Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Oxydon 40 mg Prolonged-release tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each prolonged-release tablet contains 40 mg oxycodone hydrochloride corresponding to 35.9 mg oxycodone.

Excipient(s) with known effect:
Each prolonged-release tablet contains a maximum of 12 mg sucrose.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Prolonged-release tablet

Orange, biconvex, oblong prolonged-release tablets with a breakline on both sides.

The prolonged-release tablets can be divided into equal doses.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Severe pain, which can be adequately managed only with opioid analgesics.

Oxydon Prolonged-release tablets are indicated in adults and adolescents aged 12 years and older.

4.2 Posology and method of administration

Posology
The dose should be adjusted to the intensity of the pain and the sensitivity of the individual patient.
For doses not practicable with this medicinal product other strengths are available.

Adults and adolescents (12 years of age and older)
Starting dose
The usual starting dose for an opioid naïve patient is 10 mg oxycodone hydrochloride per dose at intervals of 12 hours. Some patients may benefit from a starting dose of 5 mg to minimise the incidence of adverse reactions.

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

10 to 13 mg oxycodone hydrochloride correspond to approximately 20 mg of morphine sulphate, both in the prolonged-release formulation.

Dose adjustment
Some patients who take Oxydon Prolonged-release tablets following a fixed schedule need rapid release analgesics as rescue medication in order to control breakthrough pain. Oxydon is not intended for therapy of breakthrough pain. The single dose of the rescue medication should amount to 1/6 of the equianalgesic daily dose of Oxydon Prolonged-release tablets. Use of the rescue medication more than twice daily indicates that the dose of Oxydon Prolonged-release tablets needs to be increased. The dose should not be adjusted more often than once every 1-2 days until a stable 12 hourly administration has been achieved.

Following a dose increase from 10 mg to 20 mg oxycodone hydrochloride taken every 12 hours dose adjustments should be made in steps of approximately one third of the daily dose until the desired effect is obtained. The aim is a patient specific 12 hourly dose that will maintain adequate analgesia with acceptable undesirable effects and as little rescue medication as possible as long as pain control is necessary.

Even administration (the same dose in the morning and in the evening) following a fixed schedule (every 12 hours) is appropriate for the majority of the patients. For some patients it may be beneficial to arrange the doses unevenly. In general, the lowest effective analgesic dose should be chosen.

For the treatment of non-malignant pain a daily dose of 40 mg oxycodone hydrochloride is generally sufficient; but higher doses may be necessary.
Patients with cancer-related pain may require doses of 80 to 120 mg oxycodone hydrochloride, which in individual cases can be increased to up to 400 mg.

Duration of administration
Oxycodone should not be used for longer than necessary. If long-term treatment is necessary due to the type and severity of the illness, careful and regular monitoring is required to determine whether and to what extent treatment should be continued.

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.

Elderly patients
A dose adjustment is usually not necessary in elderly patients without clinically manifest impairment of hepatic or renal function.

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 of oxycodone hydrochloride orally in opioid naïve patients), and each patient should be titrated to adequate pain control according to their clinical situation. In such cases oxycodone hydrochloride 5 mg prolonged-release tablets can be used.

Other patients at risk
Patients with low body weight or slow metabolisers, who are opioid naïve should initially receive half the dose usually recommended for adults. Therefore, 10 mg of oxycodone hydrochloride per dose at intervals of 12 hours may not be suitable as a starting dose and in such cases oxycodone hydrochloride 5 mg prolonged-release tablets can be used.

Children under 12 years of age
Oxydon Prolonged-release tablets are not recommended for use in children under 12 years of age due to insufficient data on safety and efficacy.

Method of administration
Oral use.

Oxydon Prolonged-release tablets should be taken twice daily based on a fixed schedule at the dose determined.

The prolonged-release tablets may be taken with or without food with sufficient liquid.

Oxydon Prolonged-release tablets can be divided into equal halves. However, the tablets must not be further broken, crushed or chewed.

4.3 Contraindications

- hypersensitivity to the active substance or to any of the excipients listed in section 6.1
- severe respiratory depression with hypoxia
- elevated carbon dioxide levels in the blood (hypercarbia)
- severe chronic obstructive lung disease

- cor pulmonale
- severe bronchial asthma
- paralyticileus

4.4 Special warnings and precautions for use

The major risk of opioid excess is respiratory depression.

Caution should be exercised in
- elderly or debilitated patients,
- patients with severe impairment of pulmonary function, impaired hepatic or renal function,
- patients with myxedema,
- hypothyroidism,
- Addison's disease,
- prostatic hypertrophy,
- toxic psychosis,
- alcoholism, delirium tremens, known opioid dependence,
- diseases of the biliary tract,
- pancreatitis,
- obstructive and inflammatory bowel disorders,
- head injury (due to risk of increased intracranial pressure),
- hypotension,
- hypovolaemia,
- epilepsy or predisposition to convulsions,
- in patients taking sedative medicinal products such as benzodiazepines or other centrally depressant active substances including alcohol (see also section 4.5)
- in patients taking MAO inhibitors or within 2 weeks of discontinuation of their use (see also section 4.5)

With the occurrence or suspicion of paralytic ileus, oxycodone should be immediately discontinued.

Risk from concomitant use of sedative medicinal products such as benzodiazepines or related medicinal products
Concomitant use of oxycodone and sedative medicinal products such as benzodiazepines or related medicinal products may result in sedation, respiratory depression, coma and death. Because of these risks, concomitant prescribing with these sedative medicinal products should be reserved for patients for whom alternative treatment options are not possible. If a decision is made to prescribe oxycodone concomitantly with sedative medicinal products, 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).

Tolerance and dependence
The patient may develop tolerance to the active substance with chronic use and require progressively higher doses to maintain pain control. Prolonged use of this medicinal 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. Withdrawal symptoms may include yawning, mydriasis, lacrimation, rhinorrhoea, tremor, hyperhidrosis, anxiety, agitation, convulsions, insomnia or myalgia.

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.

Opioid Use Disorder (abuse and dependence)
Tolerance and physical and/or psychological dependence may develop upon repeated administration of opioids such as oxycodone. Iatrogenic addiction following therapeutic use of opioids is known to occur.
Repeated use of Oxydon may lead to Opioid Use Disorder (OUD). Abuse or intentional misuse of Oxydon 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).
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.

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

To avoid damage to the controlled-release properties of the prolonged-release tablets, the Oxydon Prolonged-release tablets must not be broken, chewed or crushed. The administration of broken, chewed or crushed tablets leads to rapid release and absorption of a potentially fatal dose of oxycodone (see section 4.9). However, the tablets can be divided into equal halves (see sections 3 and 4.2).

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.

Surgical procedures
Oxydon Prolonged-release tablets are not recommendedfor pre-operative use or 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 postoperative treatment with Oxydon depends on a careful risk-benefit assessment for each individual patient.
As with all opioid preparations, oxycodone-containing medicinal 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.

Paediatric population
Oxydon is not recommended for use in children below the age of 12 years due to insufficient data on safety and efficacy.

Alcohol
Concomitant use of alcohol and Oxydon may increase the undesirable effects of oxycodone; concomitant use should be avoided.

Endocrine system
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 be manifest from these hormonal changes.

This medicinal product contains sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicinal product.

Anti-Doping warning
Athletes must be aware that this medicinal product may cause a positive reaction to sports doping control tests. Use of Oxydon as a doping agent may become a health hazard.

4.5 Interaction with other medicinal products and other forms of interactions

Sedative medicinal products such as benzodiazepines or related medicinal products:
The concomitant use of opioids with sedative medicinal products such as benzodiazepines or related medicinal products 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).
CNS depressant active substances are for example sedatives (including benzodiazepines), hypnotics, phenothiazines, neuroleptics, antidepressants, antihistamines, antiemetics or other opioids.

Alcohol may enhance the pharmacodynamic effects of Oxydon; concomitant use should be avoided.

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 dose may need to be reduced in patients using these medicinal products.

Medicinal products with anticholinergic effects (e.g. tricyclic antidepressants, antihistamines, antiemetics, psychotropic medicinal products, muscle relaxants, medicinal products against Morbus Parkinson) may intensify the anticholinergic adverse drug reactions of oxycodone, such as constipation, dry mouth or dysfunction of urinary excretion.

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

A clinically relevant decrease or increase of INR (International Normalised Ratio) has been observed in individual cases in simultaneous use of oxycodone and coumarin anticoagulants.

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. In the following paragraphs these interactions are explained in detail.

CYP3A4 inhibitors, such as macrolide antibiotics (e.g. clarithromycin, erythromycin or telithromycin), azol-antifungals (e.g. ketoconazole, voriconazole, itraconazole or posaconazole), protease inhibitors (e.g. boceprevir, ritonavir, indinavir, nelfinavir or 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 of CYP3A4 enzyme inhibition are provided as follows:

- 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, carbamazepin, phenytoin or 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 of CYP3A4 enzyme induction are provided as follows:

- 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 or 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. Oxycodone passes the placenta. 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 newborn of mothers undergoing treatment with oxycodone.

Breast-feeding
Oxycodone may be excreted into breast milk and may cause sedation and respiratory depression in the breast-fed infant. Therefore, oxycodone should not be used in breast-feeding mothers.

Fertility
Human data are not available. Studies in rats have not shown any effects upon 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. This is particularly likely at the initiation of treatment with oxycodone, after dose increase or product rotation and if oxycodone is combined with other CNS depressant agents. Patients stabilised on a specific dose will not necessarily be restricted. Therefore, the physician should decide whether the patient is allowed to drive or use machinery.

4.8 Undesirable effects

Due to its pharmacological properties oxycodone can cause respiratory depression, miosis, bronchial spasm and spasm of the smooth muscles and may 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 most commonly in elderly or debilitated patients.

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

Metabolism and nutrition disorders
Common: decreased appetite up to loss of appetite
Uncommon: dehydration
Rare: increased appetite

Psychiatric disorders
Common: anxiety, confusional state, depression, decreased activity, restlessness, psychomotor hyperactivity, nervousness, insomnia, abnormal thinking
Uncommon: agitation, affect lability, euphoric mood, perception disturbances such as hallucinations, derealisation; 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, convulsion (especially in persons with epileptic disorder or predisposition to convulsions), concentration impaired, migraine, hypertonia, involuntary muscle contractions, hypoaesthesia, coordination disturbances, 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: tachycardia, palpitations (in the context of withdrawal syndrome)

Vascular disorders
Uncommon: vasodilatation
Rare: hypotension, orthostatic hypotension

Respiratory, thoracic and mediastinal disorders
Common: dyspnoea, bronchospasm
Uncommon: respiratory depression, dysphonia, cough
Not known: central sleep apnoea syndrome

Gastrointestinal disorders
Very common: constipation, vomiting, nausea
Common: abdominal pain, diarrhoea, dry mouth, hiccups, dyspepsia
Uncommon: mouth ulceration, stomatitis, dysphagia, flatulence, eructation, ileus
Rare: melaena, tooth disorders, gingival bleeding
Not known: dental caries

Hepatobiliary disorders
Uncommon: increased hepatic enzymes
Not known: cholestasis, biliary colic

Skin and subcutaneous tissue disorders
Very common: pruritus
Common: skin reaction/rash, hyperhidrosis
Uncommon: dry skin
Rare: urticaria

Renal and urinary disorders
Common: dysuria, micturition urgency
Uncommon: urinary retention

Reproductive system and breast disorders
Uncommon: erectile dysfunction, hypogonadism
Not known: amenorrhoea

General disorders and administration site conditions
Common: asthenic conditions, fatigue
Uncommon: chills, drug withdrawal syndrome, pain (e.g. chest pain), malaise, oedema, peripheral oedema, drug tolerance, thirst
Rare: weight increase, weight decrease
Not known: drug withdrawal syndrome neonatal

Injury, poisoning and procedural complications
Uncommon: injuries from accidents

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 of intoxication
Acute overdose with oxycodone can be manifested by respiratory depression, somnolence progressing up to stupor or coma, hypotonia, miosis, bradycardia, hypotension, lung oedema and death.

Therapy of intoxication
A patent airway must be maintained. The pure opioid antagonists such as naloxone are specific antidotes against symptoms from opioid overdose. Other supportive measures should be employed as needed.

Opioid antagonists: Naloxone (e.g. 0.4 to 2 mg intravenously). Administration should be repeated at 2 to 3 minute intervals as necessary, or by an infusion of 2 mg in 500 ml of 0.9% sodium chloride or 5% dextrose (0.004 mg/ml naloxone). The infusion should be run at a rate related to the previously administered bolus doses and should be in accordance with the patient's response.

Other supportive measures: including artificial ventilation, oxygen, vasopressors, and fluid infusions in the management of circulatory shock accompanying overdose. Cardiac arrest or arrhythmias may require cardiac massage or defibrillation. Fluid and electrolyte metabolism should be maintained.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Analgesics; Natural opium alkaloids
ATC code: N02AA05

Oxycodone shows an affinity to kappa, mu and delta opioid receptors in the brain, spinal cord and peripheral organs. It acts at these receptors as an opioid agonist without an antagonistic effect. The therapeutic effect is mainly analgesic and sedative. Compared to rapid-release oxycodone, given alone or in combination with other substances, oxycodone prolonged-release tablets provide pain relief for a markedly longer period without increased occurrence of undesirable effects.

Endocrine system
See section 4.4.

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

5.2 Pharmacokinetic properties

Absorption
The absorption of oxycodone from Oxydon Prolonged-release tablets could be calculated biphasic with an initially relatively rapid half-life of 0.6 hours accounting for a minority of the active substance, and a slower half-life of 6.9 hours accounting for the majority of the active substance.

To avoid damage to the controlled-release properties of the prolonged-release tablets, the Oxydon Prolonged-release tablets must not be broken, chewed or crushed. The administration of broken, chewed or crushed tablets leads to rapid release and absorption of a potentially fatal dose of oxycodone (see section 4.9). However, the tablets can be divided into equal halves (see sections 3. and 4.2).

The relative bioavailability of prolonged-release oxycodone is comparable to that of rapid release oxycodone with maximum plasma concentrations being achieved after approximately 4.5-7 hours after intake of the prolonged-release tablets compared to 1 to 1.5 hours. Peak plasma concentrations and oscillations of the concentrations of oxycodone from the prolonged-release and rapid-release formulations are comparable when given at the same daily dose at intervals of 12 and 6 hours, respectively.

A fat-rich meal before the intake of the tablets does not affect the maximum concentration or the extent of absorption of oxycodone.

The absolute bioavailability of oxycodone is approximately two thirds relative to parenteral administration.

Distribution
In *steady state,* the volume of distribution of oxycodone amounts to 2.6 l/kg; plasma protein binding to 38-45%; the elimination half-life to 4 to 6 hours and plasma clearance to 0.8 l/min. The elimination half-life of oxycodone from prolonged-release tablets is 4 to 5 hours with *steady state* values being achieved after a mean of 1 day.

Biotransformation
Oxycodone is metabolised to noroxycodone and oxymorphone in the intestine and liver via the P450 cytochrome system, 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 20, 40 and 80 mg prolonged-release tablets are bioequivalent in a dose proportional manner 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 reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity and genotoxicity.

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 malformation in rats in doses of up to 8 mg/kg 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.
There were no effects on F2 generation.

Long-term studies on carcinogenicity have not been performed.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core:
Sugar spheres (sucrose, maize starch)
Hypromellose
Macrogol 6000
Talc
Ethyl cellulose
Hydroxypropylcellulose

Propylene glycol
Magnesium stearate
Microcrystalline cellulose
Colloidal anhydrous silica

Tablet coating:

Hypromellose
Talc
Macrogol 6000
Titanium dioxide (E 171)
Iron oxide yellow (E 172)
Iron oxide red (E 172)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

4 years.

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

Alu/PVC/PVDC blister with child-resistant closure.

Pack sizes:
10, 20, 28, 30, 40, 50, 56, 60, 100 and 112 prolonged-release tablets

HDPE bottles with child-resistant PP twist-off caps

Pack sizes:
50, 100 and 250 prolonged-release tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements for disposal.

7 MARKETING AUTHORISATION HOLDER

Rowex Ltd
Newtown
Bantry
Co. Cork
Ireland

8 MARKETING AUTHORISATION NUMBER

PA0711/115/002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 19th December 2007
Date of last renewal: 20th August 2012

10 DATE OF REVISION OF THE TEXT

May 2022