Drug assessment at a glance: A26-15[1]

Donidalorsen (hereditary angioedema)

20 August 2026

[1] This is a courtesy translation of the summary provided as a service by IQWiG. For further information on the subject matter and the result of the assessment, please refer to the dossier assessment for Project A26-15. The G-BA decides on the added benefit.

Research question for the benefit assessment

Population	For routine prevention of recurrent attacks of hereditary angioedema in adults and adolescents aged 12 years and older
Intervention	donidalorsen
Comparator	Routine prevention with a C1 esterase inhibitor or lanadelumab or berotralstat
Outcomes	At least one patient-relevant outcome

Overview of positive and negative effects

	Size of the effects	Informative value of the effects
Mortality	↔	–
Morbidity	↔	–
Symptoms	↑↑ (monthly HAE attack rate)	★
Health-related quality of life	↔	–
Side effects	↔	–
	ø No (suitable) data ↔ No advantage or disadvantage ↑ / ↓ Small advantage/disadvantage ↑↑ / ↓↓ Moderate advantage/disadvantage ↑↑↑ / ↓↓↓ Large advantage/disadvantage	– Not applicable ★ Low ★★ Moderate ★★★ High

Overall: a moderate advantage with low informative value

Evidence base and noteworthy aspects

- Evidence base: Donidalorsen was compared indirectly with berotralstat via placebo; double-blind, randomized studies were available in each case: OASIS-HAE, comparing donidalorsen (n = 45) with placebo (n = 22); APeX-2, comparing berotralstat (n = 40) with placebo (n = 40); and APeX-J, comparing berotralstat (n = 7) with placebo (n = 6).
- It was unclear how the severity of HAE attacks was assessed in the APeX studies and it was therefore not possible to compare the number of severe HAE attacks across the studies.
- The assessment of the severity of adverse events was performed by the investigator within the OASIS-HAE study and for this reason could not be analysed.

Key study findings

Outcome category	donidalorsen/berotralstat		placebo		Group difference
Outcome **Comparison** **Study**	**N**	**Mean monthly rate [95% CI]**	**N**	**Mean monthly rate [95% CI]**	**Rate ratio [95% CI]; p-value**
Morbidity					
HAE attacks					
Monthly rate					
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 [ND]	39	2.35 [ND]	0.56 [0.41; 0.78]; < 0.001
APeX-J	7	1.08 [ND]	6	2.12 [ND]	0.51 [0.33; 0.79]; < 0.003
Total					0.54 [0.42; 0.70]; < 0.001
Indirect comparison using common comparators:					
donidalorsen vs. berotralstat					0.36 [0.19; 0.69]; 0.002

Outcome category	donidalorsen/berotralstat		placebo		Group difference
Outcome Comparison Study	N	Patients with event n (%)	N	Patients with event n (%)	RR [95% CI]; p-value
Freedom from attacks					
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					1.56 [0.21; 11.54]; 0.664
Indirect comparison using common comparators:					
donidalorsen vs. berotralstat					4.39 [0.27; 72.53]; 0.302

Outcome category Outcome Comparison Study	donidalorsen/berotralstat N	 Patients with event n (%)	placebo N	 Patients with event n (%)	Group difference RR [95% CI]; p-value
Mortality					
All-cause mortality					
donidalorsen vs. placebo					
OASIS-HAE	45	0 (0)	22	0 (0)	–
berotralstat vs. placebo					
APeX-2	40	0 (0)	39	0 (0)	–
APeX-J	7	0 (0)	6	0 (0)	–
Indirect comparison using common comparators:					Not submitted
Side effects					
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	40	0 (0)	39	3 (7.7)	0.14 [0.01; 2.61]; 0.188
APeX-J	7	0 (0)	6	0 (0)	–
Indirect comparison using common comparators: **donidalorsen vs. berotralstat**					1.20 [0.02; 91.20]; 0.935
Severe AEs	No suitable data for the indirect comparison				

Outcome category Outcome Comparison Study	donidalorsen/berotralstat N	 Patients with event n (%)	placebo N	 Patients with event n (%)	Group difference RR [95% CI]; p-value
Discontinuation due to AEs					
donidalorsen vs. placebo					
OASIS-HAE	45	0 (0.0)	22	0 (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					0.57 [0.07; 4.34]; ND
Indirect comparison using common comparators:					
donidalorsen vs. berotralstat					NC

Outcome category Outcome Comparison Study	donidalorsen/berotralstat N	 Values at baseline mean (SD)	 Mean change at the end of treatment Mean (SE)	placebo N	 Values at baseline mean (SD)	 Mean change at the end of treatment Mean (SE)	Group difference MD [95% CI]; p-value
Morbidity							
Activity impairment (WPAI)							
donidalorsen vs. placebo							
OASIS-HAE	44	ND	−2.2 (0.4)	22	ND	−1.4 (0.5)	−0.83 [−2.09; 0.43]; 0.192
berotralstat vs. placebo							
APeX-2	38	3.6 (2.8)	−1.6 (0.4)	36	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							−0.20 [−1.32; 0.93]; 0.733
Indirect comparison using common comparators:							
donidalorsen vs. berotralstat							−0.63 [−2.32; 1.06]; 0.463
Health status (EQ-5D VAS)							
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	82.9 (12.6)	2.7 (1.8)	36	85.2 (10.8)	3.3 (1.8)	−0.6 [−5.8; 4.5]; 0.807
APeX-J	7	75.7 (30.6)	8.4 (4.7)	6	80.5 (26.3)	−3.6 (5.1)	12.0 [−3.7; 27.8]; 0.120
Total							0.62 [−4.28; 5.51]; 0.805
Indirect comparison using common comparators:							
donidalorsen vs. berotralstat							0.91 [−7.68; 9.50]; 0.836

Outcome category	donidalorsen/berotralstat			placebo			Group difference
Outcome **Comparison** **Study**	**N**	**Values at baseline mean (SD)**	**Mean change at the end of treatment Mean (SE)**	**N**	**Values at baseline mean (SD)**	**Mean change at the end of treatment Mean (SE)**	**MD [95% CI]; p-value**
Health-related quality of life							
AE-QoL							
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	43.0 (16.9)	−15.8 (2.7)	36	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							−6.21 [−13.34; 0.92]; 0.088
Indirect comparison using common comparators:							
donidalorsen vs. berotralstat							−12.35 [−23.92; −0.79]; 0.036
						SMD [95% CI]:	−0.45 [−0.87; −0.02]

References

Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen. Donidalorsen (hereditäres Angioödem); Nutzenbewertung gemäß § 35a SGB V; Dossierbewertung [online]. 2026 [Accessed: 19.06.2026]. URL: https://doi.org/10.60584/A26-15.

Gemeinsamer Bundesausschuss. Nutzenbewertungsverfahren zum Wirkstoff Donidalorsen (Hereditäres Angioödem, Prophylaxe, ≥ 12 Jahre) [online]. 2026 [Accessed: 19.06.2026]. URL: https://www.g-ba.de/bewertungsverfahren/nutzenbewertung/1315/.

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