LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Pemetrexed Pharmaswiss
(pemetrexed)

SE/H/1474/01-02/DC

This module reflects the scientific discussion for the approval of Pemetrexed Pharmaswiss. The procedure was finalised on 2016-03-16. For information on changes after this date please refer to the module 'Update'.

Postadress/Postal address: P.O. Box 26, SE-751 03 Uppsala, SWEDEN
Besöksadress/Visiting address: Dag Hammarskjölds väg 42, Uppsala
Telefon/Phone: +46 (0)18 17 46 00 Fax: +46 (0)18 54 85 66
Internet: www.mpa.se E-mail: registrator@mpa.se

I. INTRODUCTION

The application for Pemetrexed Pharmaswiss, 100 mg and 500 mg, powder for concentrate for solution for infusion, is a generic application made according to Article 10(1) of Directive 2001/83/EC. The applicant, PharmaSwiss Ceska republika s.r.o., applies through the Decentralised Procedure with Sweden acting as reference member state (RMS) and EE, HU, LT, LV, PL, and SI as concerned member states (CMS).

The reference medicinal product chosen for the purposes of establishing the expiry of the data protection period is Alimta, 100 mg and 500 mg, powder for concentrate for solution for infusion, authorised in Community since 2004, with Eli Lilly Nederland B.V. as marketing authorisation holder.

For approved indications, see the Summary of Product Characteristics.

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

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

III.1 Discussion on the non-clinical aspects

Since this product has been shown to be essentially similar and refer to a product approved based on a full application with regard to preclinical data, no further such data have been submitted or are considered necessary.

IV. CLINICAL ASPECTS

IV.1 Pharmacokinetics

There are no bioequivalence studies included in the application. The absence of bioequivalence studies is acceptable since the applied product is to be administered as an intravenous solution containing the same active substance in the same concentration as the currently authorised product. The applied product also contains the same excipients in similar amounts as the reference product.

IV.2 Discussion on the clinical aspects

Since this product has been shown to be essentially similar and refer to a product approved based on a full application with regard to clinical efficacy/safety data, no further such data have been submitted or are considered necessary.

IV.3 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 Pemetrexed Pharmaswiss.

Safety specification

Updated summary table of safety concerns as approved in RMP

Summary of safety concerns	
Important identified risks	Noncompliance with folic acid and vitamin B12 regimens, manifested mainly as haematological and gastrointestinal toxicities Renal events Gastrointestinal disorder Interstitial pneumonitis Radiation pneumonitis Radiation recall Sepsis Bullous skin reaction including Stevens-Johnson

Summary of safety concerns	
	syndrome and toxic epidermal necrolysis Bone marrow suppression
Important potential risks	N/A
Missing information	N/A

The Safety specification has been amended as requested and now complies with the latest version (V6.0) of the Alimta RMP

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 Risk Minimisation Plan

Summary table of risk minimisation measures

Important identified risks		
Safety concern	**Routine risk minimisation measures**	**Additional risk minimisation measures**
Noncompliance with folic acid and vitamin B12 regimens, manifested mainly as haematological and gastrointestinal toxicities	Information provided in PIL and SmPC sections 4.2, 4.4 Prescription only medicine	None
Renal disorders	Information provided in PIL and SmPC sections 4.2, 4.4, 4.5, 4.8	None

Important identified risks		
	Prescription only medicine	
Gastrointestinal disorder	Information provided in PIL and SmPC sections 4.4, 4.5, 4.8 Prescription only medicine	None
Interstitial pneumonitis	Information provided in PIL and SmPC sections 4.8 Prescription only medicine	None
Radiation pneumonitis	Information provided in PIL and SmPC sections 4.4, 4.8 Prescription only medicine	None
Radiation recall	Information provided in PIL and SmPC sections 4.4, 4.8 Prescription only medicine	None
Sepsis	Information provided in PIL and SmPC sections 4.8 Prescription only medicine	None
Bullous skin reaction including Stevens-Johnson syndrome and toxic epidermal necrolysis	Information provided in PIL and SmPC sections 4.2,4.4, 4.8 Prescription only medicine	None
Bone marrow suppression	Information provided in PIL and SmPC sections 4.4, 4.8 Prescription only medicine	None

Important potential risks		
Safety concern	**Routine risk minimisation measures**	**Additional risk minimisation measures**
None	None	None

Following a Day 145 HU comment, the RMP has been updated in line with the RMP v.6. of the original drug (AlimtaTM).

The RMP is approved.

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

A user consultation with target patient groups on the package information leaflet (PIL) has been performed on the basis of a bridging report making reference to Alimta, EMEA/H/C/000564/II/0009. The bridging report submitted by the applicant has been found acceptable.

VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

The benefit/risk ratio is considered positive and Pemetrexed Pharmaswiss, 100 mg and 500 mg, powder for concentrate for solution for infusion, is recommended for approval.

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

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

VII. APPROVAL

The Decentralised procedure for Pemetrexed Pharmaswiss, 100 mg and 500 mg, powder for concentrate for solution for infusion, was positively finalised on 2016-03-16.

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MEDICAL PRODUCTS AGENCY

Public Assessment Report – Update

Procedure number*	Scope	Product Information affected	Date of end of procedure	Approval/ non approval	Summary/ Justification for refuse

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

Postadress/Postal address: P.O. Box 26, SE-751 03 Uppsala, SWEDEN
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