Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Reltebon 40 mg Prolonged-release Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each prolonged-release tablet contains 40 mg oxycodone hydrochloride corresponding to 36 mg of oxycodone.

Excipient with known effect:
The prolonged-release tablets contain lactose monohydrate.

Each prolonged-release tablet contains 31.6 mg lactose monohydrate.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Prolonged-release tablet.

Yellow, round, biconvex tablets, 7 mm in diameter, with ‘OX 40’ debossed on one side.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Severe pain, which can be adequately managed only with opioid analgesics.
Reltebon is indicated in adults and adolescents aged 12 years and older.

4.2 Posology and method of administration

Posology

The dosage depends on the intensity of pain and the patient’s individual susceptibility to the treatment. The following general dosage recommendations apply:

Adults and adolescents 12 years of age and older

Dose titration and adjustment

In general, the initial dose for opioid naïve patients is 10 mg oxycodone hydrochloride given at intervals of 12 hours. Some patients may benefit from a starting dose of 5 mg to minimize the incidence of side effects.

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

For doses not realisable/practicable with these strengths, other strengths are available.

According to well-controlled clinical studies 10-13 mg oxycodone hydrochloride correspond to approximately 20 mg morphine sulphate, both in the prolonged-release formulation.

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

Some patients who take Reltebon prolonged-release tablets following a fixed schedule need rapid release analgesics as rescue medication in order to control breakthrough pain. Reltebon prolonged-release tablets are not indicated for the treatment of acute pain and/or breakthrough pain. The single dose of the rescue medication should amount to 1/6 of the equianalgesic daily dose of Reltebon prolonged-release tablets. Use of the rescue medication more than twice daily indicates that the dose of Reltebon prolonged-release tablets needs to be increased. The dose should not be adjusted more often than once every 1-2 days until a stable twice daily administration has been achieved.

Following a dose increase from 10 mg to 20 mg taken every 12 hours dose adjustments should be made in steps of approximately one third of the daily dose. The aim is a patient- specific dosage which, with twice daily administration, allows for adequate analgesia with tolerable undesirable effects and as little rescue medication as possible as long as pain therapy is needed.

Even distribution (the same dose mornings and evenings) following a fixed schedule (every 12 hours) is appropriate for the majority of the patients. For some patients it may be advantageous to distribute 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 is generally sufficient; but higher dosages may be necessary. Patients with cancer- related pain may require dosages of 80 to 120 mg, which in individual cases can be increased to up to 400 mg. If even higher doses are required, the dose should be decided individual balancing efficacy with the tolerance and risk of undesirable effects.

Method of administration

For oral use.

Reltebon prolonged-release tablets should be taken twice daily based on a fixed schedule at the dosage determined.

The prolonged-release tablets may be taken with or independent of meals with a sufficient amount of liquid. Reltebon prolonged release tablets must be swallowed whole, not chewed.

Duration of administration
Reltebon prolonged-release tablets should not be taken 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.

Paediatric population
There have been no studies in patients under 12 years of age, therefore oxycodone hydrochloride should not be used in patients under 12 years.

Elderly patients
A dose adjustment is not usually necessary in elderly patients.

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 their clinical situation.

Risk patients
Risk patients, for example patients with low body weight or slow metabolism of medicinal products, should initially receive half the recommended adult dose if they are opioid naïve. Dose titration should be performed in accordance with the individual clinical situation.

For instructions how to open the child resistant blisters, see section 6.6.

4.3 Contraindications

- Hypersensitivity to oxycodone or to any of the excipients listed in section 6.1.
- Severe respiratory depression with hypoxia and/or hypercapnia.
- Severe chronic obstructive pulmonary disease.
- Cor pulmonale.
- Severe bronchial asthma.
- Elevated carbon dioxide levels in the blood.
- Paralytic ileus.
- Acute abdomen, delayed gastric emptying.

4.4 Special warnings and precautions for use

Paediatric population
Reltebon prolonged-release tablets have not been studied in children younger than 12 years of age. The safety and efficacy of the tablets have not been demonstrated and the use in children younger than 12 years of age is therefore not recommended.

Elderly or debilitated patients
The major risk of opioid excess is respiratory depression. Caution is required in elderly or debilitated patients, in patients with severe impairment of lung, liver or kidney function, myxoedema, hypothyroidism, Addison's disease (adrenal insufficiency), intoxication psychosis (e.g. alcohol), prostatic hypertrophy, adrenocortical insufficiency, alcoholism, known opioid dependence, delirium tremens, pancreatitis, diseases of the biliary tract, inflammatory bowel disorders, biliary or ureteric colic, hypotension, hypovolaemia, conditions with increased brain pressure such as head injury, disturbances of circulatory regulation, epilepsy or seizure tendency and in patients taking MAO inhibitors.

Patients undergoing abdominal surgery
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 should be closely monitored.

Respiratory depression
Respiratory depression is the most significant risk induced by opioids and is most likely to occur in elderly or debilitated patients. The respiratory depressant effect of oxycodone can lead to increased carbon dioxide concentrations in blood and hence in cerebrospinal fluid. In predisposed patients opioids can cause severe decrease in blood pressure.

Long-term use, tolerance and withdrawal
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. Withdrawal symptoms may include yawning, mydriasis, lacrimation, rhinorrhoea, tremor, hyperhidrosis, anxiety, agitation, convulsions and insomnia.

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.

Dependence potential
Reltebon prolonged-release tablets have a primary dependence potential. 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. However, when used as directed in patients with chronic pain the risk of developing physical or psychological dependence is markedly reduced or needs to be assessed in a differentiated manner. There are no data available on the actual incidence of psychological dependence in chronic pain patients. In patients with a history of alcohol and drug abuse the medicinal product must be prescribed with special care.

Pre-operative use
Reltebon prolonged release tablets are not recommended for pre-operative use or within the first 12-24 hours post operatively.

Abusive parenteral venous injection
In case of abusive parenteral venous injection the tablet excipients may lead to necrosis of the local tissue, infection, increased risk of endocarditis, and valvular heart injury which may be fatal, granulomas of the lung or other serious, potentially fatal events.

Tablets must not be chewed or crushed
To avoid damage to the controlled release properties of the tablets the prolonged release tablets must be swallowed whole, and not broken, chewed or crushed. The administration of broken, chewed or crushed controlled release oxycodone tablets leads to rapid release and absorption of a potentially fatal dose of oxycodone (see section 4.9).

Alcohol
Concomitant use of alcohol and oxycodone hydrochloride prolonged-release tablets may increase the undesirable effects of oxycodone hydrochloride; concomitant use should be avoided.

Reltebon contains lactose
This medicinal product contains lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

There can be an enhanced CNS depressant effect during concomitant therapy with drugs which affect the CNS such as other opioids, sedatives, hypnotics, anti-depressants, antipsychotics, anaesthetics, muscle relaxants, antihistamines and antiemetics. MAO-inhibitors are known to interact with opioid analgesics. MAO-inhibitors causes CNS-excitation or depression associated with hypertensive or hypotensive crisis (see section 4.4). 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).

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

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

Cimetidine can inhibit the metabolism of oxycodone.

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), azol-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, carbamazepin, 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 Johns 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, fluoxetine and quinidine, may cause decreased clearance of oxycodone which could lead to an increase in oxycodone plasma concentrations.

The effect of other relevant isoenzyme inhibitors on the metabolism of oxycodone is not known. Potential interactions should be taken into account.
Clinically relevant changes in International Normalized Ratio (INR) in both directions have been observed in individuals if coumarin anticoagulants are co-applied with oxycodone hydrochloride.

There are no studies investigating the effect of oxycodone on CYP catalysed metabolism of other drugs.

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 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 breastfeeding mothers.

4.7 Effects on ability to drive and use machines

Oxycodone may impair the ability to drive and use machines.
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 adverse events considered at least possibly related to treatment are tabulated below by system organ class and absolute frequency.

Body System	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)	Frequency unknown (Cannot be estimated from the available data)
Blood and lymphatic system disorders				lymphadenopathy	
Immune system disorders			hypersensitivity		anaphylactic responses
Endocrine disorders			syndrome of inappropriate antidiuretic hormone secretion		
Metabolism and nutrition disorders		decreased appetite	dehydration		
Psychiatric disorders		anxiety, confusional state, depression, insomnia, nervousness. abnormal thinking, amnesia, isolated cases of speech disorders	agitation, affect lability, euphoric mood, hallucinations, decreased libido, drug dependence (see section 4.4), depersonalisation, change in taste, visual disturbances, hyperacousis		aggression
Nervous system disorders	somnolence, dizziness, headache	asthenia, tremor	amnesia, convulsion, hypertonia, both increased and decreased muscle tone, involuntary muscle contractions; hypaesthesia; coordination disturbances; malaise; speech disorder, syncope, paraesthesia, dysgeusia		hyperalgesia
Eye disorders			visual impairment, lacrimation disorder, miosis		
Ear and labyrinth			vertigo		

disorders					
Cardiac disorders			supraventricular tachycardia; palpitations (in the context of withdrawal syndrome)		
Vascular disorders			vasodilatation	hypotension, orthostatic hypotension	
Respiratory, thoracic and mediastinal disorders		dyspnoea, bronchospasm	increased coughing; pharyngitis; rhinitis; voice changes, respiratory depression		
Gastrointestinal disorders	constipation, nausea, vomiting	dry mouth, rarely accompanied by thirst; gastrointestinal disorders such as abdominal pain; diarrhoea; dyspepsia; loss of appetite	oral ulcers; gingivitis; stomatitis; flatulence, dysphagia, eructation, ileus	gum bleeding; increased appetite; tarry stool; tooth staining	dental caries
Hepato-biliary disorders			increased hepatic enzymes		cholestasis, biliary colic
Skin and subcutaneous tissue disorders	pruritus	skin eruptions including rash, in rare cases increased photosensitivity, in isolated cases urticaria or exfoliative dermatitis, hyperhidrosis	dry skin	herpes simplex, urticaria	
Renal and urinary disorders		micturition disturbances (increased urge to urinate)	urinary retention	haematuria	
Reproductive system and breast disorders			reduced libido; erectile disfunction		amenorrhoea
General disorders and administration site conditions		sweating, asthenic conditions	accidental injuries; pain (e.g. chest pain); oedema; migraine; physical dependence with withdrawal symptoms; drug tolerance, chills,	weight changes (increase or decrease); cellulitis	

			malaise, peripheral oedema, thirst.		

Tolerance and dependence may develop.

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 and intoxication:
Miosis, respiratory depression, somnolence, reduced skeletal muscle tone and drop in blood pressure. In severe cases circulatory collapse, stupor, coma, bradycardia, non- cardiogenic lung oedema, hypotension, and death may occur; abuse of high doses of strong opioids such as oxycodone can be fatal.

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

In the event of overdosing intravenous administration of an opiate 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.

Gastric lavage can be taken into consideration. Consider activated charcoal (50 g for adults, 10 -15 g for children), 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 prolonged release 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: Natural opium alkaloids
ATC-Code: N02A A05

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. Compared to rapid-release oxycodone, given alone or in combination with other substances, the prolonged-release tablets provide pain relief for a markedly longer period without increased occurrence of undesirable effects.

Endocrine system
Opioids 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.

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.

Clinical studies
The efficacy of Oxycodone prolonged-release tablets has been demonstrated in cancer pain, post-operative pain and severe non-malignant pain such as diabetic neuropathy, postherpetic neuralgia, low back pain and osteoarthritis. In the latter indication, treatment was continued for up to 18 months and proved effective in many patients for whom NSAIDs alone provided inadequate relief. The efficacy of Oxycodone prolonged-release tablets in neuropathic pain was confirmed by three placebo-controlled studies.

In patients with chronic non-malignant pain, maintenance of analgesia with stable dosing was demonstrated for up to three years.

5.2 Pharmacokinetic properties

Absorption:
The relative bioavailability of Reltebon prolonged-release tablets is comparable to that of rapid release oxycodone with maximum plasma concentrations being achieved approximately 3 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 tablets must not be crushed, divided or chewed as this leads to rapid oxycodone release and absorption of a potentially fatal dose of oxycodone due to the damage of the prolonged release properties.

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

Metabolism:
Oxycodone is metabolised in the intestine and liver to noroxycodone and oxymorphone as well as to several glucuronide conjugates. CYP3A4 and CYP2D6 are probably involved in the formation of noroxycodone and oxymorphone respectively. Oxymorphone has analgesic activity but is present in the plasma in low concentrations and is not considered to contribute to oxycodone´s pharmacological effect.

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 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.

Elderly
The plasma concentration of oxycodone in elderly subjects is 15% greater when compared with young subjects.

Gender
Female subjects have, on average, plasma oxycodone concentrations up to 25% higher than males on a body weight adjusted basis. The reason for this difference is unknown.

Patients with renal impairment
Patients with mild, moderate and severe renal impairment showed 1.1-, 1.4- and 1.7- fold increased plasma concentrations respectively compared to patients with normal renal function. AUC increased on average 1.5-, 1.7- and 2.3-fold respectively compared to patients with normal renal function. The elimination half-life for oxycodone increased 1.5-, 1.2- and 1.4- fold respectively compared to patients with normal renal function.

Patients with hepatic impairment
Patients with mild, moderate and severe hepatic impairment showed 1.2-, 2.0- and 1.9- fold increased plasma concentrations respectively compared to patient with normal hepatic function. AUC increased on average 1.4-, 3.2- and 3.2- fold respectively compared to patients with normal hepatic function. The elimination half-life of oxycodone increased 1.1-, 1.8- and 1.8- fold respectively compared to patients with normal hepatic function.

5.3 Preclinical safety data

Teratogenicity
Oyxcodone 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 in rabbits in doses of 125 mg/kg bodyweight. However, in rabbits, when individual foetuses 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.
In a study of peri- and postnatal development in rats, maternal body weight and food intake parameters were reduced for doses $\geq$ 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 behavioural 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.

Carcinogenicity
Long-term carcinogenicity studies were not performed.

Mutagenicity
The results of *in-vitro* and *in-vivo* studies indicate that the genotoxic risk of oxycodone to humans is minimal or absent at the systemic oxycodone concentrations that are achieved therapeutically.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Tablet core:
Lactose monohydrate
Hypromellose
Povidone K30
Stearic acid
Magnesium stearate
Colloidal anhydrous silica

Tablet coating:

Polyvinyl alcohol
Titanium dioxide (E171)
Macrogol 3350

Talc
Iron oxide, yellow (E172)

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Blister packs:
Do not store above 25°C.

HDPE container:
This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

Child resistant blister packs (PVC/PVdC/Al/PET/paper).
Pack sizes:
1, 20, 28, 30, 50, 56, 60, 98 and 100 prolonged-release tablets

Blister packs (PVC/Al) in cartons.
Pack sizes:
1, 20, 28, 30, 50, 56, 60, 98 and 100 prolonged-release tablets

White, round, HDPE tablet containers with LDPE caps.
Pack size: 98 and 100 prolonged-release tablets

White, round, child-resistant, HDPE tablet containers with LDPE caps.
Pack size: 98 and 100 prolonged-release tablets

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

Instructions for use of child resistant blisters:
1. Do not push the tablet directly out of the pocket
2. Separate one blister cell from the strip at the perforations
3. Carefully peel off the backing to open the pocket

7 MARKETING AUTHORISATION HOLDER

Actavis Group PTC ehf
Reykjavikurvegi 76-78,
220 Hafnarfjördur,
Iceland

8 MARKETING AUTHORISATION NUMBER

PA1380/129/007

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 8th August 2014

10 DATE OF REVISION OF THE TEXT

June 2017