Use of Real-world Evidence in German AMNOG Applications

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BACKGROUND

- The Statutory Health Insurance (SHI) in Germany covers 90% of the German population, and nearly all healthcare services are covered with only small copayments.
- Therefore, German health insurance claims data constitute an important basis for real-world evidence (RWE) on epidemiology and cost information.
- To counter rising healthcare costs, the Act on the Reform of the Market for Medicinal Products (AMNOG) in Germany came into effect in 2011.
- Since then, at market launch, pharmaceutical companies have to submit a benefit dossier to the Federal Joint Committee (FJC) estimating prevalence, incidence, and annual therapy costs and also proving a medical benefit in terms of mortality, morbidity, and health-related quality of life. All claims and data in those categories must be underpinned with current, high-quality evidence.
- Only if the FJC declares an additional benefit over the selected comparator therapy are pharmaceutical companies entitled to negotiate a reimbursement price on a national level.
- Until now, no analyses on utilization and quality of RWE in German AMNOG assessments and impacts on price discounts have been conducted.

OBJECTIVE

- The aim of this study was to investigate the extent to which RWE was used for estimation of prevalence and incidence in German AMNOG assessments since its introduction 4 years ago and also its impact on benefit ratings and price discounts.

METHODS

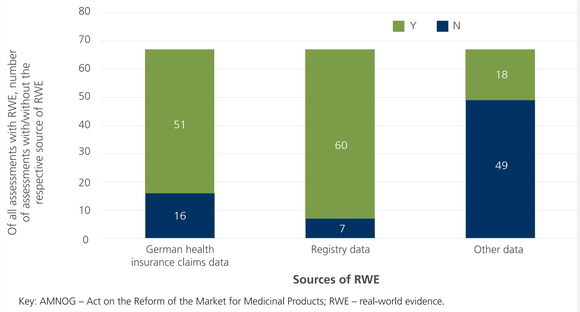
- All German AMNOG processes with published benefit assessments until March 2015 were included.
- They were screened for use of RWE in assessing the prevalence/incidence and structure/size of target populations.
- After description and discussion of methods and data sources used, statistics were applied to explore the potential influence of use and quality of RWE data on benefit ratings and level of price discounts.
- Price discounts were calculated using the official tariff list (Lauertaxe) by computing the change of ex-factory price before and after the end of negotiations.

RESULTS

Types of RWE data

- In total, 134 AMNOG assessments were included in the analyses.
- RWE was incorporated in 50% (n=67) of these dossiers to assess prevalence and incidence, as well as the size of target populations. German health insurance claims data were employed in 16 dossiers (24%), registry data in 7 dossiers (10%), and other data sources like IMS, Delphi panels, Kantar Health, INSIGHT Health, and Megapharm in 49 dossiers (73%). IMS data were included in 42 of these assessments. Multiple data sources were used in 5 dossiers.

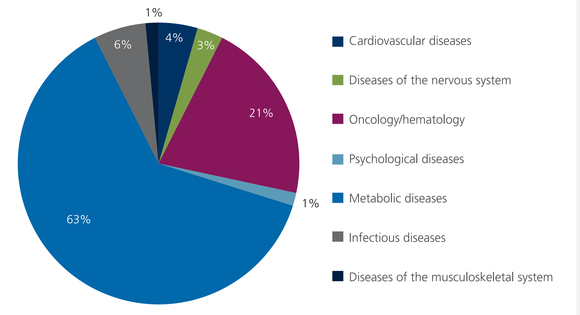
Figure 1. Data Sources of RWE in AMNOG Assessments



Key: AMNOG – Act on the Reform of the Market for Medicinal Products; RWE – real-world evidence.

- RWE was mostly considered in 2 disease areas: metabolic diseases (42 dossiers) and oncology/hematology (14 dossiers).
- German claims data and other data sources also were mainly used for metabolic diseases (8 dossiers and 34 dossiers) and in oncology/hematology (5 dossiers and 6 dossiers, respectively).
- All but 1 registry data analysis was performed in the field of oncology/hematology.

Figure 2. Disease Areas for RWE in AMNOG Assessments



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- The majority of RWE analyses assessed the prevalence of the underlying disease and size and structure of the target population; only a few tried to analyze incidence.
- Prevalence was estimated in 15 of 16 dossiers specifically using German health insurance claims data.
- Registry data, however, were mostly used to assess incidence (6 of 7) but also prevalence (4 of 7).

Assessment of populations

- The regulator will evaluate the RWE data in a dossier and discuss the findings, finally setting epidemiological numbers together with the ruling on clinical efficacy. As potential price negotiation will also factor into budget impact, it is important not to inflate potential patient numbers. Hence, a sound and robust estimate is of paramount importance from the perspective of the pharmaceutical company.
- The SHI target population was accepted as correct in 39% of the AMNOG assessments using RWE, while it was underrated in 31% and overrated in 30%.
- Of all dossiers that included claims data, the target population was accepted in 56% and underrated in 44%.
- None of the German claims data analyses overrated the SHI target population, whereas overestimations were observed in 22% of dossiers not using German claims data.
- The target population was considered by regulators to be overrated in 39% of the assessments that employed other data sources, mostly IMS data (86%).
- Particularly with regard to the following price negotiations, smaller target populations might be of advantage.

Table 1. SHI Target Population – Numbers Stated in the Dossiers Compared to Numbers Stated by the FJC

N=134		Underrated		Accepted as given*		Overrated		Total
		n	%	n	%	n	%	
RWE	Y	21	31%	26	39%	20	30%	67
	N	18	27%	43	64%	6	9%	67
German health insurance claims data	Y	7	44%	9	56%	0	0%	16
	N	32	27%	60	51%	26	22%	118
Registry data	Y	3	43%	3	43%	1	14%	7
	N	36	28%	66	52%	25	20%	127
Other data	Y	15	31%	15	31%	19	39%	49
	N	24	28%	54	64%	7	8%	85

*A margin of ±10% was assumed.

Key: FJC – Federal Joint Committee; SHI – Statutory Health Insurance; RWE – real-world evidence.

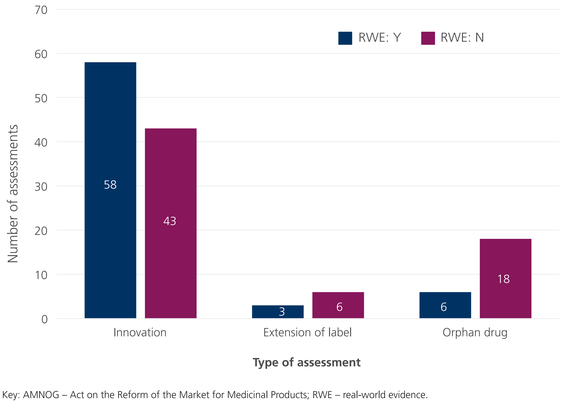
Benefit rating and price discount

- Of all AMNOG assessments using RWE, 36% were declared to prove an additional benefit of the new pharmaceutical over the selected comparator.
- However, a causal relationship between the use and quality of RWE and the benefit rating is equivocal, as the benefit rating mostly depends on clinical evidence. Rather, RWE on incidence and prevalence, as well as size of target populations, is more important for the subsequent price negotiations, as it has influence on the budget impact.
- Price negotiations were completed for 80 AMNOG assessments.
- A *t*-test evaluating the association between the use of RWE and negotiated price discounts indicated that price discounts were lower in assessments that did incorporate RWE data (P=0.049).
- However, the *t*-tests became inconclusive after stratification by data source (claims data, registry data, and other data).

Orphan drugs

- Innovation was the most common objective for submitting a dossier (101 dossiers), while only 9 dossiers aimed at an extension of the label.
- An orphan drug status was present in 24 of 134 dossiers, of which 6 used RWE for assessing target populations and 18 did not.
- In these orphan drug dossiers, RWE in terms of claims data was included in 67% (4 of 6), registry data in 50% (3 of 6), and other data in 16% (1 of 6) of cases.
- In 96% (23 of 24) of the orphan drug dossiers, the target population was underrated or accepted as reported by the company. Application of RWE resulted in only 1 case of underestimation and 5 correct estimates.
- Disease areas for orphan drug dossiers using RWE comprised oncology/hematology (4 of 6), psychological diseases (1 of 6), and cardiovascular diseases (1 of 6).

Figure 3. Use of RWE Stratified by Type of Assessment



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CONCLUSIONS

- German claims data comprise comprehensive information such as demographics, outpatient and inpatient care, prescriptions, devices and aids, incapacity to work, and sick leave payments.
- The routine documentation of diagnoses, procedures, and prescriptions, as well as the ability to evaluate patient histories over longer time periods, is particularly useful for prevalence and incidence analyses. This is of special value regarding the target population and cost estimations, which are of paramount importance in price negotiations following the AMNOG assessment.
- German claims data constitute a reliable and valid data source for assessing epidemiologic evidence in German AMNOG assessments. Indication-specific claims data analyses are a meaningful complement to literature research.
- Additional benefit ratings are most likely driven by clinical evidence, whereas price negotiations depend heavily on estimations of target populations, which should be backed up by valuable real-world evidence.

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