IPAR

Public Assessment Report for a
Medicinal Product for Human Use

Scientific Discussion

Oxycodone hydrochloride 50mg/ml solution for injection or infusion
OXYCODONE HYDROCHLORIDE
PA0281/235/002

The Public Assessment Report reflects the scientific conclusion reached by the Health Products Regulatory Authority (HPRA) at the end of the evaluation process and provides a summary of the grounds for approval of a marketing authorisation for a specific medicinal product for human use. It is made available by the HPRA for information to the public, after deletion of commercially sensitive information. The legal basis for its creation and availability is contained in Article 21 of Directive 2001/83/EC, as amended. It is a concise document which highlights the main parts of the documentation submitted by the applicant and the scientific evaluation carried out by the HPRA leading to the approval of the medicinal product for marketing in Ireland.

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I. INTRODUCTION

This product was initially authorised under procedure number UK/H/5246/1/DC with the UK as RMS. The responsibility of RMS was transferred to Ireland on 27/03/2019 under procedure number IE/H/0622/1/DC.
Please note the following detail for the product in IE:
Marketing Authorisation Number: PA0281/235/002
Marketing Authorisation Holder: Pinewood Laboratories Ltd

The current Summary of Product Characteristics (SmPC) for this medicinal product is available on the HPRA website at www.hpra.ie.

The UK public assessment report published at the time of the initial marketing authorisation is provided herein.

I INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the UK and Ireland considered that the application for Oxycodone Hydrochloride 50 mg/ml Solution for Injection or Infusion (PL 29831/0367; UK/H/5246/001/DC) could be approved. The product is a prescription-only medicine (POM).

The application was submitted using the Decentralised Procedure (DCP), with the UK as Reference Member State (RMS) and Ireland as Concerned Member State (CMS). The application was submitted under Article 10(1) of Directive 2001/83/EC, as amended, claiming to be a generic medicinal product of OxyNorm 50mg/ml solution for injection or infusion (PL 16950/0155; Napp Pharmaceuticals Limited, UK) which was authorised in the UK on 14 January 2009. The reference product authorised in the Community for more than 10 years is OxyContin 40 mg Prolonged Release Tablets authorised to Napp Pharmaceuticals Ltd in the Republic of Ireland.

The active ingredient, oxycodone (as oxycodone hydrochloride), is a full opioid agonist with no antagonist properties. It has an affinity for kappa, mu and delta opioid receptors in the brain and spinal cord. Oxycodone is similar to morphine in its action.

The product is indicated for the treatment of moderate to severe pain in patients with cancer and post-operational pain. It is also indicated for the treatment of severe pain requiring the use of a strong opioid.

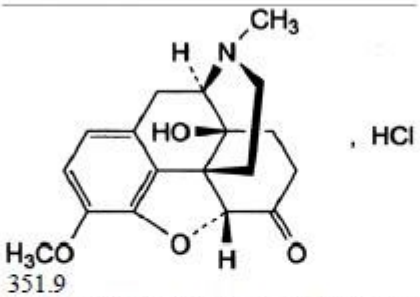
No new non-clinical or clinical studies were performed, which is acceptable given that the application was based on the product being a generic medicinal product of an originator product that has been in clinical use for over 10 years. A bioequivalence study was not necessary to support this application for a parenteral product (aqueous solution).

The RMS has been assured that acceptable standards of Good Manufacturing Practice (GMP) are in place at all sites responsible for the manufacture, assembly and batch release of this product. For manufacturing sites within the Community, the RMS has accepted copies of current manufacturer authorisations issued by inspection services of the competent authorities as certification that acceptable standards of GMP are in place at those sites.

The RMS and CMS considered that the application could be approved at the end of procedure (Day 210) on 20 June 2013. After a subsequent national phase, a licence was granted in the UK on 04 July 2013.

II. QUALITY ASPECTS

ACTIVE SUBSTANCE

INN:	Oxycodone hydrochloride
Compendial Name (European Pharacopoeia)	Oxycodone hydrochloride
Chemical Name:	4,5a-Epoxy-14-hydroxy-3-methoxy-17-methylmorphinan-6-one hydrochloride
Molecular formula:	$C_{18}H_{22}ClNO_4$
Structure:	
Molecular mass:	351.9
Appearance:	White or almost white powder, hygroscopic
Solubility:	Freely soluble in water, sparingly soluble in anhydrous ethanol, practically insoluble in toluene.

Oxycodone hydrochloride is the subject of a European Pharmacopoeia monograph.

All aspects of the manufacture and control of the active substance oxycodone hydrochloride are covered by a European Directorate for the Quality of Medicines and Healthcare (EDQM) Certificate of Suitability.

MEDICINAL PRODUCT

Other Ingredients

Other ingredients consist of the pharmaceutical excipients citric acid monohydrate, sodium citrate, sodium chloride, hydrochloric acid (for pH adjustment), sodium hydroxide (for pH adjustment) and

water for injections. Appropriate justification for the inclusion of each excipient has been provided.

All excipients comply with their respective European Pharmacopoeia monographs. Certificates of Analysis have been provided for all excipients, showing compliance with the proposed specifications.

None of the excipients contain materials of animal or human origin. No genetically modified organisms (GMO) have been used in the preparation of these excipients.

Pharmaceutical Development
The objective of the development programme was to a produce a stable formulation of oxycodone hydrochloride in a 50 mg/ml solution for injection or infusion comparable in performance to the reference product OxyNorm 50mg/ml solution for injection or infusion (Napp Pharmaceuticals Ltd, UK).

Suitable pharmaceutical development data have been provided for this application.

Comparative impurity profiles have been provided for this product and the reference product.

Manufacturing Process
A satisfactory batch formula has been provided for the manufacture of the product, along with an appropriate account of the manufacturing process. The manufacturing process has been validated with full production-scale batches that have shown satisfactory results.

Control of Finished Product
The finished product specification is acceptable. Test methods have been described that have been suitably validated. Batch data have been provided, which comply with the release specifications. Certificates of Analysis have been provided for all working standards used.

Container-Closure System
The finished product is supplied in 1 ml Type I clear, neutral glass ampoules, packed in cardboard outer cartons in pack sizes of 5 ampoules.

Satisfactory specifications and Certificates of Analysis for the primary packaging material have been provided. All primary packaging is controlled to European Pharmacopoeia standards and complies with guidance concerning materials in contact with parenteral products.

Stability of the Product
Finished product stability studies were performed in accordance with current guidelines on batches of finished product in the packaging proposed for marketing. Based on the results, a shelf-life of 2 years has been approved for the unopened product, with the storage conditions "Do not store above 25°C. Keep the ampoule in the outer carton in order to protect from light."

The injection should be given immediately after opening the ampoule. Once opened, any unused portion should be discarded.

If not used immediately, it is stated that in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8°C.

Bioequivalence/Bioavailability
A bioequivalence study was not necessary to support this application for this aqueous solution, parenteral product.

Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and Labels
The SmPC, PIL and labels are satisfactory from a pharmaceutical perspective.

User testing of the package leaflet for Oxycodone Hydrochloride 50mg/ml Solution for Injection or Infusion (PL 29831/0367) has been accepted based on a bridging report provided by the applicant making reference to the satisfactory user-testing of the PIL for Oxycodone Hydrochloride 10 mg/ml Solution for Injection or Infusion (PL 29831/0359), as the 'parent PIL'.

Marketing Authorisation Application (MAA) Form
The MAA form is satisfactory from a pharmaceutical perspective.

Expert Report (Quality Overall Summary)
The quality overall summary has been written by an appropriately qualified person and is a suitable summary of the pharmaceutical aspects of the dossier.

Conclusion
The grant of a Marketing Authorisation is recommended.

III. NON-CLINICAL ASPECTS

III.2 NON-CLINICAL ASPECTS

As the pharmacodynamic, pharmacokinetic and toxicological properties of oxycodone hydrochloride ar well-known, no new non-clinical data have been submitted and none are required.

The applicant's non-clinical overview has been written by an appropriately qualified person and is satisfactory, providing an appropriate review of the relevant non-clinical pharmacology, pharmacokinetics and toxicology.

Suitable justification has been provided for non-submission of an Environmental Risk Assessment. As this product is intended for generic substitution with a product that is already marketed, no increase in environmental burden is anticipated. Thus, the justification for non-submission of an Environmental Risk Assessment is accepted.

The grant of a Marketing Authorisation is recommended.

IV. CLINICAL ASPECTS

III.3 CLINICAL ASPECTS

Clinical Pharmacololgy

No new clinical pharmacology data have been submitted and none are required for applications of this type. A bioequivalence study was not necessary to support this application for an aqueous parenteral product. According to CPMP guidelines, bioequivalence studies are not generally required for parenteral aqueous solutions (CPMP/EWP/QWP/1401/98 Rev. 1/Corr** (Guideline on the Investigation of Bioequivalence).

Efficacy

No new efficacy data have been submitted and none are required for this type of application.

Safety

No new safety data have been submitted with this application and none are required. No new or unexpected safety concerns arose from this application. As an active ingredient, oxycodone hydrochloride has a well-established safety profile and an acceptable level of safety in the proposed indications.

Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and Labels

The SmPC, PIL and labels are acceptable from a clinical perspective. The SmPC is consistent with that for the innovator product. The PIL is consistent with the details in the SmPC and in line with the current guidance. The labelling is in line with the current guidance.

Clinical Expert Report (Clinical Overview)

The clinical overview has been written by an appropriately qualified physician and is a suitable summary of the clinical aspects of the dossier.

Pharmacovigilance System and Risk Management Plan

The Pharmacovigilance System, as described by the MAH, fulfils the requirements and provides adequate evidence that the MAH has the services of a qualified person responsible for pharmacovigilance, and has the necessary means for the notification of any adverse reaction suspected of occurring either in the Community or in a third country.

A suitable justification has been provided for not submitting a Risk Management Plan for this application.

Conclusion

The grant of a Marketing Authorisation is recommended.

V. OVERALL CONCLUSIONS

IV OVERALL CONCLUSION AND BENEFIT/RISK ASSESSMENT

QUALITY

The important quality characteristics of Oxycodone Hydrochloride 50 mg/ml Solution for Injection or Infusion are well-defined and controlled. The specifications and batch analytical results indicate consistency from batch to batch. There are no outstanding quality issues that would have a negative impact on the benefit/risk balance.

NON-CLINICAL

No new non-clinical data were submitted and none are required for this type of application.

EFFICACY

No new clinical data were submitted for this application. No bioequivalence studies were submitted or required for this application.

SAFETY

No new or unexpected safety concerns arise from this application.

PRODUCT LITERATURE

The SmPC, PIL and labelling are satisfactory and consistent with those for the reference product, where appropriate and in line with current guidance.

BENEFIT/RISK ASSESSMENT

The quality of the products is acceptable, and no new non-clinical or clinical safety concerns have been identified. The data supplied supports the claim that the applicant's product and the reference product are interchangeable. Extensive clinical experience with oxycodone hydrochloride is considered to have demonstrated the therapeutic value of the compound. The benefit/risk balance is therefore considered to be positive.

VI. REVISION DATE

22/02/2022

VII. UPDATES

This section reflects the significant changes following finalisation of the initial procedure.

SCOPE	PROCEDURE NUMBER	PRODUCT INFORMATION AFFECTED	DATE OF START OF PROCEDURE	DATE OF END OF PROCEDURE
RMS transfer	From UK/H/5246/1/DC to IE/H/0622/1/DC			