LÄKEMEDELSVERKET
SWEDISH MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Carboplatin Accord
(carboplatin)

SE/H/1908/01/E/01

This module reflects the scientific discussion for the approval of Carboplatin Accord. The procedure was finalised on 2023-02-12. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

Based on the review of the quality, safety and efficacy data, a marketing authorisation has been granted for Carboplatin Accord, 10 mg/ml, Concentrate for solution for infusion.

The active substance is carboplatin. A comprehensive description of the indication and posology is given in the SmPC.

For recommendations to the marketing authorisation not falling under Article 21a/22a/22 of Directive 2001/83/EC and conditions to the marketing authorisation pursuant to Article 21a/22a/ 22 of Directive 2001/83/EC to the marketing authorisation, please see section VI.

The application for Carboplatin Accord, 10 mg/ml, concentrate for solution for infusion, is a generic application made according to Article 10(1) of Directive 2001/83/EC. The applicant, Accord Healthcare B.V., applies for a marketing authorisation in CY, HR, RO, SI through this repeat use procedure with Sweden acting as reference member state (RMS). The product was first approved through a Decentralised Procedure (UK/H/1126/01/DC) with UK as RMS and AT, BE, CZ, DE, DK, EE, ES, FI, HU, IE, IT, LT, LV, NL, NO, PL, PT, SE, SK as concerned member states (CMS). A RMS transfer from UK to SE was completed on 5 April 2019.

The reference medicinal product chosen for the purposes of establishing the expiry of the data protection period is Paraplatin, 10 mg/ml, concentrate for solution for infusion, authorised in United Kingdom since 1991, with Bristol-Myers Squibb Holdings Limited, United Kingdom as marketing authorisation holder.

European Reference Product (ERP)

A European Reference Product is used in RMS and CY, HR, RO, SI: Paraplatin, 10 mg/ml, concentrate for solution for infusion, authorised in France with Bristol-Myers Squibb Holdings Limited, as marketing authorisation holder. The justification to use this product is based on information received from FR.

Potential similarity with orphan medicinal products

Having considered the arguments presented by the applicant and with reference to Article 8 of Regulation (EC) No 141/2000, Carboplatin Accord is considered not similar (as defined in Article 3 of Commission Regulation (EC) No. 847/2000) to Zejula. Therefore, with reference to Article 8 of Regulation (EC) No. 141/2000, the existence of any market exclusivity for Zejula in the treatment of ovarian cancer, does not prevent the granting of the marketing authorisation of Carboplatin Accord. This finding is without prejudice to the outcome of the scientific assessment of the marketing authorisation application.

II. QUALITY ASPECTS

II.1 Drug Substance

The structure of the drug substance has been adequately proven and its physico-chemical properties are sufficiently described.

The manufacture of the drug substance has been adequately described and satisfactory specifications have been provided for starting materials, reagents and solvents.

The drug substance specification includes relevant tests and the limits for impurities and degradation products have been justified. The analytical methods applied are suitably described and validated.

Stability studies confirm the retest period.

II.2 Medicinal Product

The medicinal product is formulated using excipients listed in section 6.1 in the Summary of Product Characteristics.

The manufacturing process has been sufficiently described and critical steps identified.

The tests and limits in the specification are considered appropriate to control the quality of the finished product in relation to its intended purpose.

Stability studies have been performed and data presented support the shelf life and special precautions for storage claimed in the Summary of Product Characteristics, sections 6.3 and 6.4.

III. NON-CLINICAL ASPECTS

The pharmacodynamic, pharmacokinetic and toxicological properties of carboplatin are well known. As carboplatin is a widely used, well-known active substance, no further studies are required and the applicant has not provided any. An overview based on a literature review is, thus, appropriate.

The non-clinical overview on the pre-clinical pharmacology, pharmacokinetics and toxicology is adequate.

There are no objections to approval of Carboplatin Accord from a non-clinical point of view.

Environmental Risk Assessment (ERA)

Since Carboplatin Accord is a generic product, it will not lead to an increased exposure to the environment. An environmental risk assessment is therefore not deemed necessary.

IV. CLINICAL ASPECTS

Pharmacokinetics

No studies have been conducted. The applied product is to be administered as an aqueous intravenous solution containing the same active substance as the currently authorised product. For this type of product, no bioequivalence studies are required according to the Guideline on the investigation of Bioequivalence (CHMP/QWP/EWP/1401/98 Rev. 1).

Pharmacodynamics, clinical efficacy and clinical safety

No new studies on pharmacodynamics, clinical efficacy or clinical safety have been submitted. This is a product for intravenous administration, and bioequivalence with the originator can be assumed. The efficacy and safety profiles are expected to be the same as for the originator. No additional data is necessary.

The originator Paraplatin is no longer marketed in the RMS and the application is, in the RMS, based on an ERP. However, carboplatin is an established product throughout the EU, with several generic products available.

Risk Management Plan

The MAH has submitted a risk management plan, in accordance with the requirements of Directive 2001/83/EC as amended, describing the pharmacovigilance activities and interventions designed to identify, characterise, prevent or minimise risks relating to Carboplatin Accord.

Safety specification

Important identified risk (s)	• Hypersensitivity and anaphylaxis • Myelosuppression • Use in pre-existing severe renal impairment and nephrotoxity • Concurrent therapy with nephrotoxic drugs or ototoxic drugs • Neurotoxicity • Severe hepatic dysfunction including acute liver necrosis and Venoocclusive liver disease • Ototoxicity • Tumour lysis syndrome • Haemolytic anaemia
Important potential risk (s)	• Secondary malignancies • Overdose
Missing information	• Use in Pediatric population

Pharmacovigilance Plan

Routine pharmacovigilance is suggested, and no additional pharmacovigilance activities are proposed by the applicant, which is endorsed.

Risk minimisation measures
Routine risk minimisation is suggested, and no additional risk minimisation activities are proposed by the applicant, which is endorsed.

Summary of the RMP
The submitted Risk Management Plan, version 1.1, signed 6 July 2018, is considered acceptable.

An updated RMP should be submitted:

- At the request of the RMS;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

If the dates for submission of a PSUR and the update of a RMP coincide, they can be submitted at the same time, but via different procedures.

V. USER CONSULTATION

The package leaflet has been evaluated via a user consultation study in accordance with the requirements of Articles 59(3) and 61(1) of Directive 2001/83/EC. The language used for the purpose of user testing the package leaflet was English.
The results show that the package leaflet meets the criteria for readability as set out in the Guideline on the readability of the label and package leaflet of medicinal products for human use.

VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

The application contains an adequate review of published clinical data. The quality of the drug product is acceptable. The benefit-risk ratio is considered favourable for this application.

List of recommendations not falling under Article 21a/22a/22 of Directive 2001/83/EC in case of a positive benefit risk assessment

N/A

List of conditions pursuant to Article 21a/22a or 22 of Directive 2001/83/EC

N/A

VII. APPROVAL

The mutual recognition procedure for Carboplatin Accord, 10 mg/ml, Concentrate for solution for infusion was positively finalised on 2023-02-12.

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Public Assessment Report – Update

Procedure number*	Scope	Product Information affected (Yes/No)	Date of end of procedure	Approval/ non approval	Summary/ Justification for refuse

*Only procedure qualifier, chronological number and grouping qualifier (when applicable)

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