LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Mifepristone Linepharma
mifepristone

SE/H/986/01/DC

This module reflects the scientific discussion for the approval of Mifepristone Linepharma. The procedure was finalised at 2010-12-01. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

Linepharma France has applied for a marketing authorisation for Mifepristone Linepharma tablets 200 mg claiming essential similarity to “Mifegyne 200 mg tablets marketed in Sweden by Laboratoires Exelgyn. The product contains mifepristone as active substance. For approved indications see the Summary of Product Characteristics. The reference product used in the bioequivalence study is Mifegyne tablets 200 mg from France.

II. QUALITY ASPECTS

II.1 Introduction

Mifepristone Linepharma is presented in the form of tablets containing 200 mg of mifepristone. The excipients are microcrystalline cellulose, magnesium stearate, maize starch, povidone and colloidal anhydrous silica. The tablets are packed in blisters.

II.2 Drug Substance

Mifepristone does not have a monograph in the Ph Eur.

Mifepristone is a yellowish powder which is practically insoluble in water and freely soluble in dichloromethane and methanol. The structure of mifepristone has been adequately proven and its physico-chemical properties sufficiently described. Relevant information on chirality is presented. The route of synthesis has been adequately described and satisfactory specifications have been provided for starting materials, reagents and solvents.

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

Stability studies under ICH conditions have been conducted and the data provided are sufficient to confirm the retest period.

II.3 Medicinal Product

Mifepristone Linepharma (tablet) is formulated using excipients described in the current Ph. Eur. All raw materials used in the product has demonstrated compliance with Commission Directive 2003/63/EC and the NfG on Minimising the risk of transmitting Animal Spongiform Encephalopathy Agents via human and veterinary medicinal products (EMEA/410/01).

The product development has taken into consideration the physico-chemical characteristics of the active substance.

The manufacturing process has been sufficiently described and critical steps identified. Results from the process validation studies confirm that the process is under control and ensure both batch to batch reproducibility and compliance with the product specification.

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 under ICH conditions have been performed and data presented support the shelf life claimed in the SPC, when stored below 30 °C and kept in the outer carton in order to protect from light.

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

The applicant submitted two bioequivalence studies, one with Mifegyne (approved in EES) as reference product and also one study with Mifeprex (approved in the US) as reference product. The latter is included for extrapolation of literature data where the Mifeprex product has been used. The studies were performed as single dose studies in the fasting state. The study with Mifegyne demonstrated bioequivalence for AUC, but not for C_{max} (the 90 % CI of the ratio of C_{max} arithmetical means was 103.33 – 126.66, and thus, slightly outside the upper limit of the specified interval). For the 200 mg dose proposed by the applicant for first trimester indication for Mifepristone Linepharma, the slight difference in bioequivalence was not considered a hinder for approval. The study with Mifeprex demonstrated bioequivalence for both AUC and C_{max}, and therefore extrapolation of data from studies made with Mifeprex is acceptable.

IV.2 Discussion on the clinical aspects

The applicant presented sufficient clinical data on clinical efficacy and safety investigations for treatment up to 63 days of amenorrhoea with a 200 mg dose of mifepristone provided that gemeprost 1 mg per vaginam is the chosen prostaglandin analogue.

V. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

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 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.

The risk/benefit ratio is considered positive and Mifepristone tablet 200 mg is recommended for approval.

VI. APPROVAL

The Decentralised procedure for Mifepristone tablet 200 mg was successfully finalised on 2010-12-01.

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Public Assessment Report – Update

Scope	Procedure number	Product Information affected	Date of start of the procedure	Date of end of procedure	Approval/ non approval	Assessment report attached
						Y/N (version)

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