LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report

Scientific discussion

Oxycodone Teva
(oxycodone hydrochloride)

SE/H/1423/01-03/DC

This module reflects the scientific discussion for the approval of Oxycodone Teva. The procedure was finalised on 2015-01-18. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

The application for Oxycodone Teva, 5 mg, 10 mg, 20 mg, capsule, hard is a generic application made according to Article 10(1) of Directive 2001/83/EC. The applicant, Teva Sweden AB applies through the Decentralised Procedure with Sweden acting as reference member state (RMS) and DE, DK, FI, IE, NL, NO, BG as concerned member states (CMS).

The reference medicinal product chosen for the purposes of establishing the expiry of the data protection period is OxyNorm, 20 mg, capsules, authorised in DK since 2001-05-18, with Norpharma A/S as marketing authorisation holder.

The reference product used in the bioequivalence study is OxyNorm, 5 mg and 20 mg, capsules from DK with Norpharma A/S as marketing authorisation holder.

II. QUALITY ASPECTS

II.1 Introduction

Oxycodone Teva is presented in the form of capsules containing 5, 10 or 20 mg of oxycodone hydrochloride which corresponds to 4.48, 8.96 and 17.93 mg of oxycodone, respectively. The excipients are microcrystalline cellulose, magnesium stearate, gelatine, sodium laurilsulfate, titanium dioxide, iron oxide yellow (E172), iron oxide red (E172), indigotine (E132), shellac, propylene glycol, ammonia solution (for pH-adjustment), iron oxide black (E172) and potassium hydroxide (for pH-adjustment). The capsules are packed in peel-off blister packs and push-through blister packs or filled in HDPE containers with child resistant LDPE or PP caps.

II.2 Drug Substance

Oxycodone hydrochloride has a monograph in the Ph Eur.

Oxycodone hydrochloride is a white or almost white crystalline hygroscopic powder which is freely soluble in water. Reference is made to a Certificates of Suitability issued by EDQM for the drug substance.
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.

The retest period for the drug substance is stated on the Certificate of Suitability.

II.3 Medicinal Product

Oxycodone Teva capsules are formulated using excipients described in the current Ph Eur, except for iron oxide, shellac, propylene glycol, ammonia solution, and potassium hydroxide which are controlled according to acceptable in house specifications and USP/NF monographs. 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, such as hygroscopic properties and polymorphism.

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.

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 in order to waive the 10 mg strength.

Study 1379 (5 mg)
This was a single-dose, cross-over study conducted in 32 healthy volunteers, comparing Oxikodon Teva, 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 Teva, 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 Oxycodone Teva 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 risk/benefit ratio is considered positive and Oxycodone Teva, 5 mg, 10 mg, 20 mg, capsule, hard is recommended for approval.

VI. APPROVAL

The Decentralised procedure for Oxycodone Teva, 5 mg, 10 mg, 20 mg, capsule, hard was successfully finalised on 2015-01-18.

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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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