

ANNEX I
SUMMARY OF PRODUCT CHARACTERISTICS

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

1. NAME OF THE MEDICINAL PRODUCT

Raxone 150 mg film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains 150 mg idebenone.

Excipients with known effect: Each film-coated tablet contains 46 mg of lactose (as monohydrate) and 0.23 mg of sunset yellow (E110).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet.

Orange, round, biconvex film-coated tablet of 10 mm diameter, engraved with the Santhera logo on one side and '150' on the other side.

4. Clinical particulars

4.1 Therapeutic indications

Raxone is indicated for the treatment of visual impairment in adolescent and adult patients with Leber's Hereditary Optic Neuropathy (LHON) (see section 5.1).

4.2 Posology and method of administration

Treatment should be initiated and supervised by a physician with experience in LHON.

Posology

The recommended dose is 900 mg/day idebenone (300 mg, 3 times a day).

No data regarding a continuous treatment with idebenone beyond 6 months is available from controlled clinical trials.

Special populations

Elderly

No specific dose adjustment is required for the treatment of LHON in elderly patients.

Hepatic or renal impairment

Patients with hepatic or renal impairment have not been investigated. Caution is advised in treatment of patients with hepatic or renal impairment (see section 4.4).

Paediatric population

The safety and efficacy of Raxone in LHON patients under 12 years of age have not yet been established. Currently available data are described in sections 5.1 and 5.2, but no recommendation on posology can be made.

Method of administration

Raxone film-coated tablets should be swallowed whole with water. The tablets should not be broken or chewed. Raxone should be administered with food because food increases the bioavailability of idebenone.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Monitoring

Patients should be regularly monitored according to local clinical practice.

Hepatic or renal impairment

No data are available in these populations. Therefore, caution should be exercised when prescribing Raxone to patients with hepatic or renal impairment.

Chromaturia

The metabolites of idebenone are coloured and may cause chromaturia, i.e. a reddish-brown discoloration of the urine. This effect is harmless, not associated with haematuria, and does not require any adaptation of dose or discontinuation of treatment. Caution should be exercised to ensure that the chromaturia does not mask changes of colour due to other reasons (e.g. renal or blood disorders).

Lactose

Raxone contains lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take Raxone.

Sunset yellow

Raxone contains sunset yellow (E110) which may cause allergic reactions.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies in humans have been performed.

Data from *in vitro* studies have demonstrated that idebenone and its metabolite QS10 do not exert systemic inhibition of cytochrome P450 isoforms CYP1A2, 2B6, 2C8, 2C9, 2C19, 2D6 and 3A4 at clinically relevant concentrations of idebenone or QS10. In addition, no induction of CYP1A2, CYP2B6 or CYP3A4 was observed.

Idebenone may inhibit P-glycoprotein (p-gp) with possible exposure increases of e.g. dabigatran etexilate, digoxin or aliskiren. Idebenone is not a substrate for p-gp *in vitro*.

Given the *in vitro* inhibition data, presystemic inhibition of CYP3A4 by idebenone cannot be excluded. The possible exposure increase of certain CYP3A4 substrates (e.g. midazolam, triazolam,

atorvastatin, lovastatin, simvastatin, astemizol, bepridil, cisaprid, dofetilid, levacetylmethadol, mizolastin, pimizid, quinidine, sertindol, terfenadin, dihydroergotamine, ergometrin, ergotamine, methylergometrine, eletriptan, nisoldipin and ranolazine) is unknown. Caution is advised and combination with these medicinal products should if possible be avoided.

4.6 Fertility, pregnancy and lactation

Pregnancy

The safety of idebenone in pregnant women has not been established. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity. Idebenone should only be administered to pregnant women or women of child-bearing age likely to become pregnant if it is considered that the benefit of the therapeutic effect outweighs any potential risk.

Breast-feeding

Studies in rats have shown that idebenone is excreted into maternal milk. Therefore, a decision must be made whether to discontinue breast-feeding or to discontinue therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the mother.

Fertility

There are no data concerning the effect of exposure to idebenone on human fertility.

4.7 Effects on ability to drive and use machines

Raxone has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile

The most commonly reported adverse reactions to idebenone are mild to moderate diarrhoea (usually not requiring the discontinuation of the treatment), nasopharyngitis, cough and back pain.

Tabulated list of adverse reactions

The following adverse reactions emerging from clinical trials in LHON patients or reported post-marketing in other indications are tabulated below. Frequency groupings are defined to the following convention: very common ($\geq 1/10$), common ($\geq 1/100$ to $< 1/10$), not known (cannot be estimated from the available data).

System Organ Class	Preferred Term	Frequency
Infections and Infestations	Nasopharyngitis	Very common
	Bronchitis	Not known
Blood and lymphatic system disorders	Agranulocytosis, anaemia, leukocytopenia, thrombocytopenia, neutropenia	Not known
Metabolism and nutrition disorders	Blood cholesterol increased, blood triglycerides increased	Not known
Nervous system disorders	Seizure, delirium, hallucinations, agitation, dyskinesia, hyperkinesia, poriomania, dizziness, headache, restlessness, stupor	Not known
Respiratory, thoracic and mediastinal disorders	Cough	Very common
Gastrointestinal disorders	Diarrhoea	Common
	Nausea, vomiting, anorexia, dyspepsia	Not known

Hepatobiliary disorders	Alanine aminotransferase increased, aspartate aminotransferase increased, blood alkaline phosphatase increased, blood lactate dehydrogenase increased, gamma-lutamyltransferase increased, blood bilirubin increased, hepatitis	Not known
Skin and subcutaneous tissue disorders	Rash, pruritus	Not known
Musculoskeletal and connective tissue disorders	Back pain	Common
	Pain in extremity	Not known
Renal and urinary disorders	Azotaemia, chromaturia	Not known
General disorders and administration site conditions	Malaise	Not known

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions **via the national reporting system** listed in [Appendix V](#).

4.9 Overdose

No report of overdose has been received from the RHODOS study. Doses up to 2250 mg/day have been administered in clinical studies showing a safety profile consistent with that reported in section 4.8.

There is no specific antidote for idebenone. When needed, supportive symptomatic treatment should be given.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Psychoanaleptics, Other psychostimulants and nootropics;
ATC code: N06BX13

Idebenone, a short-chain benzoquinone, is an anti-oxidant assumed to be capable of transferring electrons directly to complex III of the mitochondrial electron transport chain, thereby circumventing complex I and restoring cellular energy (ATP) generation under experimental conditions of complex I deficiency. Similarly, in LHON idebenone can transfer electrons directly to complex III of the electron transport chain, thereby bypassing complex I which is affected by all three primary mtDNA mutations causing LHON, and restoring cellular ATP generation.

According to this biochemical mode of action, idebenone may re-activate viable-but-inactive retinal ganglion cells (RGCs) in LHON patients. Depending on the time since symptom onset and the proportion of RGCs already affected, idebenone can promote recovery of vision in patients who experience vision loss.

Clinical safety and efficacy of idebenone in LHON have been assessed in one double-blind, randomised, placebo-controlled study (RHODOS).

In RHODOS a total of 85 LHON patients, 14-66 years of age, with any of the 3 primary mtDNA mutations (G11778A, G3460A or T14484C) and disease duration of not more than 5 years were enrolled. Patients received either 900 mg/day Raxone or placebo for a period of 24 weeks (6 months). Raxone was given as 3 daily doses of 300 mg each with meals.

The primary endpoint “best recovery of visual acuity (VA)” was defined as the result from the eye experiencing the most positive improvement in VA from baseline to week 24 using ETDRS charts. The main secondary endpoint “change in best VA” was measured as the difference between best VA in either the left or right eye at 24 weeks compared to baseline (Table 1).

Table 1: RHODOS: Best recovery of VA and change in best VA from baseline to week 24

Endpoint (ITT)	Raxone (N=53)	Placebo (N=29)
Primary endpoint: Best recovery of VA (mean ± SE; 95% CI)	logMAR -0.135 ± 0.041	logMAR -0.071 ± 0.053
	logMAR -0.064, 3 letters (-0.184; 0.055) p=0.291	
Main secondary endpoint: Change in best VA (mean ± SE; 95% CI)	logMAR -0.035 ± 0.046	logMAR 0.085 ± 0.060
	logMAR -0.120, 6 letters (-0.255; 0.014) p=0.078	

Analysis according to Mixed Model of Repeated Measures

One patient in the placebo group presented with ongoing spontaneous recovery of vision at baseline. Exclusion of this patient yielded similar results as in the ITT population; as could be expected, the difference between idebenone and placebo arm was slightly larger.

A pre-specified analysis in RHODOS determined the proportion of patients with an eye with baseline VA of ≤ 0.5 logMAR in whom the VA deteriorated to ≥ 1.0 logMAR. In this small subgroup of patients (n=8), 0 of 6 patients in the idebenone group deteriorated to ≥ 1.0 logMAR whereas 2 of 2 patients in the placebo group showed such a deterioration.

In a single-visit observational follow-up study of RHODOS VA assessments from 58 patients obtained on average 131 weeks after discontinuation of treatment indicates that the effect of Raxone may be maintained.

A post-hoc responder analysis was performed in RHODOS evaluating the proportion of patients who had a clinically relevant recovery of VA from baseline in at least one eye, defined as either: (i) improvement in VA from unable to read a single letter to able to read at least 5 letters on the ETDRS chart; or (ii) improvement in VA by at least 10 letters on the ETDRS chart. Results are shown in Table 2 including supporting data from 62 LHON patients using Raxone in an Expanded Access Programme (EAP) and from 94 untreated patients in a Case Record Survey (CRS).

Table 2: Proportion of patients with clinically relevant recovery of VA after 6 months from baseline

RHODOS (ITT)	RHODOS Raxone (N=53)	RHODOS Placebo (N=29)
Responders (N, %)	16 (30.2 %)	3 (10.3 %)
EAP and CRS	EAP-Raxone (N=62)	CRS-untreated (N=94)
Responders (N, %)	19 (30.6 %)	18 (19.1 %)

In the EAP the number of responders increased with longer treatment duration, from 19 out of 62 patients (30.6%) at 6 months to 17 out of 47 patients (36.2%) at 12 months.

Paediatric population

In clinical trials in Friedreich’s Ataxia, 32 patients between the ages of 8 and 11 years and 91 patients between the ages of 12 and 17 years received idebenone at ≥ 900 mg/day for up to 42 months.

In RHODOS and the EAP in LHON, a total of 3 patients between the ages of 9 and 11 years and 27 patients between the ages of 12 and 17 years received idebenone at 900 mg/day for up to 33 months.

This medicinal product has been authorised under ‘exceptional circumstances’.

This means that due to the rarity of the disease it has not been possible to obtain complete information on this medicinal product.

The European Medicines Agency will review any new information which may become available every year and this SmPC will be updated as necessary.

5.2 Pharmacokinetic properties

Absorption

Food increases the bioavailability of idebenone by approximately 5-7-fold and therefore, Raxone should always be administered with food. The tablets should not be broken or chewed.

After oral administration of Raxone, idebenone is rapidly absorbed. On repeat dosing, maximum plasma concentrations of idebenone are reached on average within 1 hour (median 0.67 h range: 0.33-2.00 h). In phase I pharmacokinetic studies, proportional increases in plasma concentrations of idebenone were observed for doses from 150 mg to 1050 mg. Neither idebenone nor its metabolites showed time-dependent pharmacokinetics.

Distribution

Experimental data have shown that idebenone passes the blood-brain barrier and is distributed at significant concentrations in cerebral tissue. Following oral administration pharmacologically relevant concentrations of idebenone are detectable in the aqueous humor of the eye.

Biotransformation

Metabolism occurs by means of oxidative shortening of the side chain and by reduction of the quinone ring and conjugation to glucuronides and sulphates. Idebenone shows a high first pass metabolism resulting in conjugates of idebenone (glucuronides and sulphates (IDE-C)) and the Phase I metabolites QS10, QS6, and QS4 as well as their corresponding Phase II metabolites (glucuronides and sulphates (QS10+QS10-C, QS6+QS6-C, QS4+QS4-C)). The main metabolites in plasma are IDE-C and QS4+QS4-C.

Elimination

Due to the high first-pass effect, the plasma concentrations of idebenone were generally only measurable up to 6 hours after oral administration of 750 mg Raxone, given either as a single oral dose or after repeated (14 days) t.i.d dosing. The main route of elimination is metabolism, with the majority of dose excreted via the kidneys as metabolites. After a single or repeated oral dose of 750 mg Raxone, QS4+QS4-C were the most prominent idebenone-derived metabolites in urine, representing on average between 49.3% and 68.3% of the total administered dose. QS6+QS6 represented 6.45% to 9.46%, whereas QS10+QS10-C and IDE+IDE-C were close to 1% or below.

Hepatic or renal impairment

No data are available in these populations.

Paediatric population

Whilst clinical trials experience in paediatrics with LHON is limited to patients of 14 years of age and above, pharmacokinetic data from population pharmacokinetic studies, which included paediatric Friedreich’s Ataxia patients of age 8 years and above, did not reveal any significant differences in the pharmacokinetics of idebenone.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction and development.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Core tablet

Lactose monohydrate
Microcrystalline cellulose
Croscarmellose sodium
Povidone K25
Magnesium stearate
Colloidal silica

Coating

Macrogol 3350
Poly(vinyl alcohol)
Talc
Titanium dioxide
Sunset yellow FCF (E110)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

5 years.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

White high-density polyethylene bottles with white polypropylene child-resistant tamper-evident twist-off caps containing 180 film-coated tablets.

6.6 Special precautions for disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Santhera Pharmaceuticals (Deutschland) GmbH
Marie-Curie Strasse 8
79539 Lörrach
Germany
Tel: +49 (0) 7621 1690 200
Fax: +49 (0) 7621 1690 201

Email: office@santhera.com

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/15/1020/001

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 8 September 2015

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency <http://www.ema.europa.eu>

ANNEX II

- A. MANUFACTURER RESPONSIBLE FOR BATCH RELEASE**
- B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE**
- C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION**
- D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT**
- E. SPECIFIC OBLIGATION TO COMPLETE POST-AUTHORISATION MEASURES FOR THE MARKETING AUTHORISATION UNDER EXCEPTIONAL CIRCUMSTANCES**

A. MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer responsible for batch release

Santhera Pharmaceuticals (Deutschland) GmbH
Marie-Curie Strasse 8
79539 Lorrach
GERMANY

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to restricted medical prescription (see Annex I: Summary of Product Characteristics, section 4.2).

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

• Periodic safety update reports

The requirements for submission of periodic safety update reports for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

The marketing authorisation holder shall submit the first periodic safety update report for this product within 12 months following authorisation.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

• Risk Management Plan (RMP)

The MAH shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the Marketing Authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

E. SPECIFIC OBLIGATION TO COMPLETE POST-AUTHORISATION MEASURES FOR THE MARKETING AUTHORISATION UNDER EXCEPTIONAL CIRCUMSTANCES

This being a marketing authorisation under exceptional circumstances and pursuant to Article 14(8) of Regulation (EC) No 726/2004, the MAH shall complete, within the stated timeframe, the following measures:

Description	Due date
In order to further investigate the benefits of Raxone in the treatment of LHON patients, the MAH should conduct and submit the results of an external natural history controlled, open-label intervention study to assess the efficacy and safety of Raxone in the treatment of LHON patients, including long-term treatment.	Interim reports should be provided at the time of annual re-assessments. Due date of final report: 31 August 2020
In order to further investigate the benefits of Raxone in the treatment of LHON patients, the MAH should maintain and extend the Historical Case Record Survey of Visual Acuity Data from Patients with LHON to serve as the external control to the open label study.	Interim reports should be provided at the time of annual re-assessments. Due date of final report: 31 August 2020
Non-interventional post-authorisation safety study (PASS): In order to further investigate the safety of Raxone in the treatment of LHON patients, the MAH should generate data based on an agreed protocol from a drug exposure registry of patients prescribed Raxone for the treatment of LHON in clinical practice. The registry should also be used to generate data on long-term effectiveness.	Reports to be provided at the time of annual re-assessment
The MAH should follow up patients in the existing Expanded Access Programme and submit the final results.	Interim reports should be provided at the time of annual re-assessments. Due date of final report: 31 August 2019

ANNEX III
LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING AND THE IMMEDIATE PACKAGING

CARTONS/ HDPE BOTTLE LABEL

1. NAME OF THE MEDICINAL PRODUCT

Raxone 150 mg film-coated tablets
idebenone

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each film-coated tablet contains 150 mg of idebenone.

3. LIST OF EXCIPIENTS

Contains lactose and sunset yellow (E110). See leaflet for further information.

4. PHARMACEUTICAL FORM AND CONTENTS

180 film-coated tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

For oral use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Santhera Pharmaceuticals (Deutschland) GmbH
Marie-Curie Straße 8
D-79539 Lörrach
Germany

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/15/1020/001

13. BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product subject to medical prescription.

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Raxone 150 mg

B. PACKAGE LEAFLET

Package leaflet: Information for the user

Raxone 150 mg film-coated tablets idebenone

▼ This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Raxone is and what it is used for
2. What you need to know before you take Raxone
3. How to take Raxone
4. Possible side effects
5. How to store Raxone
6. Contents of the pack and other information

1. What Raxone is and what it is used for

Raxone contains a substance called idebenone.

Idebenone is used to treat vision impairment in adults and adolescents with an eye disease called Leber's Hereditary Optic Neuropathy (LHON).

- This eye problem is inherited – this means it runs in families.
- It is caused by a problem with your genes (called a “genetic mutation”) that affects the ability of cells in the eye to produce the energy they need to work normally, so they become inactive.
- LHON can lead to loss of eyesight due to the inactivity of cells responsible for vision.

Treatment with Raxone can restore the ability of cells to produce energy and so allow inactive eye cells to work again. This can lead to some improvement in lost eyesight.

2. What you need to know before you take Raxone

Do not take Raxone:

- if you are allergic to idebenone or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions

Talk to your doctor or pharmacist before taking Raxone if:

- you have any blood, liver or kidney problems.

Change in urine colour

Raxone may make your urine become reddish brown. This change in colour is harmless – it does not mean your treatment needs to change. However, the change in colour could mean that you have problems with your kidneys or bladder.

- Tell your doctor if your urine changes colour.
- He or she may do a urine check to make sure the change in colour is not hiding other problems.

Tests

Your doctor will check your eye-sight before you start taking this medicine and then at regular visits while you are taking it.

Children and adolescents

This medicine should not be used in children This is because it is not known if Raxone is safe or works in patients under 12 years of age.

Other medicines and Raxone

Some medicine may interact with Raxone. Tell your doctor if you are taking, have recently taken or might take any other medicines, especially any of the following:

- to treat insomnia (midazolam, triazolam)
- to lower cholesterol levels or for prevention of cardiovascular disease (atorvastatin, lovastatin, simvastatin)
- antihistamines to treat allergies (astemizol, mizolastin, terfenadin)
- to treat high blood pressure and chest pain (bepridil, nisoldipin, ranolazine)
- to treat heartburn (cisaprid)
- to treat atrial fibrillation (dofetilid)
- for management of opioid dependence (levacetylmethadol)
- to treat muscle and speech tics associated with Tourette syndrome (pimozid)
- to treat hearth rhythm disorders (quinidine)
- antipsychotic medicines (sertindol)
- to treat migraine (dihydroergotamine, ergotamine, eletriptan)
- to control excessive bleeding after childbirth (ergometrin, methylergometrine).

Pregnancy and breast-feeding

If you are pregnant or breast-feeding, think you might be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine.

- Your doctor will prescribe Raxone to you only if the benefits of the treatment are greater than the risks to the unborn child.
- Raxone may pass into the mother's milk. If you are breast-feeding your doctor will discuss with you whether to stop breast-feeding or to stop taking the medicine. This will take into account the benefit of breast-feeding to the child and the benefit of the medicine for you.

Driving and using machines

Raxone is not expected to affect your ability to drive or use machines.

Raxone contains lactose and sunset yellow (E110)

- Raxone contains lactose (a type of sugar). If you have been told by your doctor that you have lactose intolerance or that you cannot tolerate or digest some sugars, talk to your doctor before taking this medicine.
- Raxone contains a colourant called "sunset yellow" (also called E110). This may cause allergic reactions.

3. How to take Raxone

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

How much to take

The recommended dose is 2 tablets three times a day - this is a total of 6 tablets per day.

Taking this medicine

- Take the tablets with food - this helps to get more of the medicine from your stomach into your blood.
- Swallow the tablets whole with a glass of liquid.
- Do not crush or chew the tablets.
- Take the tablets at the same time of day each day. For example in the morning at breakfast, with lunch at mid-day and with dinner in the evening.

If you take more Raxone than you should

If you take more Raxone than you should, talk to your doctor straight away.

If you forget to take Raxone

If you forget a dose, skip the missed dose. Take the next dose at the usual time. Do not take a double dose to make up for a forgotten dose.

If you stop taking Raxone

Talk to your doctor before you stop taking this medicine.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. The following side effect may happen with this medicine:

Very common (may affect more than 1 in 10 people):

- nasopharyngitis (cold)
- cough

Common (may affect up to 1 in 10 people):

- diarrhoea (mild to moderate that usually does not require discontinuation of treatment)
- back pain

Unknown frequency (frequency cannot be estimated from the available data):

- bronchitis
- changes in blood test results: low level of white blood cells, or low level of red blood cells, or low level of platelets
- increased cholesterol or fat in the blood –shown in tests
- fits, feeling confused, seeing or hearing things that are not real (hallucinations), feeling excited, movements that you cannot control, a tendency to wonder away, feeling dizzy, headache, feeling restless, lacking energy
- nausea, vomiting, loss of appetite, stomach ache
- high levels of some liver enzymes in the body which mean you have liver problems – shown in tests, high levels of “bilirubin” – this can make your skin and the whites of your eyes look yellow, hepatitis
- rash, itching
- pain in extremity
- high levels of nitrogen in the blood - shown in tests change in urine colour
- generally feeling unwell

Reporting of side effects

If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via [the national reporting system in Appendix V](#). By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Raxone

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the carton and the bottle after 'EXP'. The expiry date refers to the last day of that month.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Raxone contains

- The active substance is idebenone. Each film-coated tablet contains 150 mg of idebenone.
- The other ingredients are:
Tablet core: lactose monohydrate, microcrystalline cellulose, croscarmellose sodium, povidone K25, magnesium stearate and colloidal silica.
Tablet film-coating: macrogol, poly(vinyl alcohol), talc, titanium dioxide, sunset yellow (E110).

What Raxone looks like and contents of the pack

- Raxone film-coated tablets are orange, round tablets of 10 mm diameter, engraved with the Santhera logo on one side and '150' on the other side.
- Raxone is supplied in white plastic bottles. Each bottle contains 180 tablets.

Marketing Authorisation Holder and Manufacturer

Santhera Pharmaceuticals (Deutschland) GmbH
Marie-Curie Strasse 8
79539 Lörrach
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Tel: +49 (0) 7621 1690 200
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This leaflet was last revised in

This medicinal product has been authorised under 'exceptional circumstances'.

This means that due to the rarity of the disease it has not been possible to obtain complete information on this medicinal product.

The European Medicines Agency will review any new information which may become available every year and this leaflet will be updated as necessary.

Detailed information on this medicine is available on the European Medicines Agency web site: <http://www.ema.europa.eu>. There are also links to other websites about rare diseases and treatments.

ANNEX IV

**CONCLUSIONS ON THE GRANTING OF THE MARKETING AUTHORISATION
UNDER EXCEPTIONAL CIRCUMSTANCES PRESENTED BY THE EUROPEAN
MEDICINES AGENCY**

Conclusions presented by the European Medicines Agency on:

- **Marketing authorisation under exceptional circumstances**

The CHMP having considered the application is of the opinion that the risk-benefit balance is favourable to recommend the granting of the marketing authorisation under exceptional circumstances as further explained in the European Public Assessment Report.