Danicopan (paroxysmal nocturnal haemoglobinuria with residual haemolytic anaemia, add-on to ravulizumab or eculizumab)

Resolution of: 22 November 2024 valid until: unlimited
Entry into force on: 22 November 2024
Federal Gazette, BAnz AT 03 01 2025 B4

Therapeutic indication (according to the marketing authorisation of 19 April 2024):

Voydeya is indicated as an add-on to ravulizumab or eculizumab for the treatment of adult patients with paroxysmal nocturnal haemoglobinuria (PNH) who have residual haemolytic anaemia.

Therapeutic indication of the resolution (resolution of 22 November 2024):

See therapeutic indication according to marketing authorisation.

1. Extent of the additional benefit and significance of the evidence

Danicopan is approved as a medicinal product for the treatment of rare diseases in accordance with Regulation (EC) No. 141/2000 of the European Parliament and the Council of 16 December 1999 on orphan drugs. In accordance with Section 35a, paragraph 1, sentence 11, 1st half of the sentence SGB V, the additional medical benefit is considered to be proven through the grant of the marketing authorisation.

The Federal Joint Committee (G-BA) determines the extent of the additional benefit for the number of patients and patient groups for which there is a therapeutically significant additional benefit in accordance with Chapter 5 Section 12, paragraph 1, number 1, sentence 2 of its Rules of Procedure (VerfO) in conjunction with Section 5, paragraph 8 AM-NutzenV, indicating the significance of the evidence. This quantification of the additional benefit is based on the criteria laid out in Chapter 5 Section 5, paragraph 7, numbers 1 to 4 of the Rules of Procedure (VerfO).

Adults with paroxysmal nocturnal haemoglobinuria (PNH) who have residual haemolytic anaemia

Extent of the additional benefit and significance of the evidence of danicopan as an add-on to ravulizumab or eculizumab:

Hint for a non-quantifiable additional benefit since the scientific data does not allow quantification.

Study results according to endpoints:[1]

Adults with paroxysmal nocturnal haemoglobinuria (PNH) who have residual haemolytic anaemia

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	n.a.	The data are not assessable.
Morbidity	n.a.	The data are not assessable.
Health-related quality of life	n.a.	The data are not assessable.
Side effects	n.a.	The data are not assessable.
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		

ALPHA study:

- RCT of phase III
- Danicopan (+ eculizumab or ravulizumab) vs placebo (+ eculizumab or ravulizumab)
- 12-week randomised controlled period

Mortality

Endpoint	Danicopan		Placebo		Intervention vs control
	N	*Patients with event n (%)*	N	*Patients with event n (%)*	Effect estimator [95% CI] p value Absolute difference (AD)[a]
	No deaths occurred.				

[1] Data from the dossier assessment of the G-BA (published on 2. September 2024), and from the amendment to the dossier assessment from 29 October 2024, unless otherwise indicated.

Morbidity

Endpoint	Danicopan			Placebo			Intervention vs control
	Baseline		*Change at week 12*	*Baseline*		*Change at week 12*	*LS mean difference [95% CI] p value*
	N	*MV (SD)*	*LS mean (SE)*	*N*	*MV (SD)*	*LS mean (SE)*	*Hedges' g [95% CI]*
Change in haemoglobin value (g/dl) until week 12 compared to baseline (primary study endpoint, presented additionally)[2]							
	57	7.67 (0.95)	2.90 (0.18)	28	7.90 (1.11)	0.78 (0.25)	2.12 (1.50; 2.74) < 0.0001 n.d.

Endpoint	Danicopan		Placebo		Intervention vs control
	N	*Patients with event n (%)*	N	*Patients with event n (%)*	Relative risk [95% CI] p value Absolute difference (AD)[a]
Transfusion independence for 12 weeks (week 1–12) (presented additionally)					
	57	45 (78.9)	29	8 (27.6)	n.d. < 0.0001 AD = 51.3%
FACIT-Fatigue					
Improvement by ≥ 15% of the scale range					
	51	22 (38.6)	25	8 (27.6)	1.40 [0.74; 3.64] 0.35
Deterioration by 15% of the scale range					
	51	0 (0)	25	3 (10.3)	0.00 [0.00; 0.76] 0.036 AD = 10.3%
EQ-5D VAS - General health status					

[2] Data from the pharmaceutical company's statement of 23.09.2024

Endpoint	Danicopan		Placebo		Intervention vs control
	N	*Patients with event n (%)*	N	*Patients with event n (%)*	Relative risk [95% CI] p value Absolute difference (AD)[a]
Improvement by ≥ 15% of the scale range					
	52	20 (35.1)	24	5 (17.2)	2.04 [0.90; 7.61] 0.13
Deterioration by 15% of the scale range					
	52	0	24	3 (10.3)	0.00 [0.00; 0.76] 0.036 AD = 10.3%

Health-related quality of life

Endpoint	Danicopan		Placebo		Intervention vs control
	N	*Patients with event n (%)*	N	*Patients with event n (%)*	Relative risk [95% CI] p value Absolute difference (AD)[a]
EORTC QLQ-C30					
Improvement by ≥ 15% of the scale range					
Global health status	52	26 (45.6)	24	11 (37.9)	1.20 [0.71; 2.32] 0.65
Physical functioning	52	24 (42.1)	24	5 (17.2)	2.44 [1.01; 7.62] 0.029 AD = 24.9%
Role functioning	52	28 (49.1)	23	8 (27.6)	1.78 [0.95; 5.54] 0.07
Emotional functioning	52	13 (22.8)	24	6 (20.7)	1.10 [0.48; 3.42] 1.00

Endpoint	Danicopan		Placebo		Intervention vs control
	N	*Patients with event n (%)*	N	*Patients with event n (%)*	Relative risk [95% CI] p value Absolute difference (AD)[a]
Cognitive functioning	52	20 (35.1)	24	10 (34.5)	1.02 [0.55; 2.17] 1.00
Social functioning	52	20 (35.1)	24	5 (17.2)	2.04 [0.90; 7.61] 0.13
Deterioration by 15% of the scale range					
Global health status	52	4 (7.0)	24	5 (17.2)	0.41 [0.10; 1.63] 0.16
Physical functioning	52	0	24	5 (17.2)	0.00 [0.00; 0.40] 0.0034 AD = 17.2%
Role functioning	52	7 (12.3)	23	9 (31.0)	0.40 [0.15; 1.01] 0.044 AD = 18.7%
Emotional functioning	52	1 (1.8)	24	4 (13.8)	0.13 [0.01; 0.90] 0.042 AD = 12.0%
Cognitive functioning	52	6 (10.5)	24	7 (24.1)	0.44 [0.15; 1.36] 0.12
Social functioning	52	3 (5.3)	24	5 (17.2)	0.31 [0.04; 1.34] 0.11

Side effects

Endpoint **MedDRA system organ classes/ preferred terms/ AEs of special interest**	**Danicopan**		**Placebo**		**Intervention vs control**
	N	*Patients with event n (%)*	N	*Patients with event n (%)*	*Relative risk* *[95% CI]* *p value*
Total adverse events (presented additionally)	57	43 (75.4)	29	18 (62.1)	-
Serious adverse events (SAE)	57	3 (5.3)	29	2 (6.9)	0.76 [0.13; 7.61] 1.00
Severe adverse events (CTCAE grade ≥ 3)	57	10 (17.5)	29	4 (13.8)	1.27 [0.45; 7.56] 0.77
Therapy discontinuation due to adverse events	57	3 (5.3)	29	1 (3.4)	1.53 [0.16; 39.19] 1.00
Severe adverse events according to MedDRA (with an incidence ≥ 5% in one study arm and statistically significant difference between the treatment arms; SOC and PT)					
No significant differences					
SAEs according to MedDRA (with an incidence ≥ 5% in one study arm and statistically significant difference between the treatment arms; SOC and PT)					
No SAEs ≥ 5% occurred					
Adverse events of special interest (with statistically significant difference between the treatment arms)					
No significant differences					

[a] Indication of absolute difference (AD) only in case of statistically significant difference.

Abbreviations used:

AD = absolute difference; CTCAE = Common Terminology Criteria for Adverse Events; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer - Quality of Life Questionnaire-Core 30; EQ-5D = European Quality of Life-Five Domain Scale; FACIT = Functional Assessment of Chronic Illness Therapy; n.d.: no data available; CI = confidence interval; MedDRA = Medical Dictionary for Regulatory Activities; LS = least square; MV = mean value; N = number of patients evaluated; n = number of patients with (at least one) event; SD = standard deviation; SE = standard error; VAS = visual analogue scale; vs = versus

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

Adults with paroxysmal nocturnal haemoglobinuria (PNH) who have residual haemolytic anaemia

Approx. 70 to 350 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 Voydeya (active ingredient: danicopan) agreed upon in the context of the marketing authorisation at the following publicly accessible link (last access: 17 October 2024):

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

Treatment with danicopan should only be initiated and monitored by specialists who are experienced in the treatment of patients with haematological diseases.

4. Treatment costs

Annual treatment costs:

Adults with paroxysmal nocturnal haemoglobinuria (PNH) who have residual haemolytic anaemia

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Danicopan as an add-on to eculizumab	
Danicopan	€ 95,831.12 - € 127,740.63
Eculizumab	€ 360,213.55 - € 480,284.74
Total	€ 456,044.67 - € 608,025.37
Danicopan as an add-on to ravulizumab	
Danicopan	€ 95,831.12 - € 127,740.63
Ravulizumab	€ 313,334.58
Total	€ 409,165.70 - € 441,075.21

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 1 November 2024)

Costs for additionally required SHI services: not applicable

Other SHI services:

Designation of the therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient/ year	Costs/ patient/ year
Eculizumab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	22.8 – 30.4	€ 2,280 - € 3,040
Ravulizumab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	6.5	€ 650

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 with paroxysmal nocturnal haemoglobinuria (PNH) who have residual haemolytic anaemia

The following medicinal products with new active ingredients that can be used in a combination therapy with danicopan in the therapeutic indication of the resolution on the basis of the marketing authorisation under Medicinal Products Act are named (active ingredients and invented names) in accordance with Section 35a, paragraph 3, sentence 4 SGB V:

Ravulizumab (Ultomiris)

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.

II. **In Annex XIIa of the Pharmaceuticals Directive, the following information shall be added in alphabetical order:**

"Active ingredient of the assessed medicinal product

Danicopan

Resolution according to Section 35a paragraph 3 SGB V from

22 November 2024

Therapeutic indication of the resolution

Voydeya is indicated as an add-on to ravulizumab or eculizumab for the treatment of adult patients with paroxysmal nocturnal haemoglobinuria (PNH) who have residual haemolytic anaemia.

Patient group

Adults with paroxysmal nocturnal haemoglobinuria (PNH) who have residual haemolytic anaemia

Naming of medicinal products with new active ingredients according to Section 35a, paragraph 3, sentence 4 SGB V (active ingredients and invented names[2])

Ravulizumab (Ultomiris)

Period of validity of the designation (since... or from... to)

Since 22 November 2024

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.