LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Opidol
(tramadol hydrochloride)

SE/H/985/01-03/DC

This module reflects the scientific discussion for the approval of Opidol. The procedure was finalised at 2011-04-28. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

Brown & Burk UK Ltd has applied for a marketing authorisation for Opidol, Prolonged-release tablets, 100, 150 and 200 mg claiming essential similarity to Nobligan retard 100, 150 and 200 mg prolonged-release tablets marketed in Sweden by Grünenthal GmbH. The product contains tramadol hydrochloride as active substance. For approved indications see the Summary of Product Characteristics. The reference product used in the bio-equivalence study are Zydol SR 100 mg Tablets by Grünenthal Ltd., (Source: UK), Zydol SR 150 mg Tablets by Grünenthal Ltd., (Source: UK), TOPALGIC L.P. tablet 200 mg by Grünenthal Ltd., (Source: France), Contramal LP tablet 200 mg, Grünenthal Ltd., (Source: France).

II. QUALITY ASPECTS

II.1 Introduction

Opidol is presented in the form of prolonged-release tablets containing 100 mg, 150 mg or 200 mg of tramadol hydrochloride. The excipients are calcium hydrogen phosphate dihydrate, hydroxypropylcellulose, magnesium stearate and colloidal anhydrous silica. The tablets are packed in blister packs or plastic bottles.

II.2 Drug Substance

Tramadol hydrochloride has a monograph in the Ph Eur.

Tramadol hydrochloride is a white or almost white, crystalline powder which is freely soluble in water and methanol and very slightly soluble in acetone. The structure of tramadol hydrochloride has been adequately proven and its physico-chemical properties sufficiently described. Relevant information on polymorphism and 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 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

Opidol, prolonged-release tablet is formulated using excipients described in the current Ph Eur. All raw materials used in the product are of vegetable origin.

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 in the original package 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

More than 90% of tramadol is absorbed after oral administration. The absolute bioavailability is around 70% independent of concomitant food intake. Peak plasma concentrations are reached 1-2 hours after oral administration of an ordinary tablet. After administration of the originator's depot tablet, peak plasma concentrations are reached after about 5 hours. Elimination half-life is approximately six hours. The kinetics is linear within the therapeutic dose range.

To support the application, the applicant has submitted five bioequivalence studies. All three strengths are studied as single-dose under fasting conditions. Multiple-dose under fasting conditions has been studied for the 150 mg strength and a fed-study has been performed with the 200 mg strength. The included study package is considered sufficient to support the application.

The results of the bioequivalence studies are in favour of the application. Bioequivalence has been demonstrated for all three strengths as single-dose under fasting conditions, and the fed study and multiple-dose study also show bioequivalence. The application is recommended for approval from a pharmacokinetic point of view.

IV.2 Pharmacodynamics/Clinical efficacy/Clinical safety

Clinical efficacy and safety of tramadol are well known. As tramadol is a widely used, well-known active substance, no further studies are required and the applicant provides none. Submitted overview based on literature review is sufficient.

IV.3 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

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 risk/benefit ratio is considered positive and Opidol, Prolonged-release tablets, 100, 150 and 200 mg is recommended for approval.

VI. APPROVAL

The Decentralised procedure for Opidol, Prolonged-release tablets, 100, 150 and 200 mg was successfully finalised on 2011-04-28.

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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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