Gemeinsamer Bundesausschuss

**Bictegravir/ emtricitabine/ tenofovir alafenamide** (new therapeutic indication: HIV-1 infection, 2 to < 18 years)

Resolution of: 15 June 2023 Valid until: unlimited

Entry into force on: 15 June 2023

Federal Gazette, BAnz AT 18 07 2023 B4

**New therapeutic indication (according to the marketing authorisation of 21 November 2022):**

Biktarvy is indicated for the treatment of human immunodeficiency virus-1 (HIV-1) infection in adults and paediatric patients at least 2 years of age and weighing at least 14 kg without present or past evidence of viral resistance to the integrase inhibitor class, emtricitabine or tenofovir.

**Therapeutic indication of the resolution (resolution of 15 June 2023):**

Biktarvy is indicated for the treatment of human immunodeficiency virus-1 (HIV-1) infection in paediatric patients aged 2 to < 18 years and weighing at least 14 kg g without present or past evidence of viral resistance to the integrase inhibitor class, emtricitabine or tenofovir.

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

a) Therapy naive children with HIV-1 infection aged 2 to < 6 years without past or present evidence of viral resistance to the integrase inhibitor class, emtricitabine or tenofovir

**Appropriate comparator therapy:**

Abacavir + lamivudine or abacavir + emtricitabine, in each case in combination with

- dolutegravir or
- lopinavir/ ritonavir or
- raltegravir or
- nevirapine or
- atazanavir + ritonavir or
- darunavir + ritonavir

**Extent and probability of the additional benefit of bictegravir/ emtricitabine/ tenofovir alafenamide compared to the appropriate comparator therapy:**

An additional benefit is not proven.

b) Therapy naive children with HIV-1 infection aged 6 to < 12 years without past or present evidence of viral resistance to the integrase inhibitor class, emtricitabine or tenofovir

**Appropriate comparator therapy:**

Abacavir + lamivudine or abacavir + emtricitabine, in each case in combination with

- dolutegravir or
- atazanavir + ritonavir or
- darunavir + ritonavir

**Extent and probability of the additional benefit of bictegravir/ emtricitabine/ tenofovir alafenamide compared to the appropriate comparator therapy:**

An additional benefit is not proven.

c) Therapy naive adolescents with HIV-1 infection aged 12 to < 18 years without past or present evidence of viral resistance to the integrase inhibitor class, emtricitabine or tenofovir

**Appropriate comparator therapy:**

Tenofovir alafenamide + emtricitabine or abacavir + lamivudine or abacavir + emtricitabine, each in combination with

- dolutegravir or
- atazanavir + ritonavir or
- darunavir + ritonavir or
- elvitegravir/ cobicistat

**Extent and probability of the additional benefit of bictegravir/ emtricitabine/ tenofovir alafenamide compared to the appropriate comparator therapy:**

An additional benefit is not proven.

d) Therapy experienced children and adolescents with HIV-1 infection aged 2 to < 18 years without past or present evidence of viral resistance to the integrase inhibitor class, emtricitabine or tenofovir

**Appropriate comparator therapy:**

A patient-individual antiretroviral therapy using a selection of approved active ingredients; taking into account the previous therapy/ therapies and the reason for the change of therapy, in particular, therapy failure because of virological failure and the possible associated development of resistance or because of side effects.

**Extent and probability of the additional benefit of bictegravir/ emtricitabine/ tenofovir alafenamide compared to the appropriate comparator therapy:**

An additional benefit is not proven.

**Study results according to endpoints:**

a) Therapy naive children with HIV-1 infection aged 2 to < 6 years without past or present evidence of viral resistance to the integrase inhibitor class, emtricitabine or tenofovir

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 | ∅ | No data available. |
| 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
∅: There are no usable data for the benefit assessment.
n.a.: not assessable

b) Therapy naive children with HIV-1 infection aged 6 to < 12 years without past or present evidence of viral resistance to the integrase inhibitor class, emtricitabine or tenofovir

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 | ∅ | No data available. |
| 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>∅: There are no usable data for the benefit assessment.<br>n.a.: not assessable | | |

c) Therapy naive adolescents with HIV-1 infection aged 12 to < 18 years without past or present evidence of viral resistance to the integrase inhibitor class, emtricitabine or tenofovir

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 | ∅ | No data available. |
| 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>∅: There are no usable data for the benefit assessment.<br>n.a.: not assessable | | |

d) Therapy experienced children and adolescents with HIV-1 infection aged 2 to < 18 years without past or present evidence of viral resistance to the integrase inhibitor class, emtricitabine or tenofovir

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 | ∅ | No data available. |
| 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
∅: 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

a) Therapy naive children with HIV-1 infection aged 2 to < 6 years without past or present evidence of viral resistance to the integrase inhibitor class, emtricitabine or tenofovir

approx. 2 patients

b) Therapy naive children with HIV-1 infection aged 6 to < 12 years without past or present evidence of viral resistance to the integrase inhibitor class, emtricitabine or tenofovir

approx. 10 patients

c) Therapy naive adolescents with HIV-1 infection aged 12 to < 18 years without past or present evidence of viral resistance to the integrase inhibitor class, emtricitabine or tenofovir

approx. 22 patients

d) Therapy experienced children and adolescents with HIV-1 infection aged 2 to < 18 years without past or present evidence of viral resistance to the integrase inhibitor class, emtricitabine or tenofovir

approx. 150 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 Biktarvy (active ingredient: bictegravir/ emtricitabine/ tenofovir alafenamide) at the following publicly accessible link (last access: 28 February 2023):

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

Treatment with bictegravir/ emtricitabine/ tenofovir alafenamide should only be initiated and monitored by doctors experienced in treating patients with HIV-1.

## 4. Treatment costs

**Annual treatment costs:**

a) Therapy naive children with HIV-1 infection aged 2 to < 6 years without past or present evidence of viral resistance to the integrase inhibitor class, emtricitabine or tenofovir

| Designation of the therapy | Annual treatment costs/ patient |
|---|---|
| Medicinal product to be assessed: | |
| Bictegravir/ emtricitabine/ tenofovir alafenamide 30 mg/ 120 mg/ 15 mg | € 10171.94 |
| Appropriate comparator therapy: | |
| Abacavir + emtricitabine + atazanavir + ritonavir | € 11,460.39 - € 14,799.59 |
| Abacavir + emtricitabine + darunavir + ritonavir | € 8,541.59[1] |
| Abacavir + emtricitabine + dolutegravir | € 7,802.18 - € 10,187.70 |
| Abacavir + emtricitabine + lopinavir/ ritonavir | € 6,130.18 - € 9,192.35 |
| Abacavir + emtricitabine + nevirapine | € 6,772.58 - € 9,903.18 |
| Abacavir + emtricitabine + raltegravir | € 6,121.17 - € 8,926.08 |
| Abacavir + lamivudine + atazanavir + ritonavir | € 11,194.76 -€ 14,490.21 |
| Abacavir + lamivudine + darunavir + ritonavir | € 8,232.20[1] |
| Abacavir + lamivudine + dolutegravir | € 7,536.55 - € 9,878.31 |
| Abacavir + lamivudine + lopinavir/ ritonavir | € 5,864.55 - € 8,882.97 |
| Abacavir + lamivudine + nevirapine | € 6,506.95 - € 9,593.80 |
| Abacavir + lamivudine + raltegravir | € 5,855.54 - € 8,616.69 |

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 May 2023)

[1] According to the product information, darunavir is approved for children weighing 15 kg or more. The indicated annual treatment costs for the combinations with darunavir represent the dosage of darunavir for children weighing 15 to 30 kg.

Costs for additionally required SHI services: not applicable

b) Therapy naive children with HIV-1 infection aged 6 to < 12 years without past or present evidence of viral resistance to the integrase inhibitor class, emtricitabine or tenofovir

| Designation of the therapy | Annual treatment costs/ patient |
|---|---|
| Medicinal product to be assessed: | |
| Bictegravir/ emtricitabine/ tenofovir alafenamide 30 mg/ 120 mg/ 15 mg | € 10,171.94 |
| Bictegravir/ emtricitabine/ tenofovir alafenamide 50 mg/ 200 mg/ 25 mg | € 9,945.11 |
| Appropriate comparator therapy: | |
| Abacavir + emtricitabine + dolutegravir | € 14,808.72 - € 16,735.49 |
| Abacavir + emtricitabine + atazanavir + ritonavir | € 9,840.42 - € 13,341.41 |
| Abacavir + emtricitabine + darunavir + ritonavir | € 9,894.64 - € 12,648.83 |
| Abacavir + lamivudine + dolutegravir | € 9,050.70 - € 14,143.10 |
| Abacavir + lamivudine + atazanavir + ritonavir | € 5,656.65 - € 9,174.80 |
| Abacavir + lamivudine + darunavir + ritonavir | € 4,964.04 - € 9,229.02 |

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 May 2023)

Costs for additionally required SHI services: not applicable

c) Therapy naive adolescents with HIV-1 infection aged 12 to < 18 years without past or present evidence of viral resistance to the integrase inhibitor class, emtricitabine or tenofovir

| Designation of the therapy | Annual treatment costs/ patient |
|---|---|
| Medicinal product to be assessed: | |
| Bictegravir/ emtricitabine/ tenofovir alafenamide 50 mg/200 mg/25 mg | € 9,945.11 |
| Appropriate comparator therapy: | |
| Tenofovir alafenamide + emtricitabine + dolutegravir | € 9,052.45 |
| Tenofovir alafenamide + emtricitabine + atazanavir + ritonavir | € 5,645.50 |
| Tenofovir alafenamide + emtricitabine + darunavir + ritonavir | € 4,952.89 |

| Designation of the therapy | Annual treatment costs/ patient |
|---|---|
| Tenofovir alafenamide/ emtricitabine/ elvitegravir/ cobicistat[2] | € 9,945.11 |
| Abacavir + lamivudine + dolutegravir | € 9,050.70 |
| Abacavir + lamivudine + atazanavir + ritonavir | € 5,656.65 |
| Abacavir + lamivudine + darunavir + ritonavir | € 4,964.04 |
| Abacavir + lamivudine + elvitegravir/ cobicistat[2] | Incalculable |
| Abacavir + emtricitabine + dolutegravir | € 16,735.49 |
| Abacavir + emtricitabine + atazanavir + ritonavir | € 13,341.44 |
| Abacavir + emtricitabine + darunavir + ritonavir | € 12,648.83 |
| Abacavir + emtricitabine + elvitegravir/ cobicistat[2] | Incalculable |

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 May 2023)

Costs for additionally required SHI services: not applicable

d) Therapy experienced children and adolescents with HIV-1 infection aged 2 to < 18 years without past or present evidence of viral resistance to the integrase inhibitor class, emtricitabine or tenofovir

| Designation of the therapy | Annual treatment costs/ patient |
|---|---|
| Medicinal product to be assessed: | |
| Bictegravir/ emtricitabine/ tenofovir alafenamide 50 mg/200 mg/25 mg | € 9,945.11 |
| Appropriate comparator therapy: | |
| Individual antiretroviral therapy[3] | € 2,126.10 - € 34,184.20 |

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 May 2023)

Costs for additionally required SHI services: not applicable

[2] Elvitegravir/ cobicistat is only available as fixed combination with tenofovir alafenamide + emtricitabine on the German market

[3] Because of the different combination options in individual therapy, not all possible variants of combination therapies are presented and considered but the cost range from a cost-effective (emtricitabine/ tenofovir disoproxil + nevirapine) to a cost-intensive therapy (abacavir + emtricitabine + enfuvirtide) is specified as an example.

**5. 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 Bictegravir/ emtricitabine/ tenofovir alafenamide**

Medicinal products with new active ingredients pursuant to Section 35a, paragraph 3, sentence 4 SGB V are medicinal products with the following new active ingredients that can be used in a combination therapy with bictegravir/ emtricitabine/ tenofovir alafenamide for the treatment of HIV-1 infection in paediatric patients aged 2 to < 18 years and weighing at least 14 kg on the basis of the marketing authorisation granted under Medicinal Products Act:

a) Therapy naive children with HIV-1 infection aged 2 to < 6 years without past or present evidence of viral resistance to the integrase inhibitor class, emtricitabine or tenofovir

A designation of the concomitant active ingredients shall be made in a further resolution. The adoption of the resolution will be preceded by a written and oral written statement procedure pursuant to Chapter 5, Section 19 of the Regulation, in the course of which the pharmaceutical companies concerned will be given the opportunity to comment on the planned designation.

b) Therapy naive children with HIV-1 infection aged 6 to < 12 years without past or present evidence of viral resistance to the integrase inhibitor class, emtricitabine or tenofovir

A designation of the concomitant active ingredients shall be made in a further resolution. The adoption of the resolution will be preceded by a written and oral written statement procedure pursuant to Chapter 5, Section 19 of the Regulation, in the course of which the pharmaceutical companies concerned will be given the opportunity to comment on the planned designation.

c) Therapy naive adolescents with HIV-1 infection aged 12 to < 18 years without past or present evidence of viral resistance to the integrase inhibitor class, emtricitabine or tenofovir

A designation of the concomitant active ingredients shall be made in a further resolution. The adoption of the resolution will be preceded by a written and oral written statement procedure pursuant to Chapter 5, Section 19 of the Regulation, in the course of which the pharmaceutical companies concerned will be given the opportunity to comment on the planned designation.

d) Therapy experienced children and adolescents with HIV-1 infection aged 2 to < 18 years without past or present evidence of viral resistance to the integrase inhibitor class, emtricitabine or tenofovir

A designation of the concomitant active ingredients shall be made in a further resolution. The adoption of the resolution will be preceded by a written and oral written statement procedure pursuant to Chapter 5, Section 19 of the Regulation, in the course of which the pharmaceutical companies concerned will be given the opportunity to comment on the planned designation.

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.