PRMA Insights Focus:
Pricing and Reimbursement Success in Germany under AMNOG

This PRMA Insights Focus report provides in-depth analysis of the evidentiary and methodological issues of benefit assessment and price negotiation in Germany, and highlights key success factors to improve the likelihood of a favorable assessment to support premium pricing, impacting market access in Germany and beyond.
Market access success

Market access in Germany has become significantly more challenging since the AMNOG legislation was introduced. Even though the outcome of benefit assessment is a key driver of price negotiations, manufacturers have not always prepared dossiers adequately, compromising the outcome of the assessment and subsequent price that is agreed. In some cases, manufacturers have withdrawn from the German market in the face of substantial rebates. Lower prices in Germany will have a ripple effect across Europe and beyond, particularly in countries that use reference pricing, with implications for strategy and launch sequence.

This PRMA Insights Focus report provides in-depth analysis and understanding of the evidentiary requirements and benefit assessment process, and sets out practical recommendations and key success factors for manufacturers to ensure adequate preparation and likelihood of success.
Introduction

The benefit assessment process that was introduced as part of the AMNOG legislation in 2011 has presented manufacturers with many new market access challenges. The methodological and evidentiary requirements are stringent, and preparation of the dossier is a time-consuming and expensive task: our experts liken it to preparing the EMA submission dossier, at a likely cost of €300,000–600,000 for dossiers of 400–600 pages and up to €1 mn for a large dossier.

Analysis of the first 3 years of benefit assessment indicates that many manufacturers have not clearly understood – or met – the requirements in terms of the appropriate comparator, patient subgroups, acceptable endpoints, and methodology. Of 62 benefit assessments finalized to date, considering 113 subgroups, a resolution of “no additional benefit proven” was returned on 71 (63%); however, this was for technical reasons in the majority of cases: the dossier was incomplete in 23 (32%), the evidence was considered inappropriate by the G-BA in 27 (38%), and the appropriate comparator was not considered in 14 (20%).

Clearly this has major implications for pricing, given that the G-BA’s decision on the extent of additional benefit relative to the appropriate comparator is a key factor in the pricing negotiation – and a poor benefit assessment result will severely compromise the final reimbursed price that can be achieved. Indeed, manufacturers have seen some substantial cuts in price.

Lower prices in Germany will have a ripple effect across Europe and beyond, particularly in countries that reference price Germany. This has significant implications for strategic decisions about launch sequencing – whereas Germany has long been considered a key market in which to launch early, this may no longer be the case.
Key facts

A decision of “no additional benefit proven” was returned for 63% of the 113 subgroups considered in 62 benefit assessments to date.

However, the decision of “no additional benefit proven” was for technical reasons in 90% of cases, not because the drug did not provide additional benefit.

Based on 113 subgroups in 62 benefit assessments completed to 31 October 2013

This PRMA Insights Focus report provides in-depth analysis and understanding of the evidentiary requirements and benefit assessment process, and sets out practical recommendations and key success factors for manufacturers to ensure adequate preparation and likelihood of success.

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**Benefit assessment results**

- Not proven: 63%
- Significant: 9%
- Marginal: 20%
- Not quantifiable: 7%
- Less than 1%

**Reasons for no additional benefit proven**

- Evidence inappropriate: 38%
- Evidence incomplete: 32%
- Appropriate comparator not considered: 20%
- No benefit shown: 10%

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**PRMA Strategic Insights**

Developed by our in-house experts, PRMA Strategic Insights provide critical advice to manufacturers in planning their market access strategy.

**Key Success Factor**

Crucial factors and practical information that significantly increase the chances of a successful benefit assessment and therefore market access are highlighted.

**Case Study**

Case studies based on individual benefit assessments are used throughout the report to illustrate key points.

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Not all manufacturers have communicated with the G-BA to discuss the technical issues and challenges around preparation of the benefit dossier, or earlier to discuss the clinical trial.

**Example key issues**

**Benefit assessment**
- How will an NCE entering the German market be assessed?
- Are there any circumstances in which manufacturers can claim exemption from benefit assessment?
- What are the processes for orphan drugs? How do these differ from those for other NCEs?
- What information needs to be included in the benefit dossier?
- How are surrogate endpoints considered in the benefit assessment process?
- What can be done if the pivotal trial comparator is not the appropriate comparator defined by the G-BA?
- Will indirect treatment comparison be successful?
- How should manufacturers prepare for subgroup analysis by IQWiG and the G-BA?

**Pricing**
- What can be achieved through arbitration? Is it still worth entering the German market with a low benefit assessment rating?
- Is it always a disadvantage to be included in a reference price group?

**Strategy**
- Can a profitable price still be achieved in Germany?
- How will the price achieved in Germany affect prices elsewhere?
- Is Germany still an optimal early market for launch?

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**Consultation with G-BA prior to dossier submission**

76% Advice sought

- Reassessment 3%
- Other 5%
- Orphan drug 10%
- No/incomplete dossier 6%

Based on 62 submissions completed as at 31 October 2013

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The FAQ section provides a quick reference source of commonly asked questions, focusing on misunderstandings that our experts frequently encounter.

**Question**

What are the key aspects that determine success or failure of pricing negotiations?

**Key points**

Success will be determined by thorough preparations, the additional benefit demonstrated, prices in 15 European reference countries, the prices of the comparators, and, importantly, negotiation skills.

**Further reading**

Section 6.3 (page 121)
Scenario: endpoints were not considered patient relevant

**Drug**
- Perjeta (pertuzumab, Roche)

**General indication**
- Breast cancer, in combination with Herceptin and docetaxel

**Date of resolution**
- 1 October 2013

**Indication (EMA)**
- Adults with HER2-positive metastatic or locally recurrent unresectable breast cancer who have not received previous anti-HER2 therapy or chemotherapy for metastatic disease

**Assessment type**
- New chemical entity

**Subgroups assessed by G-BA**
- HER2-positive mBC with a visceral metastasis
- HER2-positive, locally recurrent, unresectable breast cancer

**Appropriate comparator defined by G-BA**
- Herceptin + a taxane (paclitaxel, docetaxel)
- Radiation therapy

**G-BA resolution**
- a Hint of considerable additional benefit
- b No additional benefit proven (no data provided)
- No additional benefit proven (population was not treated according to standard protocols in Germany)

**Rebate negotiated**
- Not published as at 31 Oct 2013

**HRQL data**
- Not considered because they were based on a non-validated version of the FACT-B, and were defined *post hoc*

**PFS**
- Not considered to be a patient-relevant endpoint but was accepted to support OS as a patient-relevant endpoint

**The appropriate comparator must be used according to German clinical practice**
- PFS is not always accepted as a patient-relevant endpoint; early discussion with the G-BA is recommended

**HRQL data must be generated from validated questionnaires**

**Case studies of the following are included:**
- Adcetris
- Capsalsa
- Eliquis, VTE
- Eliquis, stroke
- Elvanse
- Esbriet
- Fampryra
- Fycompa
- Gilena
- Halaven
- Incivo
- Inlyta
- Jetrea
- Perjeta
- Rapiscan
- Trajenta
- Fampyra
- Fycompa
- Gilena
- Halaven
- Incivo
- Inlyta
- Jetrea
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- Trobalt
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Author profiles

The report has been written by AMNOG experts Monika Behrens and Rachel Bosshard, supported by PRMA Consulting’s extensive cross-functional expertise in developing market access strategies.

**Monika Behrens**

Based in Germany, Monika has more than 15 years’ experience in the pharmaceutical industry and statutory health insurance in Germany. Before joining PRMA Consulting, she was responsible for market access strategy at GlaxoSmithKline in Germany, the UK, and Europe for a broad range of disease areas, including oncology, hematology, neurology, urology, and vaccines. Monika has an in-depth knowledge of the German healthcare system, particularly the AMNOG legislation, through regular attendance at workshops and training seminars, and through practical experience. She holds an MSc in Health Economics from the University of York and is a member of the DGGÖ, bdvb, and ISPOR.

**Dr Rachel Bosshard**

Rachel has experience across a broad range of consultancy work, including systematic literature reviews, HTA reviews, PRO strategies, and development of the GHE strategy for an orphan drug. She also has in-depth knowledge and understanding of the P&R system in Germany and of benefit assessment and AMNOG in particular through practical experience and regular attendance at workshops and seminars. Rachel holds a PhD in Clinical Medicine Research from Imperial College London and an MSc in Natural Sciences from the Swiss Federal Institute of Technology, and has more than 5 years’ research experience in oncology and microbiology, gained in academia and the pharmaceutical industry.

**David Sykes, Founding Partner**

David has more than 15 years’ experience in P&R, market access, and health outcomes and has held senior leadership roles at Lilly and Johnson & Johnson. He has developed European and global P&R and market access programs to quantify, capture, and communicate product value. As PRMA Consulting’s founding partner, David provides leadership and strategic input around the complex issues that manufacturers face in bringing high-value innovative products to market across a broad range of therapy areas, particularly oncology and autoimmune disease.

**Dr Casey Quinn**

Casey has 10 years’ experience in health economics and outcomes research, including economic evaluation, decision analysis, econometrics, and modeling methodologies, and in-depth understanding of the technical and evidentiary for HTA submissions in all the major markets. Casey leads a strong team of HEOR consultants and analysts providing evidence generation across economic modeling and evidence synthesis. Casey has a PhD in Health Economics from the University of York, and has taught economics, health economics, and statistics at universities in Australia, the UK, and the US.

**The report has also been reviewed and validated by an academic with 15 years’ experience in industry and consulting, specializing in healthcare and market access, and the directors and heads of market access of the German affiliates of two top-10 pharma companies, each with more than 15 years’ industry experience.**
The reimbursement price of the product at launch is determined by the manufacturer, and subject for a maximum of 1 year until the benefit assessment and price negotiation are complete. The outcome of the benefit assessment is a key determinant of the price which the price is determined through negotiation with the GKV-Spitzenverband, or inclusion in a reference price group, and also of the delay before price negotiations (the so-called “Lauer Taxe”; page 125) and negotiating prices with manufacturers.

Figure 7.1 illustrates the widespread role that this role that the GKV-Spitzenverband plays in the price negotiation. It has been argued that this widespread role violates the principle of competition, and that this role should be limited to a maximum of 1 year until the benefit assessment and price negotiation are complete.

Therefore, the price negotiations are mandatory if the GKV-Spitzenverband is involved in pricing and reimbursement. As the GKV-Spitzenverband is also a mandatory member of the G-BA, therefore, the price negotiations are mandatory if the GKV-Spitzenverband is involved in pricing and reimbursement.

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