Bundesamt für Sicherheit
im Gesundheitswesen

Public Assessment Report

Scientific discussion

Dacepton 5 mg/ml solution for infusion
Apomorphine hydrochloride hemihydrate

AT/H/0364/002/DC

This module reflects the scientific discussion for the approval of Dacepton 5 mg/ml. The procedure was finalised on 21.01.2014.

I. INTRODUCTION

The application is submitted in accordance with article 10(1) in directive 2001/83/EC: generic application.
The application concerns the addition of a new strength to the existing product Dacepton 10 mg/ml solution for injection/infusion, EVER Neuro Pharma GmbH.

The reference product is APO-go PFS 5 mg/ml solution for infusion in pre-filled syringe, Britannia Pharmaceuticals Limited, authorised since 2004-09-15.

Apomorphine is a morphine derivative with structural similarities to dopamine.
It is a short-acting dopamine agonist with balanced affinity for the D1 and D2 receptors. It does not share transport or metabolic pathways with levodopa.

The drug product is indicated for the treatment of disabling motor fluctuations ("on-off" phenomena) in patients with Parkinson's disease which persist despite individually titrated treatment with levodopa (with a peripheral decarboxylase inhibitor) and/or other dopamine agonists.

Pharmacological classification:
Pharmacotherapeutic group: Dopamine agonists
ATC code: N04BC07

II. QUALITY ASPECTS

II.1 Introduction

Dacepton 5 mg/ml is a solution for infusion which is presented in a clear glass vial, type I with bromobutyl rubber stopper and a flip-off cap.

II.2 Drug Substance

The active substance in Dacepton 5 mg/ml is apomorphine hydrochloride hemihydrate. The specification of the active substance meets the current scientific requirements. The adequate quality of the active substance has been shown by submitting the appropriate control data. The stability of the active substance has been tested under ICH conditions. The results of the stability studies support the established retest-period.

II.3 Medicinal Product

Dacepton 5 mg/ml contains the following excipients:
Sodium metabisulphite (E223) (1 mg per ml), sodium chloride (8 mg per ml), hydrochloric acid (for pH-adjustment) and water for injections.
The manufacturer responsible for batch release is EVER Neuro Pharma GmbH, Austria.
The development of the product has been sufficiently made and deemed appropriate. The usage of all the excipients has been described.
The release specification includes the check of all parameters relevant to this pharmaceutical form. Appropriate data concerning the control of the finished product support the compliance with the release specifications.
The packaging of the medicinal product complies with the current legal requirements.

Stability studies under ICH conditions have been performed and data presented support the shelf life claimed in the SmPC, with a shelf life of 30 months when stored in the original package to protect from light. Dacepton 5 mg/ml must not be refrigerated or freezed.

The pharmaceutical quality of Dacepton 5 mg/ml has been adequately shown.

II.4 Discussion on chemical, pharmaceutical and biological aspects

Information on development, manufacture and control of active substance and medicinal product has been presented in a satisfactory manner. The results of tests carried out indicate satisfactory consistency and uniformity of important product quality characteristics.

III. NON-CLINICAL ASPECTS

Pharmacodynamic, pharmacokinetic and toxicological properties of apomorphine hydrochloride are well known. As apomorphine hydrochloride is a widely used, well-known active substance, the applicant has not provided additional studies and further studies are not required. Overview based on literature review is, thus, appropriate.

Environmental Risk Assessment (ERA)
Since Dacepton is intended for generic substitution, this will not lead to an increased exposure to the environment.
In addition, the calculated Predicted Environmental Concentration (PEC) value is below 0.01µg/L and no other environmental concerns are apparent.

IV. CLINICAL ASPECTS

No clinical studies have been submitted.

Dacepton 5 mg/ml solution for infusion was developed as a product essentially similar to the originator product APO-go PFS 5mg/ml Solution for Infusion in Prefilled Syringe (Britannia Pharmaceuticals Limited). Both products are solutions intended for infusion and contain apomorphine hydrochloride hemihydrate as drug substance. The excipients, that both solutions have in common, are sodium metabisulphite, hydrochloric acid and water for injections, while Dacepton 5 mg/ml solution for infusion additionally contains sodium chloride for an improved osmolality.
During development of Dacepton 5 mg/ml solution for infusion, the originator product APO-go PFS was analysed. According to the results APO-go and Dacepton 5 mg/ml have similar profiles of most tested parameters.

According to the "Guideline on the Investigation of Bioequivalence" (CPMP/EWP/QWP/1401/98 Rev. 1/Corr**) bioequivalence testing is not required in the case of other than intravenous parenteral routes, e.g. intramuscular or subcutaneous, if the product is of the same type of solution (aqueous or oily), contains the same concentration of the same active substance and the same excipients in similar amounts as the medicinal product currently approved.

Furthermore, the guideline states that a bioequivalence study is not required for an aqueous parenteral solution with comparable excipients in similar amounts, if it can be demonstrated that the excipients have no impact on the viscosity.

These requirements are fulfilled within this application. Therefore, the waiving of bioequivalence testing of Dacepton is considered acceptable.

V. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

From a non-clinical and clinical point of view the benefit-risk ration of Dacepton is considered positive. The pharmaceutical quality of Dacepton 5 mg/ml has been adequately shown.

User consultation

The applicant submitted a bridging statement for the Dacepton 5 mg/ml Solution for infusion. According to "Consultation with target patient groups - meeting the requirements of article 59(3) without the need for a full test - recommendations for bridging" bridging will normally be acceptable for PLs for medicines in the same therapeutic class where the key safety information set out in the summary of product characteristics (and therefore the information in the PL) is similar. Moreover, bridging will normally be acceptable for PLs for medicines of the same active moiety for different strengths or routes of administration. This is applicable for Dacepton and the justification for not submitting a report is in line with the relevant guideline and therefore acceptable.

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This module reflects the procedural steps and scientific information after the finalisation of the initial procedure.

Procedure number*	Scope	Product Information affected	Date of end of procedure	Approval/ non approval	Summary/ Justification for refuse
AT/H/0364/002/DC	Line Extension: Dacepton 5 mg/ml solution for infusion	N	21/01/2014	approved	
AT/H/0364/002/II/006/G	Additional packaging site	N	09/06/2015	approved	
AT/H/0364/002/R/001	Renewal	Y	10/12/2018	approved	
AT/H/0364/002/E/001	Repeat Use Procedure to add new member states	N	19/11/2019	approved	

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