COLLEGE TER BEOORDELING VAN GENEESMIDDELEN

# Public Assessment Report

# Scientific discussion

# Oxycodon HCl 10 mg/ml Focus, oral solution

# (oxycodone hydrochloride)

## NL License RVG: 123187

## Date: 8 January 2020

**This module reflects the scientific discussion for the approval of Oxycodon HCl 10 mg/ml Focus, oral solution. The procedure was finalised on 22 July 2019. For information on changes after this date please refer to the 'steps taken after finalisation' at the end of this PAR.**

# List of abbreviations

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| ASMF | Active Substance Master File |
| CEP | Certificate of Suitability to the monographs of the European Pharmacopoeia |
| CHMP | Committee for Medicinal Products for Human Use |
| CMD(h) | Coordination group for Mutual recognition and Decentralised procedure for human medicinal products |
| CMS | Concerned Member State |
| EDMF | European Drug Master File |
| EDQM | European Directorate for the Quality of Medicines |
| EEA | European Economic Area |
| ERA | Environmental Risk Assessment |
| ICH | International Conference of Harmonisation |
| MAH | Marketing Authorisation Holder |
| Ph.Eur. | European Pharmacopoeia |
| PL | Package Leaflet |
| RH | Relative Humidity |
| RMP | Risk Management Plan |
| SmPC | Summary of Product Characteristics |
| TSE | Transmissible Spongiform Encephalopathy |

# I. INTRODUCTION

Based on the review of the quality, safety and efficacy data, the Medicines Evaluation Board (MEB) of the Netherlands has granted a marketing authorisation for Oxycodon HCl 10 mg/ml Focus, oral solution, from Focus Care Pharmaceuticals B.V.

The product is indicated for treatment of severe pain, which requires opioid analgesics to be adequately managed.

A comprehensive description of the indications and posology is given in the SmPC.

This national procedure concerns a generic application claiming essential similarity with the innovator product Oxynorm Concentrate 10 mg/ml which has been registered in the United Kingdom by Napp Pharmaceuticals Limited since 9 December 1999. In the Netherlands, Oxynorm oral solution 10 mg/ml (NL License RVG 27940) has been registered since 9 April 2003 via a national procedure.

The marketing authorisation has been granted pursuant to Article 10(1) of Directive 2001/83/EC.

# II. QUALITY ASPECTS

## II.1 Introduction

Oxycodon HCl Focus is a clear orange-red coloured oral solution. Each ml contains 10 mg oxycodone hydrochloride which corresponds to 9 mg oxycodone.

The oral solution is packed in amber coloured glass bottles with a white polypropylene screw cap and an oral polyethylene 0.5 ml or 1.0 ml syringe with an adapter. Every 1 ml mark on the dosing syringe corresponds to 10 mg oxycodone hydrochloride.

The excipients are: sodium benzoate, sodium saccharin, citric acid monohydrate, sodium hydroxide (for pH adjustment) and sun yellow FCF (E110) and water.

## II.2 Drug Substance

The active substance is oxycodone hydrochloride, an established active substance described in the European Pharmacopoeia (Ph.Eur.). Oxycodone hydrochloride is a white or almost white powder. The active substance is hygroscopic and optically active. It is freely soluble in water, sparingly soluble in anhydrous ethanol and practically insoluble in toluene.

The CEP procedure is used for the active substance. Under the official Certification Procedures of the EDQM of the Council of Europe, manufacturers or suppliers of substances for pharmaceutical use can apply for a certificate of suitability concerning the control of the chemical purity and microbiological quality of their substance according to the corresponding specific monograph, or the evaluation of reduction of Transmissible Spongiform Encephalopathy (TSE) risk, according to the general monograph, or both. This procedure is meant to ensure that the quality of substances is guaranteed and that these substances comply with the European Pharmacopoeia.

Manufacturing process

CEPs have been submitted; therefore no details on the manufacturing process have been included.

Quality control of drug substance

The active substance specification is considered adequate to control the quality and is in line with the Ph. Eur. and CEPs, with additional requirements for microbial contamination testing. Batch analytical data have been provided Batch analytical data demonstrating compliance with this specification have been provided.

Stability of drug substance

The active substance is stable for 3-5 years (depending on CEP) when stored under the stated conditions. Assessment thereof was part of granting the CEPs and has been granted by the EDQM.

## II.3 Medicinal Product

Pharmaceutical development

The product is an established pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines. The choice of excipients is justified and their functions explained. The excipients are well known and similar as in the reference product. The amber packing has been justified by photostability studies. No bioequivalence studies are required since the proposed drug product is aqueous oral solution and contains an active substance in the same concentration as the approved oral solution.

Manufacturing process

The manufacturing process includes weighing, dissolving, filtration, filling and labelling and has been validated according to relevant European guidelines. Process validation data on the product have been presented for three full-scale batches in accordance with the relevant European guidelines. The product is manufactured using conventional manufacturing techniques.

Control of excipients

These specifications comply with the Ph. Eur. and the applicable European guideline and are acceptable.

Quality control of drug product

The finished product specifications are adequate to control the relevant parameters for the dosage form. The specification includes tests for three full-scale batches. Limits in the specification have been justified and are considered appropriate for adequate quality control of the product. Satisfactory validation data for the analytical methods have been provided. Batch analytical data from six full-scale batches from the proposed production site have been provided, demonstrating compliance with the specification.

Stability of drug product

Stability data on the product have been provided for six full-scale batches stored at 25°C/60% RH (60 and 6 months), 30°C / 30% RH (24 and 6 months) and 40°C / 75% RH (12 and 6 months). The long term and accelerated conditions used in the stability studies are according to the ICH stability guideline. On basis of the data submitted, a shelf life was granted of 5 years. No specific storage conditions need to be included in the SmPC or on the label. Stability data have been provided demonstrating that the product remains stable for 3 months following first opening of the bottles.

Specific measures concerning the prevention of the transmission of animal spongiform encephalopathies

There are no substances of ruminant animal origin present in the product nor have any been used in the manufacturing of this product, so a theoretical risk of transmitting TSE can be excluded.

### II.4 Discussion on chemical, pharmaceutical and biological aspects

Based on the submitted dossier, the MEB considers that Oxycodon HCl Focus has a proven chemical-pharmaceutical quality. Sufficient controls have been laid down for the active substance and finished product. No post-approval commitments were made.

## III. NON-CLINICAL ASPECTS

### III.1 Ecotoxicity/environmental risk assessment (ERA)

Since Oxycodon HCl Focus is intended for generic substitution, this will not lead to an increased exposure to the environment. An environmental risk assessment is therefore not deemed necessary.

### III.2 Discussion on the non-clinical aspects

This product is a generic formulation of Oxynorm which is available on the European market. Reference is made to the preclinical data obtained with the innovator product. A non-clinical overview on the pharmacology, pharmacokinetics and toxicology has been provided, which

is based on up-to-date and adequate scientific literature. The overview justifies why there is no need to generate additional non-clinical pharmacology, pharmacokinetics and toxicology data. Therefore, the MEB agrees that no further non-clinical studies are required.

# IV. CLINICAL ASPECTS

## IV.1 Introduction

Oxycodone hydrochloride is a well-known active substance with established efficacy and tolerability. A clinical overview has been provided, which is based on scientific literature. The overview justifies why there is no need to generate additional clinical data. Therefore, the MEB agrees that no further clinical studies are required.

## IV.2 Pharmacokinetics

According to the current Guideline on Investigation of Bioequivalence CPMP/EWP/QWP/1401/98 Rev. 1/ Corr ** 'If the test product is an aqueous oral solution at time of administration and contains an active substance in the same concentration as an approved oral solution, bioequivalence studies may be waived'. The MAH states that according to the SmPC of Oxynorm Concentrate 10 mg/ml, the active substances and excipients are qualitatively and quantitatively the same in the test product and the reference product; thus, both medicinal products are bioequivalent. Therefore, an abridged application under Article 10(1) of Directive 2001/83/EC as amended is justified.

## 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 Oxycodon HCl Focus.

- Summary table of safety concerns as approved in RMP

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|---|---|
| Important identified risks | - Drug dependence and withdrawal reactions<br>- Abuse, misuse, diversion |
| Important potential risks | - Medication errors |
| Missing information | - Use during pregnancy |

The MEB agrees that routine pharmacovigilance activities and routine risk minimisation measures are sufficient for the risks and areas of missing information.

### IV.4 Discussion on the clinical aspects

For this authorisation, reference is made to the clinical studies and experience with the innovator product Oxynorm. No new clinical studies were conducted. Risk management is adequately addressed. This generic medicinal product can be used instead of the reference product.

## 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 test consisted of a pilot test with 3 participants, followed by two rounds with 10 participants each. The questions covered the following areas sufficiently: traceability, comprehensibility and applicability. 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

Oxycodon HCl 10 mg/ml Focus, oral solution has a proven chemical-pharmaceutical quality and is a generic form of Oxynorm Concentrate 10 mg/ml. Oxynorm is a well-known medicinal product with an established favourable efficacy and safety profile

Since both the reference and current product are aqueous oral solutions and at time of administration contain an active substance in the same concentration, no bioequivalence study is deemed necessary. A biowaiver has been granted.

The Board followed the advice of the assessors.

The MEB, on the basis of the data submitted, considered that efficacy and safety has been shown, and has therefore granted a marketing authorisation. Oxycodon HCl Focus was authorised in the Netherlands on 22 July 2019.

## STEPS TAKEN AFTER THE FINALISATION OF THE INITIAL PROCEDURE - SUMMARY

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