IS THE PROOF OF AN ADDITIONAL BENEFIT UNDER AMNOG IN GERMANY MORE DIFFICULT FOR CERTAIN DRUGS THAN FOR OTHER ONES?

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Objectives

The early benefit assessment (EBA) of pharmaceuticals was introduced in 2011 as part of the Act on the Reform of the Market for Medicinal Products (AMNOG). Regarding the discussion on AMNOG in Germany that it seems to be more difficult to prove an additional benefit (AB) for certain diseases than for other ones, a respective analysis of benefit assessments was conducted considering the following disease categories: Chronic conditions (particularly, type 2 diabetes mellitus, multiple sclerosis, and COPD), cancer (except for types treated with orphan drugs), and infectious diseases (primarily, chronic hepatitis C and HIV/AIDS).

Methods*

In total, 91 benefit assessments entailing 181 patient groups (PG) were finalized until 31 December 2014 in the context of EBA (except for drugs integrated into an existing reference price groups). Benefit assessments of orphan drugs were excluded from the current analysis, since the AB of these medications is already proved through market authorization.

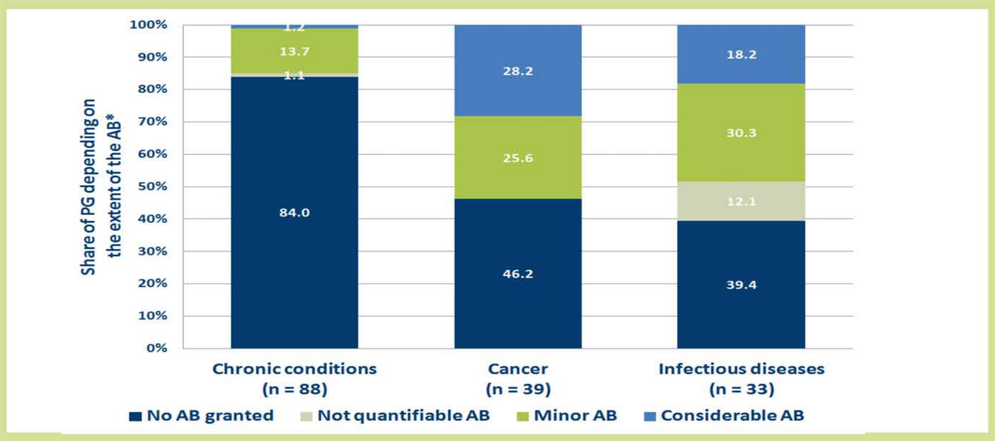
The predefined PG could be identical across several assessments (e. g. in antidiabetics). The analysis was conducted with regard to the AB granted vs. the appropriate comparator for different PG as well as with regard to the quantity of assessments with recognized AB in relation to the whole scope of assessments considered. The results are presented as percentage shares depending on the extent of the AB.

* The slightly deviating figures of this poster (in comparison to abstract PHP53 as submitted) originate from the updated version of the AMNOG analysis [1].

Results

Distribution of AB extent categories of pharmaceuticals for the considered disease categories (in terms of PG)

Figure 1: Distribution of AB extent categories in terms of PG in different disease categories



AB: Additional benefit; n: Number of PG in each disease category; PG: Patient group

* The results are presented as percentage shares of PG depending on the extent of the AB in each disease category

Since orphan drugs (16 assessments with 21 PG) were not accounted for in this current analysis, there were 75 assessments entailing 160 PG which were evaluated for AB extent.

Figure 1 presents the results of the AB analysis in the following categories:

Chronic conditions

- A total of 41 benefit assessments with 88 PG (of which 52 PG were part of antidiabetic assessments) were conducted
- An AB vs. the appropriate comparator could not be proven for 84% of PG
- For antidiabetic drugs, this number even amounted to 90% (47 of 52 PG)
- A considerable AB was granted for only 1.2% of PG (Belimumab for systemic lupus erythematosus with high disease activity)

Cancer

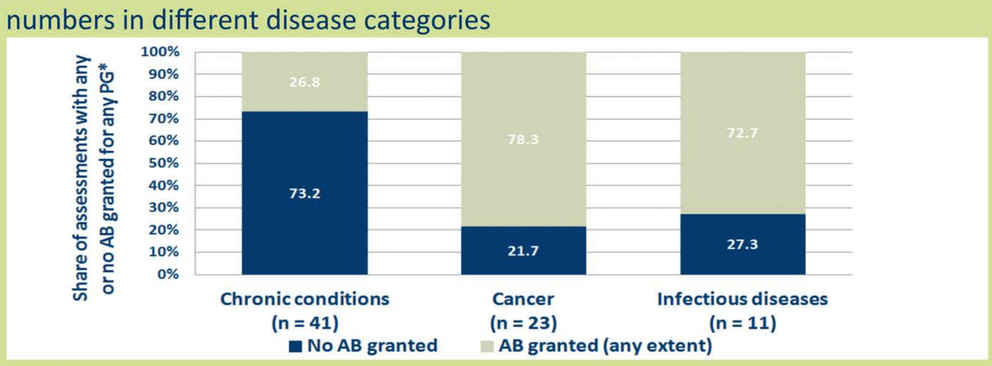
- An AB vs. the appropriate comparator could not be proven for 46.2% of PG
- A considerable AB was granted for 28.2% of PG, a minor AB for 25.6% of PG

Infectious diseases

- An AB vs. the appropriate comparator could not be proven for 39.4% of PG
- A considerable AB was granted for 18.2% of PG, a minor AB for 30.3% of PG, and 12.1% of PG received a not quantifiable AB

Distribution of AB extent categories of pharmaceuticals for the considered disease categories (in terms of assessments)

Figure 2: Distribution of AB extent categories in terms of assessment numbers in different disease categories



AB: Additional benefit; n: Number of benefit assessments in each disease category; PG: Patient group

* The results are presented as percentage shares of assessment numbers depending on the AB recognition in each disease category

Figure 2 illustrates the results of the AB analysis in the same disease categories in terms of assessment numbers (without orphan drugs):

Chronic conditions

- In case of 30 (73.2%) out of a total of 41 benefit assessments, there was no AB granted for any PG
- 11 out of 15 assessments for antidiabetic drugs were among the above mentioned 30 benefit assessments with no AB

Cancer

- Only in case of 5 (21.7%) out of a total of 23 benefit assessments, there was no AB granted for any PG

Infectious diseases

- Only in case of 3 (27.3%) out of a total of 11 benefit assessments, there was no AB granted for any PG

Possible reasons for the striking discrepancies in chance of AB recognition in different disease categories

Possible reasons for such spectacular differences in chance of AB recognition across different disease categories could be the choice of an appropriate comparator, the issues regarding patient-relevant endpoints as well as the extent of unmeet need (presented in Table 1).

Table 1: Potential reasons for discrepancies in chance of AB recognition

Potential reason	Issues regarding patient-relevant endpoints
Appropriate comparator	• **Determination:** The appropriate comparator considered a standard therapy is determined by The Federal Joint Committee (G-BA) and is usually the most cost-efficient alternative. Standards vary strongly based on the indication: The drug market for infectious and cancerous diseases offers hardly any generic alternatives whereas there are numerous generic alternatives for chronic diseases like diabetes or hypertension. • **Chance of AB recognition:** "Best supportive care" is the most common appropriate comparator for many advanced disease stages which increases dramatically the chance of AB recognition as compared to chronic diseases.
Patient-relevant endpoints	• **Mortality:** The worse the prognosis of the patient the easier is the proof of the AB (e.g. cancer (high mortality in foreseeable period) vs. diabetes (long time until death occurs as a complication)); • **Morbidity:** The severity of disease can be better assessed based on eruptive events, such as stroke or heart attack, than on slowly progressive complications, such as renal impairment, neuropathy, retinopathy, or diabetic foot; • **Quality of life (QoL):** The QoL assessment is usually based on the QoL changes over the treatment time. Therefore, cancerous diseases have a better chance of AB recognition for this endpoint as chronic or infectious conditions; • **Safety**: A lower risk of adverse events (AE) can also increase the chances of AB recognition. Even in case of assessed antidiabetic agents, the AB was granted based on the lower incidence of severe hypoglycemia.
Unmet need	• **Extent of unmet need:** The unmet need is much higher in the oncology since BSC is usually the only therapeutical option for many advanced disease stages as opposed to chronic diseases with numerous treatment alternatives.

Conclusions

It can be stated that the current EBA procedure (particularly, the obvious correlation between disease category and the chance of AB recognition) disadvantages strongly pharmaceuticals for chronic conditions, especially in case of gradually deteriorating diseases, when compared to cancerous and infectious diseases. Under such circumstances, pharmaceutical companies are forced to either entirely refuse the launch of their products on the German market or to withdraw the products from the market if no AB can be granted (meaning reimbursement on the price level of generic drugs) as it was in case of insulin degludec in 2015. As a consequence, the German patients might only gain access to such pharmaceuticals after the patent expires. These results could be relevant for the discussion on the future development of AMNOG in order to ensure availability of innovative pharmaceuticals to all PG in Germany.

References

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2. Gemeinsamer Bundesausschuss (2014): (Frühe) Nutzenbewertung nach § 35a SGB V. https://www.g-ba.de/informationen/nutzenbewertung/ (accessed 22 October 2015)