Medicines & Healthcare products Regulatory Agency

MHRA Regulating Medicines and Medical Devices

Public Assessment Report

National Procedure

OxyNorm 50 mg/ml, solution for injection or infusion

(Oxycodone hydrochloride)

PL 16950/0155

Napp Pharmaceuticals Limited

LAY SUMMARY

OxyNorm 50 mg/ml, solution for injection or infusion
<active substance(s)/common name(s)>

This is a summary of the Public Assessment Report (PAR) for OxyNorm 50 mg/ml, solution for injection or infusion (PL 16950/0155). It explains how the application for OxyNorm 50 mg/ml, solution for injection or infusion was assessed and its authorisation recommended, as well as the conditions of use. It is not intended to provide practical advice on how to use OxyNorm 50 mg/ml, solution for injection or infusion.

This product will be referred to as 'OxyNorm injection' or 'OxyNorm 50 mg/ml injection' in this lay summary for ease of reading.

For practical information about using OxyNorm injection, patients should read the package leaflet or contact their doctor or pharmacist.

What is OxyNorm injection and what is it used for?
This application is a full-dossier application. This means that the results of pharmaceutical, non-clinical and clinical tests have been submitted to show that this medicine is suitable for treating the specified indications.

OxyNorm 50 mg/ml injection is used for the treatment of moderate to severe pain.

How does OxyNorm injection work?
OxyNorm injection contains the active substance oxycodone (as oxycodone hydrochloride), which belongs to a group of medicines called pain-killers (or analgesics).

How is OxyNorm injection used?
OxyNorm 50 mg/ml injection is available as a solution for injection or infusion. OxyNorm injection will usually be prepared and administered by a health professional by injection or infusion into a vein or under the skin. The injection should be used immediately after opening.

The dose and how often the injection is given may be adjusted according to the severity of the patient's pain.

Adults (over 18 years of age)
The usual starting dose is dependent upon how the injection is given. The usual starting doses are as follows:

- As a single injection into a vein, the usual dose is 1 to 10 mg given slowly over 1 to 2 minutes. This can be repeated every 4 hours.
- As an infusion into a vein, the usual starting dose is 2 mg/hour.
- As a single injection through a fine needle into the tissue under the skin, the usual starting dose is 5 mg repeated at 4-hourly intervals if needed.
- As an infusion through a fine needle into the tissue under the skin, the usual starting dose is 7.5 mg/day.

If given by patient controlled analgesia (PCA), the dose is worked out according to the patient's weight (0.03 mg per kg of body weight). The patient's doctor or nurse will set a suitable frequency.

The patient should check with the doctor or pharmacist if the patient is unsure.

Children
Children and adolescents under 18 years of age should not be given OxyNorm injection.

Please read section 3 of the package leaflet for detailed information on dosing recommendations, the route of administration, the duration of treatment and the need for any specific monitoring of certain parameters or for diagnostic tests.

For further information on how OxyNorm injection is used, refer to the package leaflet and Summary/Summaries of Product Characteristics available on the Medicines and Healthcare products Regulatory Agency (MHRA) website.

This medicine can only be obtained with a prescription.

The patient should ask the administering healthcare practitioner if they have any questions concerning the medicine.

What benefits of OxyNorm injection have been shown in studies?
No additional studies were needed as OxyNorm injection is a line extension of the existing product OxyNorm 10mg/ml Infusion. The data submitted previously for OxyNorm 10mg/ml Infusion is sufficient to demonstrate that OxyNorm injection shows a benefit in the indications listed.

What are the possible side effects of OxyNorm injection?
Because OxyNorm injection is a line extension of the existing product OxyNorm 10mg/ml Infusion, its benefits and possible side effects are taken as being the same as OxyNorm 10mg/ml Infusion.

For the full list of all side effects reported with this medicine, see Section 4 of the package leaflet or the Summary of Product Characteristics (SmPC) available on the MHRA website.

Why was OxyNorm injection approved?
It was concluded that, as OxyNorm injection is a line extension of OxyNorm 10mg/ml Infusion, the indications and side effects observed with OxyNorm 10mg/ml Infusion are applicable to OxyNorm injection. Therefore, the MHRA decided that, as for OxyNorm 10mg/ml Infusion, the benefits are greater than the risks and recommended that OxyNorm injection can be approved for use.

What measures are being taken to ensure the safe and effective use of OxyNorm injection?
Safety information has been included in the SmPC and the package leaflet, including the appropriate precautions to be followed by healthcare professionals and patients.

Known side effects are continuously monitored. Furthermore, new safety signals reported by patients/healthcare professionals will be monitored and reviewed continuously.

Other information about OxyNorm injection

A Marketing Authorisation for OxyNorm injection was granted in the UK on 14 January 2009.

The full PAR for OxyNorm injection follows this summary.

This summary was last updated in October 2020.

TABLE OF CONTENTS

I INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the Medicines and Healthcare products Regulatory Agency (MHRA) considered that the application for OxyNorm 50 mg/ml Concentrate for Solution for Infusion (PL 16950/0155) could be approved.

The product is approved for the following indications:

- For the treatment of moderate to severe pain in patients with cancer and post-operative pain.
- For the treatment of severe pain requiring the use of a strong opioid.

Oxycodone is a full opioid agonist with no antagonist properties. It has an affinity for kappa, mu and delta opiate receptors in the brain and spinal cord. The therapeutic effect is mainly analgesic, anxiolytic and sedative.

This application was submitted under Article 8(3) of Directive 2001/83/EC, as amended, a full-dossier application. However, as this application is for a line extension of the existing product OxyNorm 10 mg/ml Infusion (PL 16950/0128), the non-clinical and clinical data are identical to those submitted previously.

The MHRA has been assured that acceptable standards of Good Manufacturing Practice (GMP) are in place for this product at all sites responsible for the manufacture, assembly and batch release of this product.

A national marketing authorisation was granted in the UK on 14 January 2009.

II QUALITY ASPECTS

II.1 Introduction

Each ml of solution for injection or infusion contains 50 mg of oxycodone hydrochloride (equivalent to 45 mg of oxycodone) as the active ingredient.

In addition to oxycodone hydrochloride, this product also contain the excipients citric acid monohydrate, sodium citrate, sodium chloride, dilute hydrochloric acid, sodium hydroxide and water for injections.

The finished product is distributed in clear 1 ml glass (type I) ampoules and packaged in cartons of 5 ampoules. Satisfactory specifications and Certificates of Analysis have been provided for all packaging components. All primary packaging complies with the current European regulations concerning materials in contact with food.

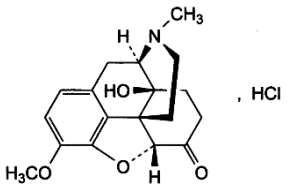
II.2 ACTIVE SUBSTANCE

rINN: Oxycodone hydrochloride

Chemical Name: Oxycodone hydrochloride

Molecular Formula: $C_{18}H_{22}ClNO_4$

Chemical Structure:



Molecular Weight: 351.9

Appearance: White crystalline powder

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 are covered by a European Directorate for the Quality of Medicines and Healthcare (EDQM) Certificate of Suitability.

II.3 DRUG PRODUCT

Pharmaceutical development

A satisfactory account of the pharmaceutical development has been provided.

All excipients comply with either their respective European/national monographs, or a suitable in-house specification. Satisfactory Certificates of Analysis have been provided for all excipients.

No excipients of animal or human origin are used in the finished product.

This product does not contain or consist of genetically modified organisms (GMO).

Manufacture of the product

A description and flow-chart of the manufacturing method has been provided.

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 and has shown satisfactory results.

Finished Product Specification
The finished product specification is satisfactory. The test methods have been described and adequately validated. Batch data have been provided that comply with the release specification. Certificates of Analysis have been provided for any working standards used.

Stability
Finished product stability studies have been conducted in accordance with current guidelines, using batches of the finished product stored in the packaging proposed for marketing. Based on the results, a shelf-life of a shelf-life of 36 months for the unopened ampoule has been set, with the storage conditions "After opening use immediately", is acceptable. For further information on use after opening see Section 6.6 of the SmPC, or the section on "Instructions for use /handling" in the leaflet for Health Professionals.

II.4 Discussion on chemical, pharmaceutical and biological aspects
The grant of a marketing authorisation is recommended.

III NON-CLINICAL ASPECTS

III.1 Introduction
As this application is for a line extension of the existing product OxyNorm 10 mg/ml Infusion (PL 16950/0128), the non-clinical data are identical to those submitted previously.

III.2 Pharmacology
No new pharmacology data were provided and none were required for this application.

III.3 Pharmacokinetics
No new pharmacokinetic data were provided and none were required for this application.

III.4 Toxicology
No new toxicology data were provided and none were required for this application.

III.5 Ecotoxicity/Environmental Risk Assessment
Suitable justification has been provided for non-submission of an Environmental Risk Assessment. As this is a line extension of an already authorised product, it is not expected that environmental exposure will increase following approval of the Marketing Authorisation for the proposed product.

III.6 Discussion on the non-clinical aspects
The grant of a marketing authorisation is recommended.

IV CLINICAL ASPECTS

IV.1 Introduction
The application is a full application made under Article 8.3(i).

This is a complex application for OxyNorm solution for injection or infusion 50 mg/ml.

The proposed product is a line extension of an authorised medicinal product. The application is for a fundamental change (addition of a new strength) to the existing product licence as referred to in Annex II of EC regulations No 1084/2003 or 1085/2003, as amended.

A line extension has been proposed to extend the flexibility of administration of the product when used in syringe drivers by increasing the oxycodone hydrochloride concentration to 50 mg/ml in 1 ml glass ampoules, thereby reducing the volume in the syringe driver, which is particularly important if dose requirements increase. In this way, the possibility of coadministration with other parenteral products may be more readily achieved in the same syringe driver, where necessary, assuming no incompatibility issues exist. This new concentration of oxycodone hydrochloride injection is intended for the management of severe pain which requires opioid treatment.

A clinical overview has been written by an adequately qualified person. The clinical overview is acceptable.

IV. 2 Pharmacokinetics

Two single dose pharmacokinetic studies using 10 mg / ml oxycodone hydrochloride injection have been performed by the applicant, in accordance with CPMP/EWP/280/96.

OXI1202 was conducted as an open, single dose, four-part, crossover study in 24 healthy, male volunteers. Each subject was randomised to the four treatments and then crossed over to compare the pharmacokinetics of oxycodone from oxycodone injection 10 mg/ml administered subcutaneously, intravenously or intramuscularly, or Oxycodone liquid 5 mg/5 ml administered orally. Twenty-one subjects completed all four study periods, however, due to a failed cannula during one i.v. injection, only 20 complete sets of data were available.

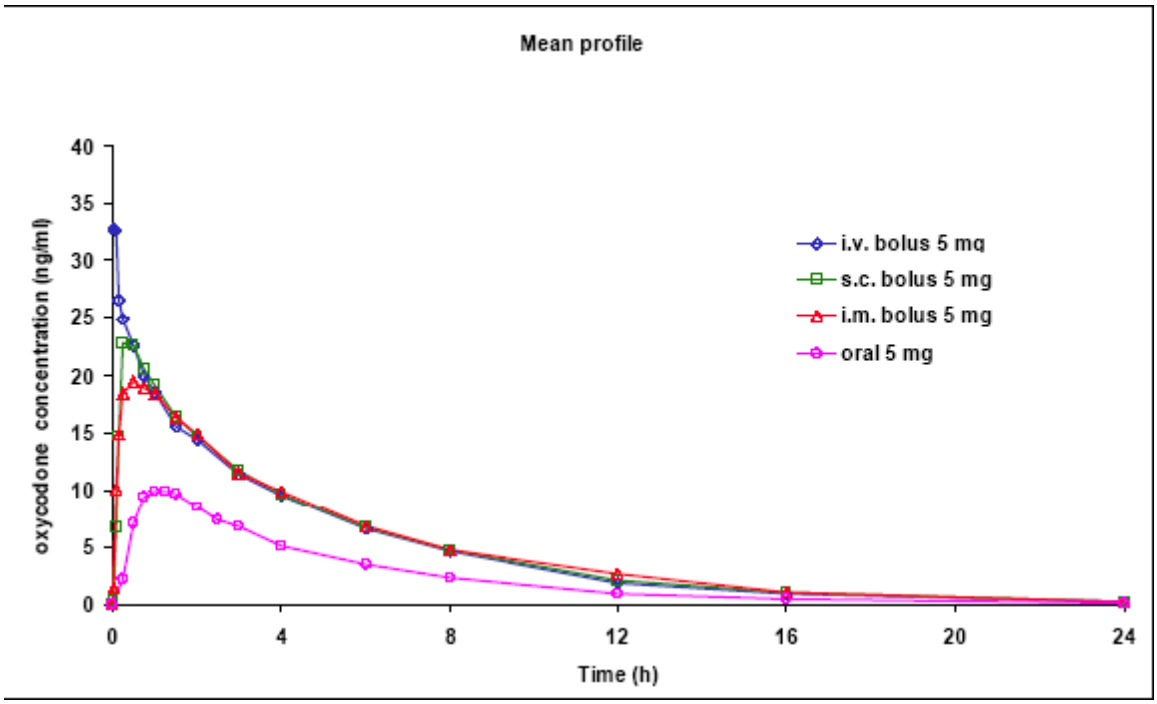
During each study period, 7 ml blood samples were taken before dosing and then at the following times after dosing for the analysis of oxycodone, noroxycodone and oxymorphone concentrations:
• Oxycodone injection 10 mg / ml (i.v., s.c. or i.m. bolus dose) -
2, 5, 10, 15, 30, 45 min and then 1, 1.5, 2, 3, 4, 6, 8, 12, 16 and 24 hours
• Oxycodone IR liquid 5 mg/5 ml (single oral dose) -
15, 30, 45 min and then 1, 1.25, 1.5, 2, 2.5, 3, 4, 6, 8, 12, 16 and 24 hours

The data were used to characterise the pharmacokinetic parameters of AUCn, AUC, Fabsn, Fabs, C_{max} $t_{max.}$ λz and t1/2z.

A large proportion of the plasma samples contained levels of oxymorphone that were below the limit of quantification for the oxymorphone assay. It was therefore not possible to carry out pharmacokinetic analysis on these data.

The 90% confidence intervals associated with the absolute bioavailability of oxycodone and noroxycodone for s.c. and i.m. administration were within the 80 -125% limits of acceptability for bioequivalence. The oxycodone oral liquid had a reduced mean availability (Fabs) of oxycodone compared with the i.v. bolus dose (46%).

As anticipated, the oxycodone C_{max} values for s.c. and i.m. administration were lower than for i.v. administration. In addition, oxycodone oral liquid had a significantly lower C_{max} than i.v. administration and C_{max} for noroxycodone was significantly higher (Figures 2.7.2.2.1).



The results demonstrate that the single subcutaneous injection and the single intramuscular injection provided an equivalent availability to the single intravenous injection.

Study OXI1203 was an open, randomised, four-part, crossover study in 24 healthy, male volunteers. The pharmacokinetics of oxycodone were compared for 0.5 ml oxycodone injection 10 mg / ml as a single i.v. and s.c. bolus dose of 5 mg and oxycodone injection 10 mg / ml as an i.v. and s.c. infusion of 10 mg over 8 hours (1.25 mg/hour). Twenty-one of the 24 subjects completed all four study periods: One subject's data was excluded from the analysis because the data did not form a complete profile characterised over the time stipulated in the protocol. During each study period, blood samples were taken before dosing and then at the following times after dosing for the analysis of oxycodone, noroxycodone and oxymorphone concentrations:

• Oxycodone injection 10 mg/ml (i.v., or s.c. bolus dose) -
2, 5, 10, 15, 30, 45 min and then 1, 2, 3, 4, 6, 8, 12, 16 and 24 hours
• Oxycodone injection 10 mg/ml (i.v., or s.c. infusion) -
1, 2, 4 and 6 hours after infusion start, immediately after infusion ends and at 5, 10, 15, 30, 45 min and 1, 2, 4, 6, 8, 12, 16 and 24 hours after infusion stopped.

The data were used to characterise the pharmacokinetic parameters of AUCn, AUC, Freln, Frel, C_{max}, tmax, λz and t½z. The primary comparisons of interest were i.v. infusion vs single i.v. bolus dose, and s.c. infusion vs single s.c. bolus dose.

Secondary comparisons of interest were single s.c. bolus dose vs single i.v. bolus dose and s.c. infusion vs i.v. infusion.

The i.v. and s.c. infusions provided an equivalent, dose-adjusted bioavailability to the i.v. and s.c. bolus doses, respectively and the different routes of administration provided an equivalent bioavailability of both oxycodone and noroxycodone.

As expected, there were significant differences, between the C_{max} values for the infusion vs. bolus doses, and the s.c. infusion vs. the s.c. bolus dose. There was also a significant difference between C_{max} values for the s.c. and i.v. bolus doses, but C_{max} values for the s.c. and i.v. infusions were comparable. As expected for the infusions, the t_{max} values coincided with the end of the infusion. The i.v. infusion t½z value was statistically significantly longer than the value for the i.v. bolus dose.

Unlike oxycodone, the C_{max} ratios for noroxycodone were all associated with 90% confidence intervals that lay within the 80 – 125% limits accepted for equivalence. The mean ratios of the AUCn values for noroxycodone relative to oxycodone were comparable for all the parenteral routes. The values were slightly higher than those recorded in OXI1202, which is probably a consequence of inter-study variability.

The infusion of oxycodone, either by the i.v. or s.c. route, provided an equivalent availability of oxycodone to a bolus injection by the same route. A bolus injection of oxycodone provided an equivalent availability of oxycodone when given subcutaneously compared with intravenously. Similarly, an infusion of oxycodone provided an equivalent availability of oxycodone when given subcutaneously compared with intravenously. The maximum plasma concentration for the subcutaneous infusion was equivalent to the intravenous infusion.

Conclusion
Although these studies were conducted with a 10 mg/ml concentration of oxycodone the results are considered applicable to the 50 mg/ml solution when given at the same dose as both are aqueous injectable solutions. The studies demonstrate that there is an equivalent availability of oxycodone when it is administered by the intravenous and subcutaneous routes as a bolus dose or as a continuous infusion over 8 hours. The data are adequate to support the proposed posology of the 50 mg/ml strength.

IV.3 Pharmacodynamics

Oxycodone belongs to the pharmacotherapeutic group: natural opium. It has an affinity for kappa, mu and delta opiate receptors in the brain and spinal cord. Oxycodone is similar to morphine in its action. The therapeutic effect is mainly analgesic, anxiolytic and sedative.

Endocrine system
Opioids may influence the hypothalamic-pituitary-adrenal or –gonadal axes. Some changes that can be seen include an increase in serum prolactin, and decreases in plasma cortisol and testosterone. Clinical symptoms may be manifest from these hormonal changes.

Other pharmacological effects
In vitro and animal studies indicate various effects of natural opioids, such as morphine, on components of the immune system; the clinical significance of these findings is unknown. Whether oxycodone, a semisynthetic opioid, has immunological effects similar to morphine is unknown

IV.4 Clinical efficacy

No new efficacy data have been submitted for this application and none were required.

IV.5 Clinical safety

No new safety data were submitted with this application and none were required. The safety profile for this product is considered to be the same as OxyNorm 10 mg/ml Infusion (PL 16950/0128).

IV.6 Risk Management Plan (RMP)

The requirement to submit an RMP with an initial marketing authorisation application came into effect on 21 July 2012. This application was submitted and approved prior to this date. Safety information has been included in the SmPC and the package leaflet for OxyNorm 50 mg/ml injection, including the appropriate precautions to be followed by healthcare professionals and patients.

IV.7 Discussion on the clinical aspects

The data are adequate to support the addition of a 50 mg/ml strength of oxycodone solution for infusion to allow for the use of a lower volume of solution in a syringe driver.

The rationale for the addition of the new strength of oxycodone is accepted. Satisfactory evidence is available that the benefit/risk balance of oxycodone is acceptable in the proposed dose range. Approval is recommended.

V USER CONSULTATION

The Patient Information Leaflet (PIL) 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 results show that the PIL 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

QUALITY

The important quality characteristics of OxyNorm 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 an application of this type.

EFFICACY

No new efficacy data were submitted for the applicant's OxyNorm 50 mg/ml Concentrate for Solution for Injection or Infusion. The applicant refers to the clinical development program for the original product line; this is acceptable.

SAFETY

No new or unexpected safety concerns arise from this application.

PRODUCT LITERATURE

The SmPC, PIL and labelling are satisfactory and in line with current guidance.

BENEFIT/RISK ASSESSMENT

The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. Extensive clinical experience with oxycodone hydrochloride is considered to have demonstrated the therapeutic value of the active substance. The risk:benefit is, therefore, considered to be positive.

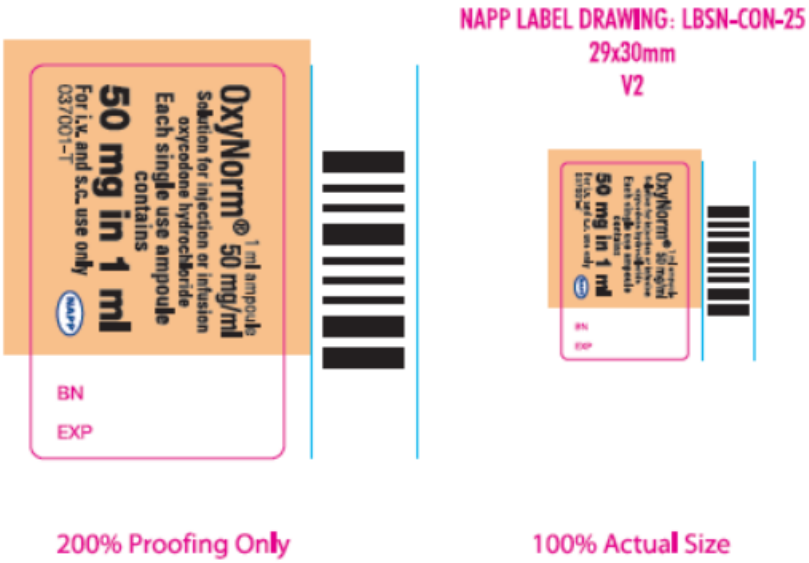
RECOMMENDATION

The grant of a Marketing Authorisation is recommended.

The SmPC, PIL and labelling are satisfactory, and in line with current guidelines.

In accordance with Directive 2012/84/EU, the current approved UK versions of the SmPCs and PILs for these products are available on the MHRA website.

The current labelling is presented below:


NAPP LABEL DRAWING: LBSN-CON-25
29x30mm
V2
OxyNorm®
1 ml ampoule
50 mg/ml
Solution for injection or infusion
oxycodone hydrochloride
Each single use ampoule contains
50 mg in 1 ml
For i.v. and s.c. use only
BN
EXP
200% Proofing Only
100% Actual Size

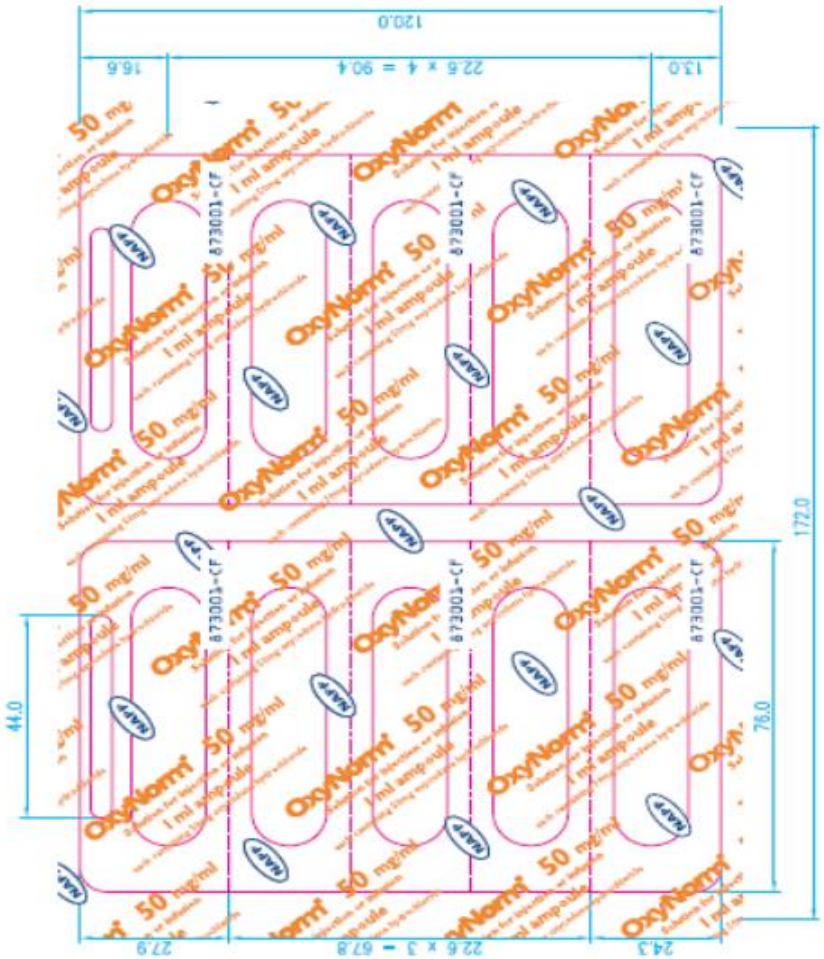

120.0
16.5
22.6 x 4 = 90.4
13.0
172.0
44.0
76.0
27.9
22.6 x 3 = 67.8
24.3

TABLE OF CONTENT OF THE PAR UPDATE

Steps taken after the initial procedure with an influence on the Public Assessment Report (non-safety variations of clinical significance).

Please note that only non-safety variations of clinical significance are recorded below and in the annexes to this PAR. The assessment of safety variations where significant changes are made are recorded on the MHRA website or European Medicines Agency (EMA) website. Minor changes to the marketing authorisation are recorded in the current SmPC and/or PIL available on the MHRA website.

Application type	**Scope**	**Product information affected**	**Date of grant**	**Outcome**	**Assessment report attached Y/N**
Type 1B	To increase the shelf life from 3 years unopened to 5 years unopened. Section 6.3 of the SmPC has been updated.	SmPC, PIL	23/04/2013	Approved	N
Type II	To update Section 5.1 (Pharmacodynamics) of the Summary of Product Characteristics (SmPC) and consequently the Leaflet, in line with the Company Core Data Sheet (CCDS).	SmPC, PIL	29/06/2013	Approved	Y – Annex 1
Type 1B	PL 16950/0155-0058 (submitted as part of CCC-Napp-16950-045 - Variation 1): To update section 4.2 of the SmPC to add information on conversion from morphine and to add statements on consideration of patient's previous history of analgesic requirements and use of lowest effective dose, and harmonisation of dilution information of 50 mg/ml strength with 10 mg/ml.	SmPC, PIL	04/09/2020	Approved	Y – Annex 2
Type II	PL 16950/0155-0060 (submitted as part of CCC-Napp-16950-045 - Variation 3): To update section 5.2 of the SmPC to update pharmacokinetic properties into ADME format and deletion of irrelevant data. [2] To update section 5.3 of the SmPC to add data on carcinogenicity and harmonisation of 10 mg/ml strength with 50 mg/ml.	SmPC	04/09/2020	Approved	Y – Annex 3

Annex 1

Our Reference: PL 16950/0155, Application 34
Product: OxyNorm 50 mg/ml, solution for injection or infusion
Marketing Authorisation Holder: Napp Pharmaceuticals Limited
Active Ingredient(s): Oxycodone hydrochloride

Type of Procedure: National
Submission Type: Variation
Submission Category: Type II
Submission Complexity: Standard
EU Procedure Number (if applicable):

Reason:
To update Section 5.1 (Pharmacodynamics) of the Summary of Product Characteristics (SmPC) and consequently the Leaflet, in line with the Company Core Data Sheet (CCDS).

Supporting Evidence
Update SmPC fragment as detailed in the table below and revised PIL.

PRESENT [10,11]	PROPOSED [10, 11]
5.1 Pharmacodynamic properties As present SPC including: Opioids may influence the hypothalamic-pituitary-adrenal or gonadal axes. Some changes that can be seen include an increase in serum prolactin and decreases in plasma cortisol and testosterone. Clinical symptoms may be manifest from these hormonal changes. In vitro and animal studies indicate various effects of natural opioids, such as morphine, on components of the immune system; the clinical significance of these findings is unknown. Whether oxycodone, a semisynthetic opioid, has immunological effects similar to morphine is unknown.	**5.1 Pharmacodynamic properties** As present SPC including: ***Gastrointestinal System*** ***Opioids may induce spasm of the sphincter of Oddi.*** ***Endocrine system*** Opioids may influence the hypothalamic-pituitary-adrenal or gonadal axes. Some changes that can be seen include an increase in serum prolactin and decreases in plasma cortisol and testosterone. Clinical symptoms may be manifest from these hormonal changes. ***Other pharmacological effects*** In vitro and animal studies indicate various effects of natural opioids, such as morphine, on components of the immune system; the clinical significance of these findings is unknown. Whether oxycodone, a semisynthetic opioid, has immunological effects similar to morphine is unknown.

Section 5.1 Pharmacodynamic Properties
A safety analysis and benefit risk assessment of biliary spasm concluded that there was insufficient evidence for a causal association between oxycodone and biliary spasm[10]. However, given the data from pharmacopoeias reviewed in the context of the safety analysis, addition of language regarding the occurrence of biliary spasm/ spasm of the sphincter of Oddi (with opioids in general) has been inserted into section 5.1.

Gastrointestinal System
Opioids may induce spasm of the sphincter of Oddi.

The sub-headings "Endocrine system" and "Other pharmacological effects" have been added, for consistency with the MAHs OxyContin (oxycodone) prolonged release tablets SmPCs.

Evaluation
The addition of sub-section headings to Section 5.1 of the SmP is acceptable. The addition of '….spasm of the sphincter of Oddi.' under the sub-section heading 'Gastrointestinal System' is also accepted.

A safety analysis and benefit risk assessment of biliary spasm concluded that there was insufficient evidence for a causal association between oxycodone and biliary spasm. Therefore, in view of the uncertainty in the causal relationship, the omission of '…spasm of the sphincter of Oddi.' in Section 4.8 of the SmPC is accepted. However the Marketing Authorisation Holder is requested to review any adverse effects related to biliary colic/spasm etcetera on a regular basis, and provide updates as necessary.

The proposed changes to the PIL are considered satisfactory.

Conclusion
The changes to the SmPC and PIL are acceptable.

Decision
Approved on 29 June 2016.

Annex 2

Reference: PL 16950/0155-0058

Product: OxyNorm 50 mg/ml, solution for injection or infusion

Type of Procedure: National

Submission category: Type IB Variation

Reason
To note: this variation was submitted as part of a Composite Coordinated Collection (CCC-Napp-16950-045). This assessment report only refers to PL 16950/0155-0058 submitted as part of variation 1 of this CCC.

To update section 4.2 of the SmPC to add information on conversion from morphine and to add statements on consideration of patient's previous history of analgesic requirements and use of lowest effective dose, and harmonisation of dilution information of 50 mg/ml strength with 10 mg/ml.

Supporting evidence
The Company has submitted an SmPC and PIL.

Evaluation
The updated documents are satisfactory.

Conclusion
The proposed changes are acceptable.

In accordance with Directive 2010/84/EU, the Summaries of Product Characteristics (SmPCs) and Patient Information Leaflets (PILs) for products granted Marketing Authorisations at a national level are available on the MHRA website.

Decision: Grant

Date: 04 September 2020.

Annex 3

Reference: PL 16950/0155-0060

Product: OxyNorm 50 mg/ml, solution for injection or infusion

Type of Procedure: National

Submission category: Type II Variation

Reason
To note: this variation was submitted as part of a Composite Coordinated Collection (CCC-Napp-16950-045). This assessment report only refers to PL 16950/0155-0060 submitted as part of variation 3 of this CCC.

1. To update section 5.2 of the SmPC to update pharmacokinetic properties into ADME format and deletion of irrelevant data.
2. To update section 5.3 of the SmPC to add data on carcinogenicity and harmonisation of 10 mg/ml strength with 50 mg/ml.

Supporting evidence
The MAH has submitted an updated SmPC.

Evaluation
The updated document is satisfactory.

Conclusion
The proposed changes are acceptable.

In accordance with Directive 2010/84/EU, the Summaries of Product Characteristics (SmPCs) and Patient Information Leaflets (PILs) for products granted Marketing Authorisations at a national level are available on the MHRA website.

Decision: Grant.

Date: 04 September 2020.