Recent Landscape of Drug Re-Assessments by G-BA – What Is the Impact of New Evidence on the Benefit Assessment Outcome?

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Lach K, Meletiche D, **Smith N** | Maple Health Group, LLC, New York, NY, USA

CONCLUSIONS

- Manufacturers largely rely on **clinical data** in their **submissions** during **G-BA re-assessments**; however, **real-world evidence** (RWE) and **indirect treatment comparisons** (ITC) can also impact the outcome of re-assessments. Manufacturers could **leverage** such study approaches to increase the likelihood of a **higher added benefit** rating in the **re-assessments** of their drugs.

INTRODUCTION

- German Federal Joint Committee (G-BA) regularly conducts re-assessments of drugs following the decision expiry or upon new data. We examined recent G-BA re-assessments to identify key drivers of the benefit re-assessment outcome, focusing on new evidence submitted by manufacturers.

METHODS

- We identified G-BA re-assessments from January 2022 to June 2023 and analyzed added benefit ratings together with data package submitted to glean insights on key drivers of re-assessment outcomes.

RESULTS

- G-BA re-assessed 16 drugs, 11 drugs in the oncology area; six drugs received orphan drug designation.
- Added benefit rating did not change after re-assessments of 12 drugs; increased for three drugs, and decreased for another one.

RESULTS (*continued*)

- New data was submitted for re-assessments of 12 drugs.
- Three drugs improved their added benefit ratings in G-BA re-assessments. Mature randomized controlled trial (RCT) data, additional RCT, a meta-analysis of RCT, single-arm registries, and natural history studies were used as part of the new data package. Positive impact on overall survival, high magnitude of effect size, availability of long-term data, contextualization of single-arm data with historical comparisons, as well as rarity and severity of disease leading to acceptance of ITC were identified as key decision drivers **(Table 1).**
- Absence of a comparator arm in submitted new studies or their insufficient follow-up time were among the reasons for no improvement in re-assessment outcomes.
- The use of RWE in re-assessments was limited (five drugs) but appeared to contribute to improved re-assessment outcome for cerliponase alfa, together with the ITC and availability of long-term survival data. Designing RWE without adhering to G-BA's criteria of comparative evidence vs. appropriate comparator therapy and sufficient follow-up time was potentially a missed opportunity in drug re-assessments without a positive outcome.

TABLE 1. G-BA RE-ASSESSMENTS FOR DRUGS WITH NEW DATA SUBMITTED (January 2022 – June 2023)

PRODUCT	INDICATION	RE-ASSESSMENT			
		NEW DATA	USE OF RWE	OUTCOME	KEY DECISION DRIVERS
Cerliponase alfa	Neuronal ceroid lipofuscinosis type 2	• Additional single-arm trial • Non-interventional observational study • Natural history external control data (local registry) • Compassionate Use Program data • Indirect comparisons (ITCs)	✓	Non-quantifiable → Major added benefit	• Advantages in overall survival vs. historical comparison with high magnitude of effect size • Rarity and severity of disease (ITC accepted) • Availability of long-term data
Olaparib	Ovarian cancer	• Final RCT data cut	×	No added benefit → considerable	• Advantage in overall survival
Abemaciclib	Breast cancer	• New RCT • Meta-analysis of new and previously submitted RCT	×	No added benefit → minor	• Advantage in overall survival
Vandetanib	Medullary thyroid carcinoma	• Post-authorization safety study	✓	Minor → no added benefit	• Absence of a comparator arm
Voretigen Neparvovec	Hereditary retinal dystrophy	• Final RCT data cut • Single-arm registry study (G-BA mandated)	✓	Considerable	• Insufficient follow-up time of the registry study
Idebenone	Leber hereditary optic neuropathy	• Two retrospective case series used as historical external control	✓	Non-quantifiable	• Absence of a comparator arm
Lumacaftor/ Ivacaftor	Cystic fibrosis	• New RCT with single-arm extension • Two single-arm comparator cohorts	✓	Non-quantifiable	• Absence of a comparator arm
Abemaciclib	Breast cancer	• Meta-analysis of two previously submitted RCTs	×	No/minor added benefit*	• No impact of new data on drug advantages in mortality, morbidity, health-related quality of life or safety
Daratumumab	Multiple myeloma	• Final RCT data cut	×	No/considerable added benefit*	
Pertuzumab	Early breast cancer	• Final RCT data cut	×	Minor added benefit	
Pertuzumab/ Trastuzumab	Early breast cancer	• Final RCT data cut	×	Minor added benefit	
Palbociclib	Breast cancer	• New RCT • Meta-analysis of new and previously submitted RCT	×	No added benefit	

BENEFIT RATING AFTER RE-ASSESSMENT: IMPROVED | NO DIFFERENCE | DECREASED

* Two subpopulations

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