PHARMACEUTICAL REIMBURSEMENT AND PRICING IN GERMANY

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Pharmaceutical Reimbursement and Pricing in Germany

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Table of contents

List of abbreviations

AMNOG	Law Reforming the Pharmaceutical Market (*Arzneimittelmarkt-Neuordnungsgesetz*)
AMVSG	Law Strengthening the Pharmaceutical Supply (*Gesetz zur Stärkung der Arzneimittelversorgung*)
G-BA	Federal Joint Committee (*Gemeinsamer Bundesausschuss*)
GKV-SV	National Association of Statutory Health Insurance Funds (*Spitzenverband Bund der Krankenkassen*)
IQWiG	Institute for Quality and Efficiency in Health Care (*Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen*)
InEK	Institute for the Hospital Remuneration System (*Institut für das Entgeltsystem im Krankenhaus*)
KHEntgG	Law on Hospital Remuneration (*Krankenhausentgeltgesetz*)
NUB	New Diagnostic and Treatment Methods (*Neue Untersuchungs- und Behandlungsmethoden*)
SGB V	Fifth Social Security Code (*Fünftes Sozialgesetzbuch*)
SHI	Statutory Health Insurance

Pharmaceutical Reimbursement and Pricing in Germany

1. Contextual background - Health care system characteristics

1. Health insurance is mandatory in Germany. The vast majority of Germany's population (90%) get coverage from statutory health insurance (hereafter SHI). The other 10 % are covered by private insurance or special schemes. The basket of goods and services covered by SHI is defined at the national level by law, in terms of general principles, and the Joint Federal Committee (*Gemeinsamer Bundesausschuss* - G-BA), through decisions on individual products or services that should be excluded from or included in the basket). Private health insurers generally cover a more or less similar basket though they are allowed to extend or restrict benefits (Paris and Docteur, 2008).

2. The basket of reimbursed pharmaceuticals is defined by the statutory exclusion of several categories of products, including OTC medicines, treatments for minor ailments and life-style medicines (see Paris and Docteur, 2008 for more details). Patients are generally required to contribute to the costs of pharmaceuticals through a 10% co-insurance rate (with a minimum of EUR 5 and a maximum of EUR 10 per prescription). When products are included in reference price clusters, subject to a unique maximum reimbursement amount, patients have to pay any difference between the market price and the maximum reimbursement amount. Compulsory health insurance (statutory and private) covers 84% of the expenditure for outpatient medicines and patients pay the rest through co-insurance payments or consumption of OTC medicines. Medicines used in inpatient care are fully covered by health insurance.

2. Pharmaceutical reimbursement and pricing in brief

3. Pricing and reimbursement policies are based on the following principles: prescription drugs are reimbursed by health insurance unless included in a negative list maintained by the G-BA); manufacturers are free to set their price; drugs can be clustered in groups of products considered to be therapeutically equivalent and subject to maximum reimbursement amounts. Since 2007, health insurance funds have been using calls for tender and contracting to obtain lower prices mainly, but not only, for generics. Prices of innovative drugs are mainly negotiated.

4. The law reforming the pharmaceutical market (*Arzneimittelmarkt-Neuordnungsgesetz* – AMNOG), which took effect in January 2011, has kept the principle of free pricing at launch but imposes a systematic and formal assessment of the

"added therapeutic benefit" of new medicines in order to negotiate the price according to the therapeutic value of the drug within twelve months after market launch. If a new drug has some added therapeutic benefit over existing standards of care, a reimbursement price is negotiated based on the prices of appropriate comparators (the current standard of care) between the national association of statutory health insurance funds (*Spitzenverband Bund der Krankenkassen* – GKV-SV) and the pharmaceutical company (see details below). If no additional therapeutic benefit is found, the new drug is included in a reference price cluster (*Festbetrag*) where possible. Otherwise, a price is negotiated that should not be higher than the price of the appropriate comparator.

5. The AMNOG evaluation and price negotiation process applies to all new patented medicines introduced in the German market, except those with annual SHI expenditure below EUR 1 million. For orphan drugs, additional therapeutic benefit is assumed by virtue of marketing authorisation without reference to an appropriate comparator in Germany for as long as annual SHI expenditure for the entire population treated with the drug remains below EUR 50 million (Bouslouk, 2016). Manufacturers are exempted from the requirement of submitting data to support additional therapeutic benefit for as long as the threshold is not exceeded but the G-BA assesses the magnitude of the additional therapeutic benefit for relevant patient groups in order to create the basis for price negotiations. Once the EUR 50 million threshold is exceeded, manufacturers are required to submit data on additional therapeutic benefit and orphan drugs are evaluated and prices renegotiated in the same manner as for all other drugs. There are no special arrangements for other expensive drugs, such as those used in oncology. However, the price negotiation process following G-BA appraisal leaves broad leeway to the negotiating parties to agree on discounts and rebates or other mechanisms that can lower prices for SHI.

6. Prices of drugs dispensed to hospital inpatients are negotiated between pharmaceutical companies and hospitals, hospital chains or group purchasing organisations. However, since 2017, prices negotiated for outpatient drugs serve as a ceiling for medicines purchased by hospitals.

7. In the outpatient sector, pharmaceutical companies must grant a 7% discount off ex-factory price to sickness funds and other health insurers on patented pharmaceuticals that are not clustered in reference price groups (SGB V, § 130a). For generics that are not clustered in reference price groups, a 6% discount applies plus an additional discount not exceeding 10%. According to the German association of research-based pharmaceutical manufacturers (*Verband forschender Arzneimittelhersteller* – VfA, 2015), statutory discounts amounted to approximately 16% of final pharmacy retail prices. Legislation also prohibits price increases, in that it requires manufacturers to grant a rebate equalling any price increase versus prices on 1 August 2009. The latter regulation, referred to as "price moratorium" was extended through 2022, subject to an adjustment for inflation as of 2018, in the 2017 law strengthening the pharmaceutical supply (*Gesetz zur Stärkung der Arzneimittelversorgung* – AMVSG).

3. Pricing and reimbursement: decision making process

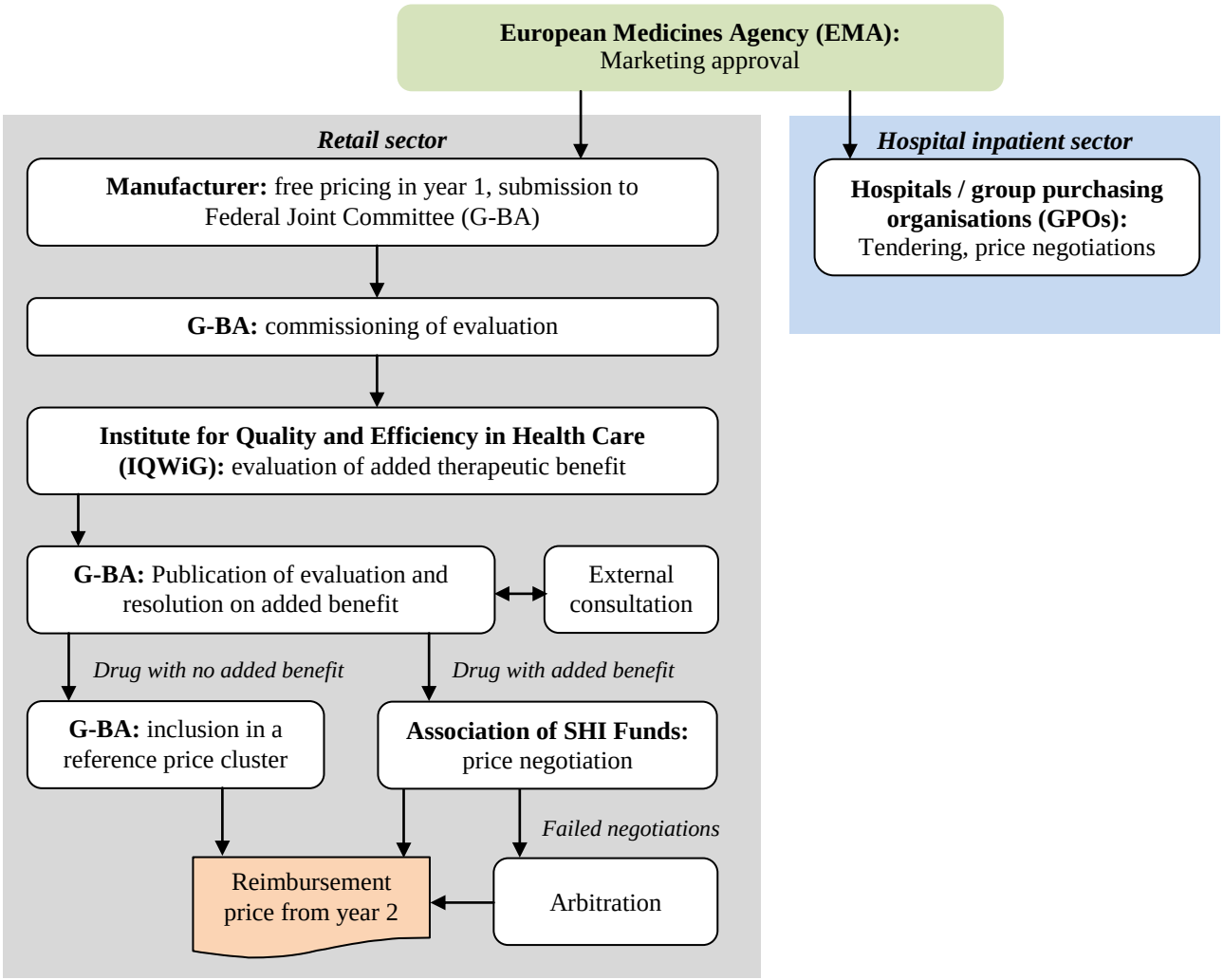
8. Unlike many other countries, the basket of pharmaceuticals reimbursed by SHI in Germany is not defined through a positive list.[1] All medicines entering the market are reimbursed by sickness funds unless they belong to a category excluded by law (e.g. OTC) or by a decision of the G-BA. The process flow for pricing after marketing authorisation is illustrated in Figure 1.

9. Pharmaceutical policy in Germany has been trying to reconcile the objectives of encouraging innovation (free pricing at market entry) and ensuring efficient use of resources (maximum reimbursement amounts for clusters of equivalent products, tendering for generics and measures to promote efficient prescribing). Since the end of 2008, however, health insurance funds did no longer want to be simple "price takers" for new medicines that cannot be clustered in reference prices. From 2007, the Health Insurance Competition Enhancing Act allowed the Institute for Quality and Efficiency in Health Care (*Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen* – IQWiG) to perform cost-benefit assessment as basis for defining reimbursement prices for these products. After several months of expert consultations and work, the IQWiG released a methodology for cost-benefit assessment, based on an efficiency frontier (IQWiG, 2009). However, before this methodology could be used to set reimbursement prices, AMNOG took effect in January 2011. Although AMNOG also provides for cost-benefit assessment, such assessments have not been used in practice thus far (von Stackelberg et al., 2016).

10. According to AMNOG, manufacturers continue to set drug prices freely at market entry. However, at the time of market launch, they must submit a dossier with the necessary data to the G-BA. The dossier must support the "added therapeutic benefit" of the medicine over the appropriated comparator (the current standard of care) determined by the G-BA. The G-BA must assess the added therapeutic benefit of the new medicine over the appropriate comparator within 3 months, or can request IQWiG or a third party to perform the assessment. In practice, IQWiG has thus far conducted all assessments at the request of the G-BA. The result of this assessment is published and external stakeholders are given the opportunity to submit written and verbal statements on the result (see below). Within an additional 3 months of the publication of the benefit assessment, the G-BA passes a binding resolution stipulating, *inter alia*, the extent of additional benefit, patient groups eligible for treatment and the cost of treatment for SHI. The resolution determines how the reimbursement price is set after the first year of marketing. If the drug has some added therapeutic benefit, the manufacturer and the national association of statutory health insurance funds (GKV-SV) negotiate a reimbursement price within another six months (see below for more details about the terms of the negotiation). If parties cannot reach an agreement, the reimbursement price is set by arbitration.

[1] See Paris and Docteur (2008) and/or Fünftes Buch Sozial Gesetzbuch –SGB V, §34 for more details.

Figure 1. Institutions and process for pricing in Germany



Source: Authors
Note: All products that are not explicitly excluded from reimbursement by SHI are reimbursed upon marketing authorisation

11. If the drug has no added therapeutic benefit over the standard of care, the G-BA will include it in a reference price cluster. If clustering is not possible, prices are negotiated in the same manner as for medicines with added benefit. However, the goal of the price negotiation is that annual treatment costs with the new medicine should not exceed those of established therapy.

3.1. Institutions, experts and stakeholders involved

12. Two institutions are involved in the assessment of new products in Germany. The first is the Federal Joint Committee (G-BA), in charge of deciding on the coverage of health goods and services, as well as establishing practice guidelines. The G-BA plays an important role in the definition of pharmaceutical coverage, through defining indications

for which OTC products may be reimbursed; making an inventory of drugs with insufficient proof of efficacy; selecting products to be excluded from coverage; and defining reference price clusters.

13. The G-BA is a college of representatives of the umbrella associations of physicians, dentists, hospitals and health insurance funds. The G-BA plenary assembly, the decision making body, is composed of an impartial chair, two other impartial members, two representatives of hospitals, two representatives of doctors, one representative of dentists and five representatives of sickness funds. All these members have voting rights. Patients' representatives attend the meetings and are consulted by the Committee.

14. Within the G-BA, the subcommittee on pharmaceuticals is in charge of the assessment of medicines. This subcommittee is composed of a chair and a vice-chair, as well as three representatives of hospitals, three representatives of doctors and six representatives of sickness funds. The pharmaceutical sub-committee of the G-BA is responsible for the assessment of benefits and added therapeutic benefits of products and delegates the task of preparing a draft assessments to working groups.

15. The second body involved in the assessment of new medicines is the Institute for Quality and Efficiency in Health Care (IQWiG). The IQWiG is an independent body in charge of evaluating the quality and efficiency of health services and health products. It was created in 2004 and its missions were initially limited to the assessment of clinical effectiveness. These missions were extended to cost-benefit assessment in 2007.

16. The IQWiG generally conducts evaluations on request of the G-BA, although the Federal Ministry of Health, patients' representatives in the G-BA or the Commissioner of the Federal Government for patients' issues can also request evaluations from IQWiG. The Institute does not produce practice guidelines or make reimbursement decisions, but rather makes available evidence-based assessments in order to inform decision makers.

17. The IQWiG employs approximately 140 staff members, half of which are scientific experts. The board of directors is composed of representatives of the Federal Ministry of Health, health insurance funds, hospitals, physicians, and of a representative of the G-BA with a consultative role.

18. In the context of the AMNOG procedure, the results of assessments are open for comment by external stakeholders. This can include physicians, physician associations and advocacy groups, academics or associations of pharmaceutical manufacturers who can submit written comments following the initial publication of an appraisal, which is followed by a public hearing. Manufacturers are allowed to submit additional data in this process and the G-BA resolution may digress from assessment recommendations based on input received.

3.2. Principles of assessment

19. The rules for the assessment of new medicines are defined in § 35a of the Fifth Social Security Code (*Fünftes Sozialgesetzbuch* - SGB V). An assessment of the additional therapeutic benefit of medicines must be undertaken in the following situations:

- For medicines marketed with new active ingredient(s), or a new combination of existing active ingredients;

- For medicines marketed with a new indication, or when a new approved indication targets a different group of patients than existing indication(s) of the product or that is attributed to a different treatment area (i.e. prevention, treatment or diagnosis);

- For medicines for which the G-BA or the pharmaceutical company requests a new assessment. Both may request an assessment because of new scientific findings but the G-BA is not obliged to accept a re-assessment requested by the company. The G-BA can also request a dossier for existing medicines.

- For medicines for which the G-BA has issued a temporary decision. New combinations of existing active ingredients shall be assessed.

20. A pharmaceutical company may request an exemption from assessment if annual SHI expenditure is not expected to exceed EUR 1 million per year.

21. The benefit for patients is assessed considering improvements in health status, reductions in the duration of the disease, survival gains, the reduction of side-effects, or an improvement in quality of life. The G-BA requires the highest possible level of evidence and prefers direct comparisons and relevant endpoints but may be flexible where needed, for example when the company can justify that evidence based on randomised controlled trials is not available (details are provided in Annex).

22. For medicines with new active ingredient(s) that have pharmacological and/or therapeutic properties comparable to those of medicines clustered in a reference price group, the additional benefit has to be proven versus alternatives in the reference price group with a complete dossier. For other medicines with new active ingredient(s), the additional benefit is assessed for each indication, by comparison to the "appropriate comparator" as defined by law. The dossier must include an estimate of the probability for the benefit improvement.

23. The additional benefit must be quantified according to a 6-level scale with the following instructions:

- A *major additional benefit* corresponds to a sustained and large improvement in therapy-relevant benefit which was not previously achieved by the appropriate comparator, such as recovery from disease, a considerable increase in life, long-term relief from severe symptoms or extensive avoidance of severe side-effects.

- A *considerable additional benefit* corresponds to a considerable improvement in therapy-relevant benefit not previously achieved by the appropriate comparator, in particular the attenuation of severe symptoms, a moderate extension of life, an "easing" of the disease noticeable by patients, or a relevant avoidance of severe or other side-effects.

- A *minor additional benefit* corresponds to a moderate or slight improvement in the therapy-relevant benefit which was not previously achieved by relevant comparators, in particular a reduction in non-severe symptoms of the disease or a relevant avoidance of side- effects.

- There is *an additional benefit which is not quantifiable* when the available scientific data does not allow its quantification.

- No additional benefit proven.
- The benefit is *less* than those of the comparator.

24. For orphan medicines, additional benefit is considered to be proven by the marketing authorisation. Nevertheless, manufacturers have to show the magnitude of the additional therapeutic benefit. Beyond market authorization, the G-BA does not initiate a complete assessment of orphan drugs, unless sales are expected to exceed 50 million Euros.

3.3. Resolution

25. The G-BA makes the binding resolution about benefit assessment within 3 months after publication of the assessment report. The resolutions are published on the internet[2] and publicly accessible. It serves as the basis for price negotiations and recommendations for appropriateness, quality and efficiency of prescription or for allocation to a reference price group (for medicines without added therapeutic benefit). The resolution includes information on:

- The therapeutic benefit of the new medicine;
- The additional benefit of the medicine over therapeutic alternatives;
- The number of patients and definition of patient groups for which the medicine represents a meaningful therapeutic improvement;
- Specific requirements to ensure appropriate use;
- The cost of the therapy, compared with those of the appropriate comparator.

3.4. Price negotiations

26. If a new medicine has some additional therapeutic benefit, the national association of statutory health insurance funds (GKV-SV) and the pharmaceutical company must negotiate a reimbursement price. The general rules for negotiation are set in § 130b SGB V and more detailed rules are determined by a framework agreement signed by the GKV-SV and associations representing the pharmaceutical industry (*Rahmenvereinbarung nach § 130b Abs. 9 SGB V*, latest version in force since 1 July 2016 (GKV-SV, 2016 and 2017)). The main content of this agreement has remained unchanged since its inception, with the additional benefit versus the comparator in the G-BA appraisal and the comparator cost being the main basis for price negotiations. The 2016 version, however, expanded the timeframe with which manufacturers can withdraw their medicine from the market before completion of the AMNOG process (opt-out) (GKV-SV, 2017).

27. The negotiations are based on the additional benefit as assessed by the G-BA. Additionally, they should take into account the annual cost of therapy of other comparable pharmaceuticals and prices paid in other European countries as reported by the company.

[2] https://www.g-ba.de/informationen/nutzenbewertung/

28. The list of countries used for international benchmarking is attached to the agreement signed between the GKV-SV and the pharmaceutical industry. It is based on three criteria: countries must be part of the European Economic Area (EEA), countries must together account for at least 80% of the population of the EEA (without Germany) and must be comparable to Germany in terms of their economic performance (Ludwig & Dintsios, 2016).[3] The pharmaceutical company must provide information on foreign ex-factory prices. If the company is not able to disclose the actual price paid in a given country, parties will agree on a method to estimate the actual price. The company is also requested to provide information on expected volumes of sales.

29. Negotiations are not open to the public and all information exchanged during the negotiation is confidential. The negotiations must be concluded within 6 months of publication of the G-BA resolution, during which, in principle, four meetings take place. Representatives of the private health insurers can also attend these meetings. Meeting results are summarised in written minutes, shared by parties to the negotiation. The GKV-SV must communicate the final reimbursement price to the umbrella organisation of private health insurers. Unless otherwise specified, the agreement is valid without a time limit. Negotiated prices apply from the second year, i.e. the 13th month, from market introduction but not retroactively to the first year, during which manufacturers are free to set a price unilaterally. Both parties to the agreement can renounce it with a three-month notice, but only after 1 year from entry into force.

30. For drugs without added therapeutic benefit that cannot be clustered in reference price groups, the price is negotiated with the goal that the annual cost of therapy should not be higher than the annual cost of therapy with the appropriate comparator.

31. If parties to the negotiations do not reach an agreement within six months of publication of the G-BA resolution, an arbitration process begins. The arbitration process is defined in regulations updated on 22 December 2010.[4] The arbitration board is composed by an impartial Chairman and two other impartial members, in addition to two members appointed by both parties to the negotiations (the GKV-SV and the pharmaceutical company). Members are appointed for four years. The Ministry of Health can dismiss a member of the arbitration board for justified reasons, after having heard the GKV-SV and the industry. Patient organisations may attend meetings of the arbitration board. Decisions are made by a simple majority vote, abstention is not allowed and if there is no majority, the vote passed by the chairman of the board will be decisive. The Board is required to make decisions within three months per § 130b, paragraph 4 of the fifth social security code (SGB V). Parties to the negotiation may appeal a decision made by the arbitration board before the competent court but appeals do not have a suspensive effect. After arbitration any party to the G-BA can ask for a cost-benefit assessment by IQWiG. This assessment has no suspensive effect but the agreed reimbursement price can be renegotiated following the assessment.

[3] The list is reviewed annually by negotiating parties and can be revised if needed. In 2012, it included 15 EU countries: Austria, Belgium, the Czech Republic, Denmark, Finland, France, Greece, Ireland, Italy, the Netherlands, Portugal, Sweden, the Slovak Republic, Spain and the United Kingdom (GKV-SV, 2016). Greece has been temporarily excluded from this group despite being listed as a reference country in the 2016 renewal of the framework agreement between the GKV-SV and the pharmaceutical industry (Ludwig & Dintsios, 2016).

[4] The arbitration board defined its own rules, which were approved by the Ministry of Health.

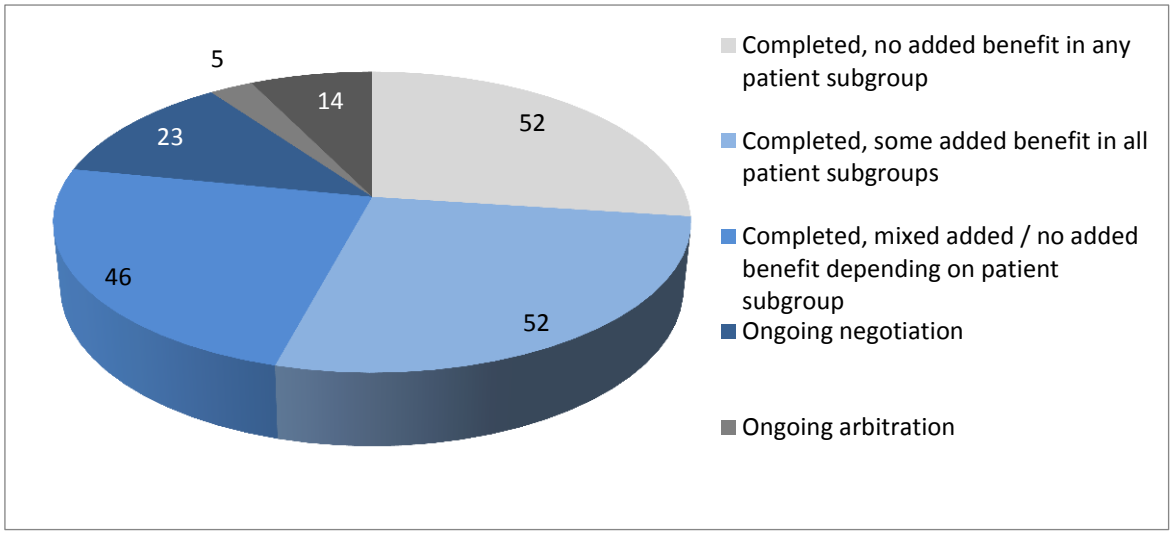
32. An agreement or an arbitration decision can be called into question by either of the parties at the earliest after one year. The price negotiated or set by arbitration, however, is valid until a new agreement is reached. A new assessment of the additional therapeutic benefit or the constitution of a reference price cluster leads to a re-negotiation of the price within one year.

4. Results

33. In 2016, products part of a reference price cluster accounted for 81% of prescriptions and 37% of total drug expenditure reimbursed by social health insurance (GKV-SV, 2017).

34. Between January 2011 and May 2018, the G-BA completed 307 assessments of medicines and published the corresponding resolutions (G-BA, 2018). As per 15 August 2017, the process of negotiating reimbursement prices had been completed for 150 medicines based on the following results of G-BA assessments: no additional benefit found for 52, additional benefit for 52 and mixed results depending on the patient group for 46 medicines. For 23 medicines, price negotiations were still underway, prices of five medicines were subject to ongoing arbitration and 14 medicines were withdrawn from the market before the process was completed (opt-out) (Figure 1). Price reductions versus list price following AMNOG appraisals between 2011 and 2016 ranged from 2 to 98% (von Stackelberg et al., 2016). In 2016, these price reductions were estimated to have reduced drug expenditure of SHI by approximately 21%, based on volumes prescribed multiplied by the reductions versus prices prior to the evaluation (von Stackelberg et al., 2017).

Figure 1. Status of price negotiations and results of G-BA assessment for completed negotiations, per 15 August 2017



Source: von Stackelberg et al, 2017

35. A significant number of assessments found varying levels of additional benefit, depending on the patient subgroup treated. For 44% of medicines for which a price has

been negotiated by July 2017 based on an assessment, negotiations were based on varying additional benefit by patient subgroup (von Stackelberg et al., 2017). The non-orphan medicines assessed provided no additional benefit for 69% of all patient subgroups considered, minor additional benefit for 12% of patient subgroups, considerable additional benefit for 14% of subgroups and major additional benefit for less than 1% of patient sub-groups; in 4% of patient sub-groups, the additional benefit could not be quantified (ibid.). Within the patient groups for which some additional benefit was found, it could only be proven in 5% of patient groups while only some indication of additional benefit was found in the remaining 95%. For orphan drugs, the additional benefit could not be quantified in 57% of patient sub-groups (ibid.).

36. An inability to quantify additional benefit can also be the result of strategic decisions of manufacturers not to submit a dossier, or to submit an incomplete dossier, to the G-BA in anticipation of a risk that the results of the G-BA appraisal could lead to a lower price than when the additional benefit cannot be quantified (von Stackelberg et al., 2016). Such behaviour was not subject to sanctions until 2017. Since May 2017, the law strengthening the pharmaceutical supply (*Gesetz zur Stärkung der Arzneimittelversorgung – AMVSG*) allows for distinguishing between medicines the additional benefit of which could not be quantified despite timely submission of a complete dossier by the manufacturer and medicines where additional benefit could not be quantified because a manufacturer failed to submit a the dossier in a timely and complete manner. In the latter case, the price of the medicine will have to be set so that costs are reasonably lower than those associated with the comparator therapy.

37. By May 2017, arbitration had been completed for a total of 28 medicines (GKV-SV, 2018). A study of 16 arbitrations completed by the end of 2015 found that 14 of the 16 products subject to arbitration had at least one generic as an appropriate comparator (Ludwig & Dintsios, 2016). Based on data reported by the same study, prices claimed by manufacturers were on average approximately 5 times the prices claimed by SHI, ranging from a factor of 1.4 for siltuximab to 18 for lixisenatide (authors' analysis based on Ludwig & Dintsios, 2016). Reimbursement prices set by arbitrations were on average 20% below the mid-point of the range between the prices claimed by manufacturers and SHI (ibid.); in only 4 of 16 cases were reimbursement prices above the midpoint, including by 31% for daclatasvir (ibid). Among 52 medicines found to have no additional benefit at all by August 2017, prices of 13 were subject to arbitration and 10 of these medicines were subsequently withdrawn from the German market (von Stackelberg et al., 2017). Another 14 of the 52 medicines with no additional benefit, which were not subject to arbitration, were withdrawn from the market before the negotiation was completed (opt-out) (ibid.).

38. A recent study of prices of all pharmaceuticals that had been appraised by the G-BA between 2011 and 2016 found that negotiated prices include premiums that reflect the added benefit identified in appraisals (Lauenroth & Stargardt, 2017). Molecules with an added benefit over comparators were estimated to achieve a price premium of approximately 230% over comparators on average. Premiums increased with the magnitude of the added benefit and were also achieved by medicines the added benefit of which could not be quantified in the appraisal. The highest premiums were achieved by medicines that had an added benefit in terms of mortality (620%), followed by medicines with an added benefit in terms of morbidity (170%) and medicines with added benefit in terms of adverse events (93%). Medicines with no added benefit over comparators were found not to achieve price premiums.

5. Negotiations and pricing for inpatient hospital drugs

39. Prices of drugs dispensed to hospital inpatients are negotiated between pharmaceutical companies and hospitals, hospital chains or group purchasing organisations (GPOs) or, in case of public hospitals, subject to public tendering according to European Union law on public procurement, which specifies a threshold above which purchases have to go through a tender process. Contrary to the outpatient sector where social insurance is legally required to cover all medicines that are not explicitly excluded from reimbursement, patients are not entitled to specific pharmaceutical treatments in hospitals. Hospitals are therefore autonomous in making purchasing decisions. Prices of medicines used in hospitals are not regulated and prices and are a result of confidential transactions, and therefore not publicly available. However, the 2017 law strengthening the pharmaceutical supply (AMVSG) introduced a rule whereby prices negotiated for the outpatient sector following appraisal under AMNOG represent ceilings for prices negotiated by hospitals. For medicines introduced before 2011 and not subject to AMNOG, manufacturers are required to submit their sales prices for the outpatient sector, which also serve as ceilings for hospitals. A large share (approximately 90%) of all hospital purchases are made directly from manufacturers. However, hospitals can also contract with wholesalers or non-hospital pharmacies and may do so especially for supply of less common products required in emergencies.

40. The cost of medicines used by hospitals is included in the payments by diagnosis-related group (DRG) for the entire treatment episode. Similar to coverage of retail drugs, hospitals may employ any technology that has not been explicitly excluded from coverage by the G-BA. Expenditures for medicines dispensed in hospitals account for 9% of total expenditure on pharmaceuticals (OECD Health data[5]).

41. Hospitals can obtain additional funding on top of DRG payments for new technologies, including medicines, when their costs have not yet been factored in DRG tariffs under the new diagnostic and treatment methods regulation (*Neue Untersuchungs- und Behandlungsmethoden - NUB*). Because DRG payment rates are set annually based on historic costs there is a time lag between the point when a new technology affects hospital costs and these additional costs are reflected in the corresponding DRG payment rate. The NUB regulation was introduced in the 2005 law on hospital remuneration (*Krankenhausentgeltgesetz* - KHEntgG) to overcome a disincentive for hospitals resulting from the time lag that could keep them from introducing beneficial new technology that is more expensive than existing treatments (Geissler et al., 2011). Under this regulation, hospitals have to apply individually for additional payments and go through three steps for new technology to be included in the regular system of DRG payments: (1) a hospital-specific application to the Institute for the Hospital Remuneration System (*Institut für das Entgeltsystem im Krankenhaus* – InEK); (2) if the hospital application with InEK is accepted, a negotiation with the sickness funds to receive the NUB payment for the

[5] Consulted on 11 May 2018.

technology; and (3) inclusion of the technology in the corresponding DRG based on data collected during the period of the NUB payment (ibid.).

42. For the calendar years 2016, 2015 and 2014, InEK received NUB applications for 710, 670 and 618 products respectively; approximately one-fourth of all applications were for drugs, with oncology and anti-inflammatory/immunology products as leading therapeutic areas for pharmaceutical applications (Freiberg et al., 2016; Friedmann et al., 2014). In 2014 and 2013, payments were approved for 18% and 10% of all products for which applications were submitted (Aggarwal et al., 2015; Friedmann et al., 2014). Approval rates were higher for drugs than for other types of products (ibid.).

Annex - Guidance for assessment of the additional benefit of new product-indications

43. Pursuant to the Decree on the Benefit Assessment of Pharmaceuticals (Verordnung über die Nutzenbewertung von Arzneimitteln nach § 35a Absatz 1 SGB V für Erstattungsvereinbarungen nach *§ 130b SGB V – AM-NutzenV*), IQWIG and the G-BA assess the additional benefits of new product-indication with pre-defined rules about the level of evidence included in the dossier. The level of the evidence is rated as follows:

Ia –Systematic review of studies of evidence level 1b;

Ib – Randomised clinical studies;

IIa – Systematic reviews of studies of evidence level IIb

IIb – Prospective comparative cohort-studies

III – Retrospective comparative studies

IV – Case series and other non-comparative studies

V – Associative observations, pathophysiological considerations, descriptive representations, single-case reports, opinions from recognised experts not proven with studies, consensus conferences and reports from expert committees.

44. The Decree also stipulates that the appropriate comparator must be identified according to international standards of evidence-based medicine. The G-BA specifies the following criteria in its rules of procedure:

- The comparator must be authorised for the specific indication assessed;
- If the comparator is a non-medical treatment, it must be deliverable within the framework of the health insurance in Germany;
- Preference should be given to therapeutic alternatives whose patient-relevant benefits have already been assessed by the G-BA.
- The comparator should be considered as an appropriate therapy according to the generally accepted state of medical knowledge.
- Initially, where several alternatives existed, the most cost-efficient had to be chosen, with a preference for medicines included in reference price clusters when possible. However, this constraint was slightly relaxed a few months after the AMNOG's implementation.

45. On this aspect, as well as on other aspects of their applications, pharmaceutical companies can seek advice from the G-BA before filing their application for assessment. The "dossier" must contain the following information by law:

- The authorised therapeutic indications;

- The "claimed" medical benefit;
- The additional medical benefit over the comparator;
- The number of patients and patient groups for whom there is a therapeutically important benefit;
- The costs of the therapy for the statutory health insurance funds: the company must indicate the pharmacy retail price of the medicine and direct costs for the statutory health insurance;
- Specific requirements to ensure "quality of care" when defining therapeutic indications.

46. The dossier must include all information related to the marketing authorisation, as well as information on results and protocols of studies sponsored or co-financed by the company or by third-parties, when available, even though studies may not have finished or have been cancelled.

47. The dossier is made publicly available except those parts including business-related confidential information or those which raise issues in terms of the protection of privacy. Some parts of the report may be kept confidential.

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