European Medicines Agency
Evaluation of Medicines for Human Use

ASSESSMENT REPORT

FOR

Rivastigmine Sandoz

International Non-proprietary Name: rivastigmine

Procedure No. EMEA/H/C/001183

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

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1. BACKGROUND INFORMATION ON THE PROCEDURE

1.1 Submission of the dossier

The applicant Sandoz Pharmaceuticals GmbH submitted on 07 May 2009 an application for Marketing Authorisation to the European Medicines Agency (EMEA) for Rivastigmine Sandoz, through the centralised procedure according to Regulation (EC) No 726/2004.

The legal basis for this application refers to Article 10c of Directive 2001/83/EC, as amended relating to informed consent from the marketing authorisation holder, Novartis Europharm Limited, for the authorised medicinal product Exelon (EU/1/98/066/001-18).

The applicant applied for the following indication:

Symptomatic treatment of mild to moderately severe Alzheimer's dementia (AD).
Symptomatic treatment of mild to moderately severe dementia in patients with idiopathic Parkinson's disease (PPD).

Scientific Advice:
The applicant did not seek scientific advice at the CHMP.

Licensing status:

The initial product, Exelon, has been given a Community Marketing Authorisation on 12 May 1998.

The Rapporteur and Co-Rapporteur appointed by the CHMP and the evaluation teams were:

Rapporteur: **Pierre Demolis** Co-Rapporteur: **Tomas P Salmonson**

Scientific Advice:

The applicant did not seek scientific advice at the CHMP.

1.2 Steps taken for the assessment of the product

- The application was received by the EMEA on 07 May 2009.
- The procedure started on 24 May 2009.
- The Rapporteur's first Assessment Report was circulated to all CHMP members on 26 June 2009.
- During the meeting on 20 – 23 July 2009, the CHMP agreed on the consolidated List of Questions to be sent to the applicant. The final consolidated List of Questions was sent to the applicant on 24 July 2009.
- The applicant submitted the responses to the CHMP consolidated List of Questions on 21 August 2009.
- The Rapporteurs circulated the Joint Assessment Report on the applicant's responses to the List of Questions to all CHMP members on 07 September 2009.
- During the meeting on 21-24 September 2009, 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 Rivastigmine Sandoz on 24 September 2009. The applicant provided the letter of undertaking on the follow-up measures to be fulfilled post-authorisation on 15 September 2009.

2. SCIENTIFIC DISCUSSION

This application has been submitted as an informed consent application in accordance with Article 10c of Directive 2001/83/EC, as amended.

Therefore the MAH of the reference product, Exelon has provided consent to allow access to Module 2 to Module 5 of the initial dossier and any subsequent post-marketing procedures submitted, assessed and approved. A satisfactory letter of consent, dated 9 February 2009 is provided and accepted.
Exelon was submitted as a full application under Art 8(3) of Directive 2001/83/EC.
The dossier submitted for Rivastigmine Sandoz consists only of Module 1 information. Taking into account that different imprint is used; also exchange pages for Module 3 was submitted during the validation phase.

As a consequence, quality, safety and efficacy of the Rivastigmine Sandoz is identical to the up-to-date quality, safety and efficacy profile of Exelon. It is important to underline that only minor information regarding the different imprint was submitted during the validation phase. Information on the scientific discussions can be found in the Exelon CHMP assessment report and in the European Public Assessment Report (EPAR).

The approved indication is: “Symptomatic treatment of mild to moderately severe Alzheimer’s dementia. Symptomatic treatment of mild to moderately severe dementia in patients with idiopathic Parkinson’s disease.”

2.1 Quality aspects

Since this application is an informed consent of the Exelon application, the quality data in support of the Rivastigmine Sandoz application are almost identical to the up-to-date quality data of the Exelon dossier which have been assessed and approved (including all post-marketing procedures). Taking into account that different imprint is used; the applicant provided minor information on this matter in Module 3.

2.2 Non-Clinical aspects

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

No ERA was submitted. The CHMP agreed with the Applicant that introduction of Rivastigmine Sandoz is unlikely to result in any significant increase in the combined sales volumes for all rivastigmine containing products. Nevertheless, a calculation of PECsw has been requested as a FUM.

2.3 Clinical Aspects

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

Rivastigmine is a slowly reversible (pseudo-irreversible), brain selective, dual inhibitor of acetylcholinesterase (AChE) and butyrylcholinesterase (BuChE) of the carbamate type. Rivastigmine exerts its therapeutic effect by enhancing cholinergic function through reversible cholinesterase inhibition, thereby increasing the concentration of acetylcholine.

Exelon, the reference product is approved in the EU through the centralized procedure as capsules, oral solution and transdermal patches.
The application under review relates to following informed consents applications:

- 1.5 mg, 3 mg, 4.5 mg and 6 mg hard capsules.
- 2mg/ml, oral solution

The proposed Product Information is in line with that of Exelon.

- **User consultation**

The Applicant performed a user consultation testing on the package leaflet. The present readability test was well designed to meet its main objectives. The results of the user testing described in the user testing report support the changes made to the PL.

2.4 Pharmacovigilance

PSUR

As requested by the MAH and agreed by the CHMP, the PSUR cycle of Rivastigmine Sandoz will correspond to the one of the cross-referred product, Exelon, until otherwise specified.

Description of the Pharmacovigilance system

The Applicant provides a statement signed from the MAH and the European Qualified Person for Pharmacovigilance (QPPV), indicating that Sandoz has their services available as QPPV and has the necessary means for the collection and notification of any adverse reaction occurring either in the Community or in a third country.
The CHMP considered that the Pharmacovigilance system as described by the applicant fulfils the legislative requirements.

Risk Management Plan

The CHMP did not require the Applicant to submit a risk management plan beyond the provision of adequate information in the SPC and suitable packaging, as well as ongoing pharmacovigilance activities to continuously monitor the safety profile of the product due to the following points:

- Safety profile of the cross-referred product Exelon has been established in both clinical trials and in post-marketing experiences
- Identified and/or potential safety events of interest related to the cross-referred product Exelon has been continuously assessed, documented and closely monitored through global pharmacovigilance activities.

The CHMP, having considered the data submitted in the application, is of the opinion that no additional risk minimisation activities are required beyond routine pharmacovigilance.

2.5 Overall conclusions, benefit/risk assessment and recommendation

Overall conclusion and Benefit/risk assessment

Rivastigmine has a well-recognised efficacy and an acceptable level of safety in the proposed indications.
Since this application is an informed consent of the Exelon application, the CHMP considered that the risk-benefit balance of Rivastigmine Sandoz was favourable and therefore recommended the granting of the marketing authorisation for the following indication:

Symptomatic treatment of mild to moderately severe Alzheimer's dementia (AD).
Symptomatic treatment of mild to moderately severe dementia in patients with idiopathic Parkinson's disease (PPD).