Resolution

Gemeinsamer Bundesausschuss

of the Federal Joint Committee on an amendment to the Pharmaceuticals Directive (AM-RL): Annex XII – Benefit Assessment of Medicinal Products with New Active Ingredients according to Section 35a SGB V Belantamab mafodotin (multiple myeloma, at least 4 prior therapies, monotherapy)

From 4. March 2021

At its session on 4. March 2021, the Federal Joint Committee (G-BA) resolved to amend the Directive on the Prescription of Medicinal Products in SHI-accredited Medical Care (Pharmaceuticals Directive, AM-RL) in the version dated 18 December 2008/22 January 2009 (Federal Gazette, BAnz. No. 49a of 31 March 2009), as last amended on TT. Monat JJJJ (Federal Gazette, BAnz AT TT.MM.JJJJ BX), as follows:

I. Annex XII shall be amended in alphabetical order to include the active ingredient Belantamab mafodotin as follows:

Belantamab mafodotin

Resolution from: 4. March 2021
Entry intro force on: 4. March 2021
BAnz AT TT. MM JJJJ Bx

Therapeutic indication (according to the marketing authorisation of 25. August 2020):

Blenrep is indicated as monotherapy for the treatment of multiple myeloma in adult patients, who have received at least four prior therapies and whose disease is refractory to at least one proteasome inhibitor, one immunomodulatory agent, and an anti-CD38 monoclonal antibody, and who have demonstrated disease progression on the last therapy.

Therapeutic indication of the resolution (resolution from the 04.03.2021):

see therapeutic indication according to marketing authorisation

1. Extent of the additional benefit and the significance of the evidence

Belantamab mafodotin is authorised as a medicinal product for the treatment of rare diseases in accordance with Regulation (EC) No. 141/2000 of the European Parliament and the Council of 16 December 1999 on orphan drugs. In accordance with section 35a, paragraph 1, sentence 11, 1st half of the sentence German Social Code, Book Five (SGB V), the additional medical benefit is considered to be proven through the grant of the marketing authorisation.

The Federal Joint Committee (G-BA) determines the extent of the additional benefit for the number of patients and patient groups for which there is a therapeutically significant additional benefit in accordance with Chapter 5, Section 12, paragraph 1, number 1, sentence 2 of its Rules of Procedure (VerfO) in conjunction with Section 5, paragraph 8 Ordinance on the Benefit Assessment of Pharmaceuticals (AM-NutzenV), indicating the significance of the evidence. This quantification of the additional benefit is based on the criteria laid out in Chapter 5, Section 5, paragraph 7, numbers 1 to 4 of the Rules of Procedure (VerfO).

Adults with multiple myeloma who have received at least four prior therapies and whose disease is refractory to at least one proteasome inhibitor, one immunomodulatory agent, and an anti-CD38 monoclonal antibody, and who have demonstrated disease progression on the last therapy.

Extend of the additional benefit and significance of the evidence of Belantamab mafodotin:

Hint for a non-quantifiable additional benefit, because the scientific data does not allow a quantification.

Study results according to endpoints:[1]

Adults with multiple myeloma who have received at least four prior therapies and whose disease is refractory to at least one proteasome inhibitor, one immunomodulatory agent, and an anti-CD38 monoclonal antibody, and who have demonstrated disease progression on the last therapy.

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ Risk of bias	Summary
Mortality	n.a.	not assessable
Morbidity	n.a.	not assessable
Health-related quality of life	n.a.	not assessable
Side effects	n.a.	not assessable

Explanations:
↑: statistically significant and relevant positive effect with low/unclear reliability of data
↓: statistically significant and relevant negative effect with low/unclear reliability of data
↑↑: statistically significant and relevant positive effect with high reliability of data
↓↓: statistically significant and relevant negative effect with high reliability of data
↔: no statistically significant or relevant difference
∅: There are no usable data for the benefit assessment.
n.a.: not assessable

[1]Data from the dossier evaluation of the G-BA (published on the 15 December 2020), unless otherwise indicated.

DREAMM-2 study: ongoing, uncontrolled phase II study[2] (data cut-offs from the 31.01.2020)

Mortality

Endpoint	Belantamab mafodotin 2,5 mg/kg body weight	
	N	Median survival time in months [95 %-KI] *Patients with event n (%)*
Overall survival		
	97	13.7 [9.9; -] 48 (49)

Morbidity

There are no suitable data.

Health-related quality of life

There are no suitable data.

Side effects

Endpoint	Belantamab mafodotin 2,5 mg/kg body weight	
	N[1)]	*Patients with event n (%)*
Total adverse events (presented additionally)		
	95	93 (98)
Serious adverse events (SAE)		
	95	40 (42)
Severe adverse events (CTCAE grade 3 or 4)		
	95	80 (84)
Therapy discontinuation because of adverse events		
	95	9 (9)
Adverse Events of special interest (AESI)		
Infusion-related reactions[2)]	95	20 (21)
Thrombocytopenia[3)]	95	36 (38)
Neutropenia	95	14 (15)
Endpoint	**Belantamab mafodotin 2,5 mg/kg body weight**	

[2] The benefit assessment refers to the treatment cohort (n = 97) from DREAMM-2 study, in which belantamab mafodotin was used in an SmPC compliant dosage of 2,5 mg/kg body weight.

	N[1)]	*Patients with event n (%)*
Corneal events		
People with ≥ 1 event on the GSK scale[3]	95	68 (72)
GSK scale grade 1	95	7 (7)
GSK scale grade 2	95	14 (15)
GSK scale grade 3	95	45 (47)
GSK scale grade 4	95	2 (2)
Blurred Vision (CTCAE)[4)]	95	24 (25)
Dry eye (CTCAE)[5)]	95	14 (15)
Keratopathy (CTCAE)[6)]	95	67 (71)
Serious AEs with incidence ≥ 5 % (PT)		
Pneumonia	95	7 (7)
Pyrexia	95	7 (7)
Severe AE (CTCAE ≥ 3) with incidence ≥ 5 % (PT)		
Thrombocytopenia	95	18 (19)
Anaemia	95	20 (21)
Keratopathy	95	28 (29)
Pneumonia	95	7 (7)
Neutropenia	95	5 (5)
Decreased lymphocyte counts	95	12 (13)
Decreased platelet counts	95	5 (5)
Decreased neutrophil counts	95	5 (5)
Hypercalcemia	95	7 (7)

1) Full Safety Set.
2) Reported Preferred Terms: Infusion-related reactions, fever, chills, diarrhoea, nausea, asthenia, hypertension, lethargy, tachycardia.
3) Reported Preferred Terms: Thrombocytopenia, lower platelets count.
4) Reported Preferred Terms: blurred vision, decreased visual acuity, visual impairment, diplopia.
5) Reported Preferred Terms: dry eye, ocular complaints, itchy eyes.
6) Reported Preferred Terms: Keratopathy, Keratitis, deficit in limbal stem cells, ulcerative keratitis.

Abbreviations used:
CTCAE = Common Terminology Criteria for Adverse Events; KG = body weight; CI = confidence interval; N = number of patients evaluated; n = number of patients with (at least one) event

[3] Corneal events were assessed using a classification scale developed by the pharmaceutical company, in addition to the CTCAE survey. This scale includes findings from a ophthalmologic keratoscopy and changes in visual acuity of patients.

2. Number of patients or demarcation of patient groups eligible for treatment

Adults with multiple myeloma, who have received at least four prior therapies and whose disease is refractory to at least one proteasome inhibitor, one immunomodulatory agent, and an anti-CD38 monoclonal antibody, and who have demonstrated disease progression on the last therapy.

Approx. 570 to 1130 patients

3. Requirements for a quality-assured application

The requirements in the product information are to be taken into account. The European Medicines Agency (EMA) provides the contents of the product information (summary of product characteristics, SmPC) for Blenrep (active ingredient: Belantamab mafodotin) at the following publicly accessible link (last access: 14. Dezember 2020):

https://www.ema.europa.eu/en/documents/product-information/blenrep-epar-product-information_de.pdf

Treatment with Belantamab mafodotin should only be initiated and monitored by specialists in internal medicine, haematology and, oncology experienced in the treatment of patients with multiple myeloma.

Under the requirements of the European Medicines Agency (EMA) regarding additional measures to risk minimisation, the pharmaceutical company should provide training materials for all belantamab mafodotin prescribing, dispensing and administering medical professionals as well as patients.

Medical professionals' training material includes a guideline on corneal side effects and a guideline on eye examination. The guideline on corneal side effects contains relevant information on the safety risk of keratopathy or microcystic epithelial changes of the cornea and details on how the safety risks addressed by the risk minimisation measures are minimised by appropriate monitoring. The eye examination guideline contains important information about corneal side effects associated with belantamab mafodotin, how to deal with side effects, and instructions for facilitating communication between the treating physician and the patient's ophthalmologist.

The patient training programme includes a guideline on corneal side effects for patients, a patient pass and a pharmacy card for eye drops.

This medicinal product was authorised under "special conditions". This means that further evidence of the benefit of the medicinal product is anticipated. The European Medicines Agency will evaluate new information on this medicinal product at a minimum once per year and update the product information where necessary.

4. Treatment costs

Annual treatment costs:

Adult patients, who have received at least four prior therapies and whose disease is refractory to at least one proteasome inhibitor, one immunomodulatory agent, and an anti-CD38 monoclonal antibody, and who have demonstrated disease progression on the last therapy.

Designation of the therapy	Annual treatment costs/patient
Belantamab mafodotin	€ 280,794.94

Costs after deduction of statutory rebates (LAUER-TAXE®, as last revised: 15. February 2021)

Costs for additionally required SHI services: not applicable

Other SHI services:

Designation of the therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient/ year	Costs/ patient/ year
Belantamab mafodotin	Surcharge for production of parenteral preparations containing cytostatic agents	€ 81	1	17.4	€ 1,409.40

II. Entry into force

1. The resolution will enter into force on the day of its publication on the internet on the G-BA website on 4. March 2021.

2. The period of validity of the resolution is limited to 1 September 2022.

The justification to this resolution will be published on the website of the G-BA at www.g-ba.de.

Berlin, 4. March 2021

Federal Joint Committee in accordance with Section 91 SGB V

Chair

Prof. Hecken