konkordanz zwischen G-BA-Beschluss und Empfehlung in Leitlinien – nach Tumorentitäten

Anzahl Patientengruppen



Quelle: HealthEcon

Abbildung 2: Die Diskordanzen zeigen sich in fast allen Tumorentitäten.

e.g. as the appropriate comparative treatment as determined by the G-BA differs from that used in the approval studies (cf. Figure 3). However, in the guideline these drugs are recommended as valuable treatment alternative or even treatment without alternative.

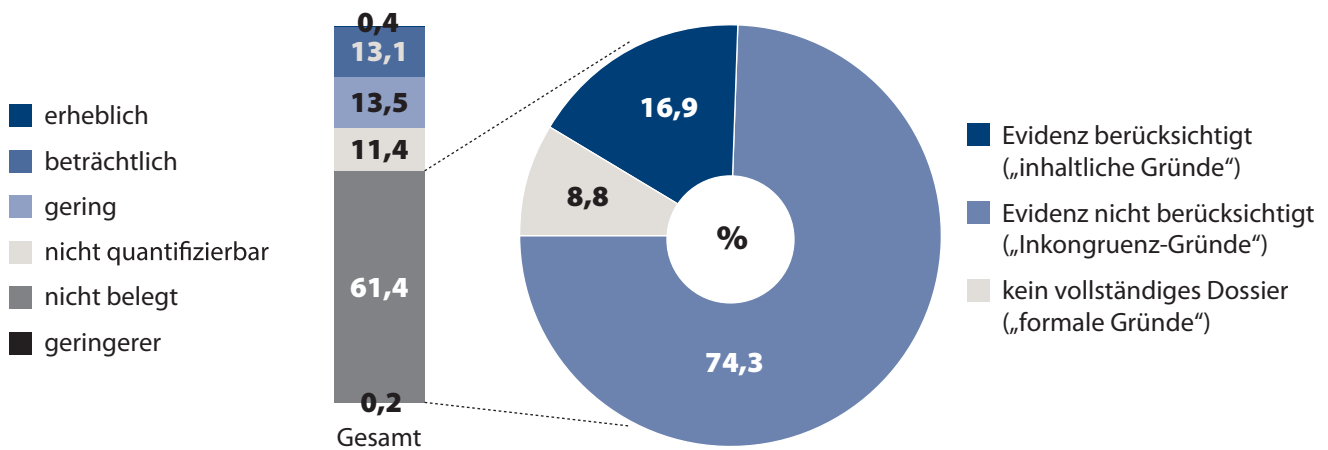
Many AMNOG decisions are now available in the indication non-small cell lung cancer (NSCLC). In 17 of the 27 patient groups, contradictions were observed between the additional benefit decision and guideline recommendations after the study (cf. Figure 4). Prescription control on the basis of the G-BA decision would thus result in a substantial deterioration in medical care for this indication, as

physicians would have significantly fewer treatment options.

The big throw

Implementation proposals by health insurance providers largely ignore these substantive problems and consider the physician information system only as technical challenge. AMNOG decisions only needed to be linked „technically“ and „interpretatively“ to be able to integrate valid treatment recommendations into the software. It is frequently forgotten, however, that the most frequent AMNOG assessment – „additional benefit not proven“ – is generally

Zusatznutzen nach Patientengruppen in abgeschlossenen Verfahren



482 Patientengruppen in 234 abgeschlossenen Verfahren; ohne wiederholte Bewertungen
 Quelle: vfa AMNOG-Verfahrensdatenbank; Stand 27.09.2017

Abbildung 3: In 74 Prozent der Fälle erfolgte die Bewertung „Zusatznutzen nicht belegt“ aus formalen Gründen.

not suitable to determine a potential therapeutic inferiority or superiority and thus its therapeutic significance. Instead, they suggest that the subcommittee „Pharmaceuticals“ of the G-BA simultaneously determines these links within the scope of the AMNOG process.

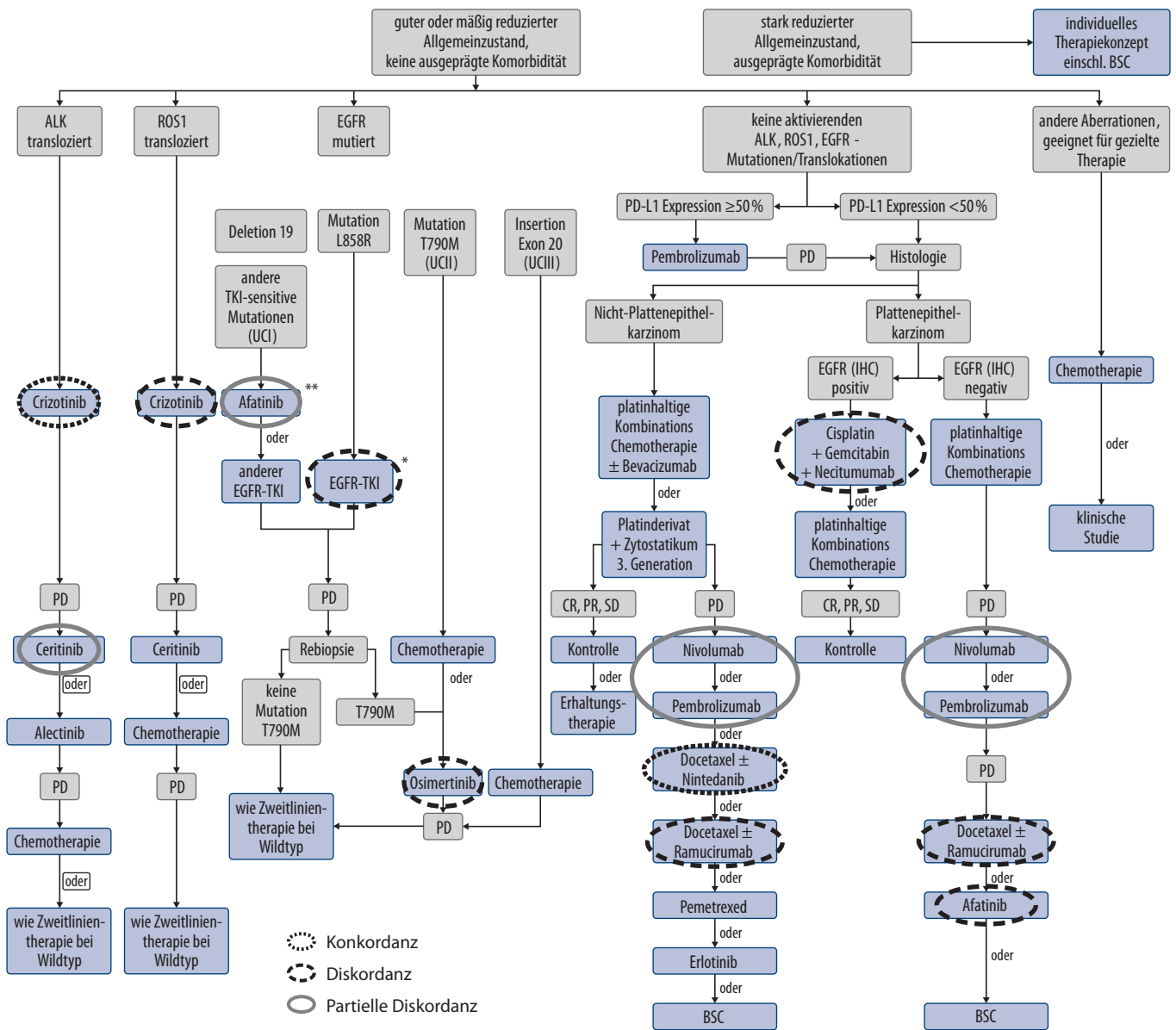
One factor which is often completely underestimated is that AMNOG decisions differ from evidence-based guidelines as a matter of principle, as they identify the best treatment options based on a given patient, while the G-BA only compares the respective active substance with the selected comparative treatment. Thus, AMNOG decisions have a different approach as compared to evidence-based guidelines and cannot simply be „converted“ into their format. This is a central dilemma in the selection of the appropriate physician information system, as physicians generally need both the „format“ and the content of the guidelines.

Health insurance providers ignore or trivialise these two

fundamental problems. A major project, i.e. creation and maintenance of treatment notes for physicians for a complex information system, is thus politically trivialised and played down to a mere „technical“ issue. The more cross-linked the contents are and the more legally binding such an information system shall be, the more relevant the requirements regarding the timeliness of the contents and juridical implications will become. A fast assessment of various AMNOG drugs compared to each other and pharmaceuticals of the so-called in-market is not possible within legally certain parameters.

Usually there is not enough information for such an evaluation and the G-BA does neither have a mandate in the AMNOG process nor sufficient evidence to determine it. Furthermore, this would result in a very complex evaluation matrix and every change of a variable (e.g. patient group or comparative treatment) would have to be evalua-

Konkordanz zwischen G-BA-Beschluss und Empfehlung in Leitlinien – Beispiel NSCLC



*Afatinib diskordant zu G-BA-Beschluss; **Keine Diskordanz bei Del 19

Quelle: HealthEcon

Abbildung 4: Bei G-BA-Beschlüssen in der Indikation NSCLC ergeben sich Widersprüche bei 17 von 27 Patientengruppen.

ted for its potential interaction in the evaluation matrix of the respective pharmaceuticals.

In short: Even ten AMNOG decisions do not add up to an overall therapeutic picture that can replace a guideline. It's not by chance that a certain pharmaceutical is classified automatically as a consequence of G-BA decisions, but the contents of G-BA decisions and guidelines must be continuously synchronised. A much broader process than AMNOG would be required in order to provide all evaluations that are required to establish a proper control mechanism in accordance with the guidelines. At present, the best solution would be to provide physicians with G-BA decisions along with evidence-based guidelines upon request. In line with evidence-based medicine, it would thus remain the responsibility of the physician to select the most appropriate treatment option in consideration of the preferences of patient (Sackett 1996).

Moreover, the development of such a „therapy guidance“ should not be left to the G-BA, as it is a true medical task. Therefore, a transparent coordination between the G-BA and scientific societies would be necessary after the additional benefit assessment process. The Association of the Scientific Medical Societies in Germany (AWMF) suggested to set up an expert commission at the BMG or approval authorities to prepare indication-specific contents for the physician information system (AWMF/DGHO 2016).

Conclusions

A lot of aspects indicate that a lean implementation of the AMVSG specifications with a practical orientation would be reasonable at the beginning. In the further course, physicians should be entrusted with the development of a more complex physician information system. But how could such a lean solution look like? For the implementation, the vfa suggests the following key parameters:

- convenient display of AMNOG decisions in the practice software (without any processing of the content, simple search function for file content),
- display of current evidence-based guidelines of medical associations in the practice software to inform the physician about the available clinical evidence,
- complete database for the physician without a pre-selection of drugs,
- clear indication of reimbursement amounts without efficiency notes for prescription, focus on information and not on physician control (no escalation and de-regionalisation of recourse pressure, no additional documentation obligations for the physician, no data feedback to health insurance providers).

With this approach, the AMNOG principle would be maintained to regulate pricing for new drugs without access restriction for patients. The relative success of AMNOG so far can be attributed to its clear structure and the fact that both freedom of medical decision and patients' demands are not affected. It makes sense to provide physicians with AMNOG decisions like evidence-based guidelines, but to leave the final assessment decision with them. Any different interpretation of the AMNOG as a volume control tool on physician level will in fact decrease treatment quality and eliminate important treatment options for patients. As the political idea behind the physician information system was to increase the quality of patient care, care should be taken that this idea is not turned upside down.

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How can the information create added value for physicians?

Dr Sibylle Steiner | Department head of the division Medical and Ordered Services of the KBV

The assessment of an additional benefit of new pharmaceuticals supports ambulatory statutory health insurance physicians in evidence-oriented prescription and thus provides an added value for the medical practice. However, certain pre-conditions must be met, such as the practical implementation of the Federal Joint Committee's (G-BA) benefit assessment decisions. Software used by physicians for the prescription of pharmaceuticals should include a compact table for the evaluated product by indication. Implementation of new legal provisions will increase expenses and costs for physicians, respectively, requiring appropriate funding schemes.

Today, any discussion about the design of „physician information systems“ (PIS) or even „pharmaceutical information system“ focuses on very specific questions. For example, for which purpose and how the decisions of the G-BA about recently launched pharmaceuticals shall be integrated into the software that statutory health insurance physicians use in their practice for the prescription of pharmaceuticals. These questions are not easy to answer and not all stakeholders have the same answers. The title of the event „Physician information for early benefit assessment – a professional challenge for all stakeholders“ illustrates that. For a solid examination of this topic, it should first be considered more closely which contents and functions of the prescription software are currently used in medical practice.

What are the features of a modern prescription software?

With the Economic Optimisation of Pharmaceutical Care Act (AVWG) dated 26 April 2006, Section 73 Para. 8 of the 5th German Social Codebook (Sozialgesetzbuch V, SGB V) was implemented, according to which ambulatory physicians in the statutory health insurance system may only use electronic programmes for the prescription of pharmaceuticals that contain information on the contents of the German Drug Prescription Directive (AM-RL), regional agreements on pharmaceuticals, as well as potential rebate agreements (1). Moreover, these electronic programmes must be approved by the National Association of Statutory Health Insurance Physicians (KBV). The medical self-governing bodies in Germany were asked to develop content specifications for a practice software to ensure high-quality and efficient pharmaceutical care and provide physicians with a manipulation-free price comparison tool for

pharmaceuticals containing further useful prescription information.

KBV and National Association of Statutory Health Insurance Funds (GKV-Spitzenverband) substantiated these legal provisions in a catalogue of requirements for prescription software. It is an annex of the Federal Collective Agreement (Bundesmantelvertrag) for physicians and was last amended on 1 October 2017. The catalogue of requirements defines the content specifications for pharmaceutical prescription software of the National Association of Statutory Health Insurance Funds and the KBV. Moreover, it is the basis for the certification of prescription software. During the review it is assessed whether the manufacturers of practice management software have met the defined requirements. At present, more than 90 practice management systems and seven pharmaceutical data bases are

being certified by the KBV.

Besides the specifications of the German Drug Prescription Directive (AM-RL) or rebate agreements, prescription software should also represent the regulations of prescription and efficiency goals for prescription control that are relevant for statutory health insurance physicians of the regional agreements on pharmaceuticals according to Section 84 Para. 1 SGB V. Figure 1 shows a good example for a reference to the KBV medication catalogue that was initially tested by the regional Pharmaceutical Initiative Saxony and Thuringia (ARMIN) and is currently used in five health insurance (KV) regions within the scope of agreements according to Section 84 or 106b SGB V as prescription control tool providing a benchmark as a criterion for the assessment of efficiency.

With the Act on Secure Digital Communication and Applications in the Healthcare System (eHealthG) (2), further contents that should be displayed during the prescription of pharmaceuticals were specified, such as functions and information required for the development and update of medication plans according to Section 31a SGB V (national medication plan).

What does the German Act on Strengthening Pharmaceutical Supply regulate?

Legal regulations were last expanded with the German Act on Strengthening Pharmaceutical Supply (AM-VSG) to provide information about G-BA decisions on early benefit assessment for the prescription of pharmaceuticals (3). The relevant legal requirements and schedules are kept short, particularly on the transcription of G-BA decisions into machine-readable version for practice management systems. Any details should be specified by a regulation by the Federal Ministry of Health. This regulation could also include specifications for the representation of regulations applica-



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Arzneimittelverordnungssoftware

Beispiel: Regionale Arzneimittelvereinbarung

The screenshot shows the MMI PHARMINDEX PLUS software interface. The main window displays the title 'Regionale Arzneimittelvereinbarungen' in a callout box. Below this, the drug 'Sortis 10 mg B2B Medical Filmtabletten' is selected. The interface shows various tabs like 'Prospekt', 'Fachinformation', 'Hautside', 'Preisvergleich', and 'Preisliste'. A table at the top right shows price comparisons for different brands. Below the drug name, there is a section for 'Arzneimittelvereinbarungen' which includes the following text:

Arzneimittelvereinbarungen

IWW-Liste, Gültigkeit: 01.04.2017 bis 30.06.2017, Erstellt am: 31.01.2017
 Atorvastatin: kein Standard bei Fettstoffwechselstörungen. Standard: =>Simvastatin oder =>Pravastatin.
 Haftungsausschluss

Vergrößerter Bildausschnitt

R Rabattarzneimittel durch bestehenden Rabattvertrag

R Hinweis, dass es für das gewählte Arzneimittel (selbst kein Rabattarzneimittel) ein vergleichbares Rabattarzneimittel gibt

Quelle: KBV: eigene Darstellung auf Basis MMI (4)

Abbildung 1: Für Vertragsärzte ist auch die Abbildung regionaler Arzneimittelvereinbarungen in der Software relevant.

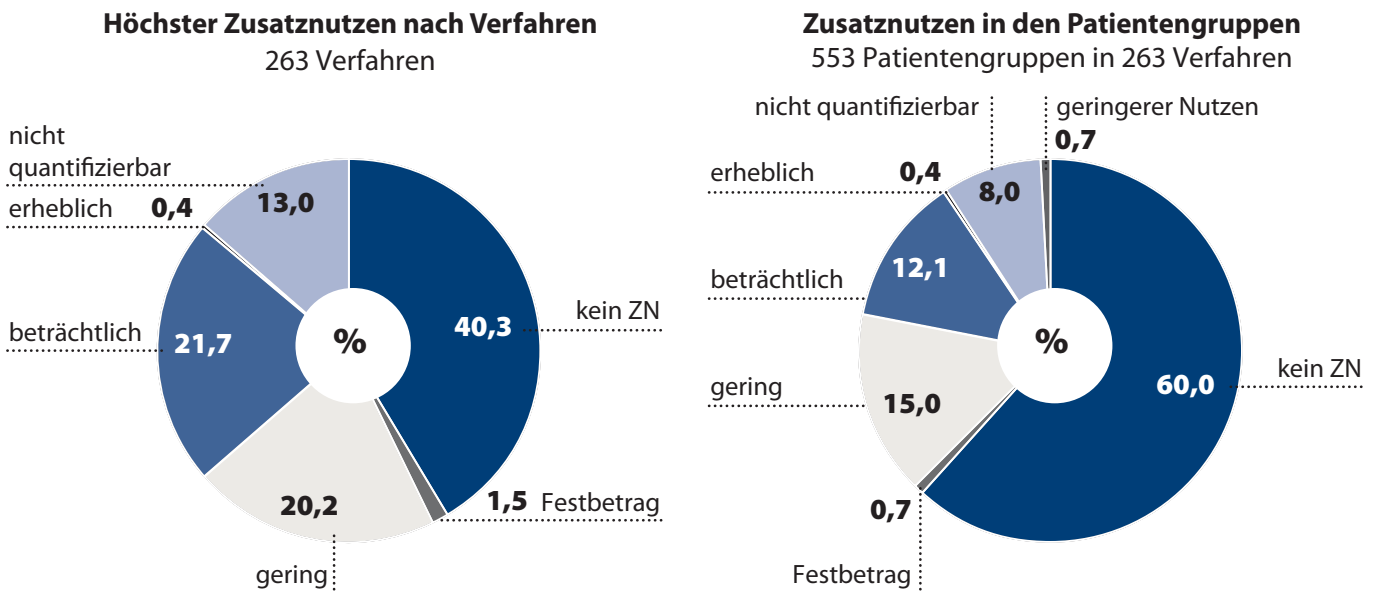
ble for statutory healthcare on the feasibility and efficiency of a prescription as compared to other treatment options.

Recent legislation is aimed at advancing both the AM-NOG procedure and pharmaceutical prescription software. The approach of providing more information about G-BA

decisions to physicians should be appreciated, if the actual intention is to provide better information. The primary goal of the additional benefit assessment is the negotiation of an adequate and economic reimbursement. Moreover, it supports physicians in the statutory health insurance

263 durchgeführte Verfahren zur frühen Nutzenbewertung

Im Durchschnitt bildet der G-BA mind. 2 Patientengruppen pro Wirkstoff



Quelle: KBV: eigene Auswertungen, Stand 09/2017 (5)

Abbildung 2: Der G-BA hat im Durchschnitt mindestens zwei Patientengruppen pro bewertetem Arzneimittel gebildet.

system in their evidence-oriented prescription decision.

As stated above, the KBV has gained considerable experience in the field of prescription software. Since the beginning of the procedures for early benefit assessment, the KBV has been publishing short summaries of the assessment on their website. Experience has shown, however, that this information must be available in the medical practice during the prescription process in order to be taken into consideration. Therefore, it must be clearly defined beforehand what goal and purpose the representation of the benefit assessment decisions shall serve and which requirements must be fulfilled by the prescription software

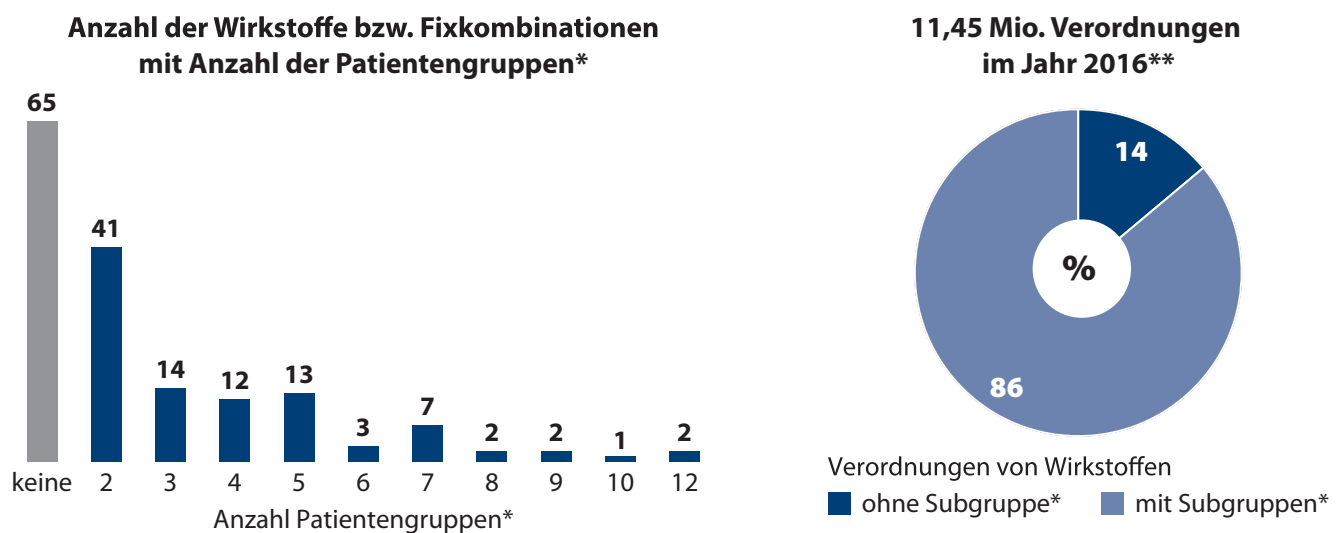
to create an added value for statutory health insurance physicians.

Physician information system: How is added value created?

For more than six years, the G-BA has been assessing the additional value of new pharmaceuticals against the current treatment standard, i.e. appropriate comparative treatment. Since then, the G-BA has conducted more than 250 procedures and attested an additional benefit of various degrees in 60 percent of the cases for at least one patient group (5). Altogether, the G-BA established more than

162 bewertete Wirkstoffe / Fixkombinationen (bis 31.12.2016)

9 von 10 Verordnungen tätigen Ärzte bei Wirkstoffen mit Unterteilung nach Patientengruppen



*Patientengruppen aller Anwendungsgebiete eines Wirkstoffes bzw. einer Fixkombination

**Schätzwert aus GKV-Verordnungen 2. Halbjahr 2016 nach Insight Health multipliziert mit Faktor 2

Quelle: KBV: eigene Auswertungen nach G-BA und Insight Health (6)

Abbildung 3: Bei 86 Prozent der Verordnungen waren die Anwendungsgebiete in zwei oder mehr Gruppen unterteilt.

550 patient groups, i.e. an average of at least two patient groups for each evaluated pharmaceutical (cf. Figure 2).

As a result, two and more patient groups (up to twelve) were established so far in almost two thirds of all evaluated active substances. According to the KBV's calculations, these new pharmaceuticals represented some 11.45 million prescriptions in 2016. In nine of ten medical prescriptions, applications were divided into two or more patient groups (see Figure 3).

This analysis shows that it is essential to identify those patient groups during the early benefit assessment that can benefit most from the respective treatment and – by

implication – those for whom the G-BA has not observed or proven an additional benefit, respectively, as compared to the appropriate comparative treatment. There are also patient groups without a proven additional benefit due to a lack of data.

All this information about new pharmaceuticals at an early stage is undoubtedly highly significant and of therapeutic value for both the medical practice itself and to support individual treatment decisions.

If there are no studies for certain patient groups against the appropriate comparative treatment, no additional benefit can be proven. However, this cannot a priori be equa-

ted with a lack of benefit. For example, in case of an intolerance or failure of the treatment standard, patients need alternatives to an approved active substance, even if an additional benefit has not or not yet been proven for one or another subgroup. Prescription of a pharmaceutical must not be regarded as an uneconomic behaviour per se. Oppositely, the use of a pharmaceutical with a proven low additional benefit must not be considered appropriate in every case.

Direct oral anticoagulants (DOACs) were, for example, classified as reserve active substance for some patient populations in the KBV medication catalogue, where new pharmaceuticals are classified as „standard active substance“, „reserve active substance“ and „subordinated prescription“ on the basis of the respective G-BA benefit assessment decisions.

This is due to the fact that in the studies the advantages of DOACs – mainly due to their decreased bleeding tendency – were less pronounced in patients with well-controlled vitamin K antagonists. In contrast to the vitamin K antagonists, long-term safety of DOACs cannot be assessed adequately.

It is evident from this that the only goal and purpose of the representation of benefit assessment decisions can be the provision of information for physicians. It is supposed to support an evidence-oriented prescription decision and not to expose physicians to the risk that prescriptions for a certain patient group without an additional benefit might be evaluated and rated as uneconomical by health insurance providers. Against the background of the mixed prices agreed between National Association of Statutory Health Insurance Funds and pharmaceutical companies – i.e. lower prices for patient groups without additional benefits and higher prices for patient groups with additional benefit – this would neither be appropriate nor fair. Thus,

case-by-case assessments are not justified in case of prescriptions of pharmaceuticals with an indication-based reimbursement amount. Otherwise, physicians will not prescribe medically reasonable innovations due to a threatening recourse.

Besides the question about goal and purpose, it is still not clear how the information shall be made available in the prescription software. In any case, several levels of information depth are required. During the prescription, the physician should be able to see that the pharmaceutical concerned has been subject to a benefit assessment at a glance. At the first level, a compact table with an overview of the pharmaceutical should be provided on the basis of the indication. As the G-BA assessed various applications for certain pharmaceuticals, the physician should only see the respective application including the defined patient groups corresponding to the patient's diagnosis. Moreover, the table should include the results of the additional benefit assessment as compared to the appropriate comparative treatment. The results of all patient-relevant endpoints of the studies used for the benefit assessment should be summarised by mortality, morbidity, safety, and quality of life. For a quick assessment, these results should be designated with the corresponding symbols. At subordinate levels, information on the requirements for a quality-assured application should be available as well as G-BA decision documents and notes on any circumstances in which a prescription would be peculiarity. Moreover, high-quality guidelines for prescription of special preparations (e.g. oncological treatment) should also be implemented in due course. Figure 4 shows the proposal for a presentation of benefit assessment decisions.

This means that the following requirements should be taken into account during the implementation of the physician information system to create added value for physi-

Arztinformationssystem

Beispiel: Frühe Nutzenbewertung von Nivolumab

OPDIVO® 10 mg/ml Konzentrat zur Herstellung einer Infusionslösung
Bristol-Myers Squibb GmbH & Co. KGaA

Navigation: **FNB** (Frühe Nutzenbewertung)

Indikation (ICD 10): C43.-Bösartiges Melanom der Haut

| Anwendungsgebiet/ Subgruppe | zweckmäßige Vergleichstherapie | Zusatznutzen* | Endpunkte |
|---|---------------------------------|-------------------------------|---------------------|
| Nicht vorbehandelte Patienten mit einem BRAF-V600-mutierten Tumor | Vemurafenib | ZN nicht belegt | Mortalität n.b. |
| | | | Morbidität n.b. |
| | | | Sicherheit n.b. |
| | | | Lebensqualität n.b. |
| Nicht vorbehandelte Patienten mit einem BRAF-V600-wildtyp Tumor | Dacarbazin oder Ipilimumab | Hinweis auf beträchtlichen ZN | Mortalität ↑ |
| | | | Morbidität n.b. |
| | | | Sicherheit ↑ |
| | | | Lebensqualität n.b. |
| Vorbehandelte Patienten | Patienten-individuelle Therapie | ZN nicht belegt | Mortalität n.b. |
| | | | Morbidität n.b. |
| | | | Sicherheit n.b. |
| | | | Lebensqualität n.b. |

Buttons: Anforderungen an qualitätsgesicherte Anwendung, Praxisbesonderheit § 130 b Abs. 2 SGB V, Beschluss G-BA, Leitlinien

Quelle: KBV: eigene Darstellung auf Basis MMI (4)

*ggf. mit Angabe, ob Orphan Drug

Abb. 4: Vorschlag zum Arztinformationssystem am Beispiel der frühen Nutzenbewertung für den Wirkstoff Nivolumab.

icians in the statutory health insurance system: Pharmaceuticals for which an early benefit assessment was performed must be clearly marked as such in the prescription software. Presentation in the prescription software should be based on the indication and all decisions pooled in one indication. For this purpose, a table with a summary of all G-

BA decisions is the best option with several subordinate levels of information. Implementation of these new legal provisions will result in additional expenses and costs for physicians, respectively, requiring appropriate funding schemes. During prescription, it should be avoided to only file G-BA decisions as PDF documents and code subgroups

Arztinformationssystem

Wie können die Informationen einen Mehrwert darstellen?





- | | |
|--------------------------------|---|
| ✓ Kennzeichnung („Button“) |  Keine bloße Hinterlegung von „pdf-Dokumenten“ |
| ✓ Indikationsbezug | |
| ✓ Kurzfassung |  Keine zusätzliche Dokumentationspflicht |
| ✓ Ebenen der Informationstiefe | |
| ✓ Darstellung der Endpunkte |  Kein bürokratischer Mehraufwand |
| ✓ Perspektivisch : Leitlinien |  Finanzierung muss geregelt sein |
-

Abbildung 5: Was bei der Konzeption eines Arztinformationssystems beachtet und was vermieden werden sollte.

and thus categories of additional benefit for a certain patient (see Figure 5).

Literature:

¹Deutscher Bundestag (2006). Economic Optimisation of Pharmaceutical Care Act (AVWG) dated 26 April 2006. Federal Law Gazette, 2006 Series, Part I No. 21, published in Bonn on 29 April 2006

²Deutscher Bundestag (2015). Act on Secure Digital Communication and Applications in the Healthcare System (eHealthG) dated 21 December 2015. Federal Law Gazette, 2015 Series, Part I No. 54, published in Bonn on 28 December 2015

³Deutscher Bundestag (2017). Act on Strengthening Pharmaceutical Supply in Statutory Health Insurance (AMVSG) dated 4 May 2017. Federal Law Gazette, 2017 Series, Part I No. 25, published in Bonn on 12 May 2017

⁴National Association of Statutory Health Insurance Physicians (KBV) (2017). Own presentation on the basis of MMI

⁵National Association of Statutory Health Insurance Physicians (KBV) (2017). Own analysis according to G-BA as of September 2017

⁶National Association of Statutory Health Insurance Physicians (KBV) (2017). Own analysis according to G-BA and Insight Health

Updating benefit assessments – is this reasonable and feasible?

Dr Thomas Kaiser | Institute for Quality and Efficiency in Healthcare (IQWiG), Cologne, Germany

Decisions on the early benefit assessment should be made available to physicians via the practice software. The aim is to support decision-making in medical practices. For this purpose, decisions should provide current and relevant information. The categories new evidence and new research questions are of practical relevance for an update. In a pilot project, new evidence was identified for four of five evaluated active substances, and in two of the four cases an update was recommended. Analysis of 36 assessments performed in 2014 revealed that in some ten percent of the cases the research question has changed fundamentally justifying an update. Based on these results, a proposal for a systematic approach to update early benefit assessments is made.

B **ackground**
The Act on Strengthening Pharmaceutical Supply in Statutory Health Insurance (AMVSG) specified that decisions of the Federal Joint Committee (G-BA) on the early benefit assessment of pharmaceuticals must also be published in machine-readable form [1]. This information shall also be provided to physicians by practice software. This should „help to select the pharmaceutical that is indicated for the respective treatment situation“ [1].

The provision of data gained during the early benefit assessment via practice software is intended to support treatment decisions in the medical practice. But it is not only important, in which form and how detailed this information is provided [2]; data should also provide current and relevant information. However, there are currently no plans for regular updates of decisions on the early benefit assessment of pharmaceuticals. The purpose of this article is to analyse whether and how updates of decisions on the early benefit assessment of pharmaceuticals are reasonable and feasible.

In which cases is an update required?

The necessity to update a benefit assessment of a certain pharmaceutical arises, if new evidence is available that might affect the conclusions of a previous benefit assessment. Updating an assessment can also be reasonable, if it is no longer relevant in whole or part. Two different cases can be distinguished: In the first case, the original research question of the benefit assessment is replaced by another one, e.g. as the standard of comparison (comparative treatment) has changed. In the second case, the assessment has become obsolete, i.e. there is no new relevant question, for example if the approval of a certain active substance is withdrawn.

Another reason for an update is, if the methodology of the benefit assessment is adopted in accordance with new findings and the assessment of the same data using a different methodology might lead to a different result. For example, new findings on the conduction of meta-analyses with only few studies [3, 4]. However, these essential adjustments are very rare. Moreover, they do not apply to individual assessments. In this case, it might be argued that the development of a methodology does not per se constitute an update requirement. Such a scenario would question the correctness of previous G-BA decisions. It would thus be difficult to explain, why the development of methodologies would require an update of the existing benefit assessment for new pharmaceuticals, while the review of other G-BA decisions wouldn't, e.g. for non-pharmaceutical procedures. Any methodological changes will thus no longer be considered an update reason.



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Therefore, updates can be sub-divided into three categories:

1. New evidence is available.
2. The research question has changed.
3. The present research question is obsolete and there is no new question.

These three categories will subsequently be discussed in detail, whereas practically relevant update reasons will be considered separately from theoretical, but practically irrelevant reasons.

New evidence

New evidence is typically available if a new study is published, a benefit assessment is started or the results of a new benefit assessment are available. Long-term results of a study already included in a benefit assessment (e.g. as a consequence of a new data cut-off) can also be considered new evidence.

In a broad sense, a different evaluation of data that was available at the time of the benefit assessment can also be new evidence. Based on past experiences with benefit assessments, it can be assumed that the necessity of modified evaluations is identified during the benefit assessment procedure that might lead to a time limitation. Therefore, any further update necessity does normally not arise through a new evaluation of already known data.

New research question

The research question for a benefit assessment according to AMNOG is specified by Section 35a of the 5th German Social Codebook (Sozialgesetzbuch V, SGB V) and the corresponding Pharmaceutical Products Benefit Assessment Ordinance (AM-NutzenV) [5], i.e.: Does the new active substance have an additional benefit for patients for whom the new active substance was approved regarding pati-

Kasten A: Implizite Zulassungserweiterung am Beispiel Ceritinib

Ceritinib wurde am 06.05.2015 zur Behandlung des vorbehandelten, fortgeschrittenen, Anaplastische Lymphomkinase (ALK) positiven, nicht kleinzelligen Lungenkarzinoms (NSCLC) zugelassen, und zwar nur bei solchen Patienten, die mit Crizotinib vorbehandelt wurden. Da Crizotinib zu diesem Zeitpunkt in der Zweitlinientherapie zugelassen war, konnte Ceritinib demnach erst ab der dritten Therapielinie eingesetzt werden.

Am 23.11.2015 wurde Crizotinib auch für die Erstlinienbehandlung zugelassen. Dies führte zu einer impliziten Zulassungserweiterung für Ceritinib, ohne dass hierfür ein eigenes Zulassungsverfahren für Ceritinib notwendig gewesen wäre. Denn Ceritinib kann seitdem auch ab der zweiten Therapielinie eingesetzt werden, sofern in der Erstlinie Crizotinib verwendet wurde.

ent-relevant endpoints as compared to the appropriate comparative treatment? This question can be addressed using the PICO process which is common in evidence-based medicine: Population, intervention, comparator, outcome.

Any changes in the population and intervention are usually constituted by a changed approval of the new active substance itself. According to SGB V, this results in an independent benefit assessment and it is therefore not relevant to determine whether a potential update is required. Implicit extensions of approval present an exception (see Box A on the example of ceritinib). These rare implicit extensions of approval should also be evaluated during the AMNOG procedure, as otherwise no information would be available in the practice software for a certain part of the application of a new active substance.

The endpoint categories that need to be evaluated are defined in the AM-NutzenV and substantiated by indication. More than 200 completed benefit assessments so far show that no relevant changes can be expected over time and that there is no update requirement due to „endpoints“ beyond the search for long-term data. Adaptation of a comparator as a consequence of a changed appropriate comparative treatment remains the most important criteri-

on.

In general, new scientific findings, such as new study results on existing treatment options, are an occasion for changes of the appropriate treatment. This can derive from the results of the early benefit assessment: If a new active substance has an additional benefit as compared to the previous standard treatment (appropriate comparative treatment) and proves reliable in practice, it can become the new appropriate comparative treatment. If the appropriate comparative treatment changes, the following type of situations can be distinguished:

- The appropriate comparative treatment is extended by one or more options and the initial options are still considered appropriate. In these cases, no update of the benefit assessment is required with regard to the practice software, as the statements of the completed benefit assessment are still relevant.
- The appropriate comparative treatment is changed (options are deleted or changed) and the comparative treatment of the completed benefit assessment is no longer considered appropriate. In these cases, no update of the benefit assessment is reasonable, as the result of the completed benefit assessment is no longer relevant for treatment decisions (comparison with a treatment option that is no longer appropriate).

Kasten B: Praktisch relevante Aktualisierungsgründe für Nutzenbewertungen nach §35a SGB V

Neue Evidenz

- Neue Studie(n)
- Neuer Datenschnitt der bekannten Studie(n)

Neue Fragestellung

- Wechsel der zweckmäßigen Vergleichstherapie
- Implizite Zulassungserweiterungen

Research question obsolete, no new questions

A research question can become obsolete for several reasons without any new question being raised. For example, this can be due to the active substance itself. If approval for a certain active substance X has been removed, the completed benefit assessment is no longer relevant with regard to the practice software, especially since the respective active substance X is no longer listed as treatment option in the practice software. But even if a certain active sub-

stance has become (almost) meaningless for prescription due to scientific advances in pharmacotherapy, and other active substances Y and Z are used, available data about active substance X in the practice software does not have any practical relevance. The application of boceprevir or telaprevir for patients with hepatitis C that were approved in 2011 is a good example. After approval of various direct antiviral drugs presenting an interferon-free treatment option, these two active substances have lost much of their importance. Distribution of both active substances was discontinued in Germany.

On the other hand, treatment paths can change so that previous research questions are no longer relevant regardless of the evaluated active substance, e.g. docetaxel re-treatment in prostate cancer patients after progression under docetaxel. This question was considered for abiraterone and cabazitaxel that received approval in 2011 [6, 7], but has now become obsolete (see e.g. benefit assessment on enzalutamide [8]).

The common characteristic of obsolete questions without new research questions is that they do not imply an update requirement with regard to practice software. Although deleting data on these questions would be logical, it would not be necessary. It is to be assumed that this information will not be requested and displayed due to its practical irrelevance for the treatment decision. However, the determination of obsolete questions without a new question is still relevant for the update process, as this information can be used for update prioritisation (obsolete questions do not have to be updated, see e.g. boceprevir in the pilot project mentioned below).

Overview of practically relevant update reasons

As a consequence of the above statements, not every theoretical reason for an update is of practical significance.

Box B shows an overview of practically relevant update reasons. They are limited to two categories, i.e. „new evidence“ and „new research question“. In the following two sections we will assess how many benefit assessments should be updated, if we systematically consider all practically relevant reasons in these two categories.

Evaluation for new evidence – Results of a pilot project

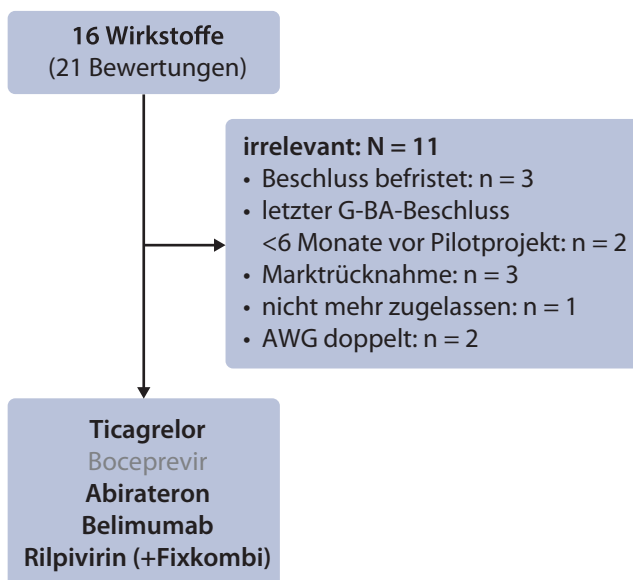
In 2016, the Institute for Quality and Efficiency in Health-care (IQWiG) conducted an internal pilot project for examination of update requirements. The aim was to develop and implement a method for the examination of update requirements of already completed benefit assessments.

Methodology of the pilot project

Five active substances of various fields of application with completed benefit assessments were selected in chronological order (starting with the first early benefit assessment of 2011). All active substances for which procedures have been completed no longer than 6 months prior to the start of the pilot project (e.g. due to expansion of the field of application) were excluded, as well as active substances with decisions with a time limitation where an update can be expected within the scope of the evaluation after expiry of the time limitation, and those that are no longer available in Germany.

A systematic search was performed for new studies and data of known studies for the selected active substances. Search was limited to directly comparative randomised and controlled trials, as pharmaceutical companies only have to submit such studies in their dossier and are not obliged to furnish other analyses (e.g. indirect comparisons). All other inclusion criteria correspond to those of the completed benefit assessment. Any new evidence was compared to the existing evidence and a recommendation for or against an update was derived.

Auswahl der Wirkstoffe für die Aktualisierungsprüfung (Pilotprojekt)



Quelle: Dr. Thomas Kaiser

Abbildung 1: Insgesamt 21 Nutzenbewertungsverfahren zu 16 Wirkstoffen wurden für das Pilotprojekt gesichtet.

Results

Figure 1 shows an overview of the selection of the five active substances to be evaluated. Overall, 21 assessments of 16 different active substances were evaluated in chronological order, i.e. ticagrelor, boceprevir, abiraterone, belimumab, and rilpivirine. Update evaluation for rilpivirine also included the fixed-dose combinations of rilpivirine with emtricitabine and tenofovir. Table 1 shows an overview of the result of the update evaluation.

Only for one active substance (belimumab), no new evidence was identified. Although new evidence was identi-

fied for ticagrelor for one of the four questions of the benefit assessment, this was derived from three small and short RCTs aimed at evaluating laboratory parameters. Despite the fact that new evidence was identified for boceprevir, examination of update requirements was cancelled. Due to the fast developing field of hepatitis C, the questions of the original dossier assessment A11-17 on boceprevir [9] were no longer relevant. For belimumab, ticagrelor and boceprevir, no update recommendations were made.

For abiraterone and rilpivirine (including fixed-dose combination) new evidence was identified resulting in an update recommendation. For abiraterone, long-term data of a known RCT were identified. For rilpivirine and the fixed-dose combination with rilpivirine, one new RCT and long-term data of three known RCTs were identified. Update recommendations for abiraterone and the fixed-dose combination with rilpivirine were limited to one of the two relevant questions, as new evidence was only identified for them.

New research questions – Analysis of dossier assessments in 2014

All dossier assessments in 2014 (a total of 36) were analysed to determine in how many cases new questions lead to an update requirement. Figure 2 shows an overview of the analysis result.

For ten of the 36 evaluations, the research questions did not have to be analysed. Three of these ten evaluations were time-limited and automatically caused an update. In the seven other cases, the respective active substances were no longer approved or withdrawn from the German market for different reasons.

In 12 of the 26 evaluations that were analysed, there were no changes of the initial research question(s). The other 14 evaluations, a change in the research question can be

expected. As indicated above about the criterion „new research question“, in four cases a new question was defined, e.g. due to a change of the appropriate comparative treatment. This corresponds to 11% of all dossier assessments performed in 2014.

Discussion

Decisions on the early benefit assessment are based on the evaluation of the available evidence for a new active substance at the time of the assessment. As with other assessments, new scientific findings can make statements made at the time of the decision obsolete. However, approaching this topic systematically shows that the theoretical entity

of update reasons should be limited to reasons of practical relevance: new evidence and new questions. The occurrence of both categories can be estimated to support a systematic approach for the update of benefit assessments.

Considering the limitations resulting from the limited number of cases in the pilot project and evaluations in 2014, the following approach is suggested:

1. Completed assessments should be evaluated regularly (e.g. every two years) for new evidence within the scope of a simplified procedure according to the pilot project, if the research questions are still relevant and an update is not planned, e.g. due to a time limitation of the decision.

Ergebnisse des Pilotprojekts zur Aktualisierungsprüfung

| Wirkstoff | Neue Evidenz identifiziert | Empfehlung zur Aktualisierung |
|--|--|-------------------------------|
| Ticagrelor | ja, für 1 der 4 Fragestellungen (3 neue RCT) | nein |
| Abirateron | ja, für 1 der 2 Fragestellungen ^a (Langzeitdaten einer bekannten RCT) | ja ^b |
| Rilpivirin | ja, für die einzige Fragestellung (1 neue RCT sowie Langzeitdaten zu 3 bekannten RCT) | ja |
| Rilpivirin / Emtricitabin / Tenofovir | ja, für 1 der 2 Fragestellungen (1 neue RCT sowie Langzeitdaten zu 3 bekannten RCT) | ja ^b |
| Belimumab | nein | nein |
| Boceprevir | ja, Aktualisierungsprüfung wurde jedoch abgebrochen ^c | nein |

a: Für eine dritte Fragestellung erfolgte keine Aktualisierungsprüfung, da diese Fragestellung inzwischen obsolet war (Docetaxel-Re-Therapie nach Progression unter Docetaxel).

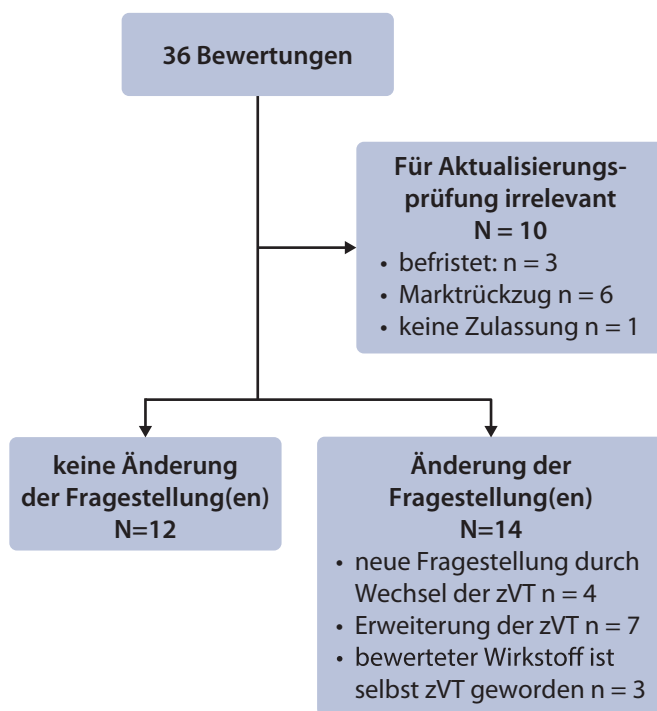
b: Die Aktualisierung wurde nur für diejenigen Fragestellungen empfohlen, für die neue Evidenz identifiziert wurde.

c: Begründung siehe nachfolgenden Text.

Quelle: Dr. Thomas Kaiser

Tabelle 1: Nur für einen Wirkstoff ist im Pilotprojekt keine neue Evidenz identifiziert worden.

Ergebnis der Prüfung: Neue Fragestellungen zu Dossierbewertungen aus 2014



Quelle: Dr. Thomas Kaiser

Abbildung 2: Von den insgesamt 36 Bewertungen im Jahr 2014 ergeben sich in 14 Fällen neue Fragestellungen.

This ensures that decisions for which no new evidence is identified, are still up-to-date even without a new benefit assessment. On the other hand, the complex update using the Section 35a procedure remains limited to active substances and questions for which an update might lead to relevant changes.

2. If decisions have a time limitation, because new evidence is expected or requested, an additional update evaluation

is not required. In the pilot project, long-term data of several studies was identified from completed benefit assessments. However, these decisions were not limited in time. In these cases, decisions should generally have a time limitation. Moreover, ongoing studies at the time of the decision should be systematically recorded (e.g. by means of searching study registries). If relevant results can be expected from ongoing studies, this should also be a reason for a limitation of the decision.

3. If the appropriate comparative treatment for a certain field of application is modified within the scope of other procedures, it should be examined which already completed evaluations will be affected and a decision taken for or against an update of the respective evaluation. As mentioned above, this decision can be supported by prior evaluation for new evidence.

In conclusion, it cannot be guaranteed that all decisions in the practice software are up-to-date. With a systematic approach, false and irrelevant information can be limited and the effort minimised.

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Will a physician information system limit therapeutic freedom?

Professor Dr Bernhard Wörmann | German Society for Haematology and Oncology

Therapeutic freedom is a precious asset. It ensures that treatment is recommended and provided in line with the individual disease and living conditions of the respective patient. The steadily growing database is a particular challenge in many specialist fields, currently mainly in oncology and both knowledge and evaluation of these data are an integral part of medical treatment recommendations. Determinations of the early benefit assessment for new pharmaceuticals can be another important element, if they are presented in detail and integrated into the current state of knowledge in diagnostics and therapy.

Therapeutic freedom: Physicians have a certain freedom in the selection of the treatment they deem appropriate for the individual disease and living conditions of the patient. This therapeutic freedom is a precious asset of the medical profession [1]. In current discussions about the introduction of a physician information system based on the determinations of the Federal Joint Committee (G-BA) on the additional benefit of new pharmaceuticals, doubts and fears have arisen as to a potential limitation of physicians' therapeutic freedom in favour of a stronger consideration of the efficiency of prescriptions or even prescription control.

However, therapeutic freedom is not a *carte blanche*. It is limited by demands on the quality of medical practice on the one hand and rights and freedom of the patient on the other hand. In the key statement of a ruling relevant for the definition of medical therapeutic freedom of the First Senate of the Federal Constitutional Court (BVerfGE) dated 6 December 2005 the rights of the patient were defined as follows [2]: „It is not compatible with the fundamental rights of Art. 2 Sec. 1 of the Basic Law for the Federal Republic of Germany (GG, Grundgesetz) in combination with the social state principle and Art. 2 Sec. 2 Sentence 1 GG to exclude patients insured under the statutory health insurance for whose life-threatening or usually fatal disease an established treatment is not available according to general medical standard from an applied medical treatment method selected by the patient, if a not entirely unrealistic expectation of cure or a detectable positive effect on the course of the disease is present.“

At the same time, limits of therapeutic freedom were defined: „The quality and efficiency of the services must be in accordance with the generally accepted state of medical knowledge in consideration of the medical progress.“ The-

therapeutic freedom is not an absolute individual right, but must be socially integrated. It enables the physician to select and suggest a treatment option that is adapted to the individual requirements of the patient.

However, an ever increasing wealth of information of highly varying quality makes data capture and evaluation very difficult for the individual physician. Thus, recommendations of professional associations and other organisations become more and more important. Most of them are based on evidence-based medicine. In 1996, the German Medical Association defined the following categories of recommendation [3]:

Directives: Rules of action and omission issued by an institution that only leave limited freedom for the individual physician.

Guidelines: Systematically developed decision-making aids about appropriate approaches granting the individual physician a certain degree of individual choice and „corri-

dors of action“ which can be derogated from in justified individual cases.

Recommendations: Aim at guiding physicians and the general public to areas requiring modification and attention.

Memorandum: Serves at providing comprehensive information and clarification; they shall also be useful to differentiate between the current state of knowledge and obsolete knowledge.

Guidelines

The majority of recommendations of professional scientific associations are guidelines. Their significance and legal framework was clarified in the lawsuit proceedings of a pharmaceutical company against the non-recommendation of a certain pharmaceutical product in a national care guideline (NVL, Nationale Versorgungsleitlinie) on pain management in 2011 / 2012 [4]. The developers of the guideline were sued, in this case the Association of the Scientific Medical Societies in Germany (AWMF), the German Medical Association, and the National Association of Statutory Health Insurance Physicians (KBV). Cologne District Court dismissed the action by judgement of 30. November 2011 stating: „If the procedure is performed on the basis of a statement – like in this case – the distinction whether it is a factual claim or expression of opinion will be of particular importance. (...) It is accepted by the jurisdiction, that any expression of opinion associated with the publication of such tests does not represent an illegal infringement, if the assessment and evaluation were performed neutrally, objectively, expertly, and thoroughly using reasonable evaluation methods.“ The judgement was affirmed in the second instance by the Higher Regional Court on 6 November 2012 and added: „In general, AWMF, BÄK, and KBV as developers and editors are responsible for the content. The



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same applies for medical associations who develop and publish guidelines under their own responsibility... These statements are evaluations and expressions of opinion.“ An appeal against the decision was not allowed.

But the physician also has a choice with guidelines to use. For example, in the field of oncology there are various options:

- Guidelines Programme Oncology by the AWMF and German Cancer Aid (Deutsche Krebshilfe) [5]
- National scientific associations, e.g. Onkopedia [6]
- Consensus meetings
- European scientific associations, e.g. ESMO [7] or EAU [8]

- American scientific associations [9]
- National Comprehensive Cancer Network [10].

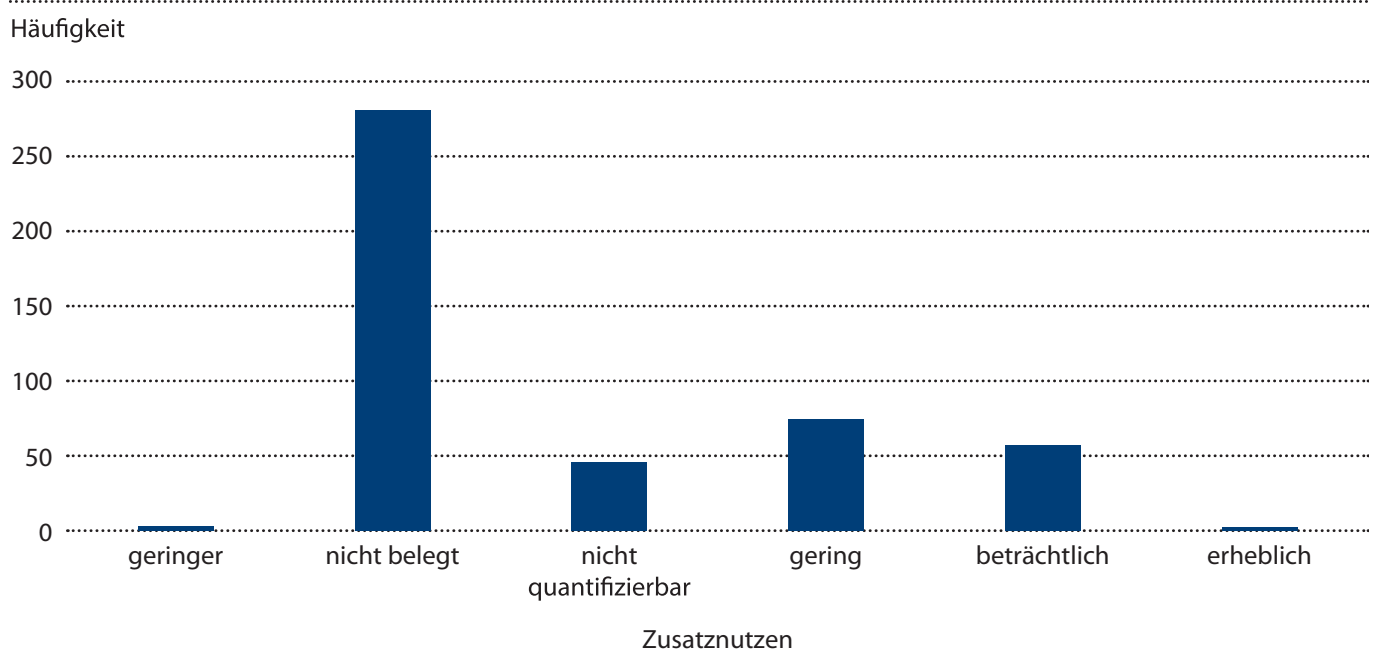
Selecting the best suitable recommendations by the physician mainly depends on the status of the issuing institution, independence of experts, comprehensive representation of practical contents, readability, and timeliness.

Guidelines are legally non-binding. They reflect standard and not individual situations and thus correspond to the principle of therapeutic freedom.

Benefit assessment according to the AMNOG

Since its introduction in 2011, the early benefit assessment

Festlegungen des G-BA zum Zusatznutzen neuer Arzneimittel 2011 – 2016



Quelle: AWMF

Abbildung 1: In etwa zwei Drittel der bewerteten Subgruppen wurde der Zusatznutzen als nicht belegt angesehen. [11]

of new pharmaceuticals as a basis for a fair pricing has quickly established itself as an effective procedure and has also attracted international attention. It provides additional transparency by presenting detailed study data of pharmaceutical companies, allows critical discussions by means of reports and statements, and forms a solid base for a fair pricing. Approximately two thirds of all evaluated sub-groups are classified as „additional benefit not proven“ (see Figure 1) [11].

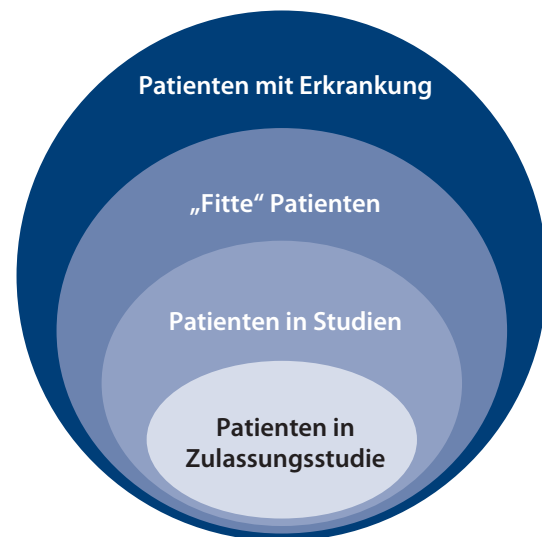
Analysis of 224 procedures between 2011 and 2016 by the Ad hoc Commission „Early Benefit Assessment“ of the AWMF confirmed the positive aspects of the procedure, but also highlighted deficiencies. However, legal certainty of an overall mixed price remains unclear and the evaluation of patient-relevant outcomes is still unsatisfactory. Moreover, any evaluation is only as sound as the underlying data that supports it. Both determination and approval are often based on one study only and not in all cases on randomised studies with appropriate comparative treatments. Study patients are a selection of all patients in the respective indication (see Figure 2).

An analysis of the results of 469 sub-groups and 224 procedures from 2011 to 2016 demonstrates the uncertainty of these determinations (see Table 1) [11]. Only in one percent of the completed procedures data were sufficient to consider the determination well proven. Almost three quarters of all determinations did not include a statement on the level of certainty.

This high proportion is mainly based on the fact that the G-BA's „additional benefit not proven“ does not include any statement on the reliability of the results. This is especially critical, as the determination can be based on various study situations ranging from lack of data to a negative result of a meta-analysis.

Payers complain that the G-BA's decisions are not reflec-

Selektion von Patienten in Zulassungsstudien



Quelle: Eigene Darstellung

Abbildung 2: Patienten in klinischen Studien repräsentieren nur einen Teil aller Patienten in der Indikation.

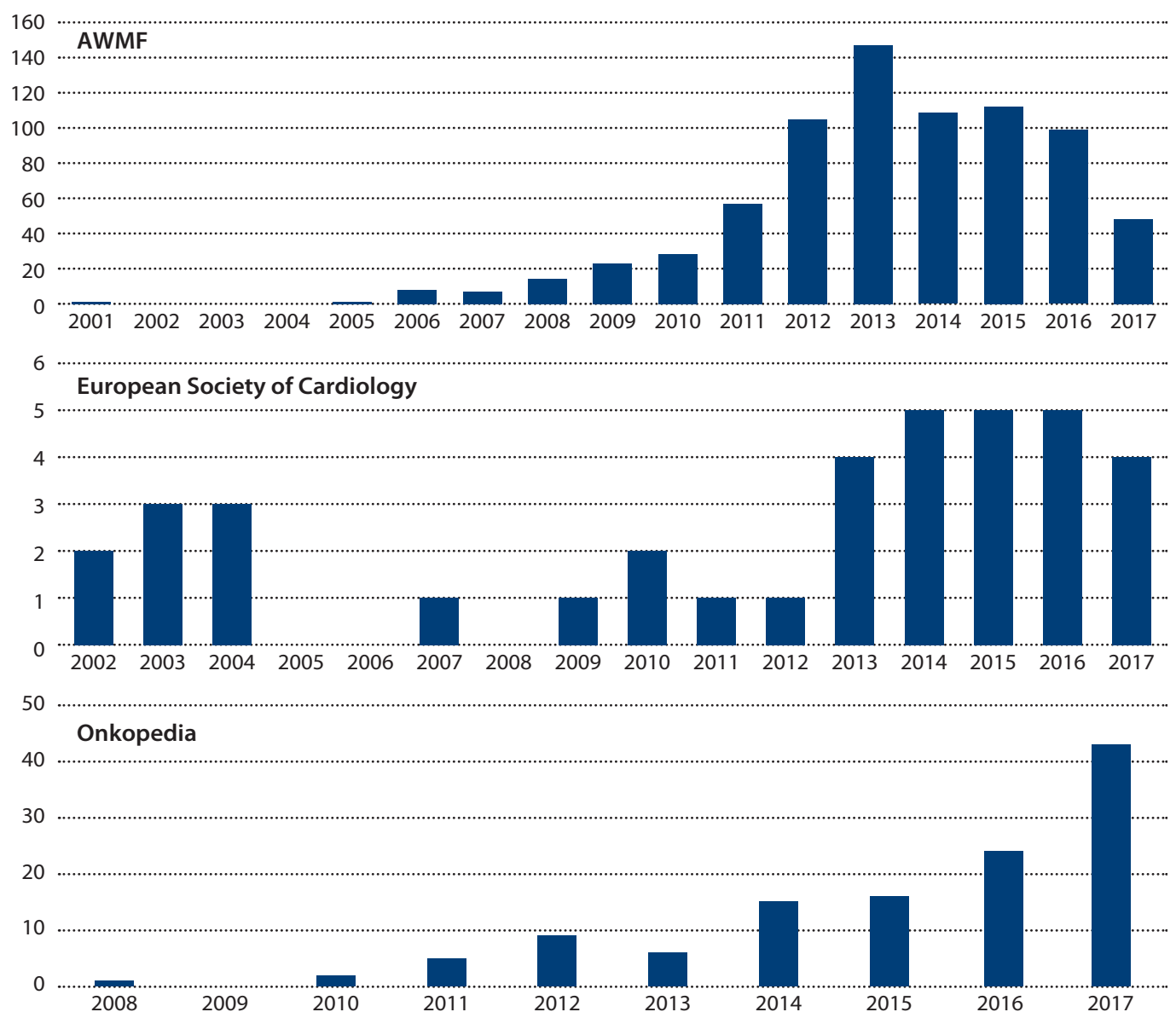
Aussagesicherheit von Festlegung der frühen Nutzenbewertung nach dem AMNOG [11]

| Aussagesicherheit | n | % |
|-------------------|-----|------|
| Beleg | 5 | 1,1 |
| Hinweis | 53 | 11,3 |
| Anhaltspunkt | 68 | 14,5 |
| keine Aussage | 343 | 73,1 |
| alle | 469 | 100 |

Quelle: AWMF

Tabelle 1: Die Analyse von 469 Subgruppen zeigt die Unsicherheit der Festlegungen durch den G-BA. [11]

Aktualisierung von Leitlinien der AWMF [5], der European Society of Cardiology [12] und von Onkopedia [6]



Quelle: Eigene Auswertung, Stand 9/2017

Abbildung 3: Fachgesellschaften kämpfen mit dem Problem der Aktualisierung ihrer Leitlinien.

ted in the prescription behaviour of physicians. In response, the German Government committed itself during the Pharmadialog 2016 to develop a concept for a physician information system for a better and faster communication of the results of the benefit assessment. It was implemented with the German Act on Strengthening Pharmaceutical Supply in Statutory Health Insurance (AMVSG). Details on the procedure will now be determined by the Federal Ministry of Health within the scope of an ordinance.

Current state of knowledge

Steadily growing amounts of data represent a particular challenge in many specialist fields, currently mainly in medical oncology. In recent years, nearly every month a new oncology drug or indication was approved by the EMA. But also other medical fields struggle with updating their recommendations (see Figure 3).

Besides the challenge of handling these large amounts of new data, this figure also reflects the problem of elaborating guidelines. An active collaboration of medical experts in the respective specialist area is the prerequisite for the development and/or update of a guideline. However, physicians collaborate on a voluntary basis which becomes increasingly difficult against the background of the steady increase of workload in inpatient and outpatient care. The delegation of guideline development to HTA organisations is helpful for the evaluation of data, but often does not result in the development of generally accepted and practically implemented recommendations.

Although clinically accepted standards are available for many of the practically required decision-making points, randomised studies are missing. These issues should also be addressed in guidelines. The above mentioned criticism of the G-BA as well as payers / sick funds regarding the lack of perception of determinations within the scope of the

Therapierrelevante Änderungen im Onkopedia-Arzneimittelportal innerhalb von 12 Monaten

| Arzneimittelbewertungen | n | % |
|---|----|----|
| Arzneimittel und Indikationen | 93 | |
| Änderungen gegenüber der vorherigen Version | 39 | |
| • therapierrelevant | | 10 |
| • nicht therapierrelevant | | 29 |

Quelle: AWMF

Tabelle 2: Im Onkopedia-Arzneimittelportal sind inzwischen über 90 Arzneimittel abgebildet.

early benefit assessment also reflects the poor readability of these comprehensive documents, lack of authenticity in the definition of comparative treatments and sub-groups, as well as the lack of updating of many determinations.

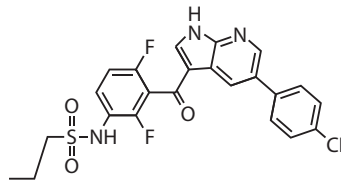
Physician information on new pharmaceuticals

In 2016, the German Society for Haematology and Medical Oncology (DGHO) opened a new portal for the information of prescribers about new oncology drugs. More than 90 pharmaceuticals and indications were included so far [13]. In the recent update, all required the necessary amendments with regard to therapy relevance were classified (see Table 2).

Studies published in peer-review-Journals were analysed. Treatment-relevant were mainly new studies, e.g. on dosing or compared to other control arms, new data of studies that have already been evaluated e.g. on the quality of life, and subsequent evaluations with already evaluated endpoints e.g. on the overall survival. This analysis reveals treatment-relevant changes in approximately ten

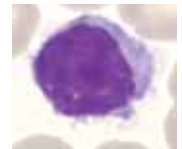
Inhalte eines Informationssystems zu neuen Arzneimitteln

Arzneimittel (ATC)



Indikation (ICD)

Stadium
weitere Charakterisierung



Frühe Nutzenbewertung

Spezifizierung
(Subgruppe)

Vergleichs-
therapie

Festlegung

Endpunkte

Status
(Orphan)

Beschlüsse
Tragende Gründe

Therapie-Algorithmen
Leitlinien

Datum der aktuell gültigen Festlegung

Quelle: Prof. Dr. Wörmann

Abbildung 4: Informationssystem, das die erforderlichen Elemente enthält und die ärztliche Therapiefreiheit achtet.

percent of the procedures within one year. All this should be considered in the design of the physician information system.

Figure 4 was developed based on previous experience. It comprises all information from the benefit assessment we consider necessary as well as links to guidelines and current therapy algorithms. Such an information system will support the physician while respecting his therapeutic freedom.

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aerztliche-Therapiefreiheit-Vom-Durchschnitt-zum-Individuum

² BVerfG, Decision of the First Senate dated 6 December 2005 - 1 BvR 347/98 - Rn. (1-69), http://www.bverfg.de/e/rs20051206_1bvr034798.html

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Physician information system – to find the ideal design is like a Herculean task

Von Florian Staeck

DThe implementation of the physician information systems (PIS) as proposed by authorities in the German Act on Strengthening Pharmaceutical Supply in Statutory Health Insurance (AM-VSG) will be associated with a number of challenges. Contents and scope of the electronic information provided will be stipulated by the ordinance of the Federal Ministry of Health which was not yet available in October 2017. The design will probably lie somewhere between the two extremes a „mere information of physicians about the contents of G-BA decisions on the early benefit assessment“ and „further information on the efficiency of prescriptions“.

The participants of the 6th meeting of the „Interdisciplinary Platform on Benefit Assessment“ on 6/7 October 2017 in Kelkheim near Frankfurt were convinced that the development of a PIS will be a complex task – regardless of its design. One of the starting points for any PIS is the fact that – according to several studies – only approximately 12 percent of all physicians take note of the G-BA decisions on the early benefit assessment of new pharmaceuticals. There are several reasons for this and the extent of information, i.e. often several dozen pages, is only one aspect. Moreover, AMNOG only evaluates a new active substance as compared to the appropriate comparative treatment (ACT), but does not provide any horizontal orientation for the physician regarding its therapeutic range. In light of the legal provisions, AMNOG does also not provide any information about the relationship of a new pharmaceutical to the existing market (i.e. drugs that came to the German market before 2011). Besides, G-BA decisions were created by lawyers for lawyers which does not really facilitate reading of the documents.

Even the „mere“ transcription of G-BA decisions into a sort of short text for a practice software systems (PSS)

might present a lot of challenges, participants warned. The goal must be to segment these complex decisions in a standardised manner. In this vision, short texts will be displayed to the physician in the PSS as before, but backed with underlying figures where appropriate intended to process the contents of the respective decision. The AMVSG only contains a few binding requirements, e.g. conversion of the decisions into a machine-readable form within set time frames.

The desired depth of information about the decisions in the PSS will be an important aspect for the actual implementation. It already contains e.g. information on rebate agreements that are available for a certain active substance as well as on regional agreements for pharmaceuticals on KV (Kassenärztliche Vereinigung) level. In future, the PSS should also provide a note that an early benefit assessment is available as well as information on the field of application, on the ACT, as well as endpoints. Thus, arrows could be used to indicate a potential additional benefit as well as its potential extent with regard to the dimensions mortality, morbidity, and quality of life.

Which information can the physician click away?

On a subordinate information level, the PSS could only provide a link to G-BA decisions and information about a quality-assured application. However, it needs to be determined which information should be mandatory for the physician and which should he be allowed to click away. General consensus was that the mere linking to Annex XII of the German Drug Prescription Directive (AM-RL) in the PIS will not be sufficient for the future. Annex XII contains all G-BA decisions in the context of the early benefit assessment.

Updating the PIS at two-weeks' intervals as specified is currently not realisable. In some 40 percent of all practices

of statutory health insurance physicians, the PSS does not have an online connection, but the update is provided on DVD on a quarterly basis. At present, there is a transitional period until 2020. As soon as the telematics infrastructure will be established, updates at two-weeks' intervals will be possible.

Even on the level of supposedly unbiased information there were challenges with regard to several generations of G-BA decisions. Decisions and integrated evaluations must be linked, for example in those cases where the ACT within a pharmaceutical class has changed over time. If this fact would not be mentioned, the respective active substance might unjustifiably placed at a disadvantage or advantage, respectively.

This classification was considered a „slightly appraising link“ causing a discussion about whether this step would be desirable and who should take care of information processing. This step could not be delegated to an IT service provider, but should rather be carried out by the G-BA itself. It is even questionable whether this link of individual evaluations in a pharmaceutical class would be possible in the G-BA without an additional hearing procedure. In this context, participants referred back to various legal confrontations about GBA's therapeutic advices. In the past, judicial bodies applied very strict standards on the evaluation of information. Even the slightest deviations from the approval text would not have passed a review by the courts. Thus, the participants were concerned that every shortening that is necessary for the PIS provides a new potential legal target for the G-BA.

Requirements will be even higher, if the PIS shall only contain efficiency notes as stipulated by the AMVSG. During the platform meeting, there was a widespread discussion about the pros and cons. If the G-BA should be obliged by the ordinance to provide efficiency notes, a new

formal procedure would be required for these notes. Such a new ruling procedure by the G-BA would have a binding effect for the prescribing physician through the German Drug Prescription Directive.

Info tool or control instrument?

Participants argue that two poles can be identified for a potential design: If the PIS is a mere information tool, the full responsibility would remain in the prescribing physician's hands. But if protection of the physician against a potential recourse is the ultimate goal, information in the PIS must have a higher binding effect. However, it should be mentioned that efficiency notes shall only ensure that a physician prescribes the more economic product, if there is the same probability of achieving a treatment goal with two alternative pharmaceuticals.

The goal is to get sustainable, additional benefit-oriented prices to achieve a financial balance of different substances on a larger scale. This goal would be characterised by the general contradictions already seen with the AM-NOG. Thus, during negotiations of the reimbursement amount, the European price level is taken into consideration, although this has no direct correlation with the additional benefit rating.

It was argued that a higher market penetration of new pharmaceuticals with proven additional benefit could only be successful in case of prescription security of statutory health insurance physicians (i.e. no risk of recourse). It was advocated that if a substance is used in line with the indication, prescription in sub-groups without additional benefit should also be considered feasible, if the appropriate comparative treatment was not tolerated by the patient or remained ineffective.

The reimbursement amount negotiated between the National Association of Statutory Health Insurance Funds

(GKV Spitzenverband) and the pharmaceutical company would reflect parts of the patient populations with and without additional benefit – resulting in the mixed price. At present, there is controversy on the mixed price against the background of an appealable decision by the Berlin-Brandenburg Superior State Social Court.

Physicians reacted sensitively to economic efficiency issues in connection with their treatment responsibility. This is all the more applicable given that the planned PIS should also be a response to the so far insufficient reception of G-BA decisions. It would thus be advisable that physicians should initially become accustomed to receiving support in the prescription process via the PSS. However, economic issues should not become the core message, as this might lead to the refusal of this tool by physicians. Participants recalled that AMNOG was a mere pricing tool – to reshape it as an access barrier in the prescription process would not be in line with the initial approach of the law.

In the further course, the participants discussed these two aspects:

- Integration of guidelines into the PIS: There was controversy on the option to provide notes on the appropriateness and efficiency even with the use of guidelines. For in many cases, G-BA decisions and treatment recommendations were not congruent. Individual G-BA decisions would not add up to an overall therapeutic image for the physician. G-BA decisions were based on substance logic, while guidelines were based on patient-related indication logic.

Other participants replied that the majority of guidelines had significantly varying levels of evidence-basing. As the individual guidelines were very heterogeneous, they should first be stratified and one „lead guideline“ specified. The broader data basis is a clear advantage: While the G-BA decision mainly refers back to comparative and randomi-

sed studies in accordance with its legal mandate, guidelines would also contain data sources of lower evidence categories, such as single-arm studies or real-world data.

Recruitment of guideline authors is difficult

Participants therefore argued that the process of guideline development must be professionalised. In particular, clinical scientific associations should accept and fulfil their leading role. Recently, the number of annual guidelines had not increased. This was also due to the fact that finding renowned experts for this volunteer work is quite difficult. As a consequence, there is an increasing number of guidelines that is older than four years.

There was general support for the proposal to support the development of guidelines with an annual budget of ten million Euros in accordance with the AWMF codices. This might help to simplify these processes at a high level. One proposal was to take the required financial resources from the innovation fund for healthcare research.

- Required regular update of G-BA decisions: Participants mentioned that regular updating would be reasonable and feasible, even if it was not possible for all decisions. There were a variety of update reasons, for example due to new studies or new evaluation of already known data. An update could also be required in case of amendments, changes, or extension of the ACT. Moreover, it was important to identify almost meaningless substances in the prescription environment. This could contribute to the prioritisation of reviews – with regard to prescription-relevant substances for which new evidence is available.

At the platform meeting, a continuously rotating update system for decisions was advocated. Although this would not allow for a provision of the decisions on a daily basis in the PIS, but the number of irrelevant or faulty decisions

could be reduced. Participants remarked that the urgency of an update would also depend on the life cycle of the respective drug.

They argued that a review of the decisions could have a cascade of consequences – up to the necessity of new price negotiations. It was therefore discussed whether an update of Module 4 only would be possible within the context of an early benefit assessment. In this module, methodology and results are described and patient groups with an additional benefit defined. Other participants replied that price data in Module 3 would then have to be updated. Still other participants referred to the predictable problems of selectively taking information from later decisions off-line. This became apparent, when therapeutic advices had to be deleted.

In view of the planned implementation of the physician information system and the resulting challenges, participants of the 6th platform meeting had different demands. Some demanded that physicians should participate more actively in the content-related design of the PIS. Several population surveys had shown that physicians – and not sick funds or pharmaceutical companies – enjoy the greatest level of patients' trust in selecting the appropriate therapy. In case of new pharmaceuticals, many physicians would find out quickly whether these new substances were valuable for prescription or not. This common sense should be developed by physicians and the responsible clinical scientific associations and should not be „dumped“ on other institutions, e. g. NICE in Great Britain.

Should the PIS start as a beta version?

Other participants asked to take pragmatic steps in the development of a PIS. They appealed to the self-governing bodies' willingness to establish a system that solves only 80 percent of all issues in the initial version. Stakeholders

should take the opportunity of progressively improving physician information instead of repeatedly postponing the implementation of a supposedly optimum PIS.

Other participants responded that the prescription control by the PIS as stipulated in the AM-VSG represented a far-reaching legal intervention. This applied for comparative assessments, linking of G-BA decisions, and mere provision of information by the PIS. Therefore, it would not be feasible to launch an immature version of the PIS. Others warned against quickly implementing a slim PIS version for pragmatic reasons.

The physician information system can interfere with the scientific associations' tasks regarding the description of the currently accepted state of medical knowledge. Failure to take adequate account of the associated complex processes would downgrade the development of guidelines by scientific associations to a „passionate hobby“ so that this new instrument might not be accepted and thus be ignored by physicians. From the physicians' point of view, G-BA news were usually secondary to positions of scientific associations.

Another point raised was that the implementation of a PIS is an ambitious task and it would thus not be feasible to shut the door on further development stages of the system after its introduction. Some participants regretted that authorities did not incorporate a model clause for a regional pilot project with the PIS. At the 6th platform meeting, initial implementation examples were presented indicating that sick funds and physicians are already working on potential solutions even without an ordinance. The participants were convinced that – after the implementation of „Version 1.0“ – it would certainly take up to four years until a technically matured physician information system would be available.

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Physician information via software: Ways and goals

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