Cancer drugs in Germany: HTA decisions of new and innovative oncology drugs in Germany – an analysis using the Prismaccess® database

Mayer F[1,2], Walzer S[2,3,4], Hodek J-M[1]

[1] University of Applied Sciences Ravensburg-Weingarten, Germany
[2] MArS Market Access & Pricing Strategy GmbH, Weil am Rhein, Germany
[3] State University Baden Wuerttemberg, Loerrach, Germany
[4] Medvance Germany, Weil am Rhein, Germany

The poster is available on www.marketaccess–pricingstrategy.de

Corresponding author:

Dr. Stefan Walzer
MArS Market Access & Pricing Strategy GmbH
Geffelbachstrasse 6
79576 Weil am Rhein, Germany

Contact: stefan.walzer@marketaccess-pricingstrategy.de

OBJECTIVE:

- The German Pharmaceutical Market Restructuring Act (AMNOG) enters its eighth effective year.
- The aim of the law is to disclose the added benefit of a new patented drug over existing therapies by an early assessment, which also serves as the basis for the price negotiation.
- This study is a descriptive analysis of the early benefit assessments for new oncologics in Germany.

METHODS:

- The international HTA database Prismaccess® includes all decisions by market access authorities, among others also from Germany.
- All decisions on therapeutic areas labeled for “oncology” and “cancer” launched in Germany were considered for a systematic analysis.
- Decisions of the German Federal Joint Committee (G-BA) have been extracted and analyzed regarding the extent of the added benefit, subgroups and results of the benefit assessment between January 2011 and May 2018.

RESULTS:

- Out of a total of 335 process, 84 decisions on new oncologics were identified for 43 different drugs.
- 23 of them had been assessed multiple times due to time restrictions and/or new indications. 21 (48,8%) decisions included only one single subgroup.

Table 1: AMNOG benefit assessment in a nutshell

	Total	IQWiG	G–BA
Total	828	452	376
Published	785	450	335
In process	43	2	41
Oncology	217	125	92
Published	208	124	**84**
In process	9	1	8

Table 2: Number of G–BA assessments by the G–BA

2011	2012	2013	2014	2015	2016	2017	2018	Total
0	7	6	9	11	22	18	11	84

- The mostly assessed indication between 2011 and 2018 was non-small cell lung cancer (24 assessments; 29%) followed by melanoma (13 assessments; 15%).

Table 3: Number of assessments according to therapeutic areas

Therapeutic indication	Number
Non-small cell lung cancer	24
Melanoma	13
Breast cancer	7
Prostate cancer	8
Renal cell cancer	7
(metastatic) Colorectal cancer	5
Thyroid tumor	5
Gastric cancer	3
Urothelial carcinoma / urologic tumour	3
Basal cell carcinoma	2
Liposarcoma	1
Malignant gastrointestinal stroma tumour	1
Merkel cell carcinoma	1
Ovarian cancer	2
Soft tissue sarcoma	1
Squamous cell carcinoma of head and neck	1
Total	84

- The specification of the procedures indicates whether it is a new product that is gaining market access in Germany for the first time or whether, for example, it is a new indication or combination. Table 4 shows the number of individual specifications.

Table 4: Specification of assessed products

Specification	Numer
New product	37
New indication	29
New ingredient	8
former orphan – New product	3
New combination	2
New assessment	2
Former orphan – new ingredient	1
Move to existing indication	1
Former orphan	1
Total	84

- Six of the drugs (Bavencio®, Cometriq®, Lartruvo®, Lenvima®, Lynparza®, Zejula®) are approved for the treatment of rare diseases and are therefore orphan drugs. The medicinal products with the specification “former orphan” have already lost their orphan status at the time of data collection and the benefit assessment procedures have been renewed. (Verband Forschender Arzneimittelhersteller (vfa), 2018)
- Each patient subgroup specified in the manufacturer’s dossier was evaluated individually. Thus, the total of 84 AMNOG processes result in 150 subgroups with individual ratings of their added benefit.
- In 41 proceedings only one and in 43 several (2-6) subgroups were evaluated. 54 procedures achieved a so-called pure result. All subgroups thus received either an added benefit (30) or not (24). So there were 30 cases with a mixed result and thus subgroups with and subgroups without added benefit.
- 71% (60/84) of the assessments received an added benefit in at least one subgroup. In all 150 subgroups evaluated, the following were obtained only 43% (64/150) of the added benefit. 4 of the 43 procedures with several subgroups received added benefit in more than one subgroup. Only one subgroup of 41 proceedings and several (2-6) subgroups of 43 proceedings were evaluated.

Table 5: Added benefit results – Extent of the added benefit

Extent of added benefit	Best rated subgroup per assessment	All subgroup assessments
Major	0	0
Considerable	34	35
Minor	17	20
Non-quantifiable	8	9
No added benefit	25	84
Less benefit	0	2
Total	**84**	**150**

- In addition, the added benefit was specified more precisely with the statement as to whether it was a “proof”, an “indication” with medium or a “hint” with little certainty of stating an additional benefit. (Stackelberg et al., 2016, p. 160)

Table 6: Added benefit results according to subgroups – probability of extent of added benefit

Probability of added benefit	Extent of added benefit	Number
Proof	Considerable	1
Proof	Minor	3
Proof	Non-quantifiable	6
Indication	Significant	23
Indication	Minor	8
Indication	Less benefit	1
Hint	Considerable	11
Hint	Minor	9
Hint	Non-quantifiable	3
Hint	Less benefit	1
	No added benefit	84
Total		150

- It is striking that the G-BA did not accept PFS at all as the endpoint for the benefit assessment.
- As a reason for the non-acceptance of the PFS data, the G-BA stated that PFS is regarded as a combined endpoint of the categories mortality and morbidity, that mortality is already covered by OS and that the morbidity component is not symptom-related but exclusively determined by imaging methods.
- The G-BA therefore has different views on the patient relevance of the endpoint PFS and the overall statement on the extent of the additional benefit remains unaffected.
- On the other hand, the endpoint of quality of life is considered to be of particular relevance as 36 cases of valid quality of life data were collected and almost all of them were accepted (34/36).

Table 7: Relevance of different oncology endpoints

Endpoint / Relevance	Mortality (OS)	Morbidity (PFS)	Quality of Life	Adverse Event (AE)	Serious Adverse Event (SAE)	Discontinuation due to AEs
Significant	45	44	15	6	25	22
Accepted by the G–BA	65	0	34	68		

CONCLUSIONS:

- The analysis showed that 43% (64/150) of the defined subgroups reached a positive added benefit in Germany. In most cases 71% (60/84), a drug received an added benefit for at least one subgroup.
- Furthermore, it was shown in a systematic analysis of all oncology assessment in Germany, that PFS is not accepted as a patient-relevant endpoint in Germany.