Resolution

Gemeinsamer Bundesausschuss

of the Federal Joint Committee (G-BA) on an Amendment of the Pharmaceuticals Directive (AM-RL): Annex XII – Benefit Assessment of Medicinal Products with New Active Ingredients According to Section 35a SGB V Caplacizumab (New Therapeutic Indication: Acquired Thrombotic Thrombocytopenic Purpura, 12 to < 18 Years)

of 7 January 2021

On 7 January 2021, the Federal Joint Committee (G-BA) resolved by written statement 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 DD Month YYYY (Federal Gazette, BAnz AT DD MM YYYY BX), as follows:

I. In Annex XII, the following information shall be added after No. 4 to the information on the benefit assessment of caplacizumab in accordance with the resolution of 22 March 2019, last amended on 7 May 2019:

Resolution of: 7. Januar 2021
Entry into force on: 7. Januar 2021
Federal Gazette, BAnz AT DD MM YYYY Bx

New therapeutic indication (according to the marketing authorisation of 9 June 2020):

Cablivi is indicated for the treatment of adults and adolescents of 12 years of age and older weighing at least 40 kg experiencing an episode of acquired thrombotic thrombocytopenic purpura (aTTP), in conjunction with plasma exchange and immunosuppression.

Therapeutic indication of the resolution (resolution of 7 January 2021):

Cablivi is indicated for the treatment of adolescents of 12 years of age and older weighing at least 40 kg experiencing an episode of acquired thrombotic thrombocytopenic purpura (aTTP), in conjunction with plasma exchange and immunosuppression.

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

Caplacizumab is approved as a medicinal product for the treatment of a rare disease 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 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).

<u>Adolescents from 12 to < 18 years weighing at least 40 kg experiencing an episode of acquired thrombotic thrombocytopenic purpura (aTTP)</u>

Extent of the additional benefit and significance of the evidence for caplacizumab:

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

Study results according to endpoints:

Adolescents from 12 to < 18 years weighing at least 40 kg experiencing an episode of acquired thrombotic thrombocytopenic purpura (aTTP)

There is no data that would allow for the assessment of the additional benefit.

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ Risk of bias	Summary
Mortality	∅	There are no suitable data for the benefit assessment.
Morbidity	∅	There are no suitable data for the benefit assessment.
Health-related quality of life	∅	There are no suitable data for the benefit assessment.
Side effects	∅	There are no suitable data for the benefit assessment.
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		

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

Adolescents from 12 to < 18 years weighing at least 40 kg experiencing an episode of acquired thrombotic thrombocytopenic purpura (aTTP)

approx. 2 to 3 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 Cablivi (active ingredient: caplacizumab) at the following publicly accessible link (last access: 8 October 2020):

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

Treatment with caplacizumab should only be initiated and monitored by specialists who are experienced in the therapy of patients with thrombotic microangiopathy. In accordance with EMA guidance on additional risk minimisation measures, a patient information card must be provided by the pharmaceutical company to all patients/caregivers who are expected to use caplacizumab. This patient information card is intended to convey the following primary concern:

- Inform physicians about medical blockade of the von Willebrand factor in order to reduce the risk of a major bleeding episode, especially in an emergency (e.g. an accident).

4. Treatment costs

Annual treatment costs:

Adolescents from 12 to < 18 years weighing at least 40 kg experiencing an episode of acquired thrombotic thrombocytopenic purpura (aTTP)

Designation of the therapy	Annual treatment costs/patient
Caplacizumab	€ 149,661.00 – 277,955.86 [1,2]

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 December 2020

Costs for additionally required SHI services: not applicable

II. The resolution will enter into force with effect from the day of its publication on the internet on the website of the G-BA.

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

Berlin, 7 January 2021

Federal Joint Committee
in accordance with Section 91 SGB V
The Chair

Prof. Hecken

[1] For the lower limit of treatment duration, the median treatment duration with caplacizumab in the double-blind phase of the HERCULES study is used (according to the product information Cablivi® Section 5.1). According to the product information of Cablivi®, the continuation of the daily administration caplacizumab is recommended if signs of residual immunologic disease are present at the end of the 30-day period following completion of daily plasma exchange. In the clinical development program, caplacizumab was administered daily for up to 65 days, which is assumed to be the upper limit of treatment duration.

[2] Caplacizumab is used in combination with plasmapheresis and immunosuppression. Plasmapheresis and immunosuppression are standard therapies for acquired thrombotic thrombocytopenic purpura that are different for each individual patient and are given without the use of caplacizumab. Therefore, only the costs of caplacizumab and not the total treatment costs are presented.