Public Assessment Report
Scientific discussion

Fosfomycin Labiana 2 g and 3 g granules for oral solution in sachets

(Fosfomycin trometamol)

Registration number in Spain:xxx

EU-procedure number:
ES/H/0332/01-02/DC

Applicant: Labiana Pharmaceuticals, S.L.U.
MA Holder: Labiana Pharmaceuticals, S.L.U.

This module reflects the scientific discussion for the approval of **Fosfomycin Labiana 2 g and 3 g granules for oral solution in sachets**. The procedure was finalised on March 2016. For information on changes after this date please refer to the module 'Update'.

I. INTRODUCTION

This decentralised procedure concerns a generic application claiming essential similarity with the innovator product Monuril® 2 g and 3 g granules for oral solution by Zambon Italy S.r.l. (group Zambon), Italy, registered since July 07th, 1986.

The legal basis of the application is Article 10(1) of Directive 2001/83/EC.

The Concerned Member States involved in these procedures are PL, PT and RO.

Fosfomycin Labiana 3 g is indicated for the treatment of acute uncomplicated cystitis caused by fosfomycin sensitive organisms in women from the age of 12 years and for periprocedural prophylaxis in diagnostic and surgical transurethral procedures in adults.

Fosfomycin Labiana 2 g is is indicated for the treatment of acute uncomplicated cystitis caused by fosfomycin sensitive organisms, in female children from the age of 6 to 11 years.

A comprehensive description of the product information is given in the SmPC.

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 authorisation issued by inspection services of the competent authorities as certification that acceptable standards of GMP are in place at those sites

RECOMMENDATION

Based on the review of the data on quality, safety and efficacy, the Member States have granted a marketing authorisation for **Fosfomycin Labiana 2 g and 3 g granules for oral solution in sachets** for Labiana Pharmaceuticals, S.L.U.

II. SCIENTIFIC OVERVIEW AND DISCUSSION

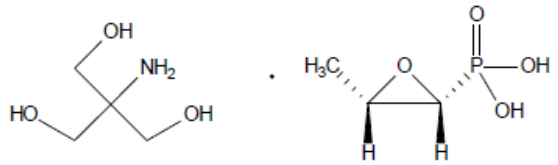
II-1 Quality aspects

INTRODUCTION

The drug product are granules for oral solution containing 2000 mg and 3000 mg of Fosfomycin (Trometamol), as active ingredient.
The excipients used are common for the manufacture of pharmaceutical preparations. The specifications for excipients are based on the specification given in the corresponding Eur. Ph. monographs.

Primary packaging complies with the current European regulations concerning materials in contact with food.

DRUG SUBSTANCE

INN Name	:	Fosfomycin Trometamol
Chemical name	:	2-Amino-2-(hydroxymethyl) propane-1,3-diol hydrogen (2R, 3S)-(3-methyloxiran-2-yl)phosphonate
Structure	:	
Molecular Formula	:	$C_7H_{18}NO_7P$
Molecular Weight	:	259.2 g/mol
Description	:	white or almost white, hygroscopic powder

Fosfomycin Trometamol is the subject of a European Pharmacopoeia monograph.

The manufacture and control of Fosfomycin Trometamol are covered by a Certificate of Suitability.

MEDICINAL PRODUCT

The drug products containing 2000 mg and 3000 mg of Fosfomycin (Trometamol) are similar to MONURIL® (reference).

The Pharmaceutical development has been supported on the basis of the similarity between the reference product and the proposed formulation.

The Applicant cross-refers to the reference product MONURIL®. Comparative studies between the proposed product and the reference product were performed and show essential similarity with respect to major physicochemical parameters.

The manufacturing process of the product has been described and validated.

The finished product specifications are considered acceptable. The analytical procedures have been described and are considered suitably validated. The analytical batch data results confirm the satisfactory uniformity of the product and indicate the manufacturing process is under control.

Finished product stability studies have been conducted in accordance with current guidelines and in the packaging proposed for marketing

Based on the results, a shelf-life of 36 months with the storage condition ñDo not store above 30ºC. Store in the original packageò is authorized when packed in the proposed packaging material surlyn/polyethylene/aluminium/paper sachets for both strengths.

II-2 Non-clinical aspects

A non-clinical overview on the pharmacology, pharmacokinetics and toxicology of the active substance has been provided, which is based on up-to-date and adequate scientific literature. The non-clinical overview on the pre-clinical pharmacology, pharmacokinetics and toxicology is adequate and the Member States agreed that no further non-clinical studies are required.

Environmental Risk Assessment (ERA)

No ERA was submitted. The medicinal product has the same quantitative and qualitative composition in active substances and a similar pharmaceutical form to the reference product. The introduction on the market of this medicinal product will not mean an increased exposure to the environment, since the generic medicinal product is intended to substitute the reference medicinal product as well as other generic products in the market.
In accordance with the Guideline on the Environmental Risk Assessment for medicinal products for human use (CPMP/SWP/4447/00), the absence of this Environmental Risk Assessment is therefore justified.

II.3 Clinical aspects

Introduction

Fosfomycin is a well-known drug with established efficacy and safety.

No new clinical efficacy or safety studies were conducted, which is acceptable for this abridged application. A clinical overview has been provided, which is based on scientific literature. The Member States agreed that no further clinical studies are required.

Biowaiver

The Applicant did not conduct any clinical study to support this application. The clinical bioequivalence studies are not necessary in view that both the reference product and the proposed product are aqueous oral solutions containing the same active substance at the same concentration as the currently approved product. The qualitative composition is identical and the quantitative composition is very similar. Therefore, there is no difference able to affect bioavailability.

According to the òGuideline on the Investigation of Bioequivalenceò a bioequivalence study is not required for an oral solution with the same excipients in very similar amounts.

Bioequivalence

Not applicable.

Risk Management Plan

A risk management plan in accordance with the requirements of Directive 2001/83/EC as amended has been submitted.

No additional risk minimization activities were required beyond those included in the product information.

Discussion on the clinical aspects

A bioequivalence study is not required for an oral solution at the same concentration with the same excipients in very similar amounts.

Efficacy and safety of the active substance fosfomycin are well documented for the reference medicinal product.

III OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

According to the "Guideline on the Investigation of Bioequivalence" a bioequivalence study is not required for an oral solution at the same concentration with the same excipients in very similar amounts.

The SmPC, PIL and labelling are considered satisfactory and consistent with the information for the reference medicinal product. The user testing of the Package Information Leaflet has been tested in accordance with Article 59(3) of Directive 2001/83/EC, as amended by Directive 2004/27/EC.

The benefit/risk balance was considered to be positive.

Agreement between Member States was reached during the procedure. The decentralised procedure was finalised with a positive outcome in March 2016.