ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

RILUTEK 50 mg film-coated tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains 50 mg of riluzole

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Film-coated tablet
The tablets are capsule-shaped, white and engraved with “RPR 202” on one side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

RILUTEK is indicated to extend life or the time to mechanical ventilation for patients with amyotrophic lateral sclerosis (ALS).

Clinical trials have demonstrated that RILUTEK extends survival for patients with ALS (see section 5.1). Survival was defined as patients who were alive, not intubated for mechanical ventilation and tracheotomy-free.
There is no evidence that RILUTEK exerts a therapeutic effect on motor function, lung function, fasciculations, muscle strength and motor symptoms. RILUTEK has not been shown to be effective in the late stages of ALS.

Safety and efficacy of RILUTEK has only been studied in ALS. Therefore, RILUTEK should not be used in patients with any other form of motor neurone disease.

4.2 Posology and method of administration

Treatment with RILUTEK should only be initiated by specialist physicians with experience in the management of motor neurone diseases.

Posology
The recommended daily dose in adults or older people is 100 mg (50 mg every 12 hours).
No significant increased benefit can be expected from higher daily doses.

Special populations
Impaired renal function
RILUTEK is not recommended for use in patients with impaired renal function, as studies at repeated doses have not been conducted in this population (see section 4.4).

Older people
Based on pharmacokinetic data, there are no special instructions for the use of RILUTEK in this population.

Impaired hepatic function
See sections 4.3, 4.4 and 5.2.

Paediatric population
RILUTEK is not recommended for use in paediatric population, due to a lack of data on the safety and efficacy of riluzole in any neurodegenerative diseases occurring in children or adolescents.

Method of administration
Oral use

4.3 Contraindications

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

Hepatic disease or baseline transaminases greater than 3 times the upper limit of normal.

Patients who are pregnant or breast-feeding.

4.4 Special warnings and precautions for use

Liver impairment
Riluzole should be prescribed with care in patients with a history of abnormal liver function, or in patients with slightly elevated serum transaminases (ALT/SGPT; AST/SGOT up to 3 times the upper limit of the normal range (ULN)), bilirubin and/or gamma-glutamyl transferase (GGT) levels. Baseline elevations of several liver function tests (especially elevated bilirubin) should preclude the use of riluzole (see section 4.8).

Because of the risk of hepatitis, serum transaminases, including ALT, should be measured before and during therapy with riluzole. ALT should be measured every month during the first 3 months of treatment, every 3 months during the remainder of the first year, and periodically thereafter. ALT levels should be measured more frequently in patients who develop elevated ALT levels.

Riluzole should be discontinued if the ALT levels increase to 5 times the ULN. There is no experience with dose reduction or rechallenge in patients who have developed an increase of ALT to 5 times ULN. Readministration of riluzole to patients in this situation cannot be recommended.

Neutropenia
Patients should be warned to report any febrile illness to their physicians. The report of a febrile illness should prompt physicians to check white blood cell counts and to discontinue riluzole in case of neutropenia (see section 4.8).

Interstitial lung disease
Cases of interstitial lung disease have been reported in patients treated with riluzole, some of them were severe (see section 4.8). If respiratory symptoms develop such as dry cough and/or dyspnoea, chest radiography should be performed, and in case of findings suggestive of interstitial lung disease (e.g. bilateral diffuse lung opacities), riluzole should be discontinued immediately. In the majority of the reported cases, symptoms resolved after medicinal product discontinuation and symptomatic treatment.

Renal impairment
Studies at repeated doses have not been conducted in patients with impaired renal function (see section 4.2).

Sodium
This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially “sodium free”.

4.5 Interaction with other medicinal products and other forms of interaction

There have been no clinical studies to evaluate the interactions of riluzole with other medicinal products.

In vitro studies using human liver microsomal preparations suggest that CYP 1A2 is the principal isozyme involved in the initial oxidative metabolism of riluzole. Inhibitors of CYP 1A2 (e.g. caffeine, diclofenac, diazepam, nicergoline, clomipramine, imipramine, fluvoxamine, phenacetin, theophylline, amitriptyline and quinolones) could potentially decrease the rate of riluzole elimination, while inducers of CYP 1A2 (e.g. cigarette smoke, charcoal-broiled food, rifampicin and omeprazole) could increase the rate of riluzole elimination.

4.6 Fertility, pregnancy and lactation

Pregnancy
RILUTEK is contraindicated in pregnancy (see sections 4.3 and 5.3).
Clinical experience with riluzole in pregnant women is lacking.

Breast-feeding
RILUTEK is contraindicated in breast-feeding women (see sections 4.3 and 5.3).
It is not known whether riluzole is excreted in human milk.

Fertility
Fertility studies in rats revealed slight impairment of reproductive performance and fertility at doses of 15 mg/kg/day (which is higher than the therapeutic dose), probably due to sedation and lethargy.

4.7 Effects on ability to drive and use machines

Patients should be warned about the potential for dizziness or vertigo, and advised not to drive or operate machinery if these symptoms occur.

No studies on the effects on the ability to drive and use machines have been performed.

4.8 Undesirable effects

Summary of safety profile
In phase III clinical studies conducted in ALS patients treated with riluzole, the most commonly reported adverse reactions were asthenia, nausea and abnormal liver function tests.

Tabulated summary of adverse reactions
Undesirable effects ranked under headings of frequency are listed below, using the following convention: very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000), very rare (<1/10,000), not known (cannot be estimated from the available data).

	Very common	Common	Uncommon	Not known
Blood and lymphatic system disorders			Anaemia	Severe neutropenia (see section 4.4)
Immune system disorders			Anaphylactoid reaction, angioedema	
Nervous system disorders		Headache, dizziness, oral paraesthesia, somnolence		
Cardiac disorders		Tachycardia		
Respiratory, thoracic and mediastinal disorders			Interstitial lung disease (see section 4.4)	
Gastrointestinal disorders	Nausea	Diarrhoea, abdominal pain, vomiting	Pancreatitis	
Skin and subcutaneous tissue disorders				Rash
Hepato-biliary disorders	Abnormal liver function tests			Hepatitis
General disorders and administration site conditions	Asthenia	Pain		

Description of selected adverse reactions

Hepato-biliary disorders

Increased alanine aminotransferase usually appeared within 3 months after the start of therapy with riluzole; they were usually transient and levels returned to below twice the ULN after 2 to 6 months while treatment was continued. These increases could be associated with jaundice. In patients (n=20) from clinical studies with increases in ALT to more than 5 times the ULN, treatment was discontinued and the levels returned to less than 2 times the ULN within 2 to 4 months in most cases (see section 4.4).

Study data indicate that Asian patients may be more susceptible to liver function test abnormalities - 3.2% (194/5995) of Asian patients and 1.8% (100/5641) of Caucasian patients.

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

Neurological and psychiatric symptoms, acute toxic encephalopathy with stupor, coma, and methaemoglobinaemia have been observed in isolated cases.

In case of overdose, treatment is symptomatic and supportive.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: other nervous system drugs, ATC code: N07XX02.

Mechanism of action
Although the pathogenesis of ALS is not completely elucidated, it is suggested that glutamate (the primary excitatory neurotransmitter in the central nervous system) plays a role for cell death in the disease.

Riluzole is proposed to act by inhibiting glutamate processes. The mode of action is unclear.

Clinical efficacy and safety
In a trial, 155 patients were randomised to riluzole 100 mg/day (50 mg twice daily) or placebo and were followed-up for 12 to 21 months. Survival, as defined in the second paragraph of section 4.1, was significantly extended for patients who received riluzole as compared to patients who received placebo. The median survival time was 17.7 months versus 14.9 months for riluzole and placebo, respectively.

In a dose-ranging trial, 959 patients with ALS were randomised to one of four treatment groups: riluzole 50, 100, 200 mg/day, or placebo and were followed-up for 18 months. In patients treated with riluzole 100 mg/day, survival was significantly higher compared to patients who received placebo. The effect of riluzole 50 mg/day was not statistically significant compared to placebo and the effect of 200 mg/day was essentially comparable to that of 100 mg/day. The median survival time approached 16.5 months versus 13.5 months for riluzole 100 mg/day and placebo, respectively.

In a parallel group study designed to assess the efficacy and safety of riluzole in patients at a late stage of the disease, survival time and motor function under riluzole did not differ significantly from that of placebo. In this study the majority of patients had a vital capacity less than 60%.

In a double-blind placebo-controlled trial designed to assess the efficacy and safety of riluzole in Japanese patients, 204 patients were randomised to riluzole 100 mg/day (50 mg twice daily) or placebo and were followed-up for 18 months. In this study, the efficacy was assessed on inability to walk alone, loss of upper limb function, tracheostomy, need for artificial ventilation, gastric tube feeding or death. Tracheostomy-free survival in patients treated with riluzole did not differ significantly from placebo. However, the power of this study to detect differences between treatment groups was low. Meta-analysis including this study and those described above showed a less striking effect on survival for riluzole as compared to placebo although the differences remained statistically significant.

5.2 Pharmacokinetic properties

The pharmacokinetics of riluzole have been evaluated in healthy male volunteers after single oral administration of 25 to 300 mg and after multiple-dose oral administration of 25 to 100 mg bid. Plasma levels increase linearly with the dose and the pharmacokinetic profile is dose-independent. With multiple dose administration (10 day-treatment at 50 mg riluzole bid), unchanged riluzole accumulates in plasma by about 2 fold and steady-state is reached in less than 5 days.

Absorption
Riluzole is rapidly absorbed after oral administration with maximal plasma concentrations occurring within 60 to 90 minutes (C_{max}=173 ± 72 (sd) ng/ml). About 90% of the dose is absorbed and the absolute bioavailability is 60 ± 18%.

The rate and extent of absorption is reduced when riluzole is administered with high-fat meals (decrease in C_{max} of 44%, decrease in AUC of 17%).

Distribution
Riluzole is extensively distributed throughout the body and has been shown to cross the blood brain barrier. The volume of distribution of riluzole is about 245 ± 69 L (3.4 L/kg). Riluzole is about 97% protein bound and it binds mainly to serum albumin and to lipoproteins.

Biotransformation
Unchanged riluzole is the main component in plasma and is extensively metabolised by cytochrome P450 and subsequent glucuronidation. *In vitro* studies using human liver preparations demonstrated that cytochrome P450 1A2 is the principal isoenzyme involved in the metabolism of riluzole. The metabolites identified in urine are three phenolic derivatives, one ureido-derivative and unchanged riluzole.

The primary metabolic pathway for riluzole is initial oxidation by cytochrome P450 1A2 producing N-hydroxy-riluzole (RPR112512), the major active metabolite of riluzole. This metabolite is rapidly glucuronoconjugated to O- and N-glucuronides.

Elimination
The elimination half-life ranges from 9 to 15 hours. Riluzole is eliminated mainly in the urine. The overall urinary excretion accounts for about 90% of the dose. Glucuronides accounted for more than 85% of the metabolites in the urine. Only 2% of a riluzole dose was recovered unchanged in the urine.

Special populations
Impaired renal function
There is no significant difference in pharmacokinetic parameters between patients with moderate or severe chronic renal insufficiency (creatinine clearance between 10 and 50 $ml.min^{-1}$) and healthy volunteers after a single oral dose of 50 mg riluzole.

Older people
The pharmacokinetic parameters of riluzole after multiple dose administration (4.5 days of treatment at 50 mg riluzole bid) are not affected in the older people (>70 years).

Impaired hepatic function
The AUC of riluzole after a single oral dose of 50 mg increases by about 1.7 fold in patients with mild chronic liver insufficiency and by about 3 fold in patients with moderate chronic liver insufficiency.

Race
A clinical study conducted to evaluate the pharmacokinetics of riluzole and its metabolite N-hydroxyriluzole following repeated oral administration twice daily for 8 days in 16 healthy Japanese and 16 Caucasian adult males showed in the Japanese group a lower exposure of riluzole (C_{max} 0.85 [90% CI 0.68-1.08] and $AUC_{inf.}$ 0.88 [90% CI 0.69-1.13]) and similar exposure to the metabolite. The clinical significance of these results is not known.

5.3 Preclinical safety data

Riluzole did not show any carcinogenicity potential in either rats or mice.

Standard tests for genotoxicity performed with riluzole were negative. Tests on the major active metabolite of riluzole gave positive results in two in vitro tests. Intensive testing in seven other standard *in vitro* or *in vivo* assays did not show any genotoxic potential of the metabolite. On the basis of these data, and taking into consideration the negative studies on the carcinogenesis of riluzole in the mouse and rat, the genotoxic effect of this metabolite is not considered to be of relevance in humans.

Reductions in red blood cell parameters and/or alterations in liver parameters were noted inconsistently in subacute and chronic toxicity studies in rats and monkeys. In dogs, haemolytic anaemia was observed.
In a single toxicity study, the absence of corpora lutea was noted at a higher incidence in the ovary of treated compared to control female rats. This isolated finding was not noted in any other study or species.

All these findings were noted at doses which were 2-10 times higher than the human dose of 100 mg/day.

In the pregnant rat, the transfer of ^{14}C-riluzole across the placenta to the foetus has been detected. In rats, riluzole decreased the pregnancy rate and the number of implantations at exposure levels at least twice the systemic exposure of humans given clinical therapy. No malformations were seen in animal reproductive studies.

In lactating rats, ^{14}C-riluzole was detected in milk.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Core:
Dibasic calcium phosphate, anhydrous
Micro crystalline cellulose
Colloidal silica, anhydrous
Magnesium stearate
Croscarmellose sodium

Coating:
Hypromellose
Macrogol 6000
Titanium dioxide (E171)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

Tablets are packaged in opaque pvc/aluminium blister cards.
Each package contains 56 tablets.

6.6 Special precautions for disposal

No special requirements.

7. MARKETING AUTHORISATION HOLDER

Sanofi Mature IP
54 rue La Boétie
75008 Paris
France

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/96/010/001

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

date of first authorisation: 10 June 1996
date of last renewal: 10 June 2006

10. DATE OF REVISION OF THE TEXT

ANNEX II

A. MANUFACTURER(S) 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

A. MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer(s) responsible for batch release

Opella Healthcare International SAS
56, Route de Choisy
60200 Compiègne
France

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 (PSURs)**

The requirements for submission of PSURs 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.

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

- **Risk management plan (RMP)**

Not applicable

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON

1. NAME OF THE MEDICINAL PRODUCT

RILUTEK 50 mg film-coated tablets
riluzole

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each film-coated tablet contains 50 mg of riluzole.

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

56 film-coated tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.
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

Sanofi Mature IP
54 rue La Boétie
75008 Paris
France

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/96/010/001

13. BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

RILUTEK

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC:
SN:
NN:

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

PVC/ALUMINIUM BLISTER

1. NAME OF THE MEDICINAL PRODUCT

RILUTEK 50 mg film-coated tablets
riluzole

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Sanofi Mature IP

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Batch

5. OTHER

B. PACKAGE LEAFLET

Package leaflet: Information for the user

RILUTEK 50 mg film-coated tablets
Riluzole

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 RILUTEK is and what it is used for

What RILUTEK is

The active substance in RILUTEK is riluzole which acts on the nervous system.

What RILUTEK is used for

RILUTEK is used in patients with amyotrophic lateral sclerosis (ALS).

ALS is a form of motor neurone disease where attacks of the nerve cells responsible for sending instructions to the muscles lead to weakness, muscle waste and paralysis.

The destruction of nerve cells in motor neurone disease may be caused by too much glutamate (a chemical messenger) in the brain and spinal cord. RILUTEK stops the release of glutamate and this may help in preventing the nerve cells being damaged.

Please consult your doctor for more information about ALS and the reason why this medicine has been prescribed for you.

2. What you need to know before you take RILUTEK

Do not take RILUTEK
- if you are **allergic** to riluzole or any of the other ingredients of this medicine (listed in section 6),
- if you have any **liver disease** or increased blood levels of some enzymes of the liver (transaminases),
- if you are **pregnant or breast-feeding**.

Warnings and precautions
Talk to your doctor before taking RILUTEK:
- if you have any **liver problems:** yellowing of your skin or the white of your eyes (jaundice), itching all over, feeling sick, being sick
- if your **kidneys** are not working very well
- if you have any **fever**: it may be due to a low number of white blood cells which can cause an increased risk of infection

If any of the above applies to you, or if you are not sure, tell your doctor who will decide what to do.

Children and adolescents
If you are less than 18 years of age, the use of RILUTEK is not recommended because there is no information available in this population.

Other medicines and RILUTEK
Tell your doctor if you are taking, have recently taken or might take any other medicines.

Pregnancy, breast-feeding and fertility
You MUST NOT take RILUTEK if you are or think you may be pregnant, or if you are breast-feeding.

If you think you may be pregnant, or if you intend to breast-feed, ask your doctor for advice before taking RILUTEK.

Driving and using machines
You can drive or use any tools or machines, unless you feel dizzy or lightheaded after taking this medicine.

RILUTEK contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially “sodium free”.

3. How to take RILUTEK

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

The recommended dose is one tablet, twice a day.
The tablets should be taken by mouth, every 12 hours, at the same time of the day each day (e.g. in the morning and evening).

If you take more RILUTEK than you should

If you take too many tablets, contact your doctor or the nearest hospital emergency department immediately.

If you forget to take RILUTEK

If you forget to take your tablet, leave out that dose completely and take the next tablet at the usual time.
Do not take a double dose to make up for a forgotten tablet.

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.

IMPORTANT
Tell your doctor immediately
- if you experience any **fever** (increase in temperature) because RILUTEK may cause a decrease in the number of white blood cells. Your doctor may want to take a blood sample to check the number of white blood cells, which are important in fighting infections.

- if you experience any of the following symptoms: yellowing of your skin or the white of your eyes (jaundice), itching all over, feeling sick, being sick, as this may be signs of **liver disease** (hepatitis).Your doctor may do regular blood tests while you are taking RILUTEK to make sure that this does not occur.

- if you experience cough or difficulties in breathing, as this may be a sign of lung disease (called interstitial lung disease).

Other side effects
Very common side effects (may affect more than 1 in 10 people) of RILUTEK are:
- tiredness
- feeling sick
- increased blood levels of some enzymes of the liver (transaminases).

Common side effects (may affect up to 1 in 10 people) of RILUTEK are:
- dizziness
- sleepiness
- headache
- numbness or tingling of the mouth
- increase in heartbeat
- abdominal pain
- vomiting
- diarrhoea
- pain

Uncommon side effects (may affect up to 1 in 100 people) of RILUTEK are:
- anaemia
- allergic reactions
- inflammation of the pancreas (pancreatitis).

Not known: frequency cannot be estimated from the available data
- rash

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

5. How to store RILUTEK

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 blister after EXP. The expiry date refers to the last day of that month.

This medicine does not require any special storage conditions.

6. Contents of the pack and other information

What RILUTEK contains

- The active substance is riluzole.
- The other ingredients are:

Core: anhydrous dibasic calcium phosphate, micro crystalline cellulose, anhydrous colloidal silica, magnesium stearate, croscarmellose sodium;
Coating: hypromellose, macrogol 6000, titanium dioxide (E171).

What RILUTEK looks like and content of the pack

The tablets are film-coated, capsule-shaped and white. Each tablet contains 50 mg of riluzole and is engraved with "RPR 202" on one side.
RILUTEK is available in a pack of 56 tablets to be taken orally.

Marketing Authorisation Holder
Sanofi Mature IP
54 rue La Boétie
75008 Paris
France

Manufacturer
Opella Healthcare International SAS
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60200 Compiègne
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For any information about this medicinal product, please contact the local representative of the Marketing Authorisation Holder.

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This leaflet was last approved in {MM/YYYY}.

Annex IV

Scientific conclusions and grounds for the variation to the terms of the marketing authorisation(s)

Scientific conclusions

Taking into account the PRAC Assessment Report on the PSUR(s) for riluzole, the scientific conclusions of CHMP are as follows:

In view of available data on rash from spontaneous reports including in some cases a close temporal relationship, a positive de-challenge and/or re-challenge, the PRAC concluded that a causal relationship between riluzole and rash is at least a reasonable possibility and the product information of products containing riluzole should be amended accordingly.

The CHMP agrees with the scientific conclusions made by the PRAC.

Grounds for the variation to the terms of the marketing authorisation(s)

On the basis of the scientific conclusions for riluzole the CHMP is of the opinion that the benefit-risk balance of the medicinal product(s) containing riluzole is unchanged subject to the proposed changes to the product information

The CHMP recommends that the terms of the marketing authorisation(s) should be varied.