Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Oxycodone hydrochloride 10mg/ml solution for injection or infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 ml ampoule contains 10 mg oxycodone hydrochloride (equivalent to 9 mg oxycodone).
Each 2 ml ampoule contains 20 mg oxycodone hydrochloride (equivalent to 18 mg oxycodone).

Excipients with known effect:
This medicinal product contains less than 1 mmol sodium (23 mg) per 1 ml, that is to say essentially 'sodium-free'.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection or infusion.

Clear colourless solution, practically free from visible particles.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Oxycodone is indicated in adults 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.

4.2 Posology and method of administration

Posology
The dose should be adjusted according to the severity of pain, the total condition of the patient and previous or concurrent medication.

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

Intravenous - 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.

Doses should not be administered more frequently than every 4 hours.

Intravenous - 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.

Intravenous - Patient Controlled Analgesia (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.

Subcutaneous - Bolus
Use as 10 mg/ml concentration. A starting dose of 5 mg is recommended, repeated at 4-hourly intervals as required.

Subcutaneous - 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).

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. It must be emphasised that this is a guide to the dose required. Inter-patient variability requires that each patient is carefully titrated to the appropriate dose.

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

Patients with renal and hepatic impairment
The dose initiation should follow a conservative approach in these patients. The recommended adult starting dose should be reduced by 50% (for example a total daily dose of 10 mg orally in opioid naïve patients), and each patient should be titrated to adequate pain control according to their clinical situation.

Paediatric population
There are no data on the use of Oxycodone Hydrochloride 10 mg/ml solution for injection or infusion in patients under 18 years of age.

Use in non-malignant pain
Opioids are not first-line therapy for chronic non-malignant pain, nor are they recommended as the only treatment. Types of chronic pain which have been shown to be alleviated by strong opioids include chronic osteoarthritic pain and intervertebral disc disease. The need for continued treatment in non-malignant pain should be assessed at regular intervals.

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

For instruction on dilution of the medicinal product before administration, see section 6.6.

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

Discontinuation of treatment
When a patient no longer requires therapy with oxycodone, it may be advisable to taper the dose gradually to prevent symptoms of withdrawal.

4.3 Contraindications

Hypersensitivity to oxycodone 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;
· paralytic ileus;
· acute abdomen;
· severe chronic obstructive lung disease;
· cor pulmonale;
· severe bronchial asthma;
· elevated carbon dioxide levels in the blood;
· chronic constipation.

4.4 Special warnings and precautions for use

The major risk of opioid excess is respiratory depression.

Caution must be exercised when administering oxycodone to the debilitated elderly; patients with severely impaired pulmonary function, patients with impaired hepatic or renal function; patients with myxedema, hypothyroidism, Addison's disease, toxic

psychosis, prostate hypertrophy, adrenocortical insufficiency, alcoholism, delirium tremens, diseases of the biliary tract, pancreatitis, inflammatory bowel disorders, hypotension, hypovolaemia, raised intracranial pressure, head injury (due to risk of increased intracranial pressure) or patients taking benzodiazepines, other CNS depressants (including alcohol) or MAO inhibitors.

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 (see also general dose recommendation in section 4.2).

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

Oxycodone Hydrochloride 10 mg/ml solution for injection or infusion should be used with caution pre- or intra-operatively and within the first 12-24 hours post-operatively.

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.

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. There must be frequent contact between physician and patient so that dosage adjustments can be made. It is strongly recommended that the physician defines treatment outcomes in accordance with pain management guidelines. The physician and patient can then agree to discontinue treatment if these objectives are not met.

The patient may develop tolerance to the drug with chronic use and require progressively higher doses to maintain pain control. Prolonged use of this product 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 symptoms of withdrawal. 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 occur, particularly in high doses. An oxycodone dose reduction or change to an alternative opioid may be required.

Oxycodone has an abuse profile similar to other strong agonist opioids. Oxycodone may be sought and abused by people with latent or manifest addiction disorders. There is potential for development of psychological dependence [addiction] to opioid analgesics, including oxycodone. Oxycodone Hydrochloride 10 mg/ml solution for injection or infusion should be used with particular care in patients with a history of alcohol and drug abuse.

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

Concomitant use of alcohol and Oxycodone Hydrochloride 10 mg/ml solution for injection or infusion may increase the undesirable effects of Oxycodone Hydrochloride 10 mg/ml solution for injection or infusion; concomitant use should be avoided.

Opioids, such as oxycodone hydrochloride, 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.

This medicinal product contains less than 1 mmol sodium (23 mg) per 1 ml, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interactions

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 dosage and duration of concomitant use should be limited (see section 4.4).

Drugs which affect the CNS include, but are not limited to: tranquillisers, anaesthetics, hypnotics, anti-depressants, non-benzodiazepine sedatives, phenothiazines, neuroleptic drugs, alcohol, other opioids, muscle relaxants and antihypertensives.

Concomitant administration of oxycodone with anticholinergics or medicines with anticholinergic activity (e.g. tricyclic anti-depressants, antihistamines, antipsychotics, muscle relaxants, anti-Parkinson drugs) may result in increased anticholinergic adverse effects. Oxycodone should be used with caution and the dosage may need to be reduced in patients using these medications.

Monoamine oxidase (MAO) inhibitors are known to interact with narcotic analgesics. MAO-inhibitors cause CNS excitation or depression associated with hypertensive or hypotensive crisis (see section 4.4).

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.

Alcohol may enhance the pharmacodynamic effects of Oxycodone Hydrochloride 10 mg/ml solution for injection or infusion, concomitant use should be avoided.

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-antifungals (e.g. ketoconazole, voriconazole, itraconazole, and posaconazole), protease inhibitors (e.g. boceprevir, ritonavir, indinavir, nelfinavir and saquinavir), cimetidine and grapefruit juice may cause a reduced clearance of oxycodone that could cause an increase of the plasma concentrations of oxycodone. Therefore, the oxycodone dose may need to be adjusted accordingly.
Some specific examples are provided below:
• Itraconazole, a potent CYP3A4 inhibitor, administered 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 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 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 that could cause a reduction of the plasma concentrations of oxycodone. 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 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 pregnancy should be monitored for respiratory depression. Withdrawal symptoms may be observed in the newborn of mothers undergoing treatment with oxycodone.

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

Fertility
Non-clinical toxicity studies in rats have not shown any effect on fertility (see section 5.3).

4.7 Effects on ability to drive and use machines

Oxycodone may impair the ability to drive and use machines. Oxycodone may modify patients' reactions to a varying extent depending on the dosage and individual susceptibility. Therefore, patients should not drive or operate machinery, if affected.

This medicine can impair cognitive function and can affect a patient's ability to drive safely. This class of medicine is in the list of drugs included in regulations under 5a of the Road Traffic Act 1988. When prescribing this medicine, patients should be told:
• The medicine is likely to affect your ability to drive
• Do not drive until you know how the medicine affects you
• It is an offence to drive while under the influence of this medicine
• However, you would not be committing an offence (called 'statutory defence') if:
o The medicine has been prescribed to treat a medical or dental problem and
o You have taken it according to the instructions given by the prescriber or in the information provided with the medicine and
o It was not affecting your ability to drive safely

4.8 Undesirable effects

Adverse drug reactions are typical of full opioid agonists. Tolerance and dependence may occur (see section 4.4). Constipation may be prevented with an appropriate laxative. If nausea or vomiting are troublesome, oxycodone may be combined with an antiemetic.

The most serious adverse reaction, as with other opioids, is respiratory depression (see section 4.9). This is most likely to occur in elderly, debilitated or opioid-intolerant patients.

The following frequency categories form the basis for classification of the undesirable effects:

Term	Frequency
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
Frequency not known	Cannot be estimated from the available data

Immune system disorders:
Uncommon: hypersensitivity.
Frequency not known: anaphylactic reaction, anaphylactoid reaction.

Metabolism and nutrition disorders:
Common: decreased appetite.
Uncommon: dehydration.

Psychiatric disorders:
Common: anxiety, confusional state, depression, insomnia, nervousness, abnormal thinking, abnormal dreams.
Uncommon: agitation, affect lability, euphoric mood, hallucinations, decreased libido, drug dependence (see section 4.4), disorientation, mood altered, restlessness, dysphoria.
Frequency not known: aggression.

Nervous system disorders:
Very common: somnolence, dizziness, headache.
Common: tremor, lethargy, sedation.
Uncommon: amnesia, convulsion, hypertonia, hypoaesthesia, involuntary muscle contractions, speech disorder, syncope, paraesthesia, dysgeusia, hypotonia.
Frequency not known: hyperalgesia.

Eye disorders:
Uncommon: visual impairment, miosis.

Ear and labyrinth disorders:
Uncommon: vertigo.

Cardiac disorders:
Uncommon: palpitations (in the context of withdrawal syndrome), supraventricular tachycardia.

Vascular disorders:
Uncommon: vasodilatation, facial flushing.
Rare: hypotension, orthostatic hypotension.

Respiratory, thoracic and mediastinal disorders:
Common: dyspnoea, bronchospasm, cough decreased.
Uncommon: respiratory depression, hiccups.

Gastrointestinal disorders:
Very common: constipation, nausea, vomiting.
Common: abdominal pain, diarrhoea, dry mouth, dyspepsia.
Uncommon: dysphagia, flatulence, eructation, ileus, gastritis.
Frequency not known: dental caries.

Hepatobiliary disorders:
Uncommon: increased hepatic enzymes, biliary colic.
Frequency not known: cholestasis.

Skin and subcutaneous tissue disorders:
Very common: pruritus.
Common: rash, hyperhidrosis.
Uncommon: dry skin, exfoliative dermatitis.
Rare: urticaria.

Renal and urinary disorders:
Uncommon: urinary retention, ureteral spasm.

Reproductive system and breast disorders:
Uncommon: erectile dysfunction, hypogonadism.
Frequency not known: amenorrhoea.

General disorders and administration site conditions:
Common: asthenia, fatigue.

Uncommon: drug withdrawal syndrome, malaise, oedema, peripheral oedema, drug tolerance, thirst, pyrexia, chills.
Frequency not known: drug withdrawal syndrome neonatal.

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 HPRA Pharmacovigilance Earlsfort Terrace IRL - Dublin 2. Tel: +353 1 6764971; Fax: +353 1 6762517; Website: www.hpra.ie; e-mail: medsafety@hpra.ie.

4.9 Overdose

Symptoms
Acute overdose with oxycodone can be manifested by miosis, respiratory depression, hypotension and hallucinations. Nausea and vomiting are common in less severe cases. Non-cardiac pulmonary oedema and rhabdomyolysis are particularly common after intravenous injection of opioid analgesics.

Circulatory failure and somnolence progressing to stupor or coma, hypotonia, bradycardia, pulmonary oedema and death may occur in more severe cases.

The effects of overdosage will be potentiated by the simultaneous ingestion of alcohol or other psychotropic drugs.

Treatment
Primary attention should be given to the establishment of a patent airway and institution of assisted or controlled ventilation. The pure opioid antagonists such as naloxone are specific antidotes against symptoms from opioid overdose. Other supportive measures should be employed as needed.

In the case of massive overdosage, administer naloxone intravenously (0.4 to 2mg for an adult and 0.01mg/kg body weight for children) if the patient is in a coma or respiratory depression is present. Repeat the dose at 2 minute intervals if there is no response. If repeated doses are required, then an infusion of 60% of the initial dose per hour is a useful starting point. A solution of 10 mg made up in 50 ml dextrose will produce 200 micrograms/ml for infusion using an IV pump (dose adjusted to the clinical response). Infusions are not a substitute for frequent review of the patient's clinical state.
Intramuscular naloxone is an alternative in the event that IV access is not possible. As the duration of action of naloxone is relatively short, the patient must be carefully monitored until spontaneous respiration is reliably re-established. Naloxone is a competitive antagonist and large doses (4 mg) may be required in seriously poisoned patients.

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

The patient should be observed for at least 6 hours after the last dose of naloxone.

Naloxone should not be administered in the absence of clinically significant respiratory or circulatory depression secondary to oxycodone overdosage. Naloxone should be administered cautiously to persons who are known, or suspected, to be physically dependent on oxycodone. In such cases, an abrupt or complete reversal of opioid effects may precipitate pain and an acute withdrawal syndrome.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Natural opium alkaloids, ATC code: N02AA05

Oxycodone 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 therapeutic effect is mainly analgesic, anxiolytic, antitussive and sedative.

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

Endocrine system

See Section 4.4.

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.

5.2 Pharmacokinetic properties

Pharmacokinetic studies in healthy subjects demonstrated an equivalent availability of oxycodone from Oxycodone Hydrochloride 10 mg/ml solution for injection or infusion when administered as a 5mg dose by the intravenous and subcutaneous routes, as a single bolus dose or a continuous infusion over 8 hours.

Absorption
Following absorption, oxycodone is distributed throughout the entire body. Approximately 45% is bound to plasma protein. It is metabolised in the liver to produce noroxycodone, oxymorphone and various conjugated glucuronides. The analgesic effects of the metabolites are clinically insignificant.

Elimination
The active drug and its metabolites are excreted in both urine and faeces.

Special patient 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.

The drug penetrates the placenta and can be found in breast milk.

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

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, and genotoxicity.

Teratogenicity
Oxycodone had no effect on fertility or early embryonic development in male and female rats at doses as high as 8 mg/kg/d. Also, oxycodone did not induce any deformities in rats at doses as high as 8 mg/kg/d or in rabbits at doses as high as 125 mg/kg/d. Dose-related increases in developmental variations (increased incidences of extra (27) presacral vertebrae and extra pairs of ribs) were observed in rabbits when the data for individual fetuses were analyzed. However, when the same data were analyzed using litters as opposed to individual fetuses, there was no dose-related increase in developmental variations although the incidence of extra presacral vertebrae remained significantly higher in the 125 mg/kg/d group compared to the control group. Since this dose level was associated with severe pharmacotoxic effects in the pregnant animals, the fetal findings may have been a secondary consequence of severe maternal toxicity.

In a study of peri- and postnatal development in rats, maternal body weight and food intake parameters were reduced for doses ≥ 2 mg/kg/d compared to the control group. Body weights were lower in the F1 generation from maternal rats in the 6 mg/kg/d dosing group. There were no effects on physical, reflexological, or sensory developmental parameters or on behavioral and reproductive indices in the F1 pups (the NOEL for F1 pups was 2 mg/kg/d based on body weight effects seen at 6 mg/kg/d). There were no effects on the F2 generation at any dose in the study.

Mutagenicity

The results of *in vitro* and *in vivo* studies indicate that the genotoxic risk of Oxycodone Hydrochloride 10 mg/ml solution for injection or infusion to humans is minimal or absent at the systemic oxycodone concentrations that are achieved therapeutically.

Oxycodone was not genotoxic in a bacterial mutagenicity assay or in an in vivo micronucleus assay in the mouse. Oxycodone produced a positive response in the in vitro mouse lymphoma assay in the presence of rat liver S9 metabolic activation at dose levels greater than 25 µg/mL. Two in vitro chromosomal aberrations assays with human lymphocytes were conducted. In the first assay, oxycodone was negative without metabolic activation but was positive with S9 metabolic activation at the 24 hour time point but not at other time points or at 48 hour after exposure. In the second assay, oxycodone did not show any clastogenicity either with or without metabolic activation at any concentration or time point.

No animal studies to evaluate the carcinogenic potential of oxycodone have been conducted.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Citric acid monohydrate
Sodium citrate dihydrate
Sodium chloride
Hydrochloric acid
Sodium hydroxide
Water for injections

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.
Cyclizine at concentrations of 3 mg/ml or less, when mixed with Oxycodone Hydrochloride 10 mg/ml solution for injection or infusion, either undiluted or diluted with water for injections, shows no sign of precipitation over a period of 24 hours storage at 25°C. Precipitation has been shown to occur in mixtures with Oxycodone Hydrochloride 10 mg/ml solution for injection or infusion at cyclizine concentrations greater than 3 mg/ml or when diluted with 0.9% saline. It is recommended that water for injections be used as a diluent when cyclizine and oxycodone hydrochloride are co-administered either intravenously or subcutaneously as an infusion.
Prochlorperazine is chemically incompatible with Oxycodone Hydrochloride 10 mg/ml solution for injection or infusion.

6.3 Shelf life

Unopened ampoules: 30 months.

Opened ampoules: The product should be used immediately after opening the ampoule.

Prepared infusion solutions:
Chemical and physical in-use stability has been demonstrated for 24 hours at 25°C.
For instructions on dilution of the medicinal product before administration, see section 6.6.
From a microbiological point of view, the product should be used immediately. If not used immediately, 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, unless dilution has taken place in controlled and validated aseptic conditions.

6.4 Special precautions for storage

This medicinal product does not require any special temperature storage conditions.
Keep the ampoule in the outer carton in order to protect from light.
For storage conditions after first opening or dilution of the medicinal product, see section 6.3.

6.5 Nature and contents of container

Colourless glass ampoules with a nominal volume of 1 ml or 2 ml.

Pack size: 5, 10 ampoules.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Each ampoule is for single use in a single patient. This medicine should be given immediately after opening the ampoule and any unused portion should be discarded.
The medicinal product should be examined visually and should not be used if particulate matter or discolouration are present.

Oxycodone Hydrochloride 10 mg/ml solution for injection or infusion has been shown to be compatible with the following drugs:
Hyoscine butylbromide
Hyoscine hydrobromide
Dexamethasone sodium phosphate
Haloperidol
Midazolam hydrochloride
Metoclopramide hydrochloride
Levomepromazine hydrochloride

Oxycodone Hydrochloride 10 mg/ml solution for injection or infusion, undiluted or diluted to 1 mg/ml with 0.9% w/v saline, 5% w/v dextrose or water for injections, is physically and chemically stable when in contact with representative brands of polypropylene or polycarbonate syringes, polyethylene or PVC tubing, and PVC or EVA infusion bags, over a 24 hour period at 25°C.
The 10 mg/ml injection, whether undiluted or diluted to 1 mg/ml in the infusion fluids and containers detailed above, does not need to be protected from light over a 24 hour period.

Inappropriate handling of the undiluted solution after opening of the original ampoule, or of the diluted solutions may compromise the sterility of the product.

7 MARKETING AUTHORISATION HOLDER

hameln pharma plus gmbh
Langes Feld 13
317 89
Germany

8 MARKETING AUTHORISATION NUMBER

PA2237/001/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 21st December 2018

10 DATE OF REVISION OF THE TEXT

April 2019