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 Duvelisib (chronic lymphocytic leukaemia, after ≥ 2 prior therapies)

of 21 July 2022

At its session on 21 July 2022, 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 shall be amended in alphabetical order to include the active ingredient duvelisib as follows:

Duvelisib

Resolution of: 21 July 2022
Entry into force on: 21 July 2022
Federal Gazette, BAnz AT DD. MM YYYY Bx

Therapeutic indication (according to the marketing authorisation of 19 May 2021):

Copiktra monotherapy is indicated for the treatment of adult patients with:

- relapsed or refractory chronic lymphocytic leukaemia (CLL) after at least two prior therapies.
- follicular lymphoma (FL) that is refractory to at least two prior systemic therapies.

Therapeutic indication of the resolution (resolution of 21 July 2022):

Copiktra monotherapy is indicated for the treatment of adult patients with relapsed or refractory chronic lymphocytic leukaemia (CLL) after at least two prior therapies.

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

a) Adult patients with pretreated CLL who have not yet received a BTK inhibitor and/or BCL2 inhibitor

Appropriate comparator therapy:

- Ibrutinib
  or
- Venetoclax + rituximab
  or
- Chemoimmunotherapy with fludarabine in combination with cyclophosphamide and rituximab (FCR) or bendamustine in combination with rituximab (BR) or chlorambucil in combination with rituximab (ClbR) (only in the case of a long recurrence-free interval and the absence of genetic risk factors)

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

An additional benefit is not proven.

b) Adult patients with relapsed or refractory CLL after a prior therapy with at least one BTK inhibitor

Appropriate comparator therapy:

- Venetoclax + rituximab

Extent and probability of the additional benefit of duvelisib over venetoclax in combination with rituximab:

An additional benefit is not proven.

c) Adult patients with relapsed or refractory CLL after a prior therapy with at least one BCL2 inhibitor

Appropriate comparator therapy:

- Ibrutinib

Extent and probability of the additional benefit of duvelisib compared to ibrutinib:

An additional benefit is not proven.

d) Adult patients with relapsed or refractory CLL after a prior therapy with at least one BTK inhibitor and one BCL2 inhibitor

Appropriate comparator therapy:

- Patient-individual therapy with selection of:
  - idelalisib in combination with rituximab,
  - bendamustine in combination with rituximab,
  - chlorambucil in combination with rituximab and
  - best supportive care;

taking into account comorbidities, general condition, genetic risk factors as well as success and tolerability of prior therapy

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

An additional benefit is not proven.

Study results according to endpoints:

a) Adult patients with pretreated CLL who have not yet received a BTK inhibitor and/or BCL2 inhibitor

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

b) Adult patients with relapsed or refractory CLL after a prior therapy with at least one BTK inhibitor

No 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.
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c) Adult patients with relapsed or refractory CLL after a prior therapy with at least one BCL2 inhibitor

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

Summary of results for relevant clinical endpoints

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d) Adult patients with relapsed or refractory CLL after a prior therapy with at least one BTK inhibitor and one BCL2 inhibitor

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

Summary of results for relevant clinical endpoints

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

a) Adult patients with pretreated CLL who have not yet received a BTK inhibitor and/or BCL2 inhibitor

and

b) Adult patients with relapsed or refractory CLL after a prior therapy with at least one BTK inhibitor

and

c) Adult patients with relapsed or refractory CLL after a prior therapy with at least one BCL2 inhibitor

and

d) Adult patients with relapsed or refractory CLL after a prior therapy with at least one BTK inhibitor and one BCL2 inhibitor

approx. 550 – 2,060 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 Copiktra (active ingredient: duvelisib) at the following publicly accessible link (last access: 7 June 2022):
https://www.ema.europa.eu/en/documents/product-information/copiktra-epar-product-information_en.pdf

Treatment with duvelisib should only be initiated and monitored by specialists in internal medicine, haematology and oncology experienced in the treatment of patients with chronic lymphocytic leukaemia.

No data on the safety and efficacy of duvelisib are available for patients who have received a BCL2, phosphoinositide 3-kinase or Bruton tyrosine kinase inhibitor prior to therapy with duvelisib.

4. Treatment costs

Annual treatment costs:

The annual treatment costs shown refer to the first year of treatment.

a) Adult patients with pretreated chronic lymphocytic leukaemia who have not yet received a BTK inhibitor and/or BCL2 inhibitor

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Duvelisib	€ 68,451.58[1]
Best supportive care	Different from patient to patient
Appropriate comparator therapy:	
Ibrutinib monotherapy	
Ibrutinib	€ 76,273.27
Additionally required SHI costs	€ 11.40
Venetoclax + rituximab	
Venetoclax	€ 72,700.30
Rituximab	€ 19,968.67
Total	€ 92,668.97
Additionally required SHI costs	€ 48.83
Chemoimmunotherapy with FCR or BR or ClbR	
Fludarabine + cyclophosphamide + rituximab (FCR)	
Fludarabine	€ 1,893.84
Cyclophosphamide	€ 220.50
Rituximab	€ 19,968.67
Total	€ 22,083.01
Additionally required SHI costs	€ 48.83
Bendamustine + rituximab (BR)	
Bendamustine	€ 6,143.00
Rituximab	€ 19,968.67
Total	€ 26,111.67
Additionally required SHI costs	€ 48.83
Chlorambucil + rituximab (ClbR)	
Chlorambucil	€ 166.85
Rituximab	€ 19,968.67
Total	€ 20,135.52
Additionally required SHI costs	€ 48.83

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 1 July 2022)

[1] Duvelisib is currently not sold in Germany. LAUER-TAXE® last revised: 15 April 2022

b) Adult patients with relapsed or refractory chronic lymphocytic leukaemia after a prior therapy with at least one BTK inhibitor

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Duvelisib	€ 68,451.58[1]
Best supportive care	Different from patient to patient
Appropriate comparator therapy:	
Venetoclax + rituximab	
Venetoclax	€ 72,700.30
Rituximab	€ 19,968.67
Total	€ 92,668.97
Additionally required SHI costs	€ 48.83

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 1 July 2022)

c) Adult patients with relapsed or refractory chronic lymphocytic leukaemia after a prior therapy with at least one BCL-2 inhibitor

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Duvelisib	€ 68,451.58[1]
Best supportive care	Different from patient to patient
Appropriate comparator therapy:	
Ibrutinib monotherapy	
Ibrutinib	€ 76,273.27
Additionally required SHI costs	€ 11.40

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 1 July 2022)

d) Adult patients with relapsed or refractory chronic lymphocytic leukaemia after a prior therapy with at least one BTK inhibitor and one BCL-2 inhibitor

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Duvelisib	€ 68,451.58[1]
Best supportive care	Different from patient to patient
Appropriate comparator therapy:	
idelalisib in combination with rituximab	
Idelalisib	€ 52,043.65

Designation of the therapy	Annual treatment costs/ patient
Rituximab	€ 26,734.07
Total	€ 78,777.72
Additionally required SHI costs	€ 60.98
Bendamustine in combination with rituximab	
Bendamustine	€ 6,143.00
Rituximab	€ 19,968.67
Total	€ 26,111.67
Additionally required SHI costs	€ 48.83
Chlorambucil in combination with rituximab	
Chlorambucil	€ 166.85
Rituximab	€ 19,968.67
Total	€ 20,135.52
Additionally required SHI costs	€ 48.83
Best supportive care	
Best supportive care	Different from patient to patient

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 1 July 2022)

Other SHI services:

Designation of the therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient/ year	Costs/ patient/ year
Medicinal product to be assessed: Duvelisib					
Incalculable					
Appropriate comparator therapy					
Fludarabine	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 81	3	18	€ 1,458
Cyclophosphamide	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 81	3	18	€ 1,458
Rituximab in combination with idelalisib)	Surcharge for the preparation of a parenteral	€ 71	1	8	€ 568

	solution containing monoclonal antibodies				
Bendamustine	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 81	2	12	€ 972

II. The resolution will enter into force on the day of its publication on the website of the G-BA on 21 July 2022.

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

Berlin, 21 July 2022

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

Prof. Hecken