18 August 2011
EMA/718241/2011
Committee for Medicinal Products for Human Use (CHMP)

Assessment report

Levodopa/Carbidopa/Entacapone Orion

levodopa/carbidopa/entacapone

Procedure No. **EMEA/H/C/002441**

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

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List of abbreviations

CHMP	Committee for Medicinal Products for Human Use
EC	European Commission
EMA	European Medicines Agency
EPAR	European Public Assessment Report
ERA	Environmental Risk Assessment
HDPE	High Density Poly Ethylene
MAH	Marketing Authorisation Holder
PSUR	Periodic Safety Update Report

1. Background information on the procedure

1.1. Submission of the dossier

The applicant Orion Corporation submitted on 7 April 2011 an application for Marketing Authorisation to the European Medicines Agency (EMA) for Levodopa/Carbidopa/Entacapone Orion, 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 October 2010.

The applicant applied for the following indication:

"Levodopa/Carbidopa/Entacapone Orion is indicated for the treatment of adult patients with Parkinson's disease and end-of-dose motor fluctuations not stabilised on levodopa/dopa decarboxylase (DDC) inhibitor treatment. "

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, quality, non-clinical and clinical data with a letter from Orion Corporation allowing use to be made of relevant quality, non-clinical and/or clinical data.

This application is submitted in accordance with Article 82.1 of Regulation (EC) No 726/2004 as a multiple of Stalevo authorised on 17 October 2003.

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 initial product Stalevo has been given a Community Marketing Authorisation on 17 October 2003.

1.2. Steps taken for the assessment of the product

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

Rapporteur: **Jaana Kallio**

Co-Rapporteur: **Beatriz Silva Lima**

- The application was received by the EMA on 7 April 2011.
- The procedure started on 24 April 2011.
- The Rapporteur's first Assessment Report was circulated to all CHMP members on 30 May 2011. The Co-Rapporteur's first Assessment Report was circulated to all CHMP members on 26 May 2011.
- The Rapporteurs circulated the Joint Assessment Report to all CHMP members on 15 June 2011.
- During the meeting on 20-23 June 2011, 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 Levodopa/Carbidopa/Entacapone Orion on 23 June 2011.

2. Scientific discussion

2.1. Introduction

This marketing authorisation application for Levodopa/Carbidopa/Entacapone Orion (levodopa/carbidopa/entacapone) has been submitted by Orion Corporation as an informed consent application in accordance with Article 10c of Directive 2001/83/EC, as amended.

The MAH (Orion Corporation) for Stalevo, which was authorised on 17 October 2003, 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 Levodopa/Carbidopa/Entacapone Orion medicinal product are identical to the up-to-date quality, non-clinical and clinical profile of Stalevo. The application for Levodopa/Carbidopa/Entacapone Orion concerns the identical strengths and pack sizes to those approved for Stalevo and consists of only Module 1. Information on the scientific discussion can be found in the Stalevo CHMP assessment reports and in the European Public Assessment Report (EPAR) published on the EMA website.

The approved indication is:

“Stalevo is indicated for the treatment of adult patients with Parkinson’s disease and end-of-dose motor fluctuations not stabilised on levodopa/dopa decarboxylase (DDC) inhibitor treatment.”

2.2. Quality aspects

Since this application is an informed consent of the Stalevo application, the quality data in support of the Levodopa/Carbidopa/Entacapone Orion application are identical to the up-to-date quality data of the Stalevo dossier, which have been assessed and approved (including all post-marketing procedures).

2.3. Non-clinical aspects

Since this application is an informed consent of the Stalevo application, the non-clinical data in support of the Levodopa/Carbidopa/Entacapone application are identical to the up-to-date non-clinical data of the Stalevo 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 at comparable dose levels and for indications that are already approved in the European Community for the reference product Stalevo. Based on the assumption that the product is intended to substitute for identical products on the market, the approval of the referred product should not result in an increase

of the total quantity of the active ingredients released into the environment. Therefore, it should not result in any increase of the risk to the environment during storage, distribution, use and disposal.

2.4. Clinical aspects

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

2.5. 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 CHMP did not require the applicant to submit a risk management plan because the safety profile of the medicinal product subject to this application is well established. No safety concerns requiring risk minimisation activities have been identified for Stalevo.

The CHMP, having considered the data submitted, was of the opinion that routine pharmacovigilance was adequate to monitor the 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 applicant has enclosed the user testing report performed for the combined Package Leaflet (PL) of Stalevo 50/12.5/200 mg, 100/25/200 mg and 150/37.5/200 film-coated tablets. The PL version tested was the PL submitted in connection with Stalevo renewal application (EMEA/H/C/511/R/040). The conducted readability testing was considered acceptable in CHMP opinion (EMEA/498045/2008) on 25 September 2008. Since the proposed PL for Levodopa/Carbidopa/Entacapone Orion will be identical with the Stalevo PL except for the product-specific information, no further testing is warranted.

3. Benefit-Risk Balance

Since this application has been submitted by Orion Corporation as an informed consent application to Stalevo in accordance with Article 10c of Directive 2001/83/EC, as amended, the CHMP considered that the benefit-risk balance of Levodopa/Carbidopa/Entacapone Orion 50 mg/12.5 mg/200 mg, 75 mg/18.75 mg/200 mg, 100 mg/25 mg/200 mg, 125 mg/31.25 mg/200 mg, 150 mg/37.5 mg/200 mg and 200 mg/50 mg/200 mg film-coated tablets was favourable and therefore recommended the granting of the marketing authorisation for the following indication:

“Levodopa/Carbidopa/Entacapone Orion is indicated for the treatment of adult patients with Parkinson’s disease and end-of-dose motor fluctuations not stabilised on levodopa/dopa decarboxylase (DDC) inhibitor treatment. “

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 Levodopa/Carbidopa/Entacapone Orion in the treatment of Parkinson's disease is favourable and therefore recommends the granting of the marketing authorisation.

Conditions or restrictions regarding supply and use

Medicinal product subject to medical prescription.

Conditions and requirements of the Marketing Authorisation

Risk Management System and PSUR cycle

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 medicinal product is on the market.

The PSUR submission schedule should follow the PSUR submission schedule for Stalevo.

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.