SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Oxyact 10 mg film-coated tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each film-coated tablet contains 10 mg oxycodone hydrochloride equivalent to 8.97 mg oxycodone.

Excipients with known effect:
Each film-coated tablet contains 64.48 mg lactose (as monohydrate) and 0.21 mg soya lecithin.
For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablet.
Middle blue, vaulted, oblong film-coated tablets with break score on both sides.
The tablet can be divided into equal halves.
Diameter: 10.1 mm
Thickness: 3.2 mm
Width: 4.6 mm

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Oxyact is indicated in adults and adolescents (from 12 years and older) for the treatment of severe pain, which can be adequately managed only with opioid analgesics.

4.2 Posology and method of administration

Posology

The dose depends on the pain intensity and the patient's individual susceptibility to the treatment.

For doses not realisable/practicable with this strength other strengths of this medicinal product are available.

The following general dose recommendations apply:

Adults and adolescents (≥ 12 years of age)

Dose titration and adjustment

The initial dose for opioid-naïve patients is usually 5 mg oxycodone hydrochloride given at intervals of every 6 hours. The dose may be increased in steps of 25% to 50% of the respective dose. The aim is a patient-specific dose which allows for adequate analgesia with tolerable undesirable effects. Therefore, the dosing interval may be shortened to 4 hours if needed.

However, Oxyact should not be taken more often than 6 times a day.

Some patients receiving prolonged-release oxycodone medicinal products according to a fixed time schedule may require immediate-release analgesics as rescue medication for the management of breakthrough pain. Oxyact is appropriate for the management of breakthrough pain. Single doses of the rescue medication should be adjusted based on the patients' individual requirements. In general, 1/8 to 1/6 of the daily prolonged-release oxycodone dose is appropriate.

The requirement of rescue medication more than twice daily may indicate that higher doses of prolonged-release oxycodone are necessary. The aim is to establish a patient-specific dosage which ensures adequate analgesia with tolerable undesirable effects and as low rescue medication as possible for as long as pain medication is necessary in patients receiving prolonged-release oxycodone treatment twice daily.

Patients already receiving opioids may start treatment with higher doses taking into account their experience with former opioid therapies.

10-13 mg oxycodone hydrochloride correspond to approximately 20 mg morphine sulphate, both in the film-coated formulation.

Because of individual differences in sensitivity for different opioids, it is recommended that patients should start conservatively with oxycodone hydrochloride after conversion from other opioids, with 50-75% of the calculated oxycodone dose.

In general, patients should be titrated individually until pain relief is achieved, provided that undesirable adverse events can be adequately managed.

If long-term pain treatment is required, the patients should be switched to oxycodone hydrochloride prolonged-release tablets.

Method of administration

Oral Use

Oxyact film-coated tablets should be taken every 4-6 hours based on a fixed schedule at the dosage determined.

The film-coated tablets may be taken with or independent of meals with a sufficient amount of liquid.

Oxyact film-coated tablets should not be used with alcoholic beverages.

Treatment goals and discontinuation

Before initiating treatment with Oxyact film-coated tablets, 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).

DURATION OF TREATMENT

Oxycodone hydrochloride should not be taken longer than necessary.

Special populations Elderly patients

Elderly patients without clinical manifestation of impaired liver and/or kidney function usually do not require dose adjustments.

Patients with 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% (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 his/her clinical situation. It is therefore possible that the lowest single dose recommended in this SmPC, i.e. 5 mg, is not suitable as a starting dose.

Other patients at risk

Patients with low body weight or slow metabolisers who are also opioid naïve, should initially be treated with half the dose usually recommended for adults. It is therefore possible that the lowest single dose recommended in this SmPC, i.e. 5 mg, is not suitable as a starting dose.

Paediatric population

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.

Children below the age of 12 years

The safety and efficacy of oxycodone in children below 12 years of age has not yet been established. No data are available.

4.3 Contraindications

Hypersensitivity to the active substance, peanut or soya 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
- severe chronic obstructive pulmonary disease
- cor pulmonale
- severe bronchial asthma
- paralytic ileus
- acute abdomen, delayed gastric emptying

4.4 Special warnings and precautions for use

Caution should be exercised in

- elderly or debilitated patients,
- patients with severly impaired respiratory function,
- patients with impaired hepatic function,
- patients with impaired renal function,
- sleep apnoea,
- myxoedema, hypothyroidism,
- concomitant use of centrally depressant substances,
- Addison's disease (adrenal insufficiency),
- intoxication psychosis (e.g. alcohol),
- prostatic hypertrophy,
- alcoholism,
- known opioid dependence,
- drug addiction, substance or alcohol abuse,
- delirium tremens,

- head injury, increased intracranial pressure,
- impaired consciousness of unknown cause,
- hypotension,
- hypovolaemia,
- pancreatitis,
- diseases of the biliary tract, biliary or ureteric colic,
- obstructive or inflammatory intestinal diseases,
- in patients taking MAO inhibitors.

Paralytic ileus

In case of paralytic ileus or suspicion thereof Oxyact should be discontinued straight away.

Respiratory depression

The major risk of opioid excess is respiratory depression.

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. 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 Oxyact 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 Oxyact 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).

Adrenal insufficiency

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 manifest from these hormonal changes.

MAO-inhibitors

Oxycodone should be used with caution in patients administered MAO-inhibitors or who have received MAO-inhibitors during the last two weeks.

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 Oxyact 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 Oxyact 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 Oxyact 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.

Tolerance , physical dependence and tapering off

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

Oxycodone hydrochloride has a primary dependence potential. Prolonged use of oxycodone hydrochloride 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. Withdrawal symptoms may include yawning, mydriasis, lacrimation, rhinorrhoea, tremor, hyperhidrosis, anxiety, agitation, convulsions,insomnia, and myalgia.

Hyperalgesia

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.

Parenteral abuse

Abuse of oral dosage forms by parenteral administration can be expected to result in serious adverse events, which may be fatal.

Perioperative use, abdominal surgery

Oxycodone should be used with caution pre-operatively and within the first 12-24 hours post-operatively. Depending on the type and extent of surgery, the anaesthetic procedure selected, other co-medication and the individual condition of the patient, the exact timing for initiating post-operative treatment with oxycodone depends on a careful risk-benefit assessment for each individual patient.

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.

Patients with severe hepatic impairment

Patients with severe hepatic impairment should be closely monitored.

Hepatobiliary disorders

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.

Concomitant use of alcohol

and oxycodone may increase the undesirable effects of Oxyact and should be avoided.

Oxyact should be used with particular care in patients with a history of alcohol and drug abuse

Children

Oxyact has not been studied in children below 12 years of age. The safety and efficacy of the tablets have not been demonstrated and the use in children below 12 years of age is therefore not recommended.

Anti-Doping Warning

Athletes must be aware that this medicine may cause a positive reaction to “anti-doping” tests. Use of oxycodone hydrochloride as doping agent may become a health hazard.

Lactose

Oxyact contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicinal product.

Soya

Oxyact contains soya. If you are allergic to peanut or soya, do not use this medicinal product.

4.5 Interaction with other medicinal products and other forms of interaction

Alcohol
Alcohol may enhance the pharmacodynamic effects of Oxyact, concomitant use should be avoided.

Centrally depressant drugs
There can be an enhanced CNS depressant effect during concomitant therapy with drugs which affect the CNS such as sedatives, hypnotics, phenothiazines, neuroleptic drugs, antidepressants, antihistamines, antiemetics and other opioids which may enhance the adverse drug reactions, especially respiratory depression.

Concomitant administration of oxycodone with **serotonergic 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 serotoin 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.

Sedative medicines such as benzodiazepines or related drugs
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).

Anticholinergics (e.g. neuroleptics, antihistamines, antiemetics, antiparkinson medicinal products) can enhance the anticholinergic undesirable effects of oxycodone (such as constipation, dry mouth or micturition disorders).

Cimetidine can inhibit the metabolism of oxycodone.

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 Oxyact.

Interactions via the CYP system
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 medicinal products 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), increasedthe 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.

Medicinal products 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 breast-feeding.

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 sedation and respiratory depression in the breast-fed child. Oxycodone should, therefore, not be used in breast-feeding mothers.

Fertility

Human data are not available. In animal studies, oxycodone had no adverse effects on fertility (see section 5.3).

4.7 Effects on ability to drive and use machines

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:
    - The medicine has been prescribed to treat a medical or dental problem and
    - You have taken it according to the instructions given by the prescriber and in the information provided with the medicine and
    - It was not affecting your ability to drive safely

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 frequently reported undesirable effects are nausea (especially at the beginning of treatment) and constipation.

Respiratory depression is the chief hazard of an opioid overdose and occurs predominantly in elderly or debilitated patients.

Drug dependence

Repeated use of Oxyact 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).

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

Infections and infestations

Rare: herpes simplex

Immune system disorders: Uncommon: hypersensitivity

Not known: anaphylactic responses

Blood and lymphatic system disorders Rare: lymphadenopathy

Endocrine disorders

Uncommon: syndrome of inappropriate antidiuretic hormone secretion

Metabolism and nutrition disorders

Common: decreased appetite up to loss of appetite Uncommon: dehydration

Rare: Increased appetite

Psychiatric disorders

Common: altered mood and personality change (e.g. anxiety, depression), decreased activity, restlessness, psychomotor hyperactivity, nervousness, insomnia, abnormal thinking, confusion

Uncommon: agitation, affect lability, euphoric mood, perception disturbances (e.g. hallucinations, depersonalisation), decreased libido, drug dependence (see section 4.4)

Not known: aggression

Nervous system disorders

Very common: somnolence, sedation, dizziness, headache

Common: tremor, lethargy

Uncommon: amnesia, concentration impaired, convulsions (especially in persons with epileptic disorder or predisposition to convulsions), migraine, hypertonia, hypoaesthesia, involuntary muscle contractions, abnormal coordination, speech disorder, syncope, paraesthesia, dysgeusia

Not known: hyperalgesia

Eye disorders

Uncommon: visual impairment, miosis

Ear and labyrinth disorders

Uncommon: hearing impaired, vertigo.

Cardiac disorders

Uncommon: palpitation (in the context of withdrawal syndrome), tachycardia

Vascular disorders Uncommon: vasodilatation

Rare: hypotension, orthostatic hypotension

Respiratory, thoracic and mediastinal disorders Common: dyspnoea

Uncommon: Dysphonia, cough, respiratory depression

Not known: central sleep apnoea syndrome

Gastrointestinal disorders

Very common: constipation, nausea, vomiting

Common: dry mouth, rarely accompanied by thirst and difficulty swallowing; hiccups, abdominal pain, diarrhoea, dyspepsia

Uncommon: dysphagia, mouth ulceration, gingivitis, stomatitis, flatulence, eructation, ileus

Rare: gingival bleeding, melaena, tooth disorders Not known: dental caries

Hepatobiliary disorders

Uncommon: increase hepatic enzymes

Not known: cholestasis, biliary colic, sphincter of Oddi dysfunction

Skin and subcutaneous tissue disorders Very common: pruritus

Common: skin reactions/rash, hyperhidrosis Uncommon: dry skin

Rare: urticaria

Renal and urinary disorders

Common: dysuria, micturition urgency Uncommon: urinary retention

Reproductive system and breast disorders

Uncommon: reduced libido, erectile dysfunction, hypogonadism Not known: amenorrhoea

General disorders and administration site conditions Common: asthenia, tiredness

Uncommon: chills, malaise, pain (e.g. chest pain), oedema, peripheral oedema, physical dependence with withdrawal symptoms, drug tolerance, thirst

Rare: weight changes (increase or decrease)

Not known: drug withdrawal syndrome neonatal

Injury, poisoning and procedural complications

Uncommon: injuries from accidents

For infants born to mothers receiving oxycodone see section 4.6.

Paediatric population

The frequency, type and severity of adverse reactions in adolescents (12 to 18 years of age) appear similar to those in adults (see section 5.1).

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 Yellow Card Scheme,

Website: www.mhra.gov.uk/yellowcard,

or search for MHRA Yellow Card in the Google Play or Apple App Store.

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.

Therapy

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

In case of 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 sodium chloride 9 mg/ml (0.9%)or glucose 50 mg/ml (5%) 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.

Gastric lavage can be taken into consideration. The adminsitration of activated charcoal (50 g for adults, 10 -15 g for children) should be considered within 1 hour, if a substantial amount has been ingested within 1 hour, provided the airway can be protected. It may be reasonable to assume that late administration of activated charcoal may be beneficial for film-coated preparations; however there is no evidence to support this.

For speeding up the passage a suitable laxative (e.g. a PEG-based solution) may be useful.

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 and sedative.

Paediatric population

Overall, the safety data obtained with oxycodone in clinical, pharmacodynamic and pharmacokinetic studies demonstrate that oxycodone is well tolerated in paediatric patients with only minor adverse events affecting mainly the gastrointestinal and nervous system. All of the adverse events reported were consistent with the known safety profile of oxycodone as well as of other comparable strong opioids (see section 4.8 Undesirable effects).

There is no clinical trial data on longer term use in children aged 12 to 18 years.

5.2 Pharmacokinetic properties

Absorption
Maximum oxycodone plasma concentrations are achieved after approximately 1 to 1.5 hours after the intake. Plasma concentrations are linear within a dose range of 5 to 20 mg.

Distribution
The absolute oral bioavailability of oxycodone is up to 87% with an elimination half-life of about 3 hours.

Biotransformation
Oxycodone is metabolised in the intestine and liver via the cytochrome P450 system to noroxycodone and oxymorphone as well as to several glucuronide conjugates. In vitro studies suggest that therapeutic doses of cimetidine probably have no relevant effect on the formation of noroxycodone. In man, quinidine reduces the production of oxymorphone while the pharmacodynamic properties of oxycodone remain largely unaffected. The contribution of the metabolites to the overall pharmacodynamic effect is irrelevant.

Elimination
Oxycodone and its metabolites are excreted via urine and faeces. Oxycodone crosses the placenta and is found in breast milk.

Linearity/non-linearity
The 5, 10 and 20 mg film-coated tablets are dose-proportional with regard to the amount of active substance absorbed as well as comparable with regard to the rate of absorption.

5.3 Preclinical safety data

Non-clinical data based on conventional studies of safety pharmacology, repeated dose toxicity and genotoxicity reveal no special hazards for humans beyond those already outlined in other sections of the SmPC.

Oxycodone showed 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 peri- 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 performed.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core
Sodium starch glycolate type A
Lactose monohydrate
Cellulose, microcrystalline
Colloidal anhydrous silica
Magnesium stearate

Tablet coating
Polyvinyl alcohol
Talc
Titanium dioxide (E 171)
Macrogol 3350
Lecithin, soya (E 322)
Indigo carmine, aluminium lake (E 132)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

5 years

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

Child resistant PVC/PVdC//aluminium blisters containing 10, 20, 30, 56 and 60, film-coated tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Any unused product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

G.L. Pharma GmbH, Schlossplatz 1, 8502 Lannach, Austria

8 MARKETING AUTHORISATION NUMBER(S)

PL 21597/0042

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

11/10/2018

10 DATE OF REVISION OF THE TEXT

25/02/2025