LÄKEMEDELSVERKET
SWEDISH MEDICAL PRODUCTS AGENCY

# Public Assessment Report
# Scientific discussion

# Oxycodone G.L.
# (oxycodone hydrochloride)

# SE/H/1704/01-03/DC

**This module reflects the scientific discussion for the approval of Oxycodone G.L.. The procedure was finalised on 2018-04-24. For information on changes after this date please refer to the module 'Update'.**

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# I. INTRODUCTION

The application for Oxycodone G.L., 10 mg/ml, solution for injection/infusion and oral solution, 1 mg/ml and 10 mg/ml, is a generic application made according to Article 10(1) of Directive 2001/83/EC. The applicant, G.L. Pharma GmbH applies through the Decentralised Procedure with Sweden acting as reference member state (RMS) and AT and UK as CMS in SE/H/1704/01-03/DC.

The reference medicinal product chosen for the purposes of establishing the expiry of the data protection period is OxyNorm concentrate, 10 mg/ml, oral solution authorised in UK since 1999 with Napp Pharmaceuticals Ltd as marketing authorisation holder.

No bioequivalence studies have been performed and a biowaiver is applied for Oxycodone 10mg/ml solution for injection/infusion, Oxycodone 1mg/ml oral solution and Oxycodone 10mg/ml oral solution.

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/EC 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

No bioequivalence studies have been performed and a biowaiver is applied for Oxycodone 10mg/ml solution for injection/infusion, Oxycodone 1mg/ml oral solution and Oxycodone 10mg/ml oral solution.

Biowaiver for Oxycodone 1mg/ml oral solution and Oxycodone 10mg/ml oral solution
According to the Guideline on the investigation of Bioequivalence (CHMP/QWP/EWP/1401/98 Rev. 1) and further clarified in a published Q&A document (6.3 Clarification on how to apply the reference made in Appendix II of the Guideline on the investigation of bioequivalence (CPMP/EWP/QWP/1401/98 Rev.1/Corr**), when waiving in vivo studies for oral solutions-NEW December 2016), biowaiver for oral solutions is possible under certain conditions. One condition is that the amount of excipients that might affect the bioavailability should be qualitatively and quantitatively the same in the test and reference product. In addition, for a solution containing a BCS class II-IV substance, qualitatively similarity and very close quantitative similarity of excipients is expected. According to the data presented in the dossier, oxycodone is considered as a highly soluble drug substance (see Quality AR) and may therefore be classified as either a BCS class I or III substance. The applicant has not discussed if oxycodone is as a BCS class I or III substance, i.e. if the absorption can be classified as complete (≥85%) or not. According to literature oxycodone has an oral bioavailability of 50-87% and based on this information oxycodone could be considered as borderline between BCS class I and III.

Regarding Oxycodone 1mg/ml oral solution:
There are quantitative differences in composition between the applied product and the reference product regarding the excipient hypromellose. The difference in hypromellose content is however assessed as acceptable even for a BCS class III substance since there is comparable viscosity between the applied product and the reference product. Hypromellose is available in several grades to give different viscosity of a solution and different amounts of hypromellose can thus be used to generate the same viscosity of a solution. The other differences in composition between the applied product and the reference product are acceptable for both a BCS class I and BCS class III substance. Thus waiver of bioequivalence studies with Oxycodone 1mg/ml is acceptable.

Regarding Oxycodone 10mg/ml oral solution:
There are differences in composition between the applied product and the reference product which is acceptable for both a BCS class I and BCS class III substance. Thus waiver of bioequivalence studies with Oxycodone 10mg/ml is acceptable.

## 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 G.L.

Safety specification
The following safety concerns are included in RMP as agreed:

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

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

Risk minimisation measures

| **Safety concern** | **Routine risk minimisation measures** | **Additional risk minimisation measures** |
|---|---|---|
| **Important identified risk:**<br><br>**Respiratory depression** | *Information in following sections of the SmPC*<br><br>*Section 4.3.: Contraindications*<br><br>*Section 4.4.: Special warnings and* | None proposed |

| | | |
|---|---|---|
| | *precautions for use*<br><br>*Section 4.5.: Interaction with other medicinal products and other forms of interaction*<br><br>*Section 4.6.: Fertility, pregnancy and lactation*<br><br>*Section 4.8.: Undesirable effects*<br><br>*Section 4.9.: Overdose*<br><br>*Legal Status:*<br>Listed as addictive drug available with a corresponding prescription only. Dispensing is limited to pharmacies. | |
| **Important identified risk:**<br><br>**Drug dependence and and withdrawal reactions** | *Information in following sections of the SmPC*<br><br>*Section 4.2. Posology and method of administration*<br><br>*Section 4.4.: Special warnings and precautions for use*<br><br>*Section 4.6.: Fertility, pregnancy and lactation*<br><br>*Section 4.8.: Undesirable effects*<br><br>*Legal Status:*<br>Listed as addictive drug available with a corresponding prescription only. Dispensing is limited to pharmacies. | None proposed |
| **Important identified risk:**<br><br>**Abuse, misuse, diversion** | *Information in following sections of the SmPC*<br><br>*Section 4.4.: Special warnings and precautions for use* | None proposed |

| Safety concern | Routine risk minimisation measures | Additional risk minimisation measures |
|---|---|---|
| | *Section 4.9.: Overdose*<br><br>*Legal Status:*<br>Listed as addictive drug available with a corresponding prescription only. Dispensing is limited to pharmacies. | |
| **Important identified risk:**<br><br>**Overdose** | *Information in following sections of the SmPC*<br><br>*Section 4.4.: Special warnings and precautions for use*<br><br>*Section 4.9.: Overdose*<br><br>*Legal Status:*<br>Listed as addictive drug available with a corresponding prescription only. Dispensing is limited to pharmacies. | None proposed |
| **Important potential risk:**<br><br>**Medication errors** | *Information in following sections of the SmPC*<br><br>*Section 4.2. Posology and method of administration*<br><br>*Section 4.4.: Special warnings and precautions for use*<br><br>*Legal Status:*<br>Listed as addictive drug available with a corresponding prescription only. Dispensing is limited to pharmacies. | None proposed |
| **Missing information**<br><br>**Use during pregnancy and lactation** | *Information in following sections of the SmPC*<br><br>*Section 4.6. Fertility, pregnancy and lactation*<br><br>*Legal Status:*<br>Listed as addictive drug available with a corresponding prescription only. Dispensing is limited to pharmacies. | None proposed |

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

Summary of the RMP

The MAH has satisfactorily responded to the questions raised and updated the RMP accordingly.

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

A user consultation with target patient groups on the package information leaflet (PIL) has been performed on the basis of a bridging report making reference to Oxycodone hydrochloride Lannacher 5 mg prolonged-release tablets (DE/H/2182+2183).
Oxycodone G.L has also referred to Vimpat syrup.
The bridging reports submitted by the applicant have been found acceptable.

# VI. OVERALL CONCLUSION, BENEFIT/RISK ASSESSMENT AND RECOMMENDATION

The quality of the generic product Oxycodone G.L., is found adequate. There are no objections to approval of Oxycodone G.L., from a non-clinical and clinical point of view. The product information is acceptable.

The application is therefore recommended for approval.

**List of recommendations not falling under Article 21a/22 of Directive 2001/83/EC 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 G.L., 10 mg/ml, solution for injection/infusion and oral solution, 1 mg/ml and 10 mg/ml was positively finalised on 2018-04-24.

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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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