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)
Migalastat (reassessment of an orphan drug after exceeding the EUR 30 million turnover limit (Fabry disease, ≥ 12 years))

of 15 February 2024

At its session on 15 February 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 migalastat in the version of the resolution of 1 December 2016 (BAnz AT 28.12.2016 B3) and of 17 February 2022 (BAnz AT 16.03.2022 B4) is repealed.**

**2. Annex XII shall be amended in alphabetical order to include the active ingredient Migalastat as follows:**

**Migalastat**

Resolution of: 15 February 2024
Entry into force on: 15 February 2024
Federal Gazette, BAnz AT DD. MM YYYY Bx

**Therapeutic indication (according to the marketing authorisation of 23 July 2021):**

Galafold is indicated for long-term treatment of adults and adolescents aged 12 years and older with a confirmed diagnosis of Fabry disease (α-galactosidase A deficiency) and who have an amenable mutation.

**Therapeutic indication of the resolution (resolution of 15 February 2024):**

See therapeutic indication according to marketing authorisation.

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

Adults and adolescents aged 12 years and older with a confirmed diagnosis of Fabry disease (α-galactosidase A deficiency) and who have an amenable mutation

**Appropriate comparator therapy:**

- Agalsidase alfa or agalsidase beta

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

An additional benefit is not proven.

**Study results according to endpoints:**[1]

Adults and adolescents aged 12 years and older with a confirmed diagnosis of Fabry disease (α-galactosidase A deficiency) and who have an amenable mutation

1 Data from the dossier assessment of the IQWiG (A23-88) and from the addendum (A24-10), unless otherwise indicated.

**Summary of results for relevant clinical endpoints**

| Endpoint category | Direction of effect/ risk of bias | Summary |
|---|---|---|
| Mortality | ↔ | No deaths occurred (no comparator data for adolescents aged 12 to < 16 years). |
| Morbidity | ↔ | No relevant differences for the benefit assessment (no comparator data for adolescents aged 12 to < 16 years). |
| Health-related quality of life | ↔ | No relevant differences for the benefit assessment (no comparator data for adolescents aged 12 to < 16 years). |
| Side effects | ↔ | No relevant differences for the benefit assessment (no comparator data for adolescents aged 12 to < 16 years). |
| Explanations:<br>↑: statistically significant and relevant positive effect with low/unclear reliability of data<br>↓: statistically significant and relevant negative effect with low/unclear reliability of data<br>↑↑: statistically significant and relevant positive effect with high reliability of data<br>↓↓: statistically significant and relevant negative effect with high reliability of data<br>↔: no statistically significant or relevant difference<br>∅: No data available.<br>n.a.: not assessable | | |

ATTRACT study: Migalastat vs enzyme replacement therapy

**Mortality**

| Endpoint | Migalastat | | Enzyme replacement therapy[a] | | Migalastat vs enzyme replacement therapy[a] |
|---|---|---|---|---|---|
| | N | Patients with event n (%) | N | Patients with event n (%) | RR [95% CI]; p value[b] |
| Overall mortality | 34 | 0 (0) | 18 | 0 (0) | - |

**Morbidity**

| **Endpoint** | Migalastat | | Enzyme replacement therapy[a] | | Migalastat vs enzyme replacement therapy[a] |
|---|---|---|---|---|---|
| | N | Patients with event n (%) | N | Patients with event n (%) | RR [95% CI]; p value[b] |
| Endpoint on clinical morbidity of Fabry disease (composite endpoint) | No suitable data | | | | |
| Renal morbidity (composite endpoint) | No suitable data | | | | |
| Cardiac morbidity (composite endpoint) | 34 | 2 (6) | 18 | 3 (17) | 0.39 [0.08; 1.96]; 0.254 |
| Symptomatic arrhythmia with need for anti-arrhythmic medication | 34 | 1 (3) | 18 | 1 (6) | n.d. |
| Ventricular tachycardia | 34 | 1 (3) | 18 | 0 (0) | n.d. |
| Cardioversion | 34 | 0 (0) | 18 | 1 (6) | n.d. |
| Heart failure | 34 | 0 (0) | 18 | 1 (6) | n.d. |
| Cerebrovascular morbidity (composite endpoint) | 34 | 0 (0) | 18 | 1 (6) | 0.38 [0.07; 2.06]; 0.261 |
| Stroke | 34 | 0 (0) | 18 | 0 (0) | – |
| Transient ischaemic attack (TIA) | 34 | 0 (0) | 18 | 1 (6) | n.d. |
| Pain (BPI-SF; improvement by 15% compared to month 18) | | | | | |
| Worst pain (item 3) | 34 | 5 (15) | 18 | 3 (17) | 0.87 [0.21; 3.69]; 0.855 |
| Pain intensity (BPI SF items 3-6) (presented additionally) | 34 | 3 (9) | 18 | 3 (17) | 0.53 [0.10; 2.72]; 0.446 |

**Health-related quality of life**

| Endpoint | Migalastat | | Enzyme replacement therapy[a] | | Migalastat vs enzyme replacement therapy[a] |
|---|---|---|---|---|---|
| | N | Patients with event n (%) | N | Patients with event n (%) | RR [95% CI]; p value[b] |
| SF-36v2 (improvement by 15% compared to month 18) | | | | | |
| Physical Component Summary (PCS) score | 34 | 1 (3) | 18 | 2 (11) | 0.32 [0.04; 2.89]; 0.309 |
| Mental Component Summary (MCS) score | 34 | 3 (9) | 18 | 2 (11) | 0.80 [0.13; 4.85]; 0.804 |

**Side effects**

| Endpoint | Migalastat | | Enzyme replacement therapy[a] | | Migalastat vs enzyme replacement therapy[a] |
|---|---|---|---|---|---|
| | N | Patients with event n (%) | N | Patients with event n (%) | RR [95% CI]; p value[b] |
| AEs (presented additionally) | 34 | 32 (94) | 18 | 18 (100) | – |
| SAEs[c] | 34 | 7 (21) | 18 | 7 (39) | 0.59 [0.26; 1.34]; 0.207 |
| Discontinuation due to AEs | 34 | 0 (0) | 18 | 0 (0) | – |
| Infusion-related reactions | No suitable data | | | | |

a. Agalsidase alfa or agalsidase beta

b. Cochran-Mantel-Haenszel method; stratified by sex and urine protein (< 100 mg / 24 h; ≥ 100 mg / 24 h)

c. contain a relevant percentage of events that can be both side effects and symptoms

**Abbreviations**: BPI-SF: Brief Pain Inventory – Short Form; CI: confidence interval; n: number of patients with (at least 1) event; N: number of patients evaluated; RR: relative risk; SD: standard deviation; SE: standard error; SF-36v2: short form-36-item health survey version 2; SAE: serious adverse event; AE: adverse event

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

Adults and adolescents aged 12 years and older with a confirmed diagnosis of Fabry disease (α-galactosidase A deficiency) and who have an amenable mutation

Approx. 20 to 460 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 Galafold (active ingredient: migalastat) at the following publicly accessible link (last access: 23 November 2023):

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

Treatment with migalastat should only be initiated and monitored by specialists who are experienced in the treatment of patients with Fabry disease. Galafold is not indicated for concomitant use with enzyme replacement therapy (ERT).

## 4. Treatment costs

**Annual treatment costs:**

Adults and adolescents aged 12 years and older with a confirmed diagnosis of Fabry disease (α-galactosidase A deficiency) and who have an amenable mutation

| Designation of the therapy | Annual treatment costs/ patient |
|---|---|
| Medicinal product to be assessed: | |
| Migalastat | € 244,639.69 |
| Appropriate comparator therapy: | |
| Agalsidase alfa | € 211,058.67 - € 351,764.45 |
| Agalsidase beta | € 200,261.67 - € 320,304.68 |

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

Costs for additionally required SHI services: not applicable

## 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 and adolescents aged 12 years and older with a confirmed diagnosis of Fabry disease (α-galactosidase A deficiency) and who have an amenable mutation

– No medicinal product with new active ingredients that can be used in a combination therapy and fulfils the requirements of Section 35a, paragraph 3, sentence 4 SGB V.

The designation of combinations exclusively serves the implementation of the combination discount according to Section 130e SGB V between health insurance funds and pharmaceutical companies. The findings made neither restrict the scope of treatment required to fulfil the medical treatment mandate, nor do they make statements about expediency or economic feasibility.

**III. The resolution will enter into force on the day of its publication on the website of the G-BA on 15 February 2024.**

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

Berlin, 15 February 2024

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

Prof. Hecken