RAXONE®
idebenone 150mg tablets

# Raxone® (idebenone)

Pharmacological treatment of visual impairment in adolescent and adult patients with Leber's hereditary optic neuropathy

Chiesi
global rare diseases

# LHON is a rare disease causing severe, painless, and progressive visual impairment[1]

### Leber's Hereditary Optic Neuropathy (LHON)

Caused by mutations in motichondrial DNA that result in mithocondrial dysfunction which particularly affect the retinal ganglion cells[4-6]

Causes rapid, painless, central loss of vision[2,3]

Leads to impaired colour vision perception[2]

### Natural history from untreated patients

Usually, loss of vision will occur in one eye, with the second eye becoming affected 6-8 weeks later[2]

25% of patients present with bilateral loss of vision[2]

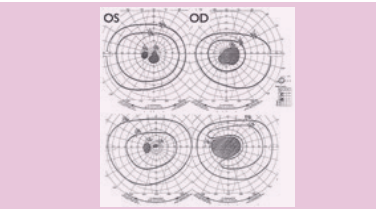
| Normal vision | LHON vision |
|---|---|
|  |  |

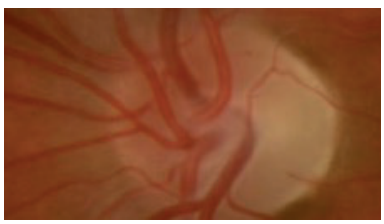
**LHON is a blinding disorder, usually leading to optic atrophy within a year of disease onset.[7]**

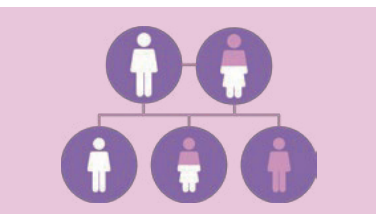
1. Yu-Wai-Man P, et al. J Med Genet. 2009;46(3):145–158 2. Yu-Wai-Man P, et al. Prog Retin Eye Res. 2011; 30:81-114. 3. Mascialino B, et al. Eur J Ophthalmol. 2012; 22:461-5. 4. Heitz FD, et al. PLoS One. 2012; 7:e45182. 5. Gueven N & Faldu D. Intractable Rare Dis Res. 2013; 2:130-135. 6. Carelli V, et al. Biochimica et Biophysica Acta. 2009; 1787:518-528. 7. Carelli V et al. J Neuroophthalmol. 2017; 37:371–81. 8. Barboni P et al. Ophthalmology. 2010;117:623–7. 9. Fraser JA et al. Surv of Ophthalmol. 2010;55(4):299–334. 10. Manole C et al, RomJOphthalmol, 2020, 64:78-82

# Diagnose early

## Suspect LHON when you see:





- **Rapid, painless vision loss in one eye then the other**[7]
- **Central or centrocecal scotoma**[1,8]
- **Males aged 15-35**[8]
- **Retinal nerve fiber layer swelling, microangiopathy and temporal optic disk pallor**[1,8]
- **Family history of LHON**[9]
- **Non-responders to glucocorticoids**[10]

**Verify the diagnosis of LHON by genetic testing**[2]

1. Yu-Wai-Man P, et al. J Med Genet. 2009;46(3):145–158 2. Yu-Wai-Man P, et al. Prog Retin Eye Res. 2011; 30:81-114. 3. Mascialino B, et al. Eur J Ophthalmol. 2012; 22:461-5. 4. Heitz FD, et al. PLoS One. 2012; 7:e45182. 5. Gueven N & Faldu D. Intractable Rare Dis Res. 2013; 2:130-135. 6. Carelli V, et al. Biochimica et Biophysica Acta. 2009; 1787:518-528. 7. Carelli V et al. J Neuroophthalmol. 2017; 37:371–81. 8. Barboni P et al. Ophthalmology. 2010;117:623–7. 9. Fraser JA et al. Surv of Ophthalmol. 2010;55(4):299–334. 10. Manole C et al, RomJOphthalmol, 2020, 64:78-82

# LHON is an inherited mitochondrial disorder

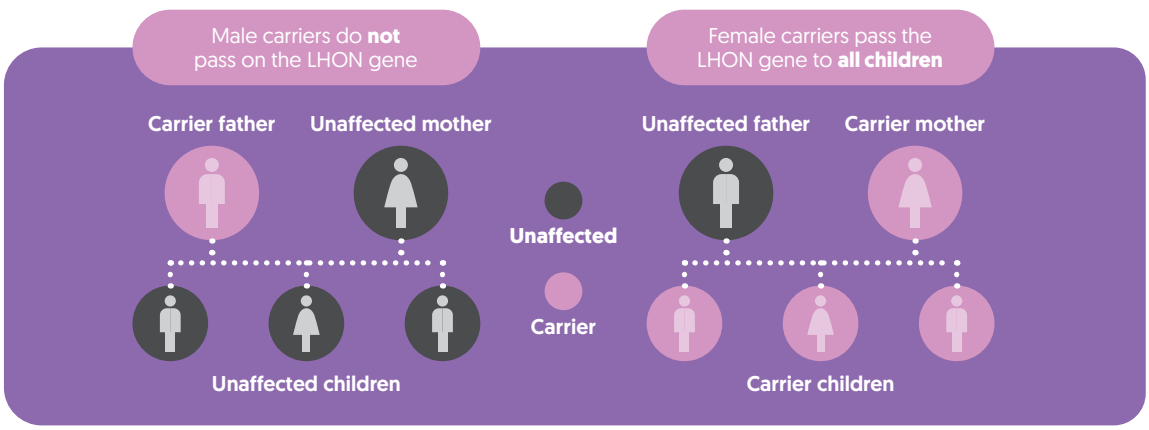
LHON mutations are passed on **typically via the mother to her children**, with no paternal contribution[2]

However, not all carriers of LHON mutations develop symptoms[1,3,4]

Interaction of **genetic and environmental factors** as well as **anatomical, physiological and hormonal factors** modulate the risk of visual loss[1,3,4]

A second form of inheritance, **autosomal recessive** has recently been described[5]

## LHON can be identified by genetic testing[6]

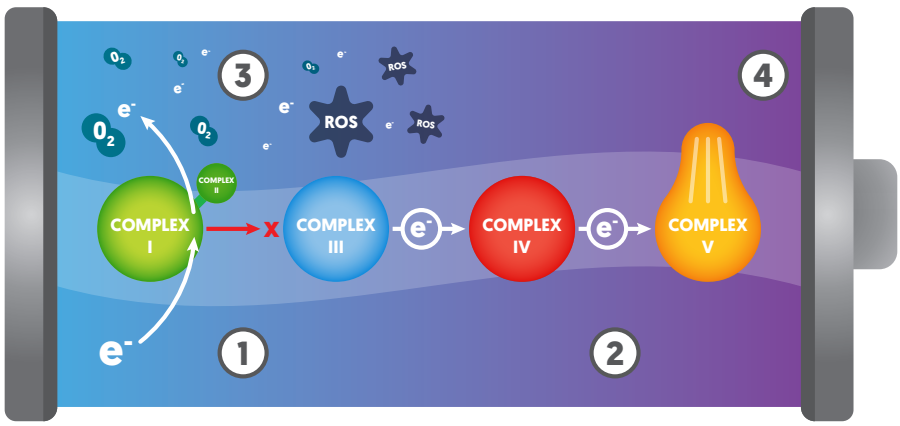



Based on Yu-Wai-Man P, et al. 2009[1]

- 60% of LHON patients know of at least one family member with vision loss[2]
- Penetrance of LHON is incomplete; only 50% of male carriers and 10% of female carriers develop the disease[1]
- Pathogenic mutations in the nuclear DNA causing LHON have been described[5]

1. Meyerson C et al. Clin Ophthalmol. 2015; 9:1165–76; 2. Yu-Wai-Man P et al. J Med Genet. 2009; 46:145–58; 3. Yu-Wai-Man P et al. Prog Retin Eye Res. 2011; 30:81–114; 4. Yu-Wai-Man P et al. Eye. 2014; 28:521–37. 5. Stenton S et al J Clin Invest . 2021 Jan 19;138267. doi: 10.1172/JCI138267 6. Yu-Wai-Man P, Chinnery PF. Leber Hereditary Optic Neuropathy. 2000 [Updated 2021]. In: Adam MP et al., eds. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993–2022. Available at: https://www.ncbi.nlm.nih.gov/books/NBK1174/ (Accessed October 2023);

# LHON is caused most often by mitochondrial DNA mutations coding for complex I subunits[5]




Based on Yu-Wai-Man P, et al. 20091 and Yu-Wai-Man P, et al. 2011.[2]

Mutations causing LHON result in selective RGC degeneration, leading to rapid, painless and progressive central vision loss and impaired colour perception.[1–5]

1. Over 90% of LHON cases are caused by point mutations in complex I (G11778A, T14484C,G3460A)[1,2]
2. These mutations break the electron transfer chain, decreasing ATP production[1,2]
3. Leaked electrons react with O2 to create ROS, contributing to oxidative stress[1,2]
4. Over time, RGCs become dysfunctional and eventually undergo apoptosis. This leads to vision loss[1]

ATP = adenosine triphosphate; LHON = Leber's hereditary optic neuropathy; RGC = retinal ganglion cell; ROS = reactive oxygen species.

1.Yu-Wai-Man P, et al. J Med Genet. 2009;46(3):145–158; 2. Yu-Wai-Man P, et al. Prog Retinal Eye Res. 2011;30(2):81–114; 3. Meyerson C, et al. Clin Ophthalmol. 2015;9:1165–1176; 4. Yu-Wai-Man P, et al. Eye. 2014;28(5):521–537; 5. Stenton SL, et al. J Clin Invest. 2021;131(6):e138267. 6. Yu-Wai-Man P, Chinnery PF. Leber Hereditary Optic Neuropathy. 2000 [Updated 2021]. In: Adam MP et al., eds. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993–2022. Available at: https://www.ncbi.nlm.nih.gov/books/NBK1174/ (Accessed October 2023);

# Differentiating between LHON and optic neuritis[1-6]

Clinical features of LHON and optic neuritis are similar. However, the presence of one or more of the following “red flags” can aid in differentiation, even before mtDNA testing.

| Red flags suggestive of LHON | Red flags suggestive of optic neuritis |
|---|---|
| Male (80% of cases) | Female (~65% of cases) |
| Painless | Periocular pain, particularly with eye movement |
| Subacute loss of vision - worsening symptoms for 4-6 weeks (per eye) | Acute loss of vision - worsening symptoms up to 2 weeks |
| No spontaneous recovery* | Spontaneous recovery within 2-3 weeks (~90% of cases) |
| Bilateral vision loss (usually sequential) | Unilateral vision loss |
| Pupillary reflexes preserved | Relative afferent pupillary defect |
| Absence of retinal disc leakage on fluorescein angiography | Retinal disc leakage may be present on fluorescein angiography |
| No / few other signs of MS** | There may be other signs suggestive of MS |
| MRI findings not typical of MS (no CNS lesions) | MRI findings typical of MS (CNS lesions) |
| Family history of LHON symptoms, or confirmed carriers within family | No family history of LHON |
| Lack of response to glucocorticoids | Response to glucocorticoids |

*Spontaneous recovery is relatively rare, particularly within the same timeframe of optic neuritis spontaneous recovery (< 2 months since onset)

**In rare cases, LHON patients can present with other symptoms suggestive of MS

1. Fraser J et al. Surv Ophthalmol. 2010; 55:299–334; 2. Yu-Wai-Man P et al. J Med Genet. 2009; 46: 145–58; 3. Beck RW et al. Ophthalmology 1995; 102:1504–8; 4. Petzold A et al. Nat Rev Neurol. 2014; 10:447–58; 5. Sawaya R et al. Postgrad Med J. 2015; 91:698–703; 6. Voss E et al. Ther Adv Neurol Disord. 2011; 4:123–34; 7. Hoorbakht H & Bagherkashi F. Open Ophthalmol J. 2012; 6:65–72.

Learn more about Leber's Hereditary Optic Neuropathy (LHON) at LHONaware.se. The site offers information both for you as a doctor, and for your patient.

# Therapeutic indication

**Raxone® (idebenone, 150 mg tablets) is approved in EU for the treatment of visual impairment in adolescent and adult patients with Leber's hereditary optic neuropathy (LHON).[1]**

# Raxone® restores mitochondrial function in retinal ganglion cells

Raxone addresses impaired mitochondrial function by:

- restoring cellular ATP generation[2,3,5]
- acting as antioxidant[2-5]

Therefore, Raxone may reactivate viable, but inactive RGCs, thereby promoting recovery of vision in patients who experience vision loss, as suggested by studies in LHON patients in acute or chronic phase treated with idebenone [1,6,7]

1. Raxone Produktresumé, fass.se; 2. Lyseng-Williamson KA. Drugs. 2016; 76:805–13; 3. Haefeli RH et al. PLoS One. 2011; 6:e17963; 4. Gueven N and Faldu D. Expert Opin Orphan Drugs. 2013; 1:331–9; 5. Gueven N et al, Redox Biol. 2021 Jan; 38: 101812. 6. Pemp B et al. Graefe's Archive for Clinical and Experimental Ophthalmology (2019) 257:2751–2757; 7. Pemp B et al. J. Clin. Med. 2021, 10, 151. https://doi.org/10.3390/jcm10010151

# Raxone® formulation, dosing and administration[1]

Raxone® is an oral medication, supplied as **film-coated tablets** containing **150 mg idebenone**

The recommended dose is **900 mg/day** idebenone. **Two tablets (300 mg)** should be taken **three times** a day

Raxone® tablets should be **swallowed whole with water**; the tablets should not be broken or chewed

Raxone® should be **taken with food**, as food increases the bioavailability of idebenone

**Morning**

**150** mg **150** mg

**Afternoon**

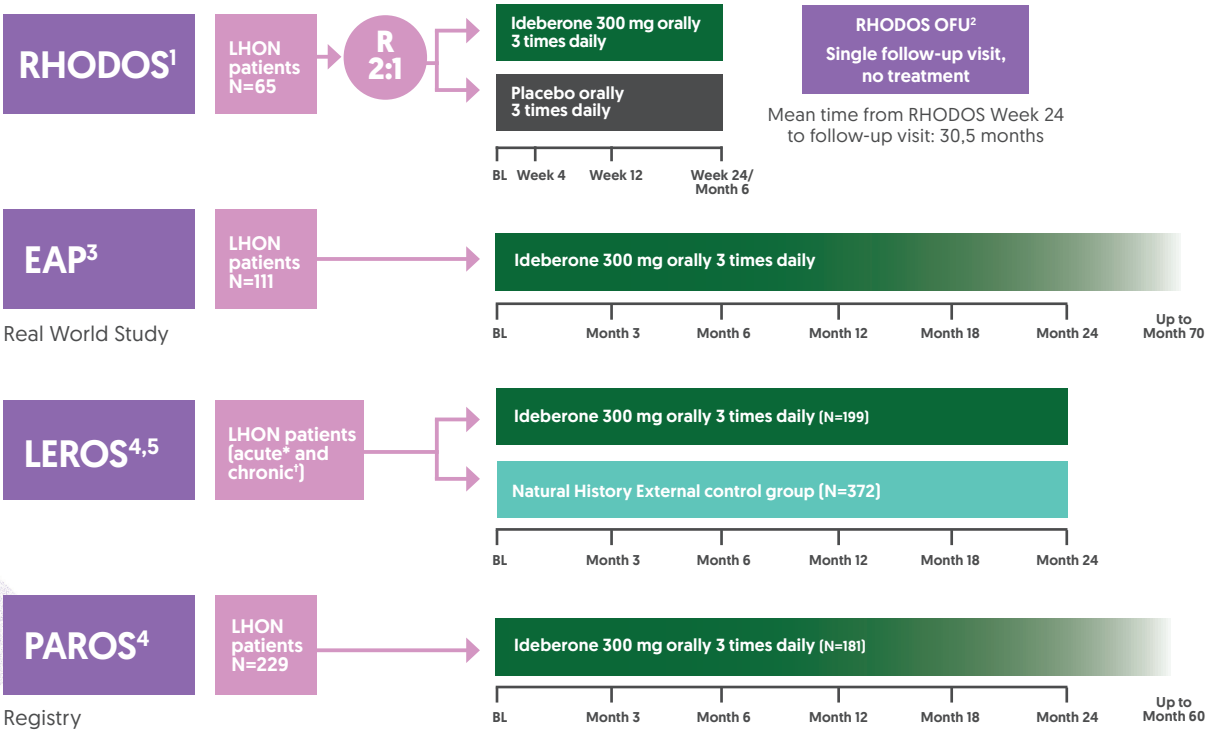
**150** mg **150** mg

**Evening**

**150** mg **150** mg

1. Raxone Produktresumé, fass.se.

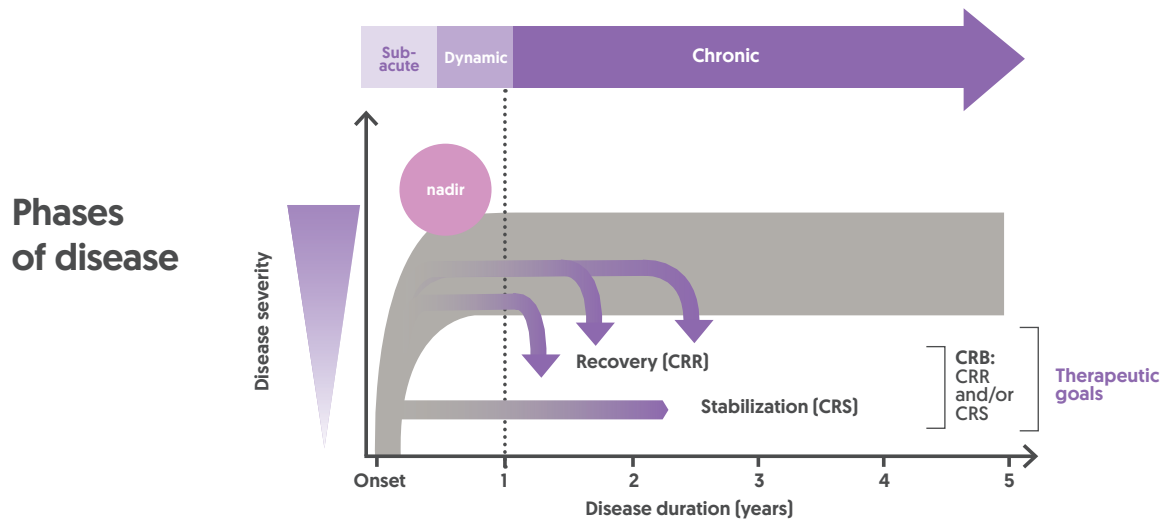
# Raxone has been studied in a randomised clinical trial and real-world studies

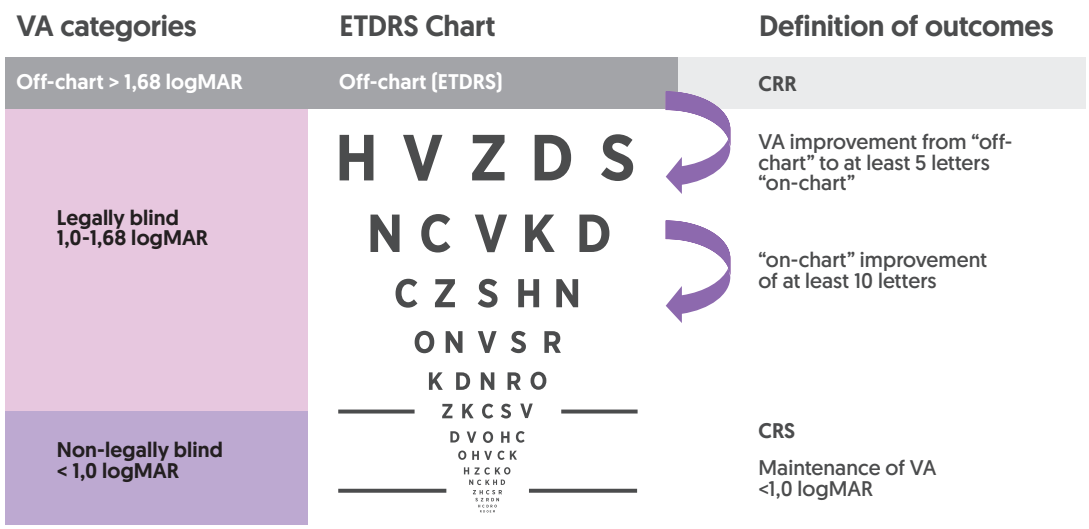



*Patients enrolled with LHON onset ≤1 year; †Patients enrolled with LHON onset >1 year and ≤5 years. BL = baseline; EAP = expanded access programme; LHON = Leber's hereditary optic neuropathy; OFU = observational follow-up; R = randomisation; RCT = randomised controlled trial; RWE = real-world evidence.

1. Klopstock T, et al. A randomized placebo-controlled trial of idebenone in Leber's hereditary optic neuropathy, Brain 2011;134:2677–2686 2. Klopstock T, et al. Persistence of the treatment effect of idebenone in Leber's hereditary optic neuropathy, Brain. 2013;136(2);e230. 3. Catarino C et al., Real-World Clinical Experience With Idebenone in the Treatment of Leber Hereditary Optic Neuropathy,J Neuro-Ophthalmol. 2020; 40:558-65. 4. Raxone Produktresumé, fass.se. 5. Yu-Wai-Man et al., Cell Reports Medicine 5, 101437 March 19, 2024.6. Carelli V et al, International Consensus Statement on the Clinical and Therapeutic Management of Leber Hereditary Optic Neuropathy. J Neuroophthalmol. 2017 Dec;37(4):371-381. 7. Gueven N. Optic Neurodegeneration: Time to Act, Biol Med. 2014; 1:1–6.

# Recovery and/or stabilization of visual acuity as important therapeutic objectives in the studies with idebenone in LHON[3,5-7]




**CRB: clinically relevant benefit; CRS: clinically relevant stabilization; CRR: clinically relevant recovery; VA: visual acuity**

1. Klopstock T, et al. A randomized placebo-controlled trial of idebenone in Leber's hereditary optic neuropathy, Brain 2011;134:2677–2686 2. Klopstock T, et al. Persistence of the treatment effect of idebenone in Leber's hereditary optic neuropathy, Brain. 2013;136(2);e230. 3. Catarino C et al., Real-World Clinical Experience With Idebenone in the Treatment of Leber Hereditary Optic Neuropathy,J Neuro-Ophthalmol. 2020; 40:558-65. 4. Raxone Produktresumé, fass.se. 5. Yu-Wai-Man et al., Cell Reports Medicine 5, 101437 March 19, 2024.6. Carelli V et al, International Consensus Statement on the Clinical and Therapeutic Management of Leber Hereditary Optic Neuropathy. J Neuroophthalmol. 2017 Dec;37(4):371-381. 7. Gueven N. Optic Neurodegeneration: Time to Act, Biol Med. 2014; 1:1–6.

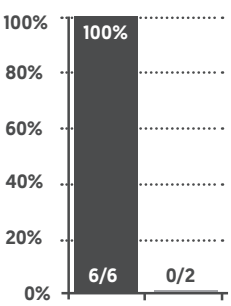
# RHODOS: Visual acuity endpoints[1]

**Estimated treatment difference (Mean and 95% CI LogMAR)***


Figure adapted from Klopstock T, et al. Brain. 2011;134:2677-2686

# Clinically Relevant Recovery (CRR) and Clinically Relevant Stabilization (CRS) in RHODOS -responder analysis[1,2,3]

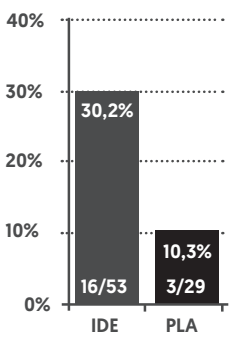
**Proportion of patients with Clinically Relevant Stabilization (CRS)[1,2]**




1,0 logMAR

**Item to be scored**
Light Perception
Hand Motion
Counting Fingers


**Proportion of patients with Clinically Relevant recovery (CRR)[2,3]**

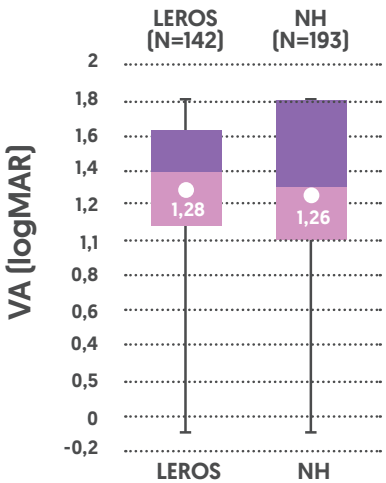



*Pre-planned analysis based on patient stratification at study entry. The primary endpoint (in bold) was the best recovery/least worsening of VA between baseline and week 24 by ETDRS chart. CI: confidence interval; RHODOS: Rescue of Hereditary Optic Disease Outpatient Study; ITT: intent-to-treat population; VA: visual acuity.

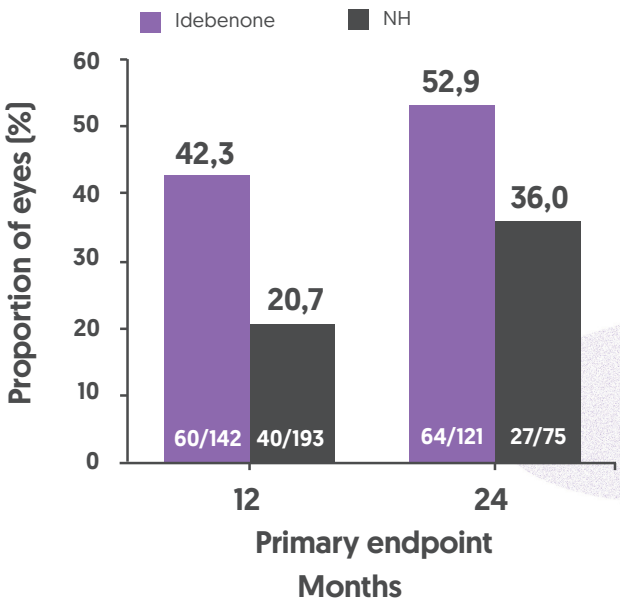
1. Klopstock T, et al. A randomized placebo-controlled trial of idebenone in Leber's hereditary optic neuropathy, Brain 2011;134:2677–2686. 2. Raxone Produktresumé, fass.se. 3. Raxone EPAR, September 2015.

# Long-term treatment with idebenone resulted in prolonged clinical benefit in patients with LHON in the subacute/ dynamic phase[1,2]

**VA at baseline**
LEROS mITT and NH
mached 12-month datasets



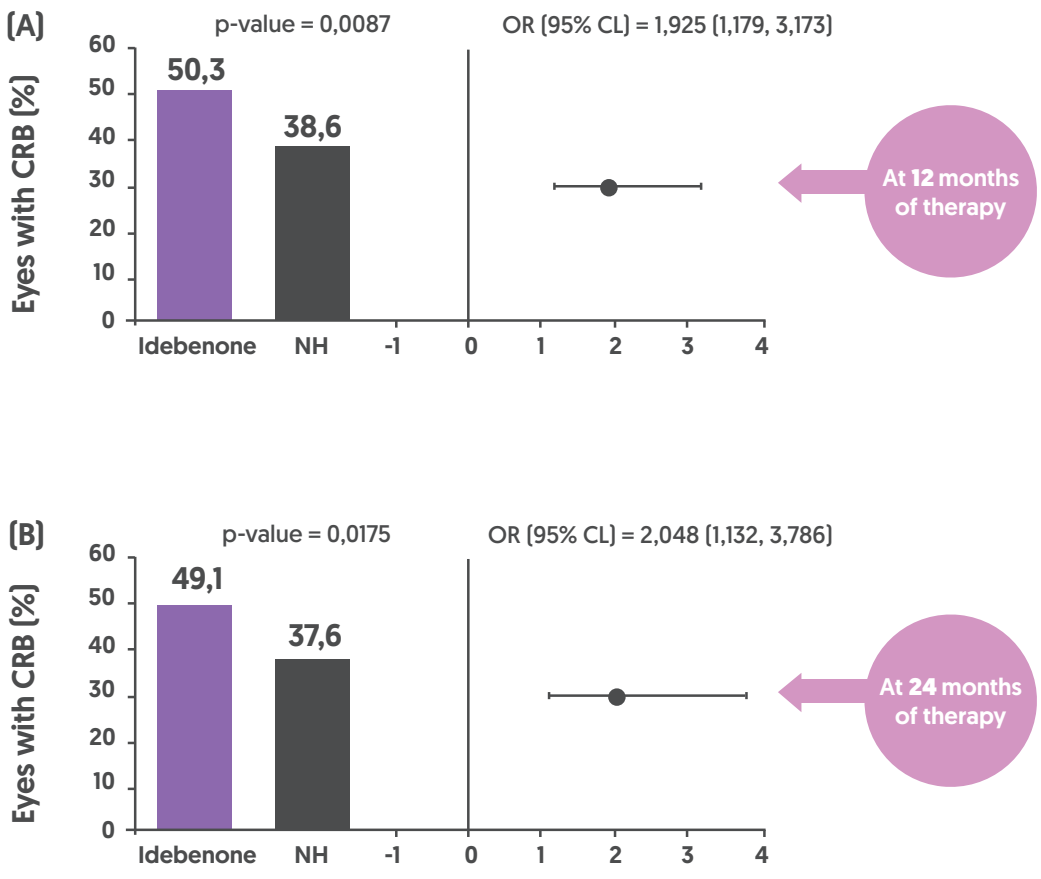

**Subacute/dynamic eyes with CRB**




| | OR | 95% CL | p-value |
|---|---|---|---|
| 12 months | 2,29 | 1,35 - 3,88 | 0,0020 |
| 24 months | 2,08 | 1,07 - 4,10 | 0,0297 |

1. Raxone Produktresumé, fass.se. 2 Yu-Wai-Man et al., Cell Reports Medicine 5, 101437 March 19, 2024

# Clinically relevant benefit (CRB) of idebenone treatment in patients with LHON in the chronic stage (1-5 years since onset of symptoms in the second eye)[1,2]




1. Raxone Produktresumé, fass.se. 2 Yu-Wai-Man et al., Cell Reports Medicine 5, 101437 March 19, 2024

# Raxone - Most commonly reported adverse events profile[1]

| System organ class | Preferred term | Frequency |
|---|---|---|
| Infections and infestations | Nasopharyngitis | Very common |
| Respiratory, thoracic and mediastinal disorders | Cough | Very common |
| Gastrointestinal disorders | Diarrhoea | Common |
| Musculoskeletal and connective tissue disorders | Back pain | Common |

Data presented are adverse reactions emerging from clinical trials in LHON patients reported post marketing in other indications. Very common: 1/10; common: 1/100–1/10

Adapted from Raxone® (idebenone) Summary of Product Characteristics, 2025.[1]

For complete information on adverse events, see the Summary of Product Characteristics.[1]

# Summary safety profile[1-5]

### RHODOS study in patients with LHON treated with Raxone (900 mg/day) or placebo for six months showed:[1,2]

- The nature, severity and frequency of adverse events were similar across study groups[2]
- No fatal adverse events were reported
- Two serious adverse events were reported[2]: one in the Raxone group (infected epidermal cyst assessed as not-related to treatment by the Investigator and one in the placebo group (epistaxis)

### Safety profile of Raxone in patients treated for up to five years in the Expanded Access Programme (EAP)[1,4]

- Adverse events were mainly mild or moderate in severity[4]
- Gastrointestinal disorders (n=17) with diarrhea were the most frequent (n=5)[4]
- There were no serious adverse events, or deaths related to idebenone[4]
- Nine patients discontinued idebenone treatment due to the occurrence of adverse events[4]

### In LEROS and PAROS studies no new safety concerns were observed with long-term treatment with Raxone[1,5]

- Adverse events reported were mainly of mild or moderate severity
- In PAROS there was one fatal case, an 81-year-old male who died of terminal prostate carcinoma, assessed by the Investigator as unrelated to Raxone
- Ten (5.1%) patients in LEROS and thirty-four (15.2%) patients in PAROS discontinued idebenone treatment due to the occurrence of adverse events

1. Raxone Produktresumé, fass.se. 2. Klopstock T et al. Brain. 2011;134(Pt 9):2677–86. 3. Raxone EPAR, September 2015; 4. Catarino CB, von Livonius B, Priglinger C et al., Real-World Clinical Experience With Idebenone in the Treatment of Leber Hereditary Optic Neuropathy J Neuro-Ophthalmol 2020; 00: 1-8. 5. Yu-Wai-Man P, Carelli V, Newman NJ et al., Therapeutic benefit of idebenone in patients with Leber hereditary optic neuropathy: The LEROS nonrandomized controlled trial. Cell Reports Medicine 5, 101437 March 19, 2024

RAXONE®
idebenone 150mg tablets

▼ **Detta läkemedel är föremål för utökad övervakning.**

**Raxone (idebenon) filmdragerad tablett 150 mg. Rx.** (F) subventioneras endast för behandling av nedsatt syn hos ungdomar och vuxna med Lebers hereditära optikusneuropati (LHON). ATC-kod: N06BX13: Psykoanaleptika, Psykostimulantia och nootropika. **Indikation:** För behandling av nedsatt syn hos ungdomar och vuxna med Lebers hereditära optikusneuropati (LHON). **Dosering och administreringssätt:** Behandling ska inledas och övervakas av en läkare med erfarenhet av LHON. Raxone filmdragerade tabletter ska sväljas hela med vatten. Tabletterna ska inte brytas eller tuggas. Raxone ska ges tillsammans med föda eftersom föda ökar idebenons biotillgänglighet. **Varning & försiktighet:** Patienterna bör regelbundet övervakas i enlighet med lokal klinisk praxis. Försiktighet bör iakttas när Raxone förskrivs till patienter med nedsatt lever- eller njurfunktion. Kan orsaka kromaturi. **Graviditet & amning:** Ska enbart ges till gravida kvinnor eller kvinnor som kan bli gravida om nyttan överväger potentiell risk. Ska enbart ges till ammande kvinnor efter att man tagit hänsyn till fördelen med amning för barnet och fördelen med behandling för kvinnan. **Biverkningar:** De oftast rapporterade biverkningarna som orsakas av idebenon är lindrig till måttlig diarré (som vanligtvis inte kräver att behandlingen avbryts), nasofaryngit, hosta och ryggsmärta. **Förpackningar:** 180 tabletter (burk). **Innehavare av godkännande för försäljning:** Chiesi Farmaceutici S.p.A., Via Palermo 26/A, 43122 Parma, Italien **Kontakt:** Chiesi Pharma AB, Tel: + 46 8 753 35 20, E-post: infonordic@chiesi.com. Förkortad produktresumé baserad på SPC från 08/2025. För ytterligare information samt priser se www.fass.se.

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chiesipharma.se

15510-10.09.2025

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