INTRODUCTION
In Germany, with the introduction of the new Arzneimittelmarktneuordnungsgesetz (AMNOG) in 2011, the pricing regulations for newly authorized pharmaceuticals and their reimbursement by statutory health insurance providers has changed.
Now, there are three main stakeholders: the Joint Federal Committee (G-BA), the Institute for Quality and Efficiency in Health Care (IQWiG) and the National Association of Statutory Health Insurance Funds (GKV-SV). G-BA is a committee of the joint self-government of physicians, hospitals and health insurance funds. It evaluates the benefits of pharmaceuticals using a standardized procedure that follows the criteria of evidence-based medicine. IQWiG helps G-BA to fulfill its legal responsibilities by issuing scientific recommendations.\(^1\)

\(^{1}\) The list price of a product is set by the manufacturer upon launch. After negotiations with the GKV-SV, the list price is reduced by the average rebate.

\(^{2}\) The manufacturer has the option to unilaterally withdraw the drug from the market.\(^{1}\)

\(^{3}\) The rebate negotiated with the GKV decreases significantly by 13.1% if any added benefit is determined.\(^{6}\)

\(^{4}\) Linear regression was used to assess the impact of a drug’s added benefit on rebate. Linear regression was used to assess the impact of added benefit in all at least one subgroup of a drug on the extent of the rebate.

\(^{5}\) The positive impact of quality of life, morbidity, and adverse events might be related to the added benefit demonstrated through the use of direct ZVT comparators.

\(^{6}\) All G-BA decisions up to March 2014 were included in the analysis. The dossier submitted by the manufacturer as well as the IQWiG assessment, G-BA decisions and price rebates were reviewed. Information was obtained directly from the G-BA website.\(^{7}\) Where needed, external sources were consulted.\(^{8}\)

\(^{7}\) Under AMNOG, the benefit is assessed for every subgroup identified by IQWiG and G-BA for each product, and the outcome may be different between these subgroups. Hence, assessment outcomes were analyzed by subgroup and not by product, unless otherwise specified. Relative risk calculations as well as discrete logistic regression were used to investigate the relationship of G-BA decisions with product and study characteristics assumed as relevant.\(^9\)

\(^{8}\) As an added benefit is automatically assumed for orphan drugs, the G-BA does not require a relevant scientific assessment by IQWiG. Submissions do not need to provide documents on comparators.

\(^{9}\) The assessment of the added benefit is not associated with the drug’s price level.

\(^{10}\) In 12 out of 13 benefit assessments where IQWiG and G-BA disagreed if added benefit was proven, G-BA concluded an added benefit for 70% (86%), among 40 subgroups with ATC-code L (27 drugs),\(^{11}\). The positive impact of quality of life, morbidity, and adverse events might be related to the added benefit demonstrated through the use of direct ZVT comparators.

\(^{11}\) The benefit of a drug can be assessed if any benefit ranging from not quantifiable to major was considered added benefit. Independent variables:

- Disease area (ATC-code)\(^{5}\)
- Study design of submitted trials (superiority/non-inferiority), comparators used (in/direct; adequate comparator (ZVT) according to GBA)\(^{5}\), surrogate endpoints used (y/n)\(^{5}\)
- Main area of claimed benefit e.g. overall survival (OS), price level (low - very high)\(^{5}\)
- Linear regression was used to assess the impact of a drug’s added benefit on rebate. Linear regression was used to assess the impact of added benefit in all at least one subgroup of a drug on the extent of the rebate.

\(^{2}\) Two to three times as likely if the G-BA accepted evidence on improvements in OS, quality of life, morbidity, or adverse events (p<0.1; 2.2; 3.5; 2.9)\(^{5}\).

\(^{3}\) Out of 68 G-BA decisions (120 subgroups), most drugs belong to ATC-codes L and A (39.7% and 19.1% of all decisions).\(^{1}\) In total, 60.3% of all G-BA drug assessments resulted in an added benefit.\(^{1}\)

\(^{4}\) Among 40 subgroups with ATC-code L (27 drugs), G-BA concluded an added benefit for 70% (86%) with 50% of them demonstrating added benefit in OS. Out of 38 subgroups with ATC-code A (13 drugs), 13% (31%) resulted in added benefit, with 0% demonstrating added benefit in OS.

\(^{5}\) In 12 out of 13 benefit assessments where IQWiG and G-BA disagreed if added benefit was proven, G-BA granted a higher added benefit for the new drug than IQWiG. Even if assessment outcomes were equivalent between IQWiG and G-BA, decisions were sometimes substantiated differently.

\(^{6}\) Manufacturers presented surrogate endpoints in 21 submissions (excluding orphan drugs),\(^{1}\) which were accepted by IQWiG in three cases.

\(^{7}\) Key factors for a positive G-BA benefit assessment are improved OS, morbidity, and adverse events, demonstrated through the use of direct ZVT comparators.

CONCLUSIONS & DISCUSSION
- Key factors for a positive G-BA benefit assessment are improved OS, morbidity, and adverse events, demonstrated through the use of direct ZVT comparators.
- The positive impact of quality of life, morbidity, and adverse events might be related to the added benefit of OS. While univariate analysis has shown that they are significant predictors, multivariate analyses need to be conducted to study more complex associations within the data and test hypothesis.

FOOTNOTES
\(^{1}\) As an added benefit is automatically assumed for orphan drugs, the G-BA does not require a relevant scientific assessment by IQWiG. Submissions do not need to provide documents on comparators.

\(^{2}\) For 27 drugs, no pricing data was available at the time of abstract submission.

\(^{3}\) See also Chance et al. 2014. A comparison of factors influencing reimbursement and coverage decision in Scotland (SMC), the Netherlands (ZNT) and Germany (G-BA). ISPOR Poster PHIP 155

\(^{4}\) Added benefit per drug was defined if the IQWiG/G-BA assessed an added benefit in at least one subgroup.

\(^{5}\) ATC codes: A Alimentary tract and metabolism; C Cardiovascular system; J Antiinfectives for systemic use; L Antineoplastic and immunomodulating agents

\(^{6}\) For some subgroups, no data on study design and comparators were available, e.g. in cases where no evidence was submitted, or where G-BA defined subgroups different to the manufacturer.

PREDICTORS OF GERMAN AMNOG DECISIONS AND GKV REBATE NEGOTIATIONS: A DATABASE ANALYSIS
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RESULTS

\(^{1}\) Gemeinsame Bundesauschuss (G-BA), www.g-ba.de, last accessed October 2014.
\(^{2}\) Institute for Quality and Efficiency in Health Care (IQWiG), www.iqwig.de, last accessed October 2014.
\(^{5}\) http://www.Clincialtrials.gov

access through evidence