15 March 2012
EMA/241210/2012

Assessment report

Riluzole Zentiva

International non-proprietary name: **riluzole**

Procedure No. **EMEA/H/C/002622**

Assessment Report as adopted by the CHMP with all information of a commercially condidential nature deleted.

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List of abbreviations

ALS	Amyotrophic Lateral Sclerosis
CHMP	Committee for Medicinal Products for Human Use
EC	European Commission
EMA	European Medicines Agency
EPAR	European Public Assessment Report
ERA	Environmental Risk Assessment
MAH	Marketing Authorisation Holder
PSUR	Periodic Safety Update Report
RMP	Risk Management Plan

1. Background information on the procedure

1.1. Submission of the dossier

The applicant Aventis Pharma S.A. submitted on 28 November 2011 an application for Marketing Authorisation to the European Medicines Agency (EMA) for Riluzole Zentiva, through the centralised procedure under Article 3 (2)(a) of Regulation (EC) No 726/2004. The eligibility to the centralised procedure was agreed upon by the EMA/CHMP on 26 September 2011.

The applicant applied for the following indication:

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

Clinical trials have demonstrated that Riluzole Zentiva extends survival for patients with ALS. Survival was defined as patients who were alive, not intubated for mechanical ventilation and tracheotomy-free.

There is no evidence that Riluzole Zentiva exerts a therapeutic effect on motor function, lung function, fasciculations, muscle strength and motor symptoms. Riluzole Zentiva has not been shown to be effective in the late stages of ALS.

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

The legal basis for this application refers to:

Article 10(c) of Directive 2001/83/EC – informed consent application.

The application submitted is composed of administrative information with a letter from Aventis Pharma S.A. allowing that use be made of relevant quality, non-clinical and/or clinical data contained in the Rilutek marketing authorisation dossier.

This application was submitted in accordance with Article 82.1 of Regulation (EC) No 726/2004 as a duplicate of Rilutek authorised on 10 June 1996.

Information on Paediatric requirements

Not applicable.

Information relating to orphan market exclusivity

Similarity

Not applicable.

Market Exclusivity

Not applicable.

Scientific Advice

The applicant did not seek scientific advice at the CHMP.

Licensing status

The reference product Rilutek was given a Community Marketing Authorisation on 10 June 1996.

1.2. Steps taken for the assessment of the product

The Rapporteur appointed by the CHMP was:

Rapporteur: Ian Hudson

- The application was received by the EMA on 28 November 2011.
- The procedure started on 18 December 2011.
- The Rapporteur's first Assessment Report was circulated to all CHMP members on 27 January 2012.
- The Rapporteur circulated the updated Assessment Report to all CHMP members on 8 February 2012.
- During the meeting on 13-16 February 2012, the CHMP, in the light of the overall data submitted and the scientific discussion within the Committee, issued a positive opinion for granting a Marketing Authorisation to Riluzole Zentiva on 16 February 2012.

2. Scientific discussion

2.1. Introduction

This marketing authorisation application for Riluzole Zentiva (riluzole) has been submitted by Aventis Pharma S.A. as an informed consent application in accordance with Article 10c of Directive 2001/83/EC, as amended.

The MAH (Aventis Pharma S.A.) for Rilutek, which was authorised on 10 June 1996, provided consent to make use of the pharmaceutical, non-clinical and clinical documentation of the initial dossier of this authorised product and any subsequent post-marketing procedures submitted, assessed and approved.

As a consequence, quality, safety and efficacy of the Riluzole Zentiva medicinal product are identical to the up-to-date quality, non-clinical and clinical profile of Rilutek. The application for Riluzole Zentiva concerns the strength and package size identical to those approved for Rilutek and consists of only Module 1. Information on the scientific discussion can be found in the Rilutek CHMP assessment reports and in the European Public Assessment Report (EPAR) published on the EMA website.

The approved indication is:

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

Clinical trials have demonstrated that Riluzole Zentiva extends survival for patients with ALS. Survival was defined as patients who were alive, not intubated for mechanical ventilation and tracheotomy-free.

There is no evidence that Riluzole Zentiva exerts a therapeutic effect on motor function, lung function, fasciculations, muscle strength and motor symptoms. Riluzole Zentiva has not been shown to be effective in the late stages of ALS.

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

2.2. Quality aspects

Since this is an informed consent application referring to the Rilutek marketing authorisation, the quality data in support of the Riluzole Zentiva application are identical to the up-to-date quality data of the Rilutek dossier, which have been assessed and approved (including all post-marketing procedures).

2.3. Non-clinical aspects

Since this is an informed consent application referring to the Rilutek marketing authorisation, the non-clinical data in support of the Riluzole Zentiva application are identical to the up-to-date non-clinical data of the Rilutek dossier, which have been assessed and approved (including all post-marketing procedures).

The ERA provided for this application consists of an adequate justification for the absence of specific study data. The medicinal product subject to this application is intended to be administered in the indication and with posology already approved in the European Community for Rilutek. Based on the assumption that the product is intended to substitute for an identical product on the market, the approval of Riluzole Zentiva should not result in an increase of the total quantity of the active ingredients released in to the environment. Therefore, the CHMP was of the view that it should not result in an increase of risk to the environment during storage, distribution, use and disposal.

2.4. Clinical aspects

Since this an informed consent application referring to the Rilutek marketing authorisation, the clinical data in support of the Riluzole Zentiva application are identical to the up-to-date clinical data of the Rilutek dossier, which have been assessed and approved (including all post-marketing procedures).

2.5. Pharmacovigilance

Detailed description of the pharmacovigilance system

The applicant has provided documents that set out a detailed description of the system of pharmacovigilance (version 3.1, dated on April 18th, 2011). The CHMP considered that the Pharmacovigilance system as described by the applicant fulfils the requirements and provides adequate evidence that the services of a qualified person responsible for pharmacovigilance and of the necessary means for notification of any adverse reaction suspected of occurring either in the Community or in a third country are available.

Risk Management Plan

The CHMP did not request that the applicant submit a risk management plan because the safety profile of the medicinal product subject to this application is well established and there have been no safety concerns with the reference product that would warrant a need for an RMP. As no RMP is in place for the reference product, the CHMP agreed that a risk management plan for Riluzole Zentiva would not be required and expressed the view that routine pharmacovigilance would be adequate to monitor safety of the product.

2.6. User consultation

A justification for not performing a full user consultation with target patient groups on the package leaflet has been submitted by the applicant and has been found acceptable for the following reasons: The Package Leaflet of Rilutek has been successfully user tested in the framework of variation

EMEA/H/C/109/II/30 for which the Commission Decision was granted on 22 April 2008. Since the proposed Package Leaflet for the current application is essentially identical to the Package Leaflet of Rilutek, no further testing is warranted.

3. Benefit-Risk Balance

Since this application has been submitted by Aventis Pharma S.A. as an informed consent application to Rilutek in accordance with Article 10c of Directive 2001/83/EC, as amended, the CHMP considered that the benefit-risk balance of Riluzole Zentiva 50 mg film-coated tablets was favourable and therefore recommended the granting of the marketing authorisation for the following indication:

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

Clinical trials have demonstrated that Riluzole Zentiva extends survival for patients with ALS. Survival was defined as patients who were alive, not intubated for mechanical ventilation and tracheotomy-free.

There is no evidence that Riluzole Zentiva exerts a therapeutic effect on motor function, lung function, fasciculations, muscle strength and motor symptoms. Riluzole Zentiva has not been shown to be effective in the late stages of ALS.

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

4. Recommendations

Outcome

Based on the CHMP review of data on quality, safety and efficacy, the CHMP considers by consensus that the risk-benefit balance of Riluzole Zentiva in the treatment of amyotrophic lateral sclerosis to extend life or the time to mechanical ventilation is favourable and therefore recommends the granting of the marketing authorisation subject to the following conditions:

Conditions or restrictions regarding supply and use imposed on the MAH

Medicinal product subject to restricted medical prescription

Conditions or restrictions with regard to the safe and effective use of the medicinal product

Not applicable

Other Conditions

Risk Management System and PSUR cycle

The Marketing Authorisation Holder will provide Periodic Safety Update Report every two years until otherwise decided by the Committee for Medicinal Products for Human Use (CHMP).