SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Lindoxa 10 mg/ml solution for injection/infusion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml contains 10 mg oxycodone hydrochloride corresponding to 9 mg oxycodone.

Excipients with known effect:
Each ml contains 7.5 mg sodium chloride.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection or infusion

Lindoxa 10 mg/ml solution for injection/infusion is a clear, colourless to slightly yellowish solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Severe pain, which requires opioid analgesics to be adequately managed.
For adults only.

4.2 Posology and method of administration

Posology

The dosage depends on the pain intensity, the total condition of the patient, previous or concurrent medication, the patient's individual susceptibility to the treatment, body weight, and sex (higher plasma concentrations in females).

The following general dosage recommendations apply:

The following starting doses are recommended. A gradual increase in dose may be required if analgesia is inadequate or if pain severity increases.

Adults (≥ 18 years of age)
i.v. (Bolus): Dilute to 1 mg/ml in 0.9% saline, 5% dextrose or water for injections.
Administer a bolus dose of 1 to 10 mg slowly over 1-2 minutes to opioid-naïve patients.
Doses should not be administered more frequently than every 4 hours.

i.v. (Infusion): Dilute to 1 mg/ml in 0.9% saline, 5% dextrose or water for injections.
A starting dose of 2 mg/hour is recommended in opioid-naïve patients.

i.v. (PCA): Dilute to 1 mg/ml in 0.9% saline, 5% dextrose or water for injections.
Bolus doses of 0.03 mg/kg should be administered with a minimum lock-out time of 5 minutes to opioid-naïve patients.

s.c. (Bolus): Use as 10 mg/ml concentration. A starting dose of 5 mg is recommended, repeated at 4-hourly intervals in opioid-naïve patients as required.

s.c. (Infusion): Dilute in 0.9% saline, 5% dextrose or water for injections if required.
A starting dose of 7.5 mg/day is recommended in opioid naïve patients, titrating gradually according to symptom control. Cancer patients transferring from oral oxycodone may require much higher doses (see below).

Particular attention should be paid to the treatment of opioid side effects.

Conversion from morphine
The dose should be based on the following ratio: 1 mg of parenteral morphine is equivalent to 1 mg of parenteral oxycodone. It must be emphasised that this is a guide to the dose required. Inter-patient variability requires that the dosage is carefully titrated to each individual patient. Initially, a lower-than equivalent dose may be advisable.

Transferring patients between oral and parenteral oxycodone
The dose should be based on the following ratio: 2 mg of oral oxycodone is equivalent to 1 mg of parenteral oxycodone, if only a few doses have been given. In case of shift in choice of opioid to a patient, who has been in long-term opioid-treatment (opioidrotation), it should be emphasised that the above mentioned equipotent doses are guidance only. Often it is necessary to administer less a decreased dose as equipotency recommend. Based on this and the patients interindividual variability a shift requires that the dosing is titrated carefully for every single patient.

Use in non-malignant pain
Opioids are not first-line therapy for chronic non-malignant pain, nor are they recommended as the only treatment. The need for continued treatment in non-malignant pain should be assessed at regular intervals.

Special populations
Elderly
Elderly patients should be treated with caution. The lowest dose should be administered with careful titration to pain control.

Renal or hepatic impairment
The dose initiation should follow a conservative approach in these patients. The recommended adult starting dose should be reduced by 50%, and each patient should be titrated to adequate pain control according to his/her clinical situation (also refer to section 4.4 and 5.2).

Paediatric population
Lindoxa 10 mg/ml solution for injection/infusion is not recommended for children and adolescents under 18 years of age.

Duration of treatment
Oxycodone should not be used longer than necessary.

Method of administration
Subcutaneous injection or infusion.
Intravenous injection or infusion.

Treatment goals and discontinuation
Before initiating treatment with Lindoxa, a treatment strategy including treatment duration and treatment goals, and a plan for end of the treatment, should be agreed together with the patient, in accordance with pain management guidelines. During treatment, there should be frequent contact

between the physician and the patient to evaluate the need for continued treatment, consider discontinuation and to adjust dosages if needed. When a patient no longer requires therapy with oxycodone, it may be advisable to taper the dose gradually to prevent symptoms of withdrawal. In absence of adequate pain control, the possibility of hyperalgesia, tolerance and progression of underlying disease should be considered (see section 4.4).

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Oxycodone must not be used in any situation where opioids are contraindicated:
- severe respiratory depression with hypoxia and/or hypercapnia
- elevated carbon dioxide levels in the blood
- severe chronic obstructive pulmonary disease
- cor pulmonale
- severe bronchial asthma
- paralytic ileus

4.4 Special warnings and precautions for use

Respiratory depression
The major risk of opioid excess is respiratory depression. Caution must be exercised when administering oxycodone to the debilitated elderly; sleep apnoea, patients with severely impaired pulmonary function, impaired hepatic or renal function; patients with myxoedema, hypothyroidism, toxic psychosis, prostate hypertrophy, adrenocortical insufficiency (Addison's disease), alcoholism, delirium tremens, diseases of the biliary tract, pancreatitis, inflammatory bowel disorders, constipation, hypotension, hypovolaemia, head injury (due to risk of increased intracranial pressure) or patients taking benzodiazepines, other CNS depressants (including alcohol) or MAO inhibitors (see section 4.5).

Hepatobiliary disordes
Oxycodone may cause dysfunction and spasm of the sphincter of Oddi, thus increasing the risk of biliary tract symptoms and pancreatitis. Therefore, oxycodone has to be administered with caution in patients with pancreatitis and diseases of the biliary tract.

Sleep-related breathing disorders
Opioids can cause sleep-related breathing disorders including central sleep apnoea (CSA) and sleep-related hypoxemia. Opioid use increases the risk of CSA in a dose-dependent fashion. Opioids may also cause worsening of pre-existing sleep apnoea (see section 4.8). In patients who present with CSA, consider decreasing the total opioid dosage.

Risk from concomitant use of sedative medicines such as benzodiazepines or related drugs: Concomitant use of oxycodone and sedative medicines such as benzodiazepines or related drugs may result in sedation, respiratory depression, coma and death. Because of these risks, concomitant prescribing with these sedative medicines should be reserved for patients for whom alternative treatment options are not possible. If a decision is made to prescribe oxycodone concomitantly with sedative medicines, the lowest effective dose should be used, and the duration of treatment should be as short as possible.
The patients should be followed closely for signs and symptoms of respiratory depression and sedation. In this respect, it is strongly recommended to inform patients and their caregivers to be aware of these symptoms (see section 4.5).

Oxycodone may supress the cough reflex.

Oxycodone should not be used where there is a possibility of paralytic ileus occurring. Should paralytic ileus be suspected or occur during use, Lindoxa 10 mg/ml solution for injection/infusion should be discontinued immediately.

Opioids, such as oxycodone, 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 manifest from these hormonal changes.

For appropriate patients who suffer with chronic non-malignant pain, opioids should be used as part of a comprehensive treatment programme involving other medications and treatment modalities. A crucial part of the assessment of a patient with chronic non-malignant pain is the patient's addiction and substance abuse history.

If opioid treatment is considered appropriate for the patient, then the main aim of treatment is not to minimise the dose of opioid but rather to achieve a dose which provides adequate pain relief with a minimum of side effects.

Tolerance and dependence
The patient may develop tolerance to the medicinal product with chronic use and require progressively higher doses to maintain pain control.

Prolonged use of oxycodone may lead to physical dependence and a withdrawal syndrome may occur upon abrupt cessation of therapy. When a patient no longer requires therapy with oxycodone, it may be advisable to taper the dose gradually to prevent withdrawal symptoms. The opioid abstinence or withdrawal syndrome is characterised by some or all of the following: restlessness, lacrimation, rhinorrhoea, yawning, perspiration, chills, myalgia, mydriasis and palpitations. Other symptoms also may develop, including: irritability, anxiety, backache, joint pain, weakness, abdominal cramps, insomnia, nausea, anorexia, vomiting, diarrhoea, or increased blood pressure, respiratory rate or heart rate.
Hyperalgesia that will not respond to a further dose increase of oxycodone may very rarely occur, particularly in high doses. An oxycodone dose reduction or change to an alternative opioid may be required.

Opioid Use Disorder (abuse and dependence)
Tolerance and physical and/or psychological dependence may develop upon repeated administration of opioids such as oxycodone.

Repeated use of Lindoxa may lead to Opioid Use Disorder (OUD). A higher dose and longer duration of opioid treatment can increase the risk of developing OUD. Abuse or intentional misuse of Lindoxa may result in overdose and/or death. The risk of developing OUD is increased in patients with a personal or a family history (parents or siblings) of substance use disorders (including alcohol use disorder), in current tobacco users or in patients with a personal history of other mental health disorders (e.g. major depression, anxiety and personality disorders).

Before initiating treatment with Lindoxa and during the treatment, treatment goals and a discontinuation plan should be agreed with the patient (see section 4.2). Before and during treatment the patient should also be informed about the risks and signs of OUD. If these signs occur, patients should be advised to contact their physician.

Patients will require monitoring for signs of drug-seeking behavior (e.g. too early requests for refills). This includes the review of concomitant opioids and psycho-active drugs (like benzodiazepines). For patients with signs and symptoms of OUD, consultation with an addiction specialist should be considered.

As with other opioids, infants who are born to dependent mothers may exhibit withdrawal symptoms and may have respiratory depression at birth (see section 4.6).

Alcohol
The intake of oxycodone with alcoholic beverages has to be avoided as alcohol may enhace the frequency of adverse reactions.

Surgical procedures
As with all opioid preparations, oxycodone products should be used with caution following abdominal surgery as opioids are known to impair intestinal motility and should not be used until the physician is assured of normal bowel function.
Lindoxa 10 mg/ml solution for injection/infusion should be used with caution pre- or intra-operatively and within the first 12-24 hours post-operatively.

Sodium chloride
This medicine contains less than 1 mmol sodium (23 mg) per ampoule, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

The concomitant use of opioids with sedative medicines such as benzodiazepines or related drugs increases the risk of sedation, respiratory depression, coma and death because of additive CNS depressant effect. The dose and duration of concomitant use should be limited (see section 4.4). Central nervous system depressants include, but are not limited to: other opioids, gabapentinoids such as pregabalin, anxiolytics, sedatives, hypnotics, phenothiazines, neuroleptics, anaesthetics, antidepressants, muscle relaxants, antihistamines, antiemetics or alcohol can enhance the CNS depressant effect of oxycodone, in particular respiratory depression.

Concomitant administration of oxycodone and anticholinergics (e.g. antipsychotics, tricyclic antidepressants, neuroleptics, antihistamines, antiemetics, muscle relaxants, antiparkinson medicines) can enhance the anticholinergic undesirable effects of oxycodone (such as constipation, dry mouth or micturition disorders).

Concomitant administration of oxycodone with serotonin agents, such as a Selective Serotonin Re-uptake Inhibitor (SSRI) or a Serotonin Norepinephrine Re-uptake Inhibitor (SNRI) may cause serotonin toxicity. The symptoms of serotonin toxicity may include mental-status changes (e.g., agitation, hallucinations, coma), autonomic instability (e.g., tachycardia, labile blood pressure, hyperthermia), neuromuscular abnormalities (e.g., hyperreflexia, incoordination, rigidity), and/or gastrointestinal symptoms (e.g., nausea, vomiting, diarrhoea). Oxycodone should be used with caution and the dosage may need to be reduced in patients using these medications.

Monoaminoxidase (MAO) inhibitors are known to interact with narcotic analgesics, producing CNS excitation or depression with hyper- or hypotensive crisis. Oxycodone should be used with caution in patients administered MAO-inhibitors or who have received MAO-inhibitors during the last two weeks (see section 4.4).

Clinically relevant changes in International Normalized Ratio (INR) in both directions have been observed in individuals if coumarin anticoagulants are co-applied with oxycodone.

Alcohol can enhance the pharmacodynamic effect of oxycodone, thus concomitant use should be avoided (refer to section 4.4).

Oxycodone is metabolised mainly by CYP3A4, with a contribution from CYP2D6. The activities of these metabolic pathways may be inhibited or induced by various co-administered drugs or dietary elements.

CYP3A4 inhibitors, such as macrolide antibiotics (e.g. clarithromycin, erythromycin and telithromycin), azole-type antifungals (e.g. ketoconazole, voriconazole, itraconazole, and posaconazole), protease

inhibitors (e.g. boceprevir, ritonavir, indinavir, nelfinavir and saquinavir), cimetidine and grapefruit juice may reduce the clearance of oxycodone which could result in an increase of oxycodone plasma concentrations. Therefore, the oxycodone dose may need to be adjusted accordingly.

Some specific examples are provided below:

- Itraconazole, a potent CYP3A4 inhibitor, administered as 200 mg orally for five days, increased the AUC of oral oxycodone. On average, the AUC was approximately 2.4 times higher (range 1.5-3.4).

- Voriconazole, a CYP3A4 inhibitor, administered as 200 mg twice-daily for four days (400 mg given as first two doses), increased the AUC of oral oxycodone. On average, the AUC was approximately 3.6 times higher (range 2.7-5.6).

- Telithromycin, a CYP3A4 inhibitor, administered as 800 mg orally for four days, increased the AUC of oral oxycodone. On average, the AUC was approximately 1.8 times higher (range 1.3-2.3).

- Grapefruit juice, a CYP3A4 inhibitor, administered as 200 ml three times a day for five days, increased the AUC of oral oxycodone. On average, the AUC was approximately 1.7 times higher (range 1.1-2.1).

CYP3A4 inducers, such as rifampicin, carbamazepine, phenytoin and St. John's Wort may induce the metabolism of oxycodone and cause an increased clearance of oxycodone which could result in a reduction of oxycodone plasma concentrations. The oxycodone dose may need to be adjusted accordingly.

Some specific examples are provided below:

- St. John's Wort, a CYP3A4 inducer, administered as 300 mg three times a day for fifteen days, reduced the AUC of oral oxycodone. On average, the AUC was approximately 50% lower (range 37-57%).

- Rifampicin, a CYP3A4 inducer, administered as 600 mg once daily for seven days, reduced the AUC of oral oxycodone. On average, the AUC was approximately 86% lower.

Drugs that inhibit CYP2D6 activity, such as paroxetine and quinidine, may cause decreased clearance of oxycodone which could lead to an increase in oxycodone plasma concentrations.

4.6 Fertility, pregnancy and lactation

Use of this medicinal product should be avoided to the extent possible in patients who are pregnant or lactating.

Pregnancy
There are limited data from the use of oxycodone in pregnant women. Infants born to mothers who have received opioids during the last 3 to 4 weeks before giving birth should be monitored for respiratory depression. Withdrawal symptoms may be observed in the newborns of mothers undergoing treatment with oxycodone.

Breast-feeding
Oxycodone may be secreted in breast milk and may cause respiratory depression in the newborn. Oxycodone should, therefore, not be used in breastfeeding mothers.

Fertility
No human data on the effect of oxycodone on fertility are available. In rats, there was no effect on mating or fertility with oxycodone treatment (see section 5.3)

4.7 Effects on ability to drive and use machines

Oxycodone hydrochloride may impair the ability to drive and use machines.
Oxycodone can impair alertness and reactivity to such an extent that the ability to drive and operate machinery is affected or ceases altogether.
With stable therapy, a general ban on driving a vehicle is not necessary. The treating physician must assess the individual situation.

4.8 Undesirable effects

Oxycodone can cause respiratory depression, miosis, bronchial spasms and spasms of the smooth muscles and can suppress the cough reflex.

The most common adverse reactions after intake of oxycodone are nausea and constipation, both approximately in 25-30% of the patients after oral administration. If nausea or vomiting is major, oxycodone can be combined with an antiemetic. Constipation should be expected as with any strong opioid and should be treated appropriately with laxatives. If the opioid-related adverse reactions persist, it should be investigated if they are caused by other things.

Apart from constipation, the side effects of opioid agonists tend to be reduced by continued treatment. Expecting side effects along with appropriate patient management can make them more acceptable.

The most serious side effect, as with other opioids, is respiratory depression (see also section 4.9). This is most likely to occur in elderly, weakened or opioid intolerant patients.

Sedation usually subsides after a few days. Bile and urinary tract spasms may occur in predisposed patients.

The adverse reactions considered at least possibly related to treatment are listed below by system organ class and absolute frequency. Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

Very common ≥ 1/10
Common ≥ 1/100 to < 1/10
Uncommon ≥ 1/1,000 to < 1/100
Rare ≥ 1/10,000 to < 1/1,000
Very rare < 1/10,000
Not known cannot be estimated from the available data

System organ class	Frequency	Adverse event
Immune system disorders	uncommon	Hypersensitivity
	not known	Anaphylactoid reaction Anaphylactic reaction
Metabolism and nutrition disorders	common	Decreased appetite
	uncommon	Dehydration
Psychiatric disorders	common	Anxiety Activity changes (normal suppression, occasionally excitation) Euphoric mood Confusional state

System organ class	Frequency	Adverse event
		Depression Insomnia Nervousness Abnormal thinking
	uncommon	Agitation Affect lability Dysphoria Hallucinations Decreased libido Drug dependence (see section 4.4)*
	not known	Aggression
Nervous system disorders	very common	Somnolence Sedation Dizziness Headache
	common	Weakness Tremor Lethargy
	uncommon	Amnesia Convulsion Hypertonia Hypoaesthesia Involuntary muscle contractions Speech disorder Syncope Paraesthesia Dysgeusia
	rare	Seizures, particularly in epileptic patients or patients with tendency to convulsions Muscle spasm
	not known	Hyperalgesia, sleep apnoea
Eye disorders	common	Miosis
	uncommon	Visual impairment Visual disturbances
Ear and labyrinth disorders	uncommon	Vertigo
Cardiac disorders	uncommon	Palpitation (in the context of withdrawal syndrome) Supraventricular tachycardia
Vascular disorders	common	Vasodilatation Orthostatic hypotension
	uncommon	Hypotension
Respiratory, thoracic and mediastinal disorders	common	Dyspnoea
	uncommon	Respiratory depression Broncho constriction
	not known	Central sleep apnoea syndrome
Gastrointestinal disorders	very common	Constipation Nausea Vomiting
	common	Dry mouth, rarely accompanied by thirst and difficulty swallowing Abdominal pain Diarrhoea

System organ class	Frequency	Adverse event
		Dyspepsia
	uncommon	Dysphagia Flatulence Eructation Ileus
	not known	Dental caries
Hepatobiliary disorders	uncommon	Increase hepatic enzymes Bile tract spasms
	not known	Cholestasis Biliary colic Sphincter of Oddi dysfunction
Skin and subcutaneous tissue disorders	very common	Pruritus
	common	Rash Hyperhidrosis
	uncommon	Dry skin Urticaria
Renal and urinary disorders	uncommon	Micturition disturbances (urinary retention, but also increased urge to urinate) Urinary tract spasms
	rare	Haematuria
Reproductive system and breast disorders	uncommon	Erectile dysfunction Hypogonadism
	not known	Amenorrhoea
General disorders and administration site conditions	common	Sweating Fatigue Asthenic conditions Chills
	uncommon	Malaise Oedema, peripheral oedema Physical dependence with withdrawal symptoms Drug tolerance Thirst
	rare	Weight changes (increase or decrease)
	not known	Drug withdrawal syndrome neonatal
Investigations	common	Increased ADH-excretion

* Drug dependence
Repeated use of Lindoxa can lead to drug dependence, even at therapeutic doses. The risk of drug dependence may vary depending on a patient's individual risk factors, dosage, and duration of opioid treatment (see section 4.4)

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V.

4.9 Overdose

Symptoms
Acute overdose with oxycodone can be manifested by miosis, respiratory depression, somnolence progressing to stupor or coma, reduced skeletal muscle tone and drop in blood pressure. In severe cases circulatory collapse, bradycardia and non-cardiogenic lung oedema may occur; abuse of high doses of

strong opioids such as oxycodone can be fatal. Toxic leukoencephalopathy has been observed with oxycodone overdose.

Management
Primary attention should be given to the establishment of a patent airway and institution of assisted or controlled ventilation.

In case of severe overdose, intravenous administration of an opioid antagonist (e.g. 0.4-2 mg intravenous naloxone) may be indicated. Administration of single doses must be repeated depending on the clinical situation at intervals of 2 to 3 minutes. Intravenous infusion of 2 mg of naloxone in 500 ml isotonic saline or 5% dextrose solution (corresponding to 0.004 mg naloxone/ml) is possible. The rate of infusion should be adjusted to the previous bolus injections and the response of the patient.

For less severe overdosage, administer naloxone 0.2 mg intravenously followed by increments of 0.1 mg every 2 minutes, if required.

Naloxone should only be given in cases of clinically significant respiratory or circulatory depression caused by oxycodone overdose.

Naloxone should be administered with caution to patients known or suspected to be physically dependent on oxycodone. In these cases, sudden or complete cessation of the opioid effect may cause pain and acute withdrawal syndrome.

Supportive measures (artificial respiration, oxygen supply, administration of vasopressors and infusion therapy) should, if necessary, be applied in the treatment of accompanying circulatory shock. Upon cardiac arrest or cardiac arrhythmias, cardiac massage or defibrillation may be indicated. If necessary, assisted ventilation as well as maintenance of water and electrolyte balance.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties
Pharmacotherapeutic group: Analgesics; Opioids; Natural opium alkaloids
ATC code: N02AA05

Oxycodone shows an affinity to kappa, mu and delta opioid receptors in the brain and spinal cord. It acts at these receptors as an opioid agonist without an antagonistic effect. The therapeutic effect is mainly analgesic, anxiolytic and sedative.

5.2 Pharmacokinetic properties

Absorption
Pharmacokinetic studies in healthy subjects have demonstrated an equivalent availability of oxycodone from oxycodone injection/infusion when administered by the intravenous or subcutaneous routes, as a single bolus dose or a continuous infusion over 8 hours.
Maximum oxycodone plasma concentrations are achieved after 0.5 hours after a subcutaneous injection.

Distribution
Approximately 45% is bound to plasma protein.
The volume of distribution at steady-state is 2.6 l/kg.

Biotransformation
Oxycodone is metabolised in the liver via CYP3A4 and CYP2D6 to noroxycodone, oxymorphone and noroxymorphone as well as to several glucuronide conjugates. The analgesic effect of the metabolites is considered clinically insignificant.

Elimination
Oxycodone and its metabolites are excreted via urine and faeces. Oxycodone has an elimination half-life of about 3 hours.

Special populations
The plasma concentrations of oxycodone are only minimally affected by age, being 15% greater in elderly as compared to young subjects.

Female subjects have, on average, plasma oxycodone concentrations up to 25% higher than males on a body weight adjusted basis.

When compared to normal subjects, patients with mild to severe hepatic dysfunction may have higher plasma concentrations of oxycodone and noroxycodone and lower plasma concentrations of oxymorphone. There may be an increase in the elimination half-life of oxycodone and this may be accompanied by an increase in drug effects.

When compared to normal subjects, patients with mild to severe renal dysfunction may have higher plasma concentrations of oxycodone and its metabolites. There may be an increase in the elimination half-life of oxycodone and this may be accompanied by an increase in drug effects.

5.3 Preclinical safety data

Studies showed that oxycodone had no effect on fertility and early embryonic development in male and female rats in doses of up to 8 mg/kg body weight and induced no malformations in rats in doses of up to 8 mg/kg and and in rabbits in doses of 125 mg/kg bodyweight. However, in rabbits, when individual fetuses were used in statistical evaluation, a dose related increase in developmental variations was observed (increased incidences of 27 presacral vertebrae, extra pairs of ribs). When these parameters were statistically evaluated using litters, only the incidence of 27 presacral vertebrae was increased and only in the 125 mg/kg group, a dose level that produced severe pharmacotoxic effects in the pregnant animals. In a study on pre- and postnatal development in rats F1 body weights were lower at 6 mg/kg/d when compared to body weights of the control group at doses which reduced maternal weight and food intake (NOAEL 2 mg/kg body weight). There were neither effects on physical, reflexological, and sensory developmental parameters nor on behavioural and reproductive indices.

Long-term carcinogenicity studies with oxycodone have not been conducted owing to the length of clinical experience with the drug subtance.

Oxycodone shows a clastogenic potential in in vitro assays. No similar effects were observed, however, under in vivo conditions, even at toxic doses. The results indicate that the mutagenic risk of Oxycodone hydrochloride to humans at therapeutic concentrations may be ruled out with adequate certainty.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium chloride
Citric acid monohydrate
Sodium hydroxide (for pH-adjustment)
Hydrochloric acid (for pH-adjustment)
Water for injections

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.

6.3 Shelf life

5 years

Chemical and physical in-use stability has been demonstrated for 48 hours/days at room temperature. From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8 °C, unless reconstitution, dilution has taken place in controlled and validated aseptic conditions.

6.4 Special precautions for storage

Do not freeze.
For storage conditions after dilution of the medicinal product, see section 6.3.

6.5 Nature and contents of container

Clear, colourless glass ampoules with OPC (one point cut) breaking system containig 1 ml or 2 ml solution, packed in card board fold boxes containing 1, 3, 5 or 10 ampoules.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

This medicinal product is for single use only, any unused solution should be discarded.

Lindoxa 10 mg/ml solution for injection/infusion and Lindoxa 20 mg/2 ml solution for injection/infusion may be diluted with

- Water for injections
- Sodium chloride 9 mg/mL (0.9%) solution for injection
- Glucose 50 mg/mL (5%) solution for injection
- Ringer's solution for injection
- Sodium chloride and Glucose solution for injection
  (Sodium chloride 0.18% w/v and Glucose 4% w/v)
- Lactated Ringer's solution for injection
  (Ringer Lactate solution and 5% Glucose solution).

Oxycodone hydrochloride, that was used undiluted or diluted to 1 mg/ml in various studies with different infusion solutions and under the use of representative brands of polypropylene or polycarbonate syringes, polyethylene or PVC tubing and PVC or EVA infusion bags, does not have to be protected against light.

7. MARKETING AUTHORISATION HOLDER

<to be completed nationally>

8. MARKETING AUTHORISATION NUMBER

<to be completed nationally>

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

<to be completed nationally>

10. DATE OF REVISION OF THE TEXT

20-MAR-2025