**Emicizumab** (new therapeutic indication: moderate haemophilia A, without factor VIII inhibitors, with severe bleeding phenotype)

Resolution of: 17 August 2023/16. November 2023 valid until: unlimited
Entry into force on: 17 August 2023/16. November 2023
Federal Gazette, BAnz AT 12 09 2023 B2/ BAnz AT 19 12 2023 B3

**New therapeutic indication (according to the marketing authorisation of 23 January 2023):**

Hemlibra is indicated for routine prophylaxis of bleeding episodes in patients with haemophilia A (congenital factor VIII deficiency):

- with factor VIII inhibitors
- without factor VIII inhibitors who have
  - severe disease (FVIII < 1%)
  - moderate disease (FVIII ≥ 1% and ≤ 5%) with severe bleeding phenotype.

Hemlibra can be used with all age groups.

**Therapeutic indication of the resolution (resolution of 17 August 2023):**

Emicizumab (Hemlibra) is indicated for routine prophylaxis of bleeding episodes in patients with haemophilia A (congenital factor VIII deficiency) without factor VIII inhibitors who have moderate disease (FVIII ≥ 1% and ≤ 5%) with severe bleeding phenotype in all age groups.

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

Patients with moderate haemophilia A (congenital factor VIII deficiency, FVIII ≥ 1% and ≤ 5%) and a severe bleeding phenotype without factor VIII inhibitors who are eligible for routine prophylaxis

**Appropriate comparator therapy:**

- plasma-derived or recombinant blood coagulation factor VIII preparations used as routine prophylaxis

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

An additional benefit is not proven.

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

Patients with moderate haemophilia A (congenital factor VIII deficiency, FVIII ≥ 1% and ≤ 5%) and a severe bleeding phenotype without factor VIII inhibitors who are eligible for routine prophylaxis

No suitable data versus the appropriate comparator therapy were presented.

**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:<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 | | |

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

Patients with moderate haemophilia A (congenital factor VIII deficiency, FVIII ≥ 1% and ≤ 5%) and a severe bleeding phenotype without factor VIII inhibitors who are eligible for routine prophylaxis

approx. 220 – 240 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 Hemlibra (active ingredient: emicizumab) at the following publicly accessible link (last access: 10 July 2023):

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

[1] Data from the dossier assessment of the Institute for Quality and Efficiency in Health Care (IQWiG) (A23-10) unless otherwise indicated.

Treatment with emicizumab should only be initiated and monitored by specialist doctors experienced in haemophilia treatment.

In accordance with the European Medicines Agency (EMA) requirements regarding additional risk minimisation measures, the pharmaceutical company must provide training material for medical professionals, patients/ carers (patient pass and training material) as well as laboratory personnel. The training material contains specific information on the management of thrombotic microangiopathy and thromboembolism, the use of bypassing preparations and the influence of emicizumab on coagulation tests (risk of misinterpretation).

## 4. Treatment costs

**Annual treatment costs:**

Patients with moderate haemophilia A (congenital factor VIII deficiency, FVIII ≥ 1% and ≤ 5%) and a severe bleeding phenotype without factor VIII inhibitors who are eligible for routine prophylaxis

| Designation of the therapy | Annual treatment costs/ patient | |
|---|---|---|
| Medicinal product to be assessed: | | |
| Emicizumab[2] | Adults | € 384,551.70 - € 410,681.38 |
| | 12 to < 18 years | € 275,719.98 - € 338,927.55 |
| | 6 to < 12 years | € 182,847.56 - € 204,224.15 |
| | < 6 years | € 92,872.42 - € 112,975.85 |
| Appropriate comparator therapy: | | |
| *recombinant blood coagulation factor VIII preparations* | | |
| Damoctogcog alfa pegol | | |
| | Adults | € 191,354.96 - € 268,117.32 |
| | 12 to < 18 years | € 108,480.02 - € 229,903.28 |
| Efmoroctocog alfa | | |
| | Adults | € 187,471.30 - € 312,537.77 |
| | 12 to < 18 years | € 112,162.31 - € 277,940.89 |
| | 6 to < 12 years | € 56,758.23 - € 168,515.56 |
| | < 6 years | € 33,919.45 - € 94,622.97 |
| Lonoctocog alfa | | |
| | Adults | € 130,649.31 - € 472,695.54 |
| | 12 to < 18 years | € 74,518.18 - € 414,026.77 |
| | 6 to < 12 years | € 57,099.04 - € 250,859.34 |
| | < 6 years | € 37,744.08 - € 140,764.69 |
| Moroctocog alfa | | |

[2] The costs represent the continuous administration in the maintenance phase.

| Designation of the therapy | Annual treatment costs/ patient | |
|---|---|---|
| | Adults | € 196,516.29 - € 574,322.03 |
| | 12 to < 18 years | € 111,488.15 - € 489,881.10 |
| | 6 to < 12 years | € 56,309.37 - € 294,693.70 |
| | < 6 years | € 28,718.77 - € 167,186.43 |
| Octocog alfa | | |
| | Adults | € 166,158.24 - € 485,593.85 |
| | 12 to < 18 years | € 94,255.91 - € 414,200.38 |
| | 6 to < 12 years | € 47,610.86 - € 368,102.50 |
| | < 6 years | € 24,291.47 - € 207,429.50 |
| Rurioctocog alfa pegol | | |
| | Adults | € 240,654.52 - € 293,231.11 |
| | 12 to < 18 years | € 138,595.93 - € 258,825.67 |
| Simoctocog alfa | | |
| | Adults | € 141,277.88 - € 413,430.03 |
| | 12 to < 18 years | € 79,921.61 - € 352,657.53 |
| | 6 to < 12 years | € 40,526.10 - € 180,622.08 |
| | < 6 years | € 20,830.17 - € 119,849.58 |
| Turoctocog alfa | | |
| | Adults | € 165,965.42 - € 398,170.94 |
| | 12 to < 18 years | € 94,628.26 - € 351,582.51 |
| | 6 to < 12 years | € 72,787.00 - € 260,590.55 |
| | < 6 years | € 48,039.82 - € 141,218.25 |
| Turoctocog alfa pegol | | |
| | Adults | € 274,483.41 |
| | 12 to < 18 years | € 154,327.13 - € 243,957.25 |
| *Human plasma-derived preparations* | | |
| | Adults | € 119,808.78 - € 357,636.13 |
| | 12 to < 18 years | € 68,300.47 - € 305,578.00 |
| | 6 to < 12 years | € 34,714.93 - € 179,663.95 |
| | < 6 years | € 17,921.54 - € 102,422.65 |

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 1 August 2023)

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:

Patients with moderate haemophilia A (congenital factor VIII deficiency, FVIII ≥ 1% and ≤ 5%) and a severe bleeding phenotype without factor VIII inhibitors who are eligible for routine prophylaxis

No medicinal product with new active ingredients that can be used in a combination therapy that 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.