

Idebenone

Resolution of: 17 March 2016 / 22 November 2019
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Valid until: 1 April 2022

Approved therapeutic indication (according to the marketing authorisation of 8 September 2015):

Idebenone (Raxone®) is indicated for the treatment of visual impairment in adolescent and adult patients with Leber's Hereditary Optic Neuropathy (LHON).

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

Idebenone 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 10, 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). 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).

Extent of the additional benefit:

Non-quantifiable

Study results of the RHODOS study according to endpoints:¹

Mortality				
No events were observed.				
Morbidity				
Endpoint	Estimated change ^a [95% CI] (change in letters)		Estimated difference ^a Mean ± standard error [95% CI] (change in letters)	p value
	Idebenone	Placebo	Idebenone vs placebo	
Best improvement in visual acuity after 24 weeks^{b, c, d}				
N ^e	53	29		
Week 24	-0.135 [-0.216; -0.054] (+6 letters)	-0.071 [-0.176; 0.034] (+3 letters)	-0.064 ± 0.061 [-0.184; 0.055] (3 letters)	0.291
Change in best visual acuity after 24 weeks^{b, d}				
N ^f	53	29		
Week 24	-0.035 [-0.126; 0.055] (+1 letter)	0.085 [-0.032; 0.203] (-4 letters)	-0.120 ± 0.068 [-0.255; 0.014] (6 letters)	0.078
Change in visual acuity of the best eye (from start of study) after 24 weeks^{b, d}				
N ^e	53	29		
Week 24	-0.030 [-0.120; 0.060] (+1 letter)	0.098 [-0.020; 0.215] (-4 letters)	-0.128 ± 0.068 [-0.262; 0.006] (6 letters)	0.061
Endpoint	Estimated change ^a [95% CI]		Estimated difference ^a Mean ± standard error [95% CI]	p value
	Idebenone	Placebo	Idebenone vs placebo	
Change in protan and tritan colour perception (colour contrast sensitivity) since start of study^{b, d, g}				
N ^g	54	22		
Protan (% colour confusion)				
Week 24	1.37 [-4.67; 7.41]	5.25 [-2.47; 12.97]	-3.88 ± 3.28 [-10.37; 2.60]	0.239
Tritan (% colour confusion)				
Week 24	-7.27 [-16.63; 2.09]	6.36 [-5.58; 18.30]	-13.63 ± 5.05 [-23.61; -3.66]	0.008
Quality of life				
No usable data are available.				

¹ Data from the RHODOS study from the G-BA benefit assessment of 4 January 2016.

Side effects	Idebenone (N = 55) n (%)	Placebo (N = 30) n (%)	RR [95% CI] ^h ARR [95% CI] ^h	p value ⁱ
Patients with at least one AE	49 (89.1)	26 (86.7)	1.26 [0.33; 4.85] 0.02 [-0.12; 0.17]	0.737
Of which patients with at least one treatment-related AE	4 (7.3)	1 (3.3)	2.27 [0.24; 21.33] 0.04 [-0.05; 0.13]	0.652
Patients with at least one severe AE	2 (3.6)	0	2.85 [0.13; 61.33] 0.04 [-0.03; 0.11]	0.538
Of which patients with at least one severe treatment related AE	1 (1.8)	0	1.68 [0.07; 42.49] 0.02 [-0.04; 0.08]	1.000
Patients with at least one SAE ^j	1 (1.8)	1 (3.3)	0.54 [0.03; 8.90] -0.02 [-0.09; 0.06]	1.000
Death	0	0	cannot be estimated	
Patients with AE leading to therapy discontinuation ^k	1 (1.8)	0	1.68 [0.07; 42.49] 0.02 [-0.04; 0.08]	1.000
Patients with SAE leading to therapy discontinuation ^k	0	0	cannot be estimated	

a Analysis in accordance with MMRM (Observed cases: at week 24 data were imputed to the respective population for 6 patients).

b ANCOVA model

c Primary endpoint of the Rhodos study

d Exclusion of three patients from analysis because insufficient visual acuity data at baseline or week 24

e N = number of patients in the analysis

f N = number of eyes/patients in the analysis

g Monocentric survey; N = number of eyes in analysis

h Additionally specified in the dossier by the pharmaceutical company. This information cannot be found in the study report.

i Exact Fisher test

j SOC and PT

k Therapy discontinuations because of AE after 24 weeks

Abbreviations used:

ARR: absolute risk reduction; CI: confidence interval; N: number of patients or eyes in the analysis; n: patients with event; PT: preferred term; RR: relative risk; SOC: system organ class; AE: adverse event; SAE: serious adverse event

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

approx. 1,500 - 3,000 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 Raxone® (active ingredient: idebenone) at the following publicly accessible link (last access: 18 January 2016): http://www.ema.europa.eu/docs/de_DE/document_library/EPAR_-_Product_Information/human/003834/WC500193836.pdf

Treatment should be initiated and monitored by a physician experienced in the treatment of Leber's Hereditary Optic Neuropathy (LHON).

There is no data from controlled clinical trials on continuous treatment with idebenone for more than six months.

This medicinal product was authorised under "exceptional circumstances". This means that because of the rarity of the disease, it was not possible to obtain complete information about the medicinal product. The EMA will examine any new information made available and update the summary of product characteristics as appropriate.

4. Treatment costs

Annual treatment costs²:

Designation of the therapy	Annual treatment costs per patient
Medicinal product to be assessed	
Idebenone	€ 99,070.13

²Medicinal product costs after deduction of statutory rebates (LAUER-TAXE®) as last revised: 1 February 2016