LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Oxikodon Actavis
(oxycodone hydrochloride)

SE/H/1226/01-03/DC

Applicant: Actavis Group PTC ehf., Iceland

This module reflects the scientific discussion for the approval of Oxikodon Actavis. The procedure was finalised at 2012-12-05. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

Actavis Group PTC ehf. has applied for a marketing authorisation for Oxikodon Actavis, 5 mg, 10 mg and 20 mg, capsule, hard, claiming essential similarity to OxyNorm, 5 mg, 10 mg and 20 mg, capsule, hard, marketed in Sweden by Mundipharma AB. The product contains oxycodone hydrochloride as active substance. For approved indications see the Summary of Product Characteristics. The reference product used in the bio-equivalence study is OxyNorm 5 mg and 20 mg, capsules, marketed by Norpharma A/S in Denmark.

II. QUALITY ASPECTS

II.1 Introduction

Oxikodon Actavis is presented in the form of hard capsules containing 5 mg, 10 mg and 20 mg of oxycodone hydrochloride which corresponds to 4.48 mg, 8.96 mg and 17.93 mg of oxycodone. The excipients are microcrystalline cellulose and magnesium stearate. The capsule shells consist of, gelatine, sodium laurilsulfate, titanium dioxide (E71), iron oxide yellow (E172), iron oxide red (E172), indigotine (E132) and are printed with ink containing, shellac, iron oxide black (E172) and potassium hydroxide. The capsules are packed in PVC/PVDC/Al/PET/paper blisters and HDPE bottles with LDPE caps.

II.2 Drug Substance

Oxycodone hydrochloride has a monograph in Ph Eur.

Oxycodone hydrochloride is a white or almost white powder, freely soluble in water, sparingly soluble in anhydrous ethanol and practically insoluble in toluene. The structure of Oxycodone hydrochloride has been adequately proven and its physico-chemical properties sufficiently described. 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

Oxikodon Actavis hard capsule is formulated using excipients described in the current Ph Eur, except for the colouring agents which comply with the regulation Commission Directive 2008/128/EC. The printing ink consists of excipients controlled according to monographs in USP and NF. 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, with the storage restriction, do not store above 30°C.

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

Bioequivalence was evaluated in two bioequivalence studies; one with the 5 mg strength and one with the 20 mg strength. As the compositions of the capsules are not quantitatively proportional bioequivalence need to be demonstrated at both the highest (20 mg) and the lowest (5 mg) strength.

Study 1379 (5 mg)

This was a single-dose, cross-over study conducted in 32 healthy volunteers, comparing Oxikodon Actavis, 5 mg, capsule with OxyNorm, 5 mg, capsule under fasting conditions. The study was conducted at Bio Pharma Services Inc, Toronto, Canada between 2011/10/01 and 2011/10/10. Blood samples were collected pre-dose and up to 24 hours post-dose. The study design is considered acceptable. Plasma concentrations of oxycodone were determined with an adequately validated LC/MS/MS method. For AUC_{0-t} and C_{max} the 90% confidence interval for the ratio of the test and reference products fell within the conventional acceptance range of 80.00-125.00%.

Study C11-0236 (20 mg)

This was a single-dose, two-way crossover study conducted in 32 healthy volunteers, comparing Oxikodon Actavis, 20 mg, capsule with OxyNorm, 20 mg, capsule under fasting conditions. The study was conducted at Cetero Research, Mississauga, Ontario, Canada between 2011/06/16 and 2011/06/24. Blood samples were collected pre-dose and up to 24 hours post-dose. The study design is considered acceptable. Plasma concentrations of oxycodone were determined with a validated LC/MS/MS method. For AUC_{0-t} and C_{max} the 90% confidence interval for the ratio of the test and reference products fell within the conventional acceptance range of 80.00-125.00%.

Bioequivalence has been shown for Oxikodon Actavis 5 mg and 20 mg capsules. The results from the study with the 20 mg strength can be extrapolated to the 10 mg strength.

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.

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 with the 20 mg capsule can be extrapolated to the 10 mg strength 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 Oxikodon Actavis, 5 mg, 10 mg and 20 mg, capsule, hard, is recommended for approval.

VI. APPROVAL

The Decentralised procedure for Oxikodon Actavis, 5 mg, 10 mg and 20 mg, capsule, hard, was successfully finalised on 2012-12-05.

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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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