LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Olvion
(Sildenafil)

SE/H/1061/01-03/DC

This module reflects the scientific discussion for the approval of Olvion. The procedure was finalised at 2011-05-26. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

Medochemie Ltd, Cyprus has applied for a marketing authorisation for Olvion, film-coated tablets, 25 mg, 50 mg and 100 mg, claiming essential similarity to Viagra, film-coated tablets, 25 mg, 50 mg and 100 mg marketed in the EU by Pfizer Limited. The product contains sildenafil as active substance. For approved indications, see the Summary of Product Characteristics. The reference product used in the bio-equivalence study is Viagra, 100 mg, film-coated tablets marketed by Pfizer Limited in United Kingdom.

II. QUALITY ASPECTS

II.1 Introduction

Olvion is presented in the form of film-coated tablets containing 25 mg, 50 mg and 75 mg of sildenafil which corresponds to 35.12 mg, 70.34 mg and 140.48 mg of sildenafil citrate. The excipients are microcrystalline cellulose, calcium hydrogen phosphate (anhydrous), croscarmellose sodium, magnesium stearate, hypromellose, titanium dioxide (E171), lactose and triacetin. The tablets are packed in PVC/Aluminium foil blisters.

II.2 Drug Substance

Sildenafil citate does not have a monograph in the Ph Eur.

Sildenafil citrate is white to off-white crystalline powder which is sparingly soluble in glacial acetic acid and very slightly soluble in water and ethanol. The structure of sildenafil citrate has been adequately proven and its physico-chemical properties sufficiently described. Relevant information on polymorphism 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

Olvion film-coated tablets are formulated using excipients described in the current Ph Eur, except for Opadry II White which is controlled according to acceptable in house specifications. All raw materials used in the product are of vegetable origin or 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, with no special storage precautions.

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

Sildenafil has an oral bioavailability of 41% (range 25-63%). Following an oral dose in the fasting state maximal plasma concentrations occur within 30 to 120 minutes (median 60 minutes). Concomitant food intake decreases the C_{max} with 29 % and delays t_{max} with about 60 minutes. The pharmacokinetics of sildenafil are linear within the dose range 25-100 mg.

One adequately performed bioequivalence study was submitted, in which 100 mg sildenafil tablets were compared with Viagra 100 mg tablets as a single dose under fasting conditions. The study was a randomised, two-treatment, two-period, two-sequence crossover study conducted in 40 healthy volunteers. Bioequivalence was demonstrated for sildenafil under fasting conditions, as the 90% confidence intervals for the test/reference ratio of the population geometric means fell within 80-125% for both AUC_{0-t} and C_{max}.

From a pharmacokinetic point of view, absence of studies with the additional strengths 25 mg and 50 mg is acceptable, as the pharmacokinetics of sildenafil are linear within the therapeutic dose range.

IV.2 Discussion on the clinical aspects

Since this product has been shown to be essentially similar and refers 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.

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 language used for the purpose of user testing the PIL was English.
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 results of the conducted bioequivalence study can be extrapolated to other strengths since the criteria for biowaiver for additional strengths are fulfilled according to the Note for Guidance on the Investigation of Bioavailability and Bioequivalence.

The risk/benefit ratio is considered positive and Olvion, film-coated tablets, 25 mg, 50 mg and 100 mg is recommended for approval.

Commitments
The applicant for Olvion will submit batch analysis data of more (at least two) batches from each of the drug substance manufacturer (Hetero Drugs Ltd, and Cadila Pharmaceutical Ltd.) based on the applicant/drug product manufacture´s specifications at the time of commercialization.

VI. APPROVAL

The Decentralised procedure for Olvion, film-coated tablets, 25 mg, 50 mg and 100 mg, was successfully finalised on 2011-05-26.

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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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