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
Donidalorsen (hereditary angioedema, prevention, ≥ 12 years)

From 20 August 2026

At their session on 20 August 2026, 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. In Annex XII, information on the active ingredient donidalorsen shall be added in alphabetical order as follows:

Donidalorsen

Resolution of: 20 August 2026
Entry into force on: 20 August 2026
Federal Gazette, BAnz AT DD. MM YYYY Bx

Therapeutic indication (according to the marketing authorisation of 19 January 2026):

Dawnzera is indicated for routine prevention of recurrent attacks of hereditary angioedema (HAE) in adults and adolescents aged 12 years and older.

Therapeutic indication of the resolution (resolution of 20 August 2026):

See therapeutic indication according to marketing authorisation.

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

Adults and adolescents aged 12 years and older with recurrent attacks of hereditary angioedema for whom routine prevention is indicated

Appropriate comparator therapy:

- Routine prevention with C1 esterase inhibitor or lanadelumab or berotralstat

Extent and probability of the additional benefit of donidalorsen compared to berotralstat:

Hint of a minor additional benefit

Study results according to endpoints:[1]

Adults and adolescents aged 12 years and older with recurrent attacks of hereditary angioedema for whom routine prevention is indicated

Summary of results for relevant clinical endpoints

Endpoint category	Direction of effect/ risk of bias	Summary
Mortality	↔	No deaths occurred.
Morbidity	↑	Advantage in the monthly rate of HAE attacks.
Health-related quality of life	↔	No relevant difference for the benefit assessment.
Side effects	↔	No relevant difference 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

Indirect comparison via bridge comparators according to Bucher: Donidalorsen (OASIS-HAE study) vs berotralstat (APeX-2 and APeX-J studies)

Mortality

Endpoint Comparison Study	Donidalorsen or berotralstat		Placebo		Group difference
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI]; p value[a]
Mortality/ overall mortality[b]					
Donidalorsen vs placebo OASIS-HAE	45	0 (0)	22	0 (0)	–
Berotralstat vs placebo APeX-2 APeX-J	 40 7	 0 (0) 0 (0)	 39 6	 0 (0) 0 (0)	 – –
Indirect comparison via bridge comparators:	not submitted				

[1] Data from the dossier assessment of the Institute for Quality and Efficiency in Health Care (IQWiG) (A26-15) unless otherwise indicated.

Morbidity

Endpoint Comparison Study	Donidalorsen or berotralstat		Placebo		Group difference
	N	Average monthly rate [95% CI][c]	N	Average monthly rate [95% CI][c]	Rate ratio [95% CI]; p value
HAE attacks monthly rate[d, e]					
Donidalorsen vs placebo OASIS-HAE	45	0.44 [0.27; 0.73]	22	2.26 [1.66; 3.09]	0.19 [0.11; 0.35]; < 0.001
Berotralstat vs placebo APeX-2	40	1.33 [n.d.]	39	2.35 [n.d.]	0.56 [0.41; 0.78]; < 0.001
APeX-J	7	1.08 [n.d.]	6	2.12 [n.d.]	0.51 [0.33; 0.79]; < 0.003
Total[f]					0.54 [0.42; 0.70]; < 0.001
Indirect comparison via bridge comparators: Donidalorsen vs berotralstat					0.36 [0.19; 0.69]; 0.002
Laryngeal HAE attacks monthly rate[d,e]					
Donidalorsen vs placebo OASIS-HAE	45	0.01 [0.00; 0.05]	22	0.05 [0.02; 0.14]	0.22 [0.04; 1.31]; 0.097
Berotralstat vs placebo APeX-2	40	0.07 [n.d.]	39	0.17 [n.d.]	0.39 [0.16; 0.97]; 0.044
APeX-J	7	n.c.	6	n.c.	n.c.
Indirect comparison via bridge comparators: Donidalorsen vs berotralstat					0.56 [0.08; 4.17] 0.573

Endpoint Comparison Study	Donidalorsen or berotralstat		Placebo		Group difference
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI][a]; p value
Attack-free status[e, g]					
Donidalorsen vs placebo OASIS-HAE	45	14 (31.1)	22	1 (4.5)	6.84 [0.96; 48.77]; 0.055
Berotralstat vs placebo APeX-2	40	2 (5.0)	39	1 (2.6)	1.95 [0.18; 20.64]; 0.579
APeX-J	7	0 (0)	6	0 (0)	0.88 [0.02; 38.59]; 0.945
Total[f]					1.56 [0.21; 11.54]; 0.664
Indirect comparison via bridge comparators: Donidalorsen vs berotralstat					4.39 [0.27; 72.53]; 0.302

Endpoint Comparison Study	Donidalorsen or berotralstat			Placebo			Group difference
	N[h]	Values at the start of the study MV (SD)	Mean change at the end of treatment (MV (SD/SE))[i]	N[h]	Values at the start of the study MV (SD)	Mean change at the end of treatment (MV (SD/SE))[i]	MD [95% CI][i]; p value
Activity impairment (WPAI[j])							
Donidalorsen vs placebo OASIS-HAE	44	n.d.[k]	-2.2 (0.4)	22	n.d.[k]	-1.4 (0.5)	-0.83 [-2.09; 0.43]; 0.192
Berotralstat vs placebo APeX-2	38[l]	3.6 (2.8)	-1.6 (0.4)	36[l]	4.1 (2.8)	-1.2 (0.4)	-0.5 [-1.7; 0.7]; 0.406
APeX-J	7	3.3 (2.8)	1.0 (1.0)	6	1.3 (3.3)	-1.0 (1.1)	2.1 [-1.2; 5.4]; 0.200
Total[f]							-0.20 [-1.32; 0.93]; 0.733
Indirect comparison via bridge comparators: Donidalorsen vs berotralstat							-0.63 [-2.32; 1.06]; 0.463

Health status (EQ-5D VAS[m])							
Donidalorsen vs placebo OASIS-HAE	44	82.8 (15.0)	-0.9 (2.0)	22	86.8 (10.1)	-2.5 (3.0)	1.53 [-5.53; 8.59]; 0.668
Berotralstat vs placebo APeX-2	38[l]	82.9 (12.6)	2.7 (1.8)	36[l]	85.2 (10.8)	3.3 (1.8)	-0.6 [-5.8; 4.5]; 0.807
APeX-J	7	75.7 (30.61)	8.4 (4.7)	6	80.5 (26.3)	-3.6 (5.1)	12.0 [-3.7; 27.8]; 0.120
Total[f]							0.62 [-4.28; 5.51]; 0.805
Indirect comparison via bridge comparators: Donidalorsen vs berotralstat							0.91 [-7.68; 9.50]; 0.836[n]

Health-related quality of life

Endpoint Comparison Study	**Donidalorsen or berotralstat**			**Placebo**			**Group difference**
	N[h]	Values at the start of the study MV (SD)	Mean change at the end of treatment[j] MV (SD/SE)[i]	N[h]	Values at the start of the study MV (SD)	Mean change at the end of treatment[j] MV (SD/SE)[i]	MD [95% CI][k]; p value
Angioedema Quality of Life Questionnaire (AE-QoL[o])							
Total score							
Donidalorsen vs placebo OASIS-HAE	45	45.6 (16.8)	-24.8 (2.6)	22	45.4 (17.0)	-6.2 (3.8)	-18.56 [-27.67; -9.45]; < 0.001
Berotralstat vs placebo APeX-2	38[l]	43.0 (16.9)	-15.8 (2.7)	36[l]	45.9 (20.1)	-11.0 (2.7)	-4.83 [-12.39; 2.74]; 0.207
APeX-J	7	39.5 (24.8)	-17.1 (6.5)	6	40.4 (16.0)	0.1 (7.0)	-17.26 [-38.68; 4.15]; 0.103
Total[f]							-6.21 [-13.34; 0.92]; 0.088

Endpoint Comparison Study	Donidalorsen or berotralstat			Placebo			Group difference
	N[h]	Values at the start of the study MV (SD)	Mean change at the end of treatment[j] MV (SD/SE)[i]	N[h]	Values at the start of the study MV (SD)	Mean change at the end of treatment[j] MV (SD/SE)[i]	MD [95% CI][k]; p value
Indirect comparison via bridge comparators: Donidalorsen vs berotralstat							-12.35 [-23.92; -0.79]; 0.036
						SMD [95% CI]:	-0.45 [-0.87; -0.02]
Function							
Donidalorsen vs placebo OASIS-HAE	45	45.2 (22.2)	-36.7 (3.4)	22	46.6 (19.6)	-12.2 (5.0)	-24.46 [-36.42; -12.51]
Berotralstat vs placebo APeX-2	38[l]	47.1 (21.0)	-22.0 (3.4)	36[l]	45.3 (24.1)	-13.0 (3.5)	-8.97 [-18.72; 0.78]
APeX-J	7	42.0 (28.3)	-14.8 (7.0)	6	32.3 (18.3)	-1.5 (7.5)	-13.26 [-35.97; 9.45]
Fatigue/ mood							
Donidalorsen vs placebo OASIS-HAE	45	41.9 (20.2)	-11.6 (3.0)	22	34.1 (20.2)	-3.5 (4.6)	-8.07 [-19.04; 2.89]
Berotralstat vs placebo APeX-2	38[l]	38.5 (19.3)	-12.7 (3.3)	36[l]	44.5 (23.2)	-10.5 (3.3)	-2.13 [-11.41; 7.15]
APeX-J	7	21.4 (15.5)	-3.2 (7.2)	6	32.5 (18.1)	2.9 (7.8)	-6.12 [-30.56; 18.31]
Anxiety/ shame							
Donidalorsen vs placebo OASIS-HAE	45	53.3 (21.0)	-29.8 (3.3)	22	57.0 (25.8)	-5.9 (5.0)	-23.91 [-35.80; -12.03]
Berotralstat vs placebo APeX-2	38[l]	47.9 (22.9)	-16.2 (3.5)	36[l]	51.5 (26.1)	-11.2 (3.5)	-5.09 [-15.03; 4.85]
APeX-J	7	57.1 (33.1)	-32.6 (7.6)	6	61.8 (25.6)	-4.4 (8.2)	-28.21 [-53.57; -2.86]

Endpoint Comparison Study	Donidalorsen or berotralstat			Placebo			Group difference
	N[h]	Values at the start of the study MV (SD)	Mean change at the end of treatment[j] MV (SD/SE)[i]	N[h]	Values at the start of the study MV (SD)	Mean change at the end of treatment[j] MV (SD/SE)[i]	MD [95% CI][k]; p value
Nutrition							
Donidalorsen vs placebo OASIS-HAE	45	32.7 (20.7)	-21.4 (2.6)	22	36.4 (23.4)	-5.8 (3.9)	-15.65 [-24.90; -6.39]
Berotralstat vs placebo APeX-2	38[l]	31.6 (24.0)	-10.0 (3.2)	36[l]	34.0 (25.0)	-7.3 (3.3)	-2.57 [-11.68; 6.54]
APeX-J	7	26.8 (29.3)	-4.3 (8.6)	6	12.5 (15.8)	2.9 (9.3)	-7.24 [-36.49; 22.01]

Side effects

Endpoint Comparison Study	Donidalorsen or berotralstat		Placebo		Group difference
	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI]; p value[a]
Total adverse events (AEs) *(presented additionally)*					
Donidalorsen vs placebo OASIS-HAE	45	33 (73.3)	22	18 (81.8)	–
Berotralstat vs placebo APeX-2 APeX-J	 40 7	 34 (85.0) 7 (100)	 40 6	 30 (76.9) 6 (100)	 – –
Serious adverse events (SAEs)					
Donidalorsen vs placebo OASIS-HAE	45	0 (0.0)	22	1 (4.5)	0.17 [0.01; 3.93]; 0.267
Berotralstat vs placebo APeX-2 APeX-J	 40 7	 0 (0) 0 (0)	 39 6	 3 (7.7) 0 (0)	 0.14 [0.01; 2.61]; 0.188 –
Indirect comparison via bridge comparators[p]: Donidalorsen vs berotralstat					1.20 [0.02; 91.20]; 0.935

Severe adverse events					
No suitable data for indirect comparison					
Therapy discontinuation due to adverse events					
Donidalorsen vs placebo OASIS-HAE	45	0 (0)	22	0 (0)	–
Berotralstat vs placebo APeX-2	40	1 (2.5)	39	1 (2.6)	0.98 [0.06; 15.05]; 0.986
APeX-J	7	0 (0)	6	1 (16.7)	0.29 [0.01; 6.07]; 0.426
Total[f]					0.57 [0.07; 4.34]; no data available
Indirect comparison via bridge comparators[c]: Donidalorsen vs berotralstat					n.c.

a. Calculation using the fourfold table: in the case of 0 events in a study arm, the correction factor 0.5 was used in both study arms when calculating effect and CI.
b. The results on overall mortality are based on the data on fatal AEs.
c. OASIS-HAE study: A Poisson model with the rate of HAE attacks at baseline and the interaction between treatment arm and HAE attacks at baseline as covariates, and the logarithm of the duration of observation as an offset variable. APeX-2 and APeX-J studies: negative binomial model; the covariate of confirmed HAE attack rate at baseline was taken into account. The logarithm of the treatment duration was used as an offset variable.
d. In the OASIS-HAE, APeX-2 and APeX-J studies, one month was defined as 28 days.
e. OASIS-HAE and APeX-2 studies: HAE attacks confirmed by the principal investigator; APeX-J study: HAE attacks confirmed by the independent expert.
f. Meta-analysis using a fixed-effects model (inverse variance method).
g. Reduction in the number of HAE attacks by 100% during the treatment period compared to the run-in phase.
h. Number of patients who were taken into account in the effect estimate; the values at the start of the study can be based on other patient numbers.
i. OASIS-HAE study: MV (SE) and MD [95% CI]: Based on an MMRM model, in which the treatment group, the visit and an interaction variable between the visit and the treatment group are defined as fixed effects. The effect represents the difference in changes (compared to the baseline value) between the treatment groups at week 25.
APeX-2 and APeX-J studies: MV (SE) and MD [95% CI]: Based on an MMRM model, in which the baseline, the treatment group, the visit and an interaction variable between the visit and the treatment group are defined as fixed effects. The effect represents the difference in changes (compared to the baseline value) between treatment groups at week 24.
j. Question 10 of the WPAI+CIQ:SHP is used for the OASIS-HAE study; question 6 of the WPAI which corresponds to question 10 of the WPAI+CIQ:SHP is used for the APeX-2 and APeX-J studies. Lower (decreasing) values mean better symptomatology; negative effects (intervention minus comparison) mean an advantage for the intervention (scale range: 0 to 10 points).
k. According to the OASIS-HAE study protocol, the weekly scores for each 4-week period should be evaluated in aggregated form when analysing the WPAI+CIQ:SHP. As with the APeX-2 and APeX-J studies, the last 7 days were taken into account for the analysis of the dossier and the indirect comparison. The pharmaceutical company did not specify any baseline values for these in Module 4 A.
l. Number of patients with values at the end of treatment; it is unclear how many patients were included in the model.

m. Higher (increasing) values mean better symptomatology; positive effects (intervention minus comparison) mean an advantage for the intervention (scale range: 0 to 100 points).
n. IQWiG calculation.
o. Lower values mean better health-related quality of life; negative effects (intervention minus comparison) mean an advantage for the intervention (scale range: 0 to 100 points).
p. For the indirect comparison, only data from the APeX-2 study are used for the comparator side.

AE-QoL = Angioedema Quality of Life Questionnaire; HAE = hereditary angioedema; n.d. = no data available; CI = confidence interval; MD = mean difference; MMRM = mixed model for repeated measures; MV = mean value; n = number of patients with (at least 1) event; N = number of patients evaluated; RR = relative risk; SD = standard deviation; SE = standard error; SMD = standardised mean difference; SAE = serious adverse event; AE = adverse event; VAS = visual analogue scale; WPAI = Work Productivity and Activity Impairment

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

Adults and adolescents aged 12 years and older with recurrent attacks of hereditary angioedema for whom routine prevention is indicated

Approx. 140 – 450 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 Dawnzera (active ingredient: donidalorsen) at the following publicly accessible link (last access: 11 August 2026):

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

Treatment with donidalorsen should only be initiated and monitored by specialists who are experienced in the treatment of patients with hereditary angioedema.

Therapy discontinuation should be considered for patients with HAE with normal C1-INH (nC1-INH) who have shown an insufficient reduction in attacks after 4 months of treatment.

4. Treatment costs

Annual treatment costs:

Adults and adolescents aged 12 years and older with recurrent attacks of hereditary angioedema for whom routine prevention is indicated

Designation of the therapy	Annual treatment costs/ patient
Medicinal product to be assessed:	
Donidalorsen - 1st year - Subsequent years	 € 179,258.78 – € 286,814.04 € 143,407.02 – € 286,814.04
Appropriate comparator therapy:	
C1 esterase inhibitor (1st year and subsequent years)	€ 190,355.94 – € 253,738.42
Lanadelumab (1st year and subsequent years)	€ 130,499.74 – € 262,003.33
Berotralstat (1st year and subsequent years)	€ 181,327.98

Costs after deduction of statutory rebates (LAUER-TAXE® as last revised: 15 June 2026)

Costs for additionally required SHI services: not applicable

II. The resolution will enter into force on the day of its publication on the G-BA website on 20 August 2026.

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

Berlin, 20 August 2026

Federal Joint Committee
in accordance with Section 91 SGB V
The Chair

Dr Optendrenk