LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Public Assessment Report
Scientific discussion

Oxycodone Depot Teva Sweden (oxycodone hydrochloride)

SE/H/1549/01-08/DC

This module reflects the scientific discussion for the approval of Oxycodone Depot Teva Sweden. The procedure was finalised on 2016-06-16. For information on changes after this date please refer to the module 'Update'.

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I. INTRODUCTION

The application for Oxycodone Depot Teva Sweden, 5 mg, 10 mg, 15 mg, 20 mg, 30 mg, 40 mg, 60 mg, 80 mg, prolonged-release tablet, 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 AT, BE, DK, FI, NL, PL, UK as concerned member states (CMS).

The reference medicinal product chosen for the purposes of establishing the expiry of the data protection period is Oxycontin®PR, 5 mg, Tablets authorised in DK since 1996, with Norpharma A/S as marketing authorisation holder.

The reference products used in the bioequivalence study are Oxycontin®PR, 5 mg, 10 mg, 15 mg, 20 mg, 30 mg, 40 mg, 60 mg, 80 mg Tablets from DK with Norpharma A/S as marketing authorisation holder and OxyContin®, 5 mg, 80 mg Prolonged-Release Tablets from SE with Mundipharma AB as marketing authorisation holder.

For approved indications, see the Summary of Product Characteristics.

For recommendations to the marketing authorisation not falling under Article 21a/22 of Directive 2001/83 and conditions to the marketing authorisation pursuant to Article 21a or 22 of Directive 2001/83/EC to the marketing authorisation, please see section VI.

II. QUALITY ASPECTS

II.1 Drug Substance

The structure of the drug substance has been adequately proven and its physico-chemical properties are sufficiently described.

The manufacture of the drug substance has been adequately described and satisfactory specifications have been provided for starting materials, reagents and solvents.

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

Stability studies confirm the retest period.

II.2 Medicinal Product

The medicinal product is formulated using excipients listed in section 6.1 in the Summary of Product Characteristics.

The manufacturing process has been sufficiently described and critical steps identified.

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 have been performed and data presented support the shelf life and special precautions for storage claimed in the Summary of Product Characteristics, sections 6.3 and 6.4.

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

Single dose fasting studies were conducted for all strength; 5mg, 10mg, 15mg, 20mg, 30mg, 40mg, 60mg and 80mg. This is appropriate. A single dose fed study was performed at the lowest strength (5mg) and at the highest strength (80mg). Steady state studies were performed at the lowest strength (5mg), at the highest strength (80mg) and at the intermediate strength (20mg). Thus a complete study packaged is fulfilled on the lowest strength (5mg) and the highest strength (80mg). This is considered sufficient since the lowest and the highest strength is considered the worst case formulations. Thus, the study packaged is considered sufficient. The submitted studies are described below:

Eight single dose, two-way, cross-over studies were performed, where blood samples were collected pre-dose and up to 36 hours post-dose. Plasma concentrations of oxycodone were determined with a validated LC-MS/MS method. For AUC_{0-t}, $AUC_{0-\infty}$ 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%.

A combined single dose study under fed condition and a steady state study under fasting condition were performed at the 5 mg strength as a two-way cross over study. Blood samples were collected pre-dose and up to 24 hours post-dose day 1 as well as pre-dose and up to 12 hours post-dose day 5. Plasma concentrations of oxycodone were determined with a validated LC/MS/MS method. The 90% confidence interval for the ratio of the test and reference products fell within the conventional acceptance range of 80.00-125.00% for AUC_{0-t}, $AUC_{0-\infty}$ and C_{max} for the single dose study as well as for $AUC_{0-\tau}$, C_{max} and C_{min} for the multiple dose study.

A multiple dose, two-way crossover study under fasting condition was performed at the 20 mg strength. Blood samples were collected pre-dose day 1, 2, 3 and 4. On Day 5, blood samples were collected pre-dose and up to 12 hours post dose. Plasma concentrations of oxycodone were determined with a validated LC/MS/MS method. For $AUC_{0-\tau}$, C_{max} and C_{min} the 90% confidence interval for the ratio of the test and reference products fell within the conventional acceptance range of 80.00-125.00%.

A single dose, two-way crossover study under fed condition was performed at the 80 mg strength where blood samples were collected pre-dose and up to 36 hours post-dose. Plasma

concentrations of oxycodone were determined with a validated LC-MS/MS method. For AUC_{0-t}, $AUC_{0-\infty}$ 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%.

One multiple dose, two-way crossover study under fasting condition was performed at the 80 mg strength. Blood samples were collected pre-dose and up to 12 hours post dose on day 4 and day 8. Plasma concentrations of oxycodone were determined with a validated LC-MS/MS method. For $AUC_{0-\tau}$, C_{max} and C_{min} the 90% confidence interval for the ratio of the test and reference products fell within the conventional acceptance range of 80.00-125.00%.

Based on the submitted bioequivalence studies, Oxycodone Depot Teva Sweden is considered bioequivalent with OxyContin. The study packaged is considered sufficient.

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.

IV.3 Risk Management Plan

The MAH has submitted a risk management plan, in accordance with the requirements of Directive 2001/83/EC as amended, describing the pharmacovigilance activities and interventions designed to identify, characterise, prevent or minimise risks relating to Oxycodone Depot Teva Sweden.

Safety specification

Summary table of safety concerns as approved in RMP

Important identified risks	Respiratory depression Tolerance, dependence and withdrawal syndrome with prolonged use
Important potential risks	Use in children under 12 years of age Abuse/misuse
Missing information	N/A

Pharmacovigilance Plan
Routine pharmacovigilance is suggested and no additional pharmacovigilance activities are proposed by the applicant, which is endorsed.

Risk minimisation measures
Routine risk minimisation is suggested and no additional risk minimisation activities are proposed by the applicant, which is endorsed.

Summary of Safety Concerns and Planned Risk Minimisation Activities as proposed/ approved in RMP

Safety Concern	**Routine Risk Minimisation Measures**	**Additional Risk Minimisation Measures**
Important Identified Risks		

Safety Concern	Routine Risk Minimisation Measures	Additional Risk Minimisation Measures
Respiratory depression Tolerance, dependence and withdrawal syndrome with prolonged use	Routine pharmacovigilance	None
Important Potential Risks		
Use in children under 12 years of age Abuse/misuse	Routine pharmacovigilance	None

Summary of the RMP

The RMP is approved.

The MAH shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the Marketing Authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the RMS;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

If the dates for submission of a PSUR and the update of a RMP coincide, they can be submitted at the same time, but via different procedures.

V. 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.

VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

The benefit/risk ratio is considered positive and Oxycodone Depot Teva Sweden, 5 mg, 10 mg, 15 mg, 20 mg, 30 mg, 40 mg, 60 mg, 80 mg, prolonged-release tablet is recommended for approval.

List of recommendations not falling under Article 21a/22 of Directive 2001/83 in case of a positive benefit risk assessment

N/A

List of conditions pursuant to Article 21a or 22 of Directive 2001/83/EC

N/A

VII. APPROVAL

The Decentralised procedure for Oxycodone Depot Teva Sweden, 5 mg, 10 mg, 15 mg, 20 mg, 30 mg, 40 mg, 60 mg, 80 mg, prolonged-release tablet was positively finalised on 2016-06-16.

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Public Assessment Report – Update

Procedure number*	Scope	Product Information affected	Date of end of procedure	Approval/ non approval	Summary/ Justification for refuse

*Only procedure qualifier, chronological number and grouping qualifier (when applicable)

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