



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

20 September 2012
EMA/741024/2012
Committee for Medicinal Products for Human Use (CHMP)

Assessment report

Memantine Merz

International non-proprietary name: **memantine**

Procedure No. **EMA/H/C/002568**

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



Table of contents

1. Background information on the procedure	4
1.1. Submission of the dossier.....	4
1.2. Steps taken for the assessment of the product	4
2. Scientific discussion	5
2.1. Introduction	5
2.2. Non- clinical aspects	5
2.2.1. Introduction	5
2.2.2. Ecotoxicity/Environmental risk assessment.....	5
2.3. Clinical aspects	5
2.4. Pharmacovigilance.....	6
3. Benefit-risk balance	7
4. Recommendation.....	7

List of abbreviations

CHMP	Committee for Medicinal Products for Human Use
EMA	European Medicines Agency
ERA	Environmental Risk Assessment
MA	Marketing Authorisation
MAH	Marketing Authorisation Holder
PL	Package Leaflet
PSUR	Periodic Safety Update Report
RMP	Risk Management Plan

1. Background information on the procedure

1.1. Submission of the dossier

The applicant Merz Pharmaceuticals GmbH submitted on 28 May 2012 an application for Marketing Authorisation to the European Medicines Agency (EMA) for Memantine Merz, through the centralised procedure under Article 3 (2) (b) of Regulation (EC) No 726/2004. The eligibility to the centralised procedure was agreed upon by the EMA/CHMP on 15 March 2012.

The applicant applied for the following indication: treatment of moderate to severe Alzheimer's disease.

The legal basis for this application refers to Article 10(c) Informed consent application.

The application submitted is composed of administrative information together with a letter from Merz Pharmaceuticals GmbH allowing use to be made of relevant quality, non-clinical and/or clinical data of the original marketing authorisation for Axura (EU/1/02/218//001-030).

Information on paediatric requirements

Not applicable

Scientific Advice

The applicant did not seek scientific advice at the CHMP.

Licensing status

The product was not licensed in any country at the time of submission of the application. The original medicinal product Axura was approved in the EU on 17 May 2002.

1.2. Steps taken for the assessment of the product

The Rapporteur appointed by the CHMP and the evaluation team were:

Rapporteur: **Walter Janssens**

- The application was received by the EMA on 28 May 2012
- The procedure started on 22 June 2012.
- The Rapporteur's first Assessment Report was circulated to all CHMP members on 3 September 2012.
- During the meeting on 17-20 September 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 Memantine Merz on 20 September 2012.

2. Scientific discussion

1.3. Introduction

This marketing authorisation application for Memantine Merz has been submitted by Merz Pharmaceuticals GmbH as an informed consent application in accordance with Article 10c of Directive 2001/83/EC, as amended.

The MAH (Merz Pharmaceuticals GmbH) for Axura, which was authorised on 17 May 2002, 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 Memantine-Merz medicinal product are identical to the up-to-date quality, non-clinical and clinical profile of Axura. The application for Memantine Merz concerns the identical strengths to those approved for Axura and consists of only Module 1. Information on the scientific discussion can be found in the Axura CHMP assessment reports and in the European Public Assessment Report (EPAR) published on the EMA website.

The approved indication is: Treatment of patients with moderate to severe Alzheimer's disease.

Quality aspects

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

1.4. Non- clinical aspects

1.4.1. Introduction

Since this application is an informed consent of the Axura application, the non-clinical data in support of the Memantine Merz application are identical to the up-to-date non-clinical data of the Axura dossier, which have been assessed and approved.

1.4.2. Ecotoxicity/Environmental risk assessment

An Environmental Risk Assessment was submitted. However, as the introduction of Memantine Merz is considered unlikely to result in any significant increase in the combined sales volumes for all memantine containing products and the exposure of the environment to the active substance, the environmental risk is expected to be similar and not increased.

1.5. Clinical aspects

Since this application is an informed consent of the Axura application, the clinical data in support of the Memantine Merz application are identical to the up-to-date clinical data of the Axura dossier, which have been assessed and approved.

1.6. Pharmacovigilance

Detailed description of the pharmacovigilance system

The CHMP considered that the Pharmacovigilance system as described by the applicant fulfils the legislative requirements.

Risk management plan

The applicant submitted a risk management plan in line with the reference product Axura.

Table 1. Summary of the risk management plan

Safety concern	Proposed pharmacovigilance activities	Proposed risk minimization activities
<u>Prostate cancer</u>	<u>Routine pharmacovigilance activities:</u> <ul style="list-style-type: none">- Systematic and continuous capture and follow-up of all Prostate Cancer ADRs- Regular and specific reporting and presentation of reports of Prostate Cancer ADRs in PSURs <u>Additional pharmacovigilance activities:</u> <ul style="list-style-type: none">- Epidemiologic population based case control study	None
<u>Overdose with memantine pump device</u>	<u>Routine pharmacovigilance activities:</u> <ul style="list-style-type: none">- Systematic and continuous capture and follow-up of all reports of overdose and drug administration error including a monthly signal detection- Cases of overdoses/drug administration errors with the pump device will be analyzed and presented with the next PSUR.	None

The below pharmacovigilance activities in addition to the use of routine pharmacovigilance are needed to investigate further prostate cancer safety concerns:

Description	Due date
Epidemiologic population based case control study	The study is planned to be evaluated and reported until Q3 2013.

No additional risk minimisation activities were required.

In addition, the CHMP considered that the applicant should provide an updated RMP taking into account the currently on-going finalisation of the study protocol for the required post-authorisation safety study investigating "memantine use and prostate cancer" as soon as available in the post-marketing authorisation setting.

PSUR submission

The PSUR submission schedule should follow the PSUR schedule for the reference product, which is currently on a 1 yearly cycle. The next data lock point for the reference medicinal product is 15 September 2012.

User consultation

The Package Leaflet of Axura has been successfully user tested in the framework of its evaluation for which the CHMP opinion was adopted on 17 May 2012. Since the proposed Package Leaflet for the current application is identical to the Package Leaflet for Axura except for the product-specific information, no further testing is warranted.

3. Benefit-risk balance

This Marketing Authorisation application for Memantine Merz (memantine hydrochloride) has been submitted by Merz Pharmaceuticals GmbH as an informed consent application of Axura in accordance with Article 10c of Directive 2011/83/EC, as amended.

As a consequence, quality, safety and efficacy of the Memantine Merz medicinal product are identical to the up-to-date quality, non-clinical and clinical profile of the reference product.

The application for Memantine Merz concerns the identical strengths to those approved for Axura.

In line with the assessment of data undertaken in the framework of the Axura initial marketing authorisation application as well as within all post-authorisation procedures, the CHMP considers that the benefit/risk balance for Memantine Merz is positive.

Information on the scientific discussion can be found on the Axura CHMP assessment reports and in the European Public Assessment Report (EPAR) published on the EMA website.

4. Recommendation

Based on the CHMP review of data on quality, safety and efficacy, the CHMP considers by consensus that the risk-benefit balance of Memantine Merz in the treatment of treatment of Alzheimer's disease is favourable and therefore recommends the granting of the marketing authorisation subject to the following conditions:

Conditions or restrictions regarding supply and use

Medicinal product subject to restricted medical prescription

Conditions and requirements of the Marketing Authorisation

Pharmacovigilance System

The MAH must ensure that the system of pharmacovigilance, presented in Module 1.8.1 of the marketing authorisation, is in place and functioning before and whilst the product is on the market.

Risk management system

The MAH shall perform the pharmacovigilance activities detailed in the Pharmacovigilance Plan, as agreed in the Risk Management Plan (RMP) presented in Module 1.8.2 of the marketing authorisation and any subsequent updates of the RMP agreed by the CHMP.

As per the CHMP Guideline on Risk Management Systems for medicinal products for human use, the updated RMP should be submitted at the same time as the next Periodic Safety Update Report (PSUR).

In addition, an updated RMP should be submitted:

- When new information is received that may impact on the current Safety Specification, Pharmacovigilance Plan or risk minimisation activities
- Within 60 days of an important (pharmacovigilance or risk minimisation) milestone being reached
- At the request of the EMA

PSUR cycle

The PSUR cycle for the product will follow PSURs submission schedule for Axura.

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

Not applicable

Conditions or restrictions with regard to the safe and effective use of the medicinal product to be implemented by the member states.

Not applicable.