IPAR

Public Assessment Report for a
Medicinal Product for Human Use

Scientific Discussion

Paclitaxel 6 mg/ml Concentrate for Solution for Infusion
Paclitaxel
PA22709/004/001

The Public Assessment Report reflects the scientific conclusion reached by the Health Products Regulatory Authority (HPRA) at the end of the evaluation process and provides a summary of the grounds for approval of a marketing authorisation for a specific medicinal product for human use. It is made available by the HPRA for information to the public, after deletion of commercially sensitive information. The legal basis for its creation and availability is contained in Article 21 of Directive 2001/83/EC, as amended. It is a concise document which highlights the main parts of the documentation submitted by the applicant and the scientific evaluation carried out by the HPRA leading to the approval of the medicinal product for marketing in Ireland.

CONTENTS

I. INTRODUCTION

This product was initially authorised under procedure number UK/H/1847/1/DC with the UK as RMS. The responsibility of RMS was transferred to Ireland on 18/02/2019 under procedure number IE/H/0981/1/DC.
Please note the following detail for the product in IE:
Marketing Authorisation Number: PA22709/004/001
Marketing Authorisation Holder: Riemser Pharma GmbH

The current Summary of Product Characteristics (SmPC) for this medicinal product is available on the HPRA website at www.hpra.ie.

The UK public assessment report published at the time of the initial marketing authorisation is provided herein.

RECOMMENDATION

Based on the review of the data on quality, safety and efficacy, the RMS considers that the application for Paclitaxel, used in the treatment of ovarian, advanced breast cancer, non-small cell lung cancer and KS, **is approvable**.

EXECUTIVE SUMMARY

Problem statement

This Decentralised Procedure concerns a generic version of Paclitaxel, under the proposed trade name Paclitaxel 6 mg/ml concentrate for solution for infusion. In this Assessment Report, the name Paclitaxel is used.

This application refers to the reference medicinal product Taxol 6 mg/ml concentrate for solution for infusion which has been authorised for 10 years in at least a Member state or in the Community. The originator product is Taxol (6 mg/ml, concentrate for solution for infusion) by Bristol-Myers Squibb, authorised on 18th November 1993.

With the UK as the Reference Member State in this Decentralised Procedure, Peckforton Pharmaceuticals Limited is applying for the Marketing Authorisations for Paclitaxel in the following CMS: IE.

About the product

Paclitaxel is a member of the Taxane group of drugs and is an alkaloid ester derived from the Western and European Yew trees. Paclitaxel enhances tubulin polymerization, acting as a mitotic spindle poison. The stabilization of polymerization results in mitotic disruption. Paclitaxel is used clinically in the treatment of ovarian, advanced breast cancer, non-small cell lung cancer and KS. Neutropenia, thrombocytopenia and peripheral neuropathy are dose limiting toxicities. Routine pre-medication with a corticosteroid, histamine H_1 and H_2-receptor antagonists is recommended to prevent severe hypersensitivity reactions.

General comments on the submitted dossier

The application is submitted in accordance with Article 10(1) Directive 2001/83/EC as amended. The submitted documentation in relation to the proposed product is of sufficient quality and is consistent with the current EU regulatory requirements. Satisfactory quality, clinical and non-clinical overviews have been submitted.

A formal Environmental Risk Assessment has not been performed as the product is intended for generic substitution. Hence no increase in environmental risk is to be expected compared to that of the reference product.

The Applicant has supplied a justification for not submitting a European Risk Management Plan.

Other documentation relating to Pharmacovigilance systems has been provided.

Consultation with Target Patient Groups: The Applicant has carried out PIL user testing in 20 volunteers in the English Language.

General comments on compliance with GMP, GLP & GCP

The RMS has been assured that acceptable standards of GMP are in place for these product types at all sites responsible for the manufacture and assembly of this product. For manufacturing sites within the Community, the RMS has accepted copies of current manufacturer authorisations issued by inspection services of the competent authorities as certification that acceptable standards of GMP are in place at those sites. For manufacturing sites outside the Community, the RMS has accepted copies of current GMP Certificates of satisfactory inspection summary reports, 'close-out letters' or 'exchange of information' issued by the inspection services of the competent authorities (or those countries with which the EEA has a Mutual Recognition Agreement for their own territories) as certification that acceptable standards of GMP are in place at those non-Community sites.

No GCP certificate is required for this type of application.

II. QUALITY ASPECTS

Quality aspects

Drug Substance

The chemical-pharmaceutical documentation and Expert Report in relation to paclitaxel 20mg/ml solution for infusion are of sufficient quality in view of the present European regulatory requirements. The active substance paclitaxel is reported in EDMFs and relevant letters of access have been submitted to MHRA. The drug substance specification for this drug substance is generally acceptable. Stability studies have been performed with the drug substance. No significant changes in any parameters were observed. The proposed retest period of 12 months is acceptable.

Drug Product

The development of the product has been described, the choice of excipients is justified and their functions explained. The product specifications cover appropriate parameters for this dosage form. Validations reports for the analytical methods have been presented. Batch analysis has been performed on two batches of each presentation are provided. The batch analysis results show that the finished products meet the specifications proposed. The conditions used in the stability studies are according to the ICH stability guideline. The control tests and specifications for drug product are adequately drawn up. Full validation data for each presentation at commercial scale should be provided. The proposed shelf-life of 24 months is acceptable.

III. NON-CLINICAL ASPECTS

Non clinical aspects

The Applicant has provided a non-clinical Overview.

IV. CLINICAL ASPECTS

Clinical aspects

Bioequivalence studies

No new data have been submitted and none are required for this generic application.

Paclitaxel 6 mg/ml concentrate for solution for infusion is the generic version of Taxol 6 mg/ml concentrate for solution for infusion, the originator product (Bristol-Myers Squibb). The use of the reference product is well-established in the UK. Both products contain the same quantitative and qualitative composition of the active ingredient, Paclitaxel.

No new data have been submitted and none are required for this application. According to CPMP guidelines, the applicant is not required to submit a bioequivalence study if the product is to be administered as an aqueous intravenous solution containing the same active substance, in the same concentration as the currently authorised product (CPMP/EWP/1401/98, subpoint 5.1.6, Parenteral solutions).

Pharmacodynamics
No novel pharmacodynamic data are supplied or required for this application. The pharmacodynamic claims in the SPC are appropriately consistent with the innovator product.

Clinical efficacy and Safety
The clinical overview adequately reviews the published evidence to support the use of Paclitaxel in the proposed indications. The clinical overview reviews the safety data of Paclitaxel. No new safety concerns have been highlighted for the proposed indications.

Pharmacovigilance system
The Applicant has provided a description of the Pharmacovigilance system and this is acceptable.

Risk Management Plan
The Applicant has provided an acceptable justification for not submitting a European Risk Management Plan.

V. OVERALL CONCLUSIONS

BENEFIT RISK ASSESSMENT
The use of Paclitaxel is well established. It has recognised efficacy and acceptable safety. Overall the risk benefit analysis for Paclitaxel is favourable and a Marketing Authorisation was granted.

VI. REVISION DATE

22/02/2022

VII. UPDATES

This section reflects the significant changes following finalisation of the initial procedure.

SCOPE	PROCEDURE NUMBER	PRODUCT INFORMATION AFFECTED	DATE OF START OF PROCEDURE	DATE OF END OF PROCEDURE
RMS transfer	From UK/H/1847/1/DC to IE/H/0981/1/DC			