Benralizumab (new therapeutic indication: eosinophilic granulomatosis with polyangiitis)

Resolution of: 15 May 2025/29 July 2025 Valid until: unlimited
Entry into force on: 15 May 2025/29 July 2025
Federal Gazette, BAnz AT 27 06 2025 B2/ BAnz AT 22 08 2025 B7

New therapeutic indication (according to the marketing authorisation of 24 October 2024):

Fasenra is indicated as an add-on treatment for adult patients with relapsing or refractory eosinophilic granulomatosis with polyangiitis.

Therapeutic indication of the resolution (resolution of 15 May 2025):

See new therapeutic indication according to marketing authorisation.

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

a) Adults with relapsing or refractory eosinophilic granulomatosis with polyangiitis **with** organ-threatening or life-threatening manifestationsmanifestations; for add-on treatment

Appropriate comparator therapy for benralizumab as add-on treatment:

- Individualised therapy with selection of cyclophosphamide and rituximab for remission induction followed by mepolizumab for remission maintenance, each in combination with glucocorticoids

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

An additional benefit is not proven.

b) Adults with relapsing or refractory eosinophilic granulomatosis with polyangiitis **without** organ-threatening or life-threatening manifestations; for add-on treatment

Appropriate comparator therapy for benralizumab as add-on treatment:

- Mepolizumab

Extent and probability of the additional benefit of benralizumab compared to mepolizumab:

An additional benefit is not proven.

Study results according to endpoints:[1]

a) Adults with relapsing or refractory eosinophilic granulomatosis with polyangiitis **with** organ-threatening or life-threatening manifestations; for add-on treatment

No data available.

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	∅	No data available.
Morbidity	∅	No data available.
Health-related quality of life	∅	No data available.
Side effects	∅	No data available.

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) Adults with relapsing or refractory eosinophilic granulomatosis with polyangiitis **without** organ-threatening or life-threatening manifestations; for add-on treatment

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	↔	No deaths occurred.
Morbidity	↔	No relevant differences for the benefit assessment.
Health-related quality of life	↔	No relevant differences for the benefit assessment in SF-36.
Side effects	↔	No relevant differences for the benefit assessment.

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

[1] Data from the dossier assessment of the IQWiG (A24-113) and from the addendum (A25-49), unless otherwise indicated.

MANDARA study: Randomised controlled trial over 52 weeks, benralizumab versus mepolizumab each as add-on treatment to oral corticosteroids +/- immunosuppressant (basic therapy)

Mortality

Endpoint	**Benralizumab + basic therapy**		**Mepolizumab + basic therapy**		**Benralizumab versus mepolizumab**
	N	*Patients with event n (%)*	*N*	*Patients with event n (%)*	*RR [95 % CI]; p-value*[a]
Overall mortality[b] (within 52 weeks)					
	70	0 (0)	70	0 (0)	--

Morbidity

Endpoint	**Benralizumab + basic therapy**		**Mepolizumab + basic therapy**		**Benralizumab versus mepolizumab**
	N	*Patients with event n (%)*	*N*	*Patients with event n (%)*	*RR [95 % CI]; p-value*[a]
Remission (BVAS = 0 and OCS ≤ 7.5 mg/day; within the first 24 weeks until week 52)					
	70	41 (58.6)	70	40 (57.1)	1.12 [0.89; 1.40]; 0.336[c]
Absence of vasculitis disease activity (BVAS = 0; within the first 24 weeks until week 52) (presented additionally)					
	70	42 (60.0)	70	44 (62.9)	0.96 [0.73; 1.25]; 0.743[c]
Severe EGPA symptomatology					
	No suitable data				
Asthma symptomatology (ACQ-6, improvement averaged over weeks 49 to 52)[d]					
	70	24 (34.3)	70	20 (28.6)	1.20 [0.73; 1.96]; 0.531
Sinonasal symptomatology (SNOT-22, improvement at week 52)[e]					
	70	18 (25.7)	70	13 (18.6)	1.39 [0.74; 2.60]; 0.338
Activity impairment (WPAI question 6, improvement at week 52)[f]					
	70	22 (31.4)	70	20 (28.6)	1.10 [0.66; 1.83]; 0.792
Symptomatology (PGIS, improvement at week 52)[g]					

Endpoint	Benralizumab + basic therapy		Mepolizumab + basic therapy		Benralizumab versus mepolizumab
	N	*Patients with event n (%)*	*N*	*Patients with event n (%)*	*RR [95 % CI]; p-value[a]*
	70	26 (37.1)	70	33 (47.1)	0.79 [0.53; 1.17]; 0.250
Endpoint	**Benralizumab + basic therapy**		**Mepolizumab + basic therapy**		**Benralizumab versus mepolizumab**
	N	*Number of events annual rate [95% CI]*	*N*	*Number of events annual rate [95% CI]*	*Rate ratio [95% CI]; p value[i]*
Relapse[i] (deterioration or persistence of the active disease since the last visit) (presented additionally)					
	70	34 0.48 [n.d.]	70	30 0.43 [n.d.]	1.03 [0.56; 1.90]; 0.928

Health-related quality of life

Endpoint	Benralizumab + basic therapy		Mepolizumab + basic therapy		Benralizumab versus mepolizumab
	N	*Patients with event n (%)*	*N*	*Patients with event n (%)*	*RR [95 % CI]; p-value[a]*
SF-36v2 (improvement at week 52)[j]					
Physical Component Summary (PCS) score	70	7 (10.0)	70	8 (11.4)	0.88 [0.34; 2.28]; 0.862
Mental Component Summary (MCS) score	70	10 (14.3)	70	12 (17.1)	0.83 [0.39; 1.80]; 0.687

Side effects

Endpoint	Benralizumab + basic therapy		Mepolizumab + basic therapy		Benralizumab versus mepolizumab
	N	*Patients with event n (%)*	*N*	*Patients with event n (%)*	*RR [95 % CI]; p-value[a]*
Total adverse events (presented additionally)					
	70	63 (90.0)	70	67 (95.7)	–
Serious adverse events (SAE)					
	70	4 (5.7)	70	9 (12.9)	0.44 [0.14; 1.38]; 0.167
Therapy discontinuation due to adverse events					
	70	0 (0)	70	2 (2.9)	0.20 [0.01; 4.09]; 0.210

a RR unadjusted, p value: IQWiG calculation
b Fatalities were collected as part of AEs
c RR, 95% CI and p value are based on a log-binomial regression with treatment group, baseline BVAS (BVAS = 0 vs BVAS > 0) and baseline OCS dose (< 12 mg/day vs ≥ 12 mg/day) as factors.
d A mean decrease in ACQ-6 score by ≥ 0.9 points in the weeks 49-52 compared to the start of the study is considered a clinically relevant improvement (scale range 0 to 6).
e A decrease in SNOT-22 total score by ≥ 16.5 points at week 52 compared to the start of the study is considered a clinically relevant improvement (scale range 0 to 110).
f A decrease in WPAI score (question 6) by ≥ 15 points at week 52 compared to the start of the study is considered a clinically relevant improvement (scale range 0 to 100).
g A decrease by ≥ 1 point compared to the start of the study is considered a clinically relevant improvement (scale range from 0 "no symptoms" to 5 "very severe").
h Rate ratio including CI and p value is based on a negative-binomial model with treatment group, OCS dose at baseline, BVAS at baseline, region and logarithmised treatment duration (offset variable)
i Patients with at least 1 relapse: 21 (intervention) vs 21 (control) An increase in the
j PCS score by ≥ 9.4 points or MCS score by ≥ 9.6 points at week 52 compared to the start of the study is considered a clinically relevant improvement (scale range: 10.8 to 75.5 for PCS and 5.6 to 69.7 for MCS).

Abbreviations used:
ACQ: Asthma Control Questionnaire; BVAS: Birmingham Vasculitis Activity Score; EGPA: eosinophilic granulomatosis with polyangiitis; n.d.: no data available; CI: confidence Interval; MCS: Mental Component Summary; n: number of patients with (at least 1) event; N: number of patients evaluated; n.r. = not reached; OCS: oral glucocorticoids; PCS: Physical Component Summary; PGIS: Patient Global Impression of Severity, PC: pharmaceutical company, RCT: randomised controlled trial, RR: relative risk, SF-36v2: Short Form 36-item health survey version 2; SNOT-22: 22-item Sino-Nasal Outcome Test; SAE: serious adverse event; AE: adverse event; WPAI: Work Productivity and Activity Impairment

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

a) Adults with relapsing or refractory eosinophilic granulomatosis with polyangiitis **with** organ-threatening or life-threatening manifestations; for add-on treatment

and

b) Adults with relapsing or refractory eosinophilic granulomatosis with polyangiitis without organ-threatening or life-threatening manifestations; for add-on treatment

Approx. 90 – 1,360 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 Fasenra (active ingredient: benralizumab) at the following publicly accessible link (last access: 5 March 2025):

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

Treatment with benralizumab should only be initiated and monitored by doctors experienced in the therapy of EGPA.

Benralizumab is intended for long-term treatment. A decision on the continuation of therapy should be made at least once a year. Patients who develop life-threatening manifestationss of EGPA should be assessed for the need for continued therapy as Fasenra has not been studied in this patient group.

4. Treatment costs

Annual treatment costs:

a) Adults with relapsing or refractory eosinophilic granulomatosis with polyangiitis **with** organ-threatening or life-threatening manifestations; for add-on treatment

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
First year of treatment and following years	
Benralizumab	€ 31,966.35
Prednisolone	Different from patient to patient
Appropriate comparator therapy:	
Individualised therapy with selection of cyclophosphamide and rituximab for remission induction followed by mepolizumab for remission maintenance, each in combination with glucocorticoids	

Designation of the therapy	Annual treatment costs/ patient
First year of treatment	
Cyclophosphamide followed by mepolizumab	€ 25,654.16 – € 33,769.71
Cyclophosphamide[2]	€ 198.36 – € 289.14
Mepolizumab	€ 25,365.02 – € 33,571.35
Prednisolone	Different from patient to patient
Rituximab followed by mepolizumab	€ 27,595.75
Rituximab	€ 2,976.76
Mepolizumab	€ 24,618.99
Prednisolone	Different from patient to patient
Following years	
Mepolizumab	€ 48,491.95
Prednisolone	Different from patient to patient

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 April 2025)

b) Adults with relapsing or refractory eosinophilic granulomatosis with polyangiitis **without** organ-threatening or life-threatening manifestations; for add-on treatment

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Benralizumab	€ 31,966.35
Prednisolone	Different from patient to patient
Appropriate comparator therapy:	
Mepolizumab	€ 48,491.95
Prednisolone	Different from patient to patient

Costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 15 April 2025)

Costs for additionally required SHI services: not applicable

[2] Es wurden ganze Arzneimittelpackungen (N1, N2 und N3) zur Berechnung der Therapiekosten herangezogen.

Other SHI services:

Designation of the therapy	Type of service	Costs/ unit	Number/ cycle	Number/ patient/ year	Costs/ patient/ year
Cyclophosphamide	Surcharge for production of a parenteral preparation containing cytostatic agents	€ 100	1	6 - 9	€ 600 – € 900
Rituximab	Surcharge for the preparation of a parenteral solution containing monoclonal antibodies	€ 100	1	2	€ 200

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:

a) Adults with relapsing or refractory eosinophilic granulomatosis with polyangiitis **with** organ-threatening or life-threatening manifestations; for add-on treatment

The following medicinal products with new active ingredients that can be used in a combination therapy with benralizumab 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:

– Mepolizumab (Nucala)

b) Adults with relapsing or refractory eosinophilic granulomatosis with polyangiitis **without** organ-threatening or life-threatening manifestations; for add-on treatment

The following medicinal products with new active ingredients that can be used in a combination therapy with benralizumab 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:

– Mepolizumab (Nucala)

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.