# Reassessment of orphan drugs after exceeding the 50 MIO. Euro revenue threshold: Effects on added benefit and price discount

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## Background

- Since the enactment of AMNOG in Germany in 2011, pharmaceutical companies are required to provide evidence of the additional medical benefit of newly approved drugs.
- The additional benefit of orphan drugs (OD) assessed by the G-BA is already acknowledged by approval. However, if the annual costs for the statutory health insurance (SHI) exceed 50 million euros or the OD-status is lost, a standard assessment without OD privileges against an appropriate comparator (ACT) is mandatory.
- Depending on the extent of the effect in the categories mortality, morbidity, health-related quality of life and safety, the assessment can result in “major”, “considerable”, “minor”, “non-quantifiable”, “no”, or even “less” additional medical benefits (**Table 1**).
- Due to the rising deficit in the SHI spendings and external macroeconomic effects, the German government plans to change the reimbursement of drugs in Germany. This will be done depending on the extent of the additional benefit and price relative to the named ACT.
- As a result, a SHI Financial Stabilization Act is currently being processed by the German Department of Health, that foresees a significant reduction of the revenue threshold to 20 million euros. This affects not only newly licensed ODs, but also ODs that have already been assessed by G-BA. Therefore, even more OD companies that have not been affected to date should be aware of a possible reassessment.

### Table 1. The extent of the additional medical benefit

| Additional benefit | Additional benefits | Longer survival | Symptoms | Side-effects | Other |
|---|---|---|---|---|---|
| Major | **Sustained** and large improvement in the therapy-relevant benefit (recovery from the disease) | Considerable | **Long-term freedom from severe symptoms** | Extensive avoidance of severe side-effects | - |
| Considerable | **Considerable** improvement in the therapy-relevant benefit | Moderate | **Lessening of severe symptoms** | A relevant avoidance of severe side-effects or a significant avoidance of other side-effects | Relief of the disease, which is noticeable to the patients |
| Minor | **Moderate** and not merely slight improvement in the therapy-relevant benefit | - | **Reduction in non-severe symptoms of the disease** | Relevant avoidance of side-effects | - |
| Non-quantifiable | Scientific base data do not permit to quantify benefit | - | - | - | - |
| None proven | - | - | - | - | - |
| Less | - | - | - | - | - |

## Objectives

- The aim of this study was to analyze resolutions for ODs which exceed the 50 million euros threshold and to examine the change in the rating of the additional medical benefit after the reassessment, the time to reassessment and change of the price discount.

## Methods

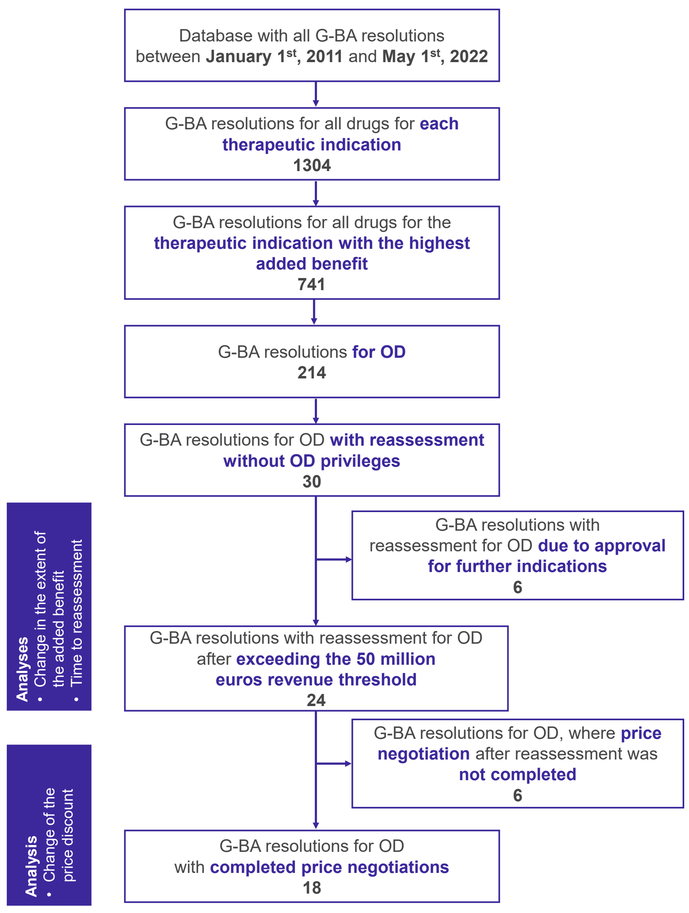
- A database containing all assessed AMNOG dossiers published on the G-BA website (https://www.g-ba.de) from January 1st, 2011 to May 1st, 2022 was screened.
- All ODs that underwent a reassessment were extracted.
- Information on the time to reassessment and the change in the extent of the additional medical benefit were retrieved.
- The change of the price discount was calculated using a database for pharmacies (Lauer Taxe) which allows a comparison of the price of the OD before and after the reassessment.
- If the G-BA assessed more than one subpopulation within the label population, the subpopulation with the highest extent of additional medical benefit was considered.

## Conclusions

- Only one fourth of reassessments resulted in an upgraded additional medical benefit.
- There seems to be a correlation between a shorter time to reassessment and the likelihood of receiving an upgrade in the additional medical benefit.
- In general, the price discount after reassessment is higher compared to the one after the initial assessment, except for drugs with an upgraded additional medical benefit.
- In light of a possible lowering of the revenue threshold as trigger for a standard assessment, companies launching drugs likely to exceed this threshold should be aware of the potential impact of reassessment.
- OD companies should seek early advice from the G-BA (including the ACT) on an appropriate study design and implement it accordingly.

## Results

### Figure 1. Flow diagram of the database search and selection process for data inclusion in the analysis



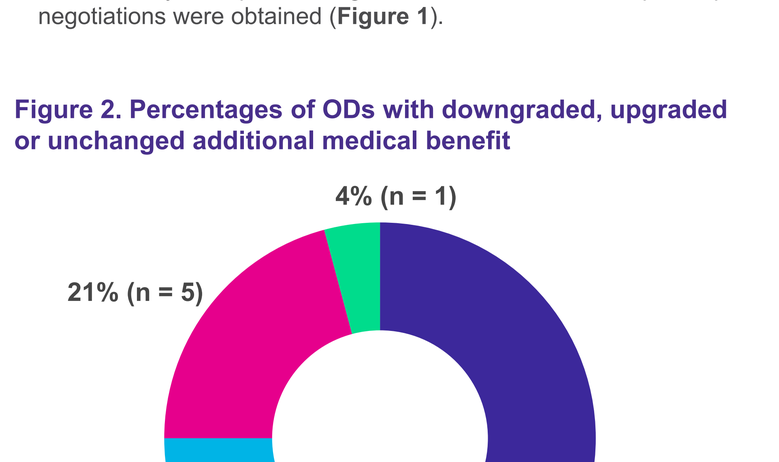

- Of the 1304 assessed subgroups within 741 published resolutions, 214 resolutions for ODs were identified (**Figure 1**).
- After excluding drugs with a reassessment due to indication extension, 24 resolutions were considered relevant (**Figure 1**).
- For the analysis of price changes 18 resolutions with completed price negotiations were obtained (**Figure 1**).

### Figure 2. Percentages of ODs with downgraded, upgraded or unchanged additional medical benefit



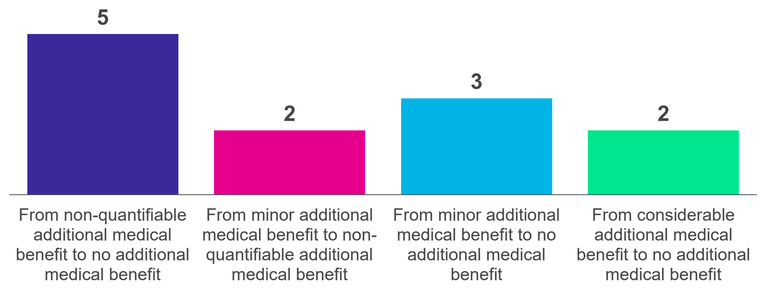

- The majority (50 %) of reassessments resulted in a downgraded additional medical benefit (**Figure 2**).
- The distribution of reassessment outcomes that remained unchanged or were upgraded were similar (21 % and 25 %, **Figure 2**).

### Figure 3. Direction of the upgrade




- The majority of the ODs were upgraded from non-quantifiable additional medical benefit to considerable additional medical benefit (**Figure 3**).

### Figure 4. Direction of the downgrade



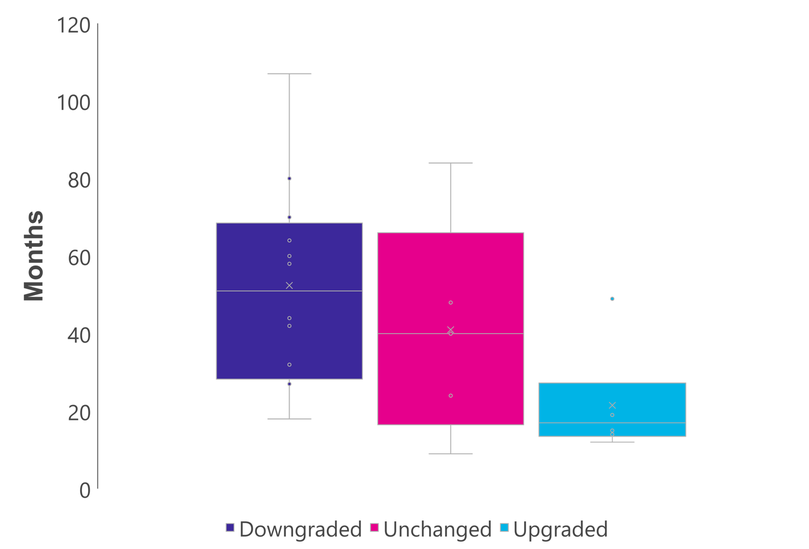

- The majority of the ODs were downgraded from non-quantifiable additional medical benefit to no additional medical benefit (**Figure 4**).

### Table 2. Reasons for the downgrade

| Reason for a downgrade (multiple reasons possible) | n/N (%) |
|---|---|
| Study comparator does not meet the ACT named by G-BA | 6/12 (50 %) |
| Incorrect presentation of study data | 6/12 (50 %) |
| No direct comparative evidence | 5/12 (42 %) |
| Study duration too short | 3/12 (25 %) |
| Incompleteness of content | 3/12 (25 %) |
| Inadequate use of indirect and historical comparisons | 2/12 (17 %) |
| Study population does not represent the label population | 1/12 (8 %) |

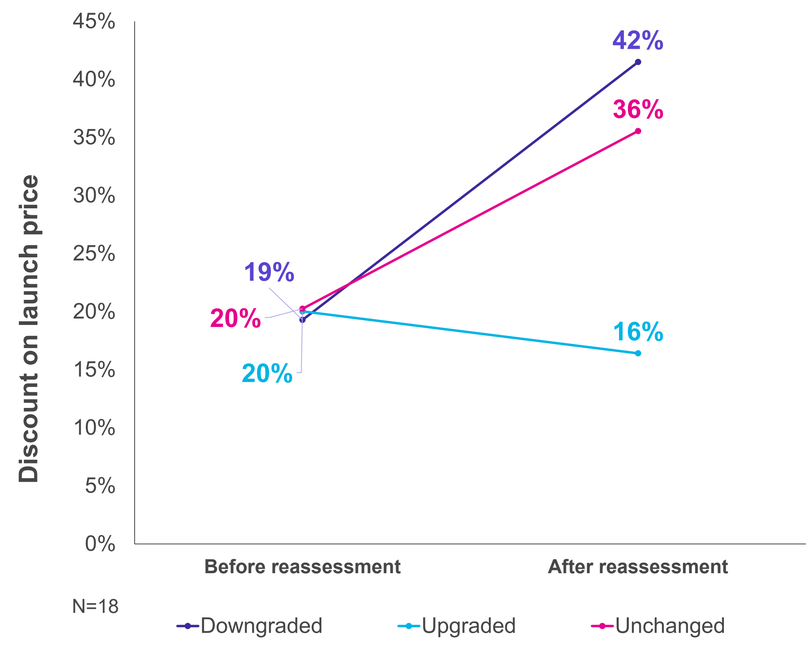
- As the reasons for an upgrade are based on presenting new evidence and the reasons for downgrading are method related, it was decided to focus on the latter.
- The main reason for a downgrade after the reassessment was due to an incorrect study design including a failure to meet the appointed ACT by G-BA (**Table 2**).

### Figure 5. Average time to reassessment




- The average time to reassessment was 52 months for drugs with a downgraded additional medical benefit after reassessment and 41 months for drugs without changes in the additional medical benefit (**Figure 5**).
- The average time to reassessment for drugs with an upgrade in the additional medical benefit was 22 months (**Figure 5**).

### Figure 6. Average discount on launch price




- The average discount on the launch price increased from 19% to 42% for drugs with a downgrade in the additional medical benefit after reassessment and from 20% to 36% for drugs with an unchanged additional medical benefit (**Figure 6**).
- The average discount on the launch price decreased from 20% to 16% for drugs with an upgrade in the additional medical benefit. (**Figure 6**).

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