Public Assessment Report for paediatric studies submitted in accordance with Article 45 of Regulation (EC) No1901/2006, as amended

Product name in RMS country:
OxyContin (prolonged release tablets)
OxyNorm (capsules, oral solution, solution for injection)
OxyNormORO (orodispersible tablets)

oxycodone hydrochloride

FR/W/0010/pdWS/01

Rapporteur:	France
Finalisation procedure (day 120):	24/03/2021

TABLE OF CONTENTS

ADMINISTRATIVE INFORMATION

Invented name of the medicinal product(s):	See section VI
INN (or common name) of the active substance(s):	Oxycodone
MAH (s):	See section VI
Pharmaco-therapeutic group (ATC Code):	N02AA05
Pharmaceutical form(s) and strength(s):	Immediate release oxycodone (tablets, capsules, oral solution, orodispersible tablets) Prolonged release oxycodone Parenteral oxycodone

I. EXECUTIVE SUMMARY

The applicant initially proposed modification of the SmPC at the start of the Article 45 procedure to extend the indication of oxycodone to children from 6 months old. Subsequently following review of studies submitted, the proposed indication was updated to paediatric subset 12 years of age and older.

Summary of outcome

☐ No change

☐ New study data

☐ New safety information

☒ Paediatric information clarified

☒ New indication

II. RECOMMENDATION

Based on the evidence submitted by the MAH, the rapporteur concludes that the data justified the use of oxycodone (oral and parenteral) in the paediatric population (adolescents aged 12 years and older) as treatment of "*Severe pain, which can be adequately managed only with opioid analgesics".*
The indication is already approved in several European countries in this population.

Oxycodone should be not recommended in patients < 6 months < 12 years old taking into account that the available data about potential doses and dose intervals are too scarce in this population.

A comprehensive description of the indications and posology is given in section 4.1 and 4.2 of the SmPC.
Section 5.1 is updated with the information in relation to the paediatric population.
The MAH does not have sufficient pharmacokinetic data in adolescent patients from oral or parenteral products to merit inclusion in section 5.2 of the SmPC.

The frequency, type and severity of adverse reactions in patients from 12 years of age and older appear similar to those in adults. This statement is included under section 4.8 with a cross reference to section 5.1.

Section 4.8 Undesirable effects should be completed with the table of the frequency and SOC of the adverse events observed in paediatric population in line with SmPC Guidance (September 2009), with all headings. These changes will need to be implemented with the filing of later a variation. As a Risk Minimisation Measure, it is emphasised that Opioids must only be used for appropriate indications and prescribed by a specialist experienced in managing severe pain in children, with careful assessments of the benefits and risks.

Moreover, section 4.4 and section 4.9 were modified according to the PRAC recommendation (November 20222) of the PSUSA oxycodone (PSUSA/00002254/202204) and the CMDh position (EMA/CMDh/852779/2022).

III. INTRODUCTION

In accordance with Article 45 of the Regulation (EC) No 1901/2006, as amended on medicinal products for paediatric use, Mundipharma submitted 17 completed paediatric studies for oxycodone.

The dossier submitted was limited, with scarce kinetic data and no real phase II/III studies with either dose determination or evaluation of efficacy and safety of oxycodone in children below 12 years.

A short critical expert overview was also provided.

In addition, the following documentation was included as per the procedural guidance:

- An annex including SmPC wording of sections 4.1 and 4.2 related to the paediatric use of the medicinal product.

During the FR/W/010/pdWS/001 EU Work-sharing procedure for paediatric studies submitted under Article 45 of EU Regulation No 1901/2006, based on the evidence submitted by the MAH, the rapporteur concluded that the data justified the use of Oxycodone (oral and parenteral) in the paediatric population. The Applicant was requested to submit a Type II Variation to update sections 4.1 and 4.2 of the SmPCs and PILs of products containing the active ingredient Oxycodone (oral and parenteral formulations) in line with the work-sharing recommendations. Furthermore, the applicant was asked to update section 5.1 Pharmacodynamic properties and section 5.2 Pharmacokinetic properties with the available data in the paediatric population.

The MAH committed to submit a variation to update the product information accordingly.

In accordance with the above-mentioned request, the MAH submitted a type II variation as an EU Worksharing procedure (FR/H/xxxx/001/WS/288). The Marketing Authorization Holder proposed an update to the Summary of Product Characteristics (SmPC) and Package Leaflet (PIL) of the products containing Oxycodone as a single pharmaceutical ingredient to include the proposed text concerning the addition of the paediatric indication in the paediatric subset 12 years of age and older as recommended and requested. Sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are proposed to be updated.

Efficacy and safety data from clinical trials conducted in paediatric patients based on clinical studies performed by the Applicant as well as publicly available literature were submitted.

IV. SCIENTIFIC DISCUSSION

IV.1 Information on the pharmaceutical formulation used in the clinical study(ies)

The pharmaceutical formulation has not been stated in the report.

IV.2 Non-clinical aspects

No data are provided.

IV.3 Clinical aspects

The MAH provided clinical data, including kinetic and efficacy studies. These data are summarized hereafter.

First author	Year		Age range	Indication	Dose	Route
Pokela	2005	PK	< 6 months	Postoperative	0.1 mg/kg	Intravenous
Kokki	2004	PK	6 – 93 months	Postoperative	0.1 mg/kg	Intravenous/buccal/ intramuscular
Kokki	2006	PK	6 – 91 months	Postoperative	0.2 mg/kg	Buccal/sublingual
Buice	1999	PK	5 – 12 yrs	Unknown	Single dose, 10 mg q12h / 5 mg q4-6h	Oral
Olkkola	1994	PK	2 – 10 yrs	Postoperative	0.1 mg/kg	Intravenous
Blumer	2001	PK	6 – 12 yrs	Unknown	Single dose, 10 mg q12h/5 mg q4-6h	Oral
Myers	2006	PK	6 – 18 yrs	Orthopaedic injury	Single dose, 0.1, 0.15, 0.2 mg/kg	Intravenous
Charney	2008	Clin	4-17 years	Triage	0.2 mg/kg	Oral
Koller	2007	Clin	6-18 years	Orthopaedic injury	0.1 mg/kg	Oral
Sharar	2002	Clin	5-14 years	Wound care	0.2 mg/kg	Oral
Murray	2002	Clin	4 – 43 mo	Preoperative	0.1 mg/kg	Oral
Kokki	2006	Clin	10 mo-12 yrs	Thoracotomy	Not stated	Intravenous
Kokki	2005	Clin	4-15 years	Abdominal pain	0.1 mg/kg	Buccal
OC92-1101	1992	Clin	9 – 17 yrs	Pain	10, 20, 40 & 80 mg q12h	Oral
Czarnecki	2004	Clin	10-19 years	Postoperative	1.24 mg/kg/day	Oral
Ganesh	2007	Clin	1-10 years	Postoperative	0.1 mg/kg 4-hourly	Oral
Luhmann	2006	Clin	5-17 years	Forearm fracture	0.2 mg/kg	Oral

The MAH submitted reports for:

- OXP3003: multicenter, double blind, randomised, dose ranging study, in paediatric patients 5 to ≤ 16 years of age receiving morphine as standard supplemental pain medication, to evaluate pharmacokinetics, efficacy and safety of Oxy paediatric liquid (1 mg/ml) versus placebo in the treatment of acute moderate to severe pain.
- OC92-1101: open-label clinical use study of controlled-release oxycodone tablets administered orally every 12 hours for the management of pain.
- OXP1005: a multicenter, inpatient, open-label, dose-ranging study to characterize the pharmacokinetics and safety of an oral liquid formulation of oxycodone in patients from birth to 4 years, who require opioid analgesia.
- OXP3004: multicenter, open-label, multiple-dose study of the conversion from immediate-release oxycodone (OxyIR®) to controlled-release (OxyContin®) to evaluate pharmacokinetics and to characterize safety and efficacy in paediatric patients 6 to ≤ 16 years of age.
- OXN9002: prospective observational cohort study: safety and efficacy of Targin® in patients with pain

The MAH submitted synopsis for:

- AWB-MF/OXY/010898: oxygesic in post-operative analgesia: study in adult patients with included patients aged from 16 to 93 (mean 54.7) years.
- AWB-GW/OXY 4407: observational pain control with oxygesic: study in adult patients with included patients aged from 17 to 96 years.

The MAH also submitted bibliographic data.

Clinical studies

OXP3003: Was a multicenter, double blind, randomised, dose ranging study, in paediatric patients 5 to ≤ 16 years of age receiving morphine as standard supplemental pain medication, to evaluate

pharmacokinetics, efficacy and safety of Oxy paediatric liquid (1 mg/ml) versus placebo in the treatment of acute moderate to severe pain

- To characterize the pharmacokinetics of Oxy Paediatric Liquid 1 mg/ml (using a population PK approach) after the first dose and after repeated dosing in paediatric patients aged 5 to ≤ 16 years.
- To evaluate the safety of Oxy Paediatric Liquid 1 mg/ml in paediatric patients aged 5 to ≤ 16 years

There were 66 paediatric patients enrolled in the study. The safety and full analysis populations consisted of 60 patients, with 50 patients completing the study. Ten patients (17%) discontinued: 3 (5%) due to adverse events, 5 (8%) due to administrative reasons and 2 (3%) due to subject's choice.

The PoPPK model presented for oxycodone by the applicant is based on PK data from 8 clinical studies performed in healthy adult volunteers or paediatric patients where all the available oxycodone formulation were administered (IR solid, IR liquid, OC or ORF). The PK dataset consisted of 5187 oxycodone concentrations from 275 patients. Paediatric PK data accounted for 25% of the entire dataset.

The modelling report states that data below limit of quantification (BLQ) have been omitted from the analysis. However, there is no mention of the amount of data being BLQ. If >10% of the data is BLQ, it is recommended to apply an appropriate likelihood-based method to handle the missing data, e.g. M3 or M4 [Ahn et al. J Pharmacokinet Pharmacodyn. 2008 Aug;35(4):401-421].

To note none of the raw PK data were available from any of the used clinical PK study.

The PopPK model was used to derive (by simulation) the optimal dose of oxycodone in a given paediatric age group (newborn - <1 month, 1 month-1 year, 2-6 year, 7-11 year, and 12-17 year) and for a given formulation (IR solid, liquid or OCR) using the extrapolation concept (matching adult AUC exposure).

The PopPK model consisted of 1 cpt PK model with first order absorption and elimination. Separate bioavailability terms (F) were incorporated into the model for the immediate release (IR), liquid (IRl), IR solid (IRs), and modified-release (MR) reformulated OxyContin (ORF) oxycodone formulations. Variability in CL/F and V/F were partially described by allometrically scaled weight. An additional effect of age on CL/F was also described for children newborn to <1 month old and for children 1 month to 1 year old.

Overall, PK parameters were estimated with a good precision (RSE <25%) for both fixed and random effects. The estimate typical CL/F and Vc/F were 90.8 L/h and 575 L with associated moderate IIV of 35.9% and 32.7%. Eta-shrinkage was particularly low (<22%).
RUV use a combined error model for each oxycodone formulation, with proportional term particularly high for IR liquid (40%) and solid (55.2%) formulation.
Although BW and age were highly correlated (0.84), BW (allometric scaling with fixed exponents of 0.75 and 1 for CL/F and Vc/F) and age (power model on CL/F for the young children group) were found to have an effect on oxycodone PK.
According to the applicant standard diagnostic plot does not show significant bias. To note no local regression line was provided. Nevertheless, on the DV *vs* IPRED for adult, along the concentration interval the model seems to under-predict concentrations whereas for low concentration the model seems to over-predict. The same trend appears particularly pronounced for low concentrations for the paediatric population.

The applicant tried to fit a 2 compartment PK model, however this was associated to no improvement of the fit.

Predictive performance were investigated using a QQ plot where the observed distribution of C_{med} (for children) or dose-normalised C_{med} (for adults) was compared to 500 replicate of simulated C_{med} (or dose normalised C_{med}). The applicant stated that good predictive performance are observed for the paediatric population. However, this is truly the case only for the fourth quartile (C_{med} > 14 ng/mL) whereas for the other quartiles, the simulated C_{med} are slightly higher than the observed C_{med}.

For the adult population, the predictive performance were particularly worst along the concentration interval and as pointed out by the applicant, when this plot was conditioned by study type, the simulated dose normalised C_{med} was lower for single dose study only. However, it should be noted that PK data from this single dose study represented more than 65% of the entire PK dataset, these data contained the main information of the PK of oxycodone.

Nevertheless, since only one observation per individual ([dose normalised] median concentration) were presented, without stratification on formulation, it was not possible to draw any conclusions regarding model predictability based on figures alone. The applicant should have provided a proper model evaluation with prediction, corrected visual predictive checks for oxycodone concentration vs time after dose [Bergstrand et al. AAPS J. 2011 Jun;13(2):143-151] and different stratifications: (1) single dose/steady state, (2) formulation [IR Oral Liquid; IR Oral Capsule; Orodispersible Tablet; PR Tablet (ORF); PR Tablet (OC)], (3) age [6 months -<2 years; 2-<4 years; 4-<6 years; 6-<12 years; 12-<18 years; ≥18 years], and (4) body weight [6-<12 kg; 12-<16 kg; 16-<20 kg; 20-<50 kg; 50-<70 kg; ≥70 kg].

The typical estimates for apparent clearance and relative bioavailability were associated with uncertainty. Despite this, there was no uncertainty reported for the Adult target AUCs, in the presented results from the simulation analysis. Uncertainties for these predictions should have been provided. The information should have been completed by including a comparison of predicted C_{max} (with uncertainty) for adults and predicted C_{max} at recommended doses for children, for each formulation and age category, respectively.

It was noted that the doses for children, to match the adult target AUC, for IR Oral Capsule, Orodispersible Tablet, and PR Tablet, were lower than the lowest strengths approved for these formulations. Boxplots should have been provided for AUC and C_{max}, showing the exposure by age compared with adult target exposure, for the recommended (approved) doses for each formulation separately (for an illustrative example, please see Modelling and simulation: Questions and Answers [https://www.ema.europa.eu/en/human-regulatory/research-development/scientific-guidelines/clinical-pharmacology-pharmacokinetics/modelling-simulation-questions-answers]).

Consequently, taking into account these data, any agreement on the suitability of the developed PopPK model used to derive the paediatric dose (per age and formulation) could not be performed.

No conclusion could be drawn regarding efficacy. Regarding safety, the incidence was comparable between groups and the nature of these AEs was, according to investigator, known adverse drug reaction or explained by the patient's underlying condition. Regarding SAEs, they were considered not related to the use of oxycodone. Nevertheless, one must take into account the few number of patients enrolled in this study: 26 for patients aged 5 to 12 years and 39 for patients aged 12 to 16 years.

In conclusion: since the developed PopPK model needed further clarifications to be considered as suitable, any agreement on the dosing recommendations in the paediatric population based on the simulation exercise, could not be performed.

OXP3004: multicenter, open-label, multiple-dose study of the conversion from immediate-release oxycodone (OxyIR®) to controlled-release (OxyContin®) to evaluate pharmacokinetics and to characterize safety and efficacy in paediatric patients 6 to ≤ 16 years of age.

The study was terminated early for administrative reasons, with 10 patients treated in the conversion phase and 7 in the long term period for a duration of three weeks. No conclusion could be drawn on the efficacy and safety of either IR or CR oxycodone due to the small number of patients. No information regarding the dose administered was available in the documentation provided.
This study provided no information to support the dosing recommendation made by the applicant for the SmPC

OXP1005: a multicenter, inpatient, open-label, dose-ranging study to characterize the pharmacokinetics and safety of an oral liquid formulation of oxycodone in patients from birth to 4 years, who require opioid analgesia.

No conclusion could be drawn as this was an open non randomised study. Supplemental pain medication was higher for the higher dose groups for oxycodone, suggesting higher pain in this population as dose was increased according to the patient's needs.

Review of Literature Presenting Studies

Wu et al. (2020) conducted a randomised, controlled study in 166 children up to 9 years of age to investigate oxycodone for pre-emptive analgesia while undergoing endoscopic plasma total adenotonsillectomy. The children were randomised to one of the following three treatment groups:

1. SPOA (postoperative sufentanil)
2. SPEA+SPOA (pre-emptive sufentanil and postoperative sufentanil)
3. OPEA+SPOA (pre-emptive oxycodone and postoperative sufentanil).

The primary endpoint was serum c-fos levels.
A dose of oxycodone (0.1 mg/kg) as pre-emptive analgesia could improve pain levels after endoscopic plasma total adenotonsillectomy in children.

Li et al. (2018) performed a retrospective comparative study to assess if intrathecal morphine (ITM) and oral analgesics provide effective pain control after posterior spinal fusion (PSF) for adolescent idiopathic scoliosis (AIS). Patients in the age of 10–17 suffering from AIS who had undergone PSF were eligible for this study. A total of 28 patients who received ITM were compared to 28 patients who received a hydromorphone epidural infusion (EPI). The ITM group received oral oxycodone (0.1 mg/kg) starting at 16 hours post injection.
ITM and oral analgesics (including oxycodone) provided safe and effective pain control after PSF for AIS. Patients can be transitioned directly to oral opioids without the need for intravenous opioids.

Rodenas et al. (2015) conducted an open-label, multicentre study to establish the efficacy and safety of twice daily oxycodone hydrochloride controlled-release tablets in 155 opioid experienced paediatric patients (6 – 16 years) suffering from moderate to severe malignant and/or non-malignant pain requiring opioid analgesics.
It was shown that oxycodone PR was safe and effective when administered to opioid-experienced paediatric patients aged 6 to 16 years suffering from moderate to severe malignant and/or non-malignant pain requiring opioid therapy.

Koller et al. (2007) performed a prospective, randomised, double-blind study to compare the effectiveness of oxycodone (0.1 mg/kg, max 10 mg), ibuprofen (10 mg/kg, max 800 mg), and the combination of oxycodone and ibuprofen (0.1 mg/kg + 10 mg/kg, max 10 mg + max 800 mg) in children (6-18 years) suffering from pain due to a suspected orthopaedic injury.
Efficacy assessment was performed using the FPS and VAS as assessed at baseline, post-immobilisation as well as at different time points post-medication.
Oxycodone, ibuprofen and the combination provided effective analgesia for mild-to-moderate orthopaedic injuries in children. Oxycodone or ibuprofen, alone, can be given alone, thereby avoiding the increase in adverse effects when given together.

Bailey et al. (2015) performed a double-blinded randomised control study in 58 children (aged 2-16 years) to evaluate paediatric post-tonsillectomy pain management using oxycodone in combination with a specific information sheet. A post-operative analgesia information sheet provided higher satisfaction and knowledge for parents using oxycodone ($p<0.001$) and children had improved post-operative pain control, most significantly at day 5 ($p<0.05$). Parent assessment of the child's analgesia was superior with the oxycodone information sheet, most significantly at day 3 and 7 post-operatively ($p<0.05$). There was also a positive correlation between the parents' observed pain score and children's self-reported pain score ($p<0.001$).

Maxwell et al. (2014) conducted a prospective cohort study to investigate pain management following major intracranial surgery in paediatric patients. Two hundred children (98 males, 102 females), aged 7.8 ± 5.8 years (range: 2 months-18.5 years), with a mean body weight of 32.2 ± 23.0 kg (range: 4.5-111.6 kg) undergoing craniectomy (51), craniotomy (96) or craniofacial reconstruction (53) were studied. Despite considerable variation in mode and route of analgesic administration, there were no differences in average pain score, length of hospital stay, or parental satisfaction with care.

Safety submitted data

Overview of data from the international drug safety database

The cases reporting use in patients in paediatric age groups identified in the international drug safety database were, in the main, associated with off label use of oxycodone. Drug abuse and dependence, medication errors and foetal exposure during pregnancy or neonatal exposure via breastmilk were commonly reported, with accidental exposure type of events more frequent in younger children and (illicit) abuse and dependence associated events more frequent in adolescent, but with few cases documented as resulting from correct medical use.

Considering the other MedDRA PTs reported in the cases, the safety profile of oxycodone in paediatric patients seems similar to the safety profile of oxycodone in adult patients when compared against terms listed in the MAH's oxycodone CCDS. In particular, more frequently reported unlisted terms or EMA IME terms do not seem to represent actual causal associations specific to paediatric patients. A limited number of cases reported drug abuse and dependence, even when pain was the reported indication. Treating physicians must be aware of the potential for drug abuse and dependence, including in patients aged 12 and over, and should accordingly use the lowest dose which sufficiently controls severe pain for the shortest duration of time, monitor the patient closely. Every effort should be made to avoid divergence into particularly the adolescent age group such as limiting number of days of prescription, and to avoid accidental exposure in younger children.

No specific concerns regarding use of oxycodone in paediatric patients in the therapeutic setting were identified during the review of the international drug safety database.

Review of EudraVigilance Data Analysis System (EVDAS)

The EVDAS data concerning use of oxycodone in paediatric patients was limited when compared to adult patients. The drug-event combinations (DECs) with a positive ROR (-) paed and a significant number of new paediatric cases in the last year include Drug dependence, Drug abuse, Substance abuse, Completed suicide, and Dependence. The data did not allow to distinguish between cases associated with medical prescription versus those with (illicit) abuse, but it was likely that the pattern would be similar to what was seen on more detailed analysis of the data in the company global safety database. Nonetheless, these DECs further supported the conclusions of the analysis of the company safety database:
Treating physicians must be aware of the potential for drug abuse and dependence, including in patients aged 12 and over, and – when an opioid analgesic is needed – should accordingly use the lowest dose which sufficiently controls severe pain for the shortest duration of time and monitor the patient closely. Every effort should be made to avoid divergence into particularly the adolescent age group such as limiting number of days of prescription, and to avoid accidental exposure in younger children.

Review of Literature

In order to identify relevant literature articles published to the evaluation of paediatric use of oxycodone, a cumulative search was undertaken on the 20 Jul 2021.
655 articles were identified in the first instance, and the abstracts of each were reviewed to identify any articles potentially reporting safety outcomes of oxycodone use in paediatric patients. The majority of articles did not report relevant information, variously studying prescription numbers and utilization of oxycodone, local analgesic protocols and procedures, oxycodone use in non-paediatric patients, and use of opioids other than oxycodone. Only 19 potentially relevant articles were identified and underwent full text review. Of the 19 articles, 15 were deemed relevant for the analysis.

Studies reported adverse events that were within the known safety profile of oxycodone use in adults.
In general, the literature review did not reveal any specific safety concerns for the use of oxycodone in paediatric patients. Nevertheless, data from Wheaton et al. (2019) presented "14 cases of paediatric patients experiencing leukoencephalopathy after ingesting opioid medications, 2 of which reported ingestion of oxycodone. Upon review, the cases described circumstances of accidental exposure or parental abuse and opioid overdose which was not representative of the proposed therapeutic use of oxycodone.

V. MEMBER STATES OVERALL CONCLUSION AND RECOMMENDATION

➢ Overall conclusion

The available efficacy and safety data provided evidence supporting the use of oxycodone in paediatric patients aged from 12 years and older.
Oxycodone should be not recommended in patients < 6 months < 12 years taking into account that the available data about potential doses and dose intervals were too scarce in this population.

Concerning section 4.1 the proposed indication "*Severe pain, which can be adequately managed only with opioid analgesics"* is acceptable.

A comprehensive description of posology is given in section 4.2 of the SmPC for adolescents from 12 years of age and older. No data are available for children below 12 years of age. The safety and efficacy of oxycodone in children below 12 years of age has not yet been established. As a Risk Minimisation Measure, it is emphasised that Opioids must only be used for appropriate indications and prescribed by a specialist experienced in managing severe pain in children, with careful assessments of the benefits and risks.

Section 5.1 was updated with the information in relation to the paediatric population.
The MAH did not have sufficient pharmacokinetic data in adolescent patients from oral or parenteral products to merit inclusion in section 5.2 of the SmPC.

The frequency, type and severity of adverse reactions in adolescents from 12 years of age and older appear similar to those in adults.
Section 4.8 Undesirable effects should be completed with the table of the frequency and SOC of the adverse events observed in paediatric population in line with SmPC Guidance (September 2009), with all headings. These changes will need to be implemented with the filing of later a variation.

Moreover, section 4.4 and section 4.9 were modified according to the PRAC recommendation (November 20222) of the PSUSA oxycodone (PSUSA/00002254/202204) and the CMDh position (EMA/CMDh/852779/2022).

➢ Recommendation

Based on the evidence submitted by the MAH, the rapporteur concludes that the data justified the use of Oxycodone (oral and parenteral) in the paediatric population (patients aged 12 years and older) as treatment of *"Severe pain, which can be adequately managed only with opioid analgesics"*.

VI. LIST OF MEDICINAL PRODUCTS AND MARKETING AUTHORISATION HOLDERS INVOLVED

Invented name of the medicinal product(s):

OxyContin (prolonged release tablets)
OxyNorm (capsules, oral solution, solution for injection)
OxyNormORO (orodispersible tablets)

MAH : MUNDIPHARMA