Dolutegravir/ abacavir/ lamivudine (new therapeutic indication: HIV infection, ≥ 14 kg to < 12 years)

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 29 09 2023 B4/ BAnz AT 19 12 2023 B4

New therapeutic indication (according to the marketing authorisation of 20 February 2023):

Triumeq is indicated for the treatment of Human Immunodeficiency Virus (HIV) infected children weighing at least 14 kg to less than 25 kg.

Triumeq is indicated for the treatment of Human Immunodeficiency Virus (HIV) infected adults, adolescents and children weighing at least 25 kg.

Before initiating treatment with abacavir-containing products, screening for carriage of the HLAB*5701 allele should be performed in any HIV-infected patient, irrespective of racial origin. Abacavir should not be used in patients known to carry the HLA-B*5701 allele.

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

Triumeq is indicated for the treatment of Human Immunodeficiency Virus (HIV) infected children weighing at least 14 kg to < 12 years.

Before initiating treatment with abacavir-containing products, screening for carriage of the HLAB*5701 allele should be performed in any HIV-infected patient, irrespective of racial origin. Abacavir should not be used in patients known to carry the HLA-B*5701 allele.

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

   a) Therapy naive children with HIV-1 infection ≥ 14 kg to < 6 years

   Appropriate comparator therapy:

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

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

   or dolutegravir + abacavir + emtricitabine

   Extent and probability of the additional benefit of dolutegravir/ abacavir/ lamivudine compared to the appropriate comparator therapy:

An additional benefit is not proven.

b) Therapy naive children with HIV-1 infection ≥ 14 kg from 6 to < 12 years

Appropriate comparator therapy:

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

- atazanavir + ritonavir or
- darunavir + ritonavir

or dolutegravir + abacavir + emtricitabine

Extent and probability of the additional benefit of dolutegravir/ abacavir/ lamivudine compared to the appropriate comparator therapy:

An additional benefit is not proven.

c) Therapy experienced children with HIV-1 infection ≥ 14 kg to < 12 years

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 dolutegravir/ abacavir/ lamivudine 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 ≥ 14 kg to < 6 years

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 ∅: No data available. n.a.: not assessable		

b) Therapy naive children with HIV-1 infection ≥ 14 kg from 6 to < 12 years

No suitable data versus the appropriate comparator therapy were presented.

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c) Therapy experienced children with HIV-1 infection ≥ 14 kg to < 12 years

No suitable data versus the appropriate comparator therapy were presented.

Summary of results for relevant clinical endpoints

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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

a) Therapy naive children with HIV-1 infection ≥ 14 kg to < 6 years

approx. 4 patients

b) Therapy naive children with HIV-1 infection ≥ 14 kg from 6 to < 12 years

approx. 15 patients

c) Therapy experienced children with HIV-1 infection ≥ 14 kg to < 12 years

approx. 67 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 Triumeq (combination of active ingredients: dolutegravir/ abacavir/ lamivudine) at the following publicly accessible link (last access: 16 May 2023):

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

Treatment with dolutegravir/ abacavir/ lamivudine 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 ≥ 14 kg to < 6 years

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Dolutegravir/ abacavir/ lamivudine	€ 9,791.53 - € 11,749.84
Appropriate comparator therapy:	
Base therapy	
Abacavir	€ 1,999.47 - € 2,832.58
Emtricitabine	€ 1,603.08 - € 2,315.56
Lamivudine	€ 1,337.45 - € 2,006.18
Abacavir + emtricitabine	€ 3,602.55 - € 5,148.14
Abacavir + lamivudine	€ 3,336.92 - € 4,838.76
Concomitant active ingredient:	
Atazanavir	€ 7,638.23 - € 9,547.79[1]
Ritonavir	€ 413.50 - € 722.70
Darunavir	€ 2,977.63[1]
Lopinavir/ ritonavir	€ 2,629.37 - € 4,319.68
Nevirapine	€ 3,170.03 - € 4,755.04
Raltegravir	€ 2,518.62 - € 3,777.93
Dolutegravir	€ 4,199.63 - € 5,039.56
Total	
Abacavir + emtricitabine + atazanavir + ritonavir	€ 11,963.48 - € 15,418.63
Abacavir + emtricitabine + darunavir + ritonavir	€ 8,539.28
Abacavir + emtricitabine + lopinavir/ ritonavir	€ 6,231.92 - € 9,467.82
Abacavir + emtricitabine + nevirapine	€ 6,772.58 - € 9,903.18
Abacavir + emtricitabine + raltegravir	€ 6,121.17 - € 8,926.08

[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 for children weighing more than 15 kg.

Designation of the therapy	Annual treatment costs/ patient
Abacavir + emtricitabine + dolutegravir	€ 7,802.18 - € 10,187.70
Abacavir + lamivudine + atazanavir + ritonavir	€ 11,697.85 - € 15,109.25
Abacavir + lamivudine + darunavir + ritonavir	€ 8,229.89
Abacavir + lamivudine + lopinavir/ ritonavir	€ 5,966.29 - € 9,158.43
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: 1 August 2023)

Costs for additionally required SHI services: not applicable

b) Therapy naive children with HIV-1 infection ≥ 14 kg from 6 to < 12 years

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Dolutegravir/ abacavir/ lamivudine	€ 11,382.97 - € -11,749.84
Appropriate comparator therapy:	
Base therapy	
Abacavir	€ 3,866.99 - € 5,155.99
Emtricitabine	€ 2,671.80 - € 3,322.11
Lamivudine	€ 2,006.18 - € 2,465.12
Abacavir/ lamivudine	€ 743.18[2]
Abacavir + emtricitabine	€ 6,538.79 - € 8,478.10
Abacavir + lamivudine	€ 743.18 [2] - € 5,873.17
Concomitant active ingredient:	
Atazanavir	€ 2,923.29 - € 4,337.78
Ritonavir	€ 413.50
Darunavir	€ 2,977.63 - € 3,805.04
Dolutegravir	€ 8,307.52
Total:	
Abacavir + emtricitabine + atazanavir + ritonavir	€ 9,875.58 - € 13,229.93
Abacavir + emtricitabine + darunavir + ritonavir	€ 9,929.93 - € 12,696.65
Abacavir + emtricitabine + dolutegravir	€ 14,846.31 - € 16,785.62
Abacavir + lamivudine + atazanavir + ritonavir	€ 5,494.47 - € 9,209.96

[2] Fixed combination of abacavir/ lamivudine not approved for children <25 kg

Designation of the therapy	Annual treatment costs/ patient
Abacavir + lamivudine + darunavir + ritonavir	€ 4,961.73 - € 9,264.30

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

Costs for additionally required SHI services: not applicable

c) Therapy experienced children with HIV-1 infection ≥ 14 kg to < 12 years

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Dolutegravir/ abacavir/ lamivudine	€ 9,791.53 - € 11,749.84
Appropriate comparator therapy:	
Individual antiretroviral therapy[3]	€ 2,126.10 - € 20,285.85
Lower range	
Abacavir/ lamivudine	€ 743.18
Nevirapine	€ 1,382.92
Abacavir/ lamivudine + nevirapine	€ 2,126.10
Upper range	
Abacavir	€ 5,155.99
Emtricitabine	€ 3,322.11
Maraviroc	€ 11,807.75
Abacavir + emtricitabine + maraviroc	€ 20,285.85

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:

[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 (abacavir/ lamivudine + nevirapine) to a cost-intensive therapy (abacavir + emtricitabine + maraviroc) is specified as an example.

a) Therapy naive children with HIV-1 infection ≥ 14 kg to < 6 years

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.

b) Therapy naive children with HIV-1 infection ≥ 14 kg from 6 to < 12 years

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.

c) Therapy experienced children with HIV-1 infection ≥ 14 kg to < 12 years

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.