Gemeinsamer Bundesausschuss

Resolution

of the Federal Joint Committee on an Amendment of the Pharmaceuticals Directive:
Annex XII – Benefit Assessment of Medicinal Products with New Active Ingredients according to Section 35a (SGB V)
Midostaurin (reassessment of an orphan drug after exceeding the 30 million euro threshold: systemic mastocytosis)

of 2 May 2024

At its session on 2 May 2024, the Federal Joint Committee (G-BA) resolved to amend the 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 by the publication of the resolution of D Month YYYY (Federal Gazette, BAnz AT DD.MM.YYYY BX), as follows:

I. Annex XII is amended as follows:

1. The information on Midostaurin in the version of the resolution of 5 April 2018 (BAnz AT 24.04.2018 B2) is repealed.

2. In Annex XII, the following information shall be added after No. 4 to the information on the benefit assessment of Midostaurin in the version of the resolution of 2 May 2024 on the therapeutic indication "in combination with standard daunorubicin and cytarabine induction and high-dose cytarabine consolidation chemotherapy, and for patients in complete response followed by Rydapt monotherapy maintenance treatment, for adult patients with newly diagnosed acute myeloid leukaemia (AML) who are FLT3 mutation-positive":

Midostaurin

Resolution of: 2 May 2024
Entry into force on: 2 May 2024
Federal Gazette, BAnz AT DD. MM YYYY Bx

Therapeutic indication (according to the marketing authorisation of 18 September 2017):

Rydapt is indicated as monotherapy for the treatment of adult patients with aggressive systemic mastocytosis (ASM), systemic mastocytosis with associated haematological neoplasm (SM-AHN), or mast cell leukaemia (MCL).

Therapeutic indication of the resolution (resolution of 2 May 2024):

See therapeutic indication according to marketing authorisation.

1. Additional benefit of the medicinal product in relation to the appropriate comparator therapy

Adults with aggressive systemic mastocytosis (ASM), systemic mastocytosis with associated haematological neoplasm (SM-AHN) or mast cell leukaemia (MCL)

Appropriate comparator therapy:

Patient-individual therapy with selection of:

- avapritinib (only for subjects after at least one prior systemic therapy and with platelet counts ≥ 50 x 10^9/l),
- cladribine *and*
- imatinib (only for subjects without KIT D816V mutation or with unknown KIT mutational status and for subjects with existing eosinophilia with FIP1L1-PDGFRA fusion gene),

taking into account the general condition, KIT mutational status and prior therapy

Extent and probability of the additional benefit of midostaurin compared to the appropriate comparator therapy:

An additional benefit is not proven.

Study results according to endpoints:[1]

Adults with aggressive systemic mastocytosis (ASM), systemic mastocytosis with associated haematological neoplasm (SM-AHN) or mast cell leukaemia (MCL)

No adequate data are available to allow an assessment of the additional benefit.

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	n.a.	There are no assessable data.
Morbidity	n.a.	There are no assessable data.
Health-related quality of life	n.a.	There are no assessable data.
Side effects	n.a.	There are no assessable data.
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 ∅: No data available. n.a.: not assessable		

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

Adults with aggressive systemic mastocytosis (ASM), systemic mastocytosis with associated haematological neoplasm (SM-AHN) or mast cell leukaemia (MCL)

Approx. 300 to 400 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 Rydapt (active ingredient: midostaurin) at the following publicly accessible link (last access: 25 March 2024):

https://www.ema.europa.eu/en/documents/product-information/rydapt-epar-product-information_en.pdf

Treatment with midostaurin should only be initiated and monitored by specialists in internal medicine, haematology and oncology experienced in the treatment of patients with

1 Data from the dossier assessment of the Institute for Quality and Efficiency in Health Care (IQWiG) (A23-111) unless otherwise indicated.

aggressive systemic mastocytosis, systemic mastocytosis with associated haematological neoplasm and mast cell leukaemia.

4. Treatment costs

Annual treatment costs:

Adults with aggressive systemic mastocytosis (ASM), systemic mastocytosis with associated haematological neoplasm (SM-AHN) or mast cell leukaemia (MCL)

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Midostaurin	€ 393,150.89
Appropriate comparator therapy:	
Avapritinib	€ 234,766.78
Cladribine	€ 10,500.72 - € 21,001.44
Imatinib	€ 2,006.08

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 April 2024)

Other SHI services:

Designation of the therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient/ year	Costs/ patient/ year
Cladribine IV	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	5	15 - 30	€ 1,500 - € 3,000

5. Designation of medicinal products with new active ingredients according to Section 35a, paragraph 3, sentence 4 SGB V that can be used in a combination therapy with the assessed medicinal product

In the context of the designation of medicinal products with new active ingredients pursuant to Section 35a, paragraph 3, sentence 4 SGB V, the following findings are made:

Adults with aggressive systemic mastocytosis (ASM), systemic mastocytosis with associated haematological neoplasm (SM-AHN) or mast cell leukaemia (MCL)

- No designation of medicinal products with new active ingredients that can be used in combination therapy pursuant to Section 35a, paragraph 3, sentence 4 SGB V, as the active ingredient to be assessed is an active ingredient authorised in monotherapy.

II. The resolution will enter into force on the day of its publication on the website of the G-BA on 2 May 2024.

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

Berlin, 2 May 2024

Federal Joint Committee (G-BA)
in accordance with Section 91 SGB V
The Chair

Prof. Hecken