

# Summary of Product Characteristics

## 1 NAME OF THE MEDICINAL PRODUCT

Dancex SR 40 mg Prolonged-Release Tablets

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

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

Excipients:

Each prolonged-release tablet contains 43.2 mg lactose anhydrous

For the full list of excipients, see section 6.1.

## 3 PHARMACEUTICAL FORM

Prolonged-release tablet.

Yellow, round, biconvex film coated prolonged-release tablets, diameter: 6.8 mm – 7.4 mm.

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic Indications

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

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

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 adverse reactions.

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

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 Dancex SR prolonged-release tablets after conversion from other opioids, with 50-75% of the calculated oxycodone dose.

Some patients who take Dancex SR prolonged-release tablets following a fixed schedule need rapid release analgesics as rescue medication in order to control breakthrough pain. Various options for the treatment of breakthrough pain exist with regard to the choice of the active substance, the route of administration and the dosage form.

Dancex SR 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 Dancex SR prolonged-release tablets. Use of the rescue medication more than twice daily indicates that the dose of Oxycodone Hydrochloride 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 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.

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 individually balancing efficacy against tolerance and the risk of undesirable effects.

For the treatment of non-malignant pain a daily dose of 40 mg is generally sufficient; but higher dosages may be necessary.

#### Duration of administration

Dancex SR 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.

#### Older people

The lowest dose should be administered with careful titration to pain control.

#### 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.

#### Special populations

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. Therefore the lowest recommended dosage, i.e. 10 mg, may not be suitable as a starting dose.

Dose titration should be performed in accordance with the individual clinical situation.

#### Children under 12 years of age

Dancex SR prolonged-release tablets are not recommended for children under 12 years of age.

#### **Method of administration**

For oral use.

Dancex SR 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. Dancex SR prolonged-release tablets must be swallowed whole, and they must not be chewed, divided or crushed.

### 4.3 Contraindications

- hypersensitivity to the active substance 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
- paralytic ileus
- elevated carbon dioxide levels in the blood

### 4.4 Special warnings and precautions for use

#### Caution should be exercised in

- elderly or debilitated patients,
- patients with severe impairment of lung, liver or kidney function,
- Addison's disease,
- intoxication psychosis (e.g. alcohol),
- prostatic hypertrophy,
- adrenocortical insufficiency,
- alcoholism, known opioid dependence,
- delirium tremens,
- pancreatitis,
- diseases of the biliary tract, biliary or ureteric colic,
- inflammatory bowel disorders
- conditions with increased brain pressure,
- disturbances of circulatory regulation (e.g. hypotensions, hypovolaemia),
- epilepsy or seizure tendency,
- in patients taking MAO inhibitors or within 2 weeks of discontinuation of their use
- and in patients taking naltrexone (see also section 4.5).

#### Respiratory depression

Respiratory depression is the most significant risk induced by opioids. The respiratory depressant effect of oxycodone can lead to increased carbon dioxide concentrations in blood and hence in cerebrospinal fluid.

#### Myxoedema, Hypothyroidism

As with all narcotics, a reduction in dosage may be advisable in patients with hypothyroidism.

#### Mixed opioid agonists/antagonists

Care should be taken when combining Dancex SR prolonged-release tablets with mixed mu-opioid agonist/antagonists (like pentazocine, nalbuphine) or partial mu-opioid agonists (like buprenorphine). In patients maintained on buprenorphine for the treatment of opioid dependence, alternative treatment options (like e.g. temporary buprenorphine discontinuation) should be considered, if administration of full  $\mu$ -agonists (like oxycodone) becomes necessary in acute pain situations. On combined use with buprenorphine, higher dose requirements for full  $\mu$ -receptor agonists have been reported and close monitoring of adverse events such as respiratory depression is required in such circumstances. (see also section 4.5).

#### Tolerance and dependence

Long-term use of Dancex SR can lead to the development of tolerance which leads to the use of higher doses in order to achieve the desired analgesic effect. There is a cross-tolerance to other opioids.

Dancex SR have a primary dependence potential. However, when used as intended in patients with chronic pain the risk of developing physical or psychological dependence is markedly reduced. There are no data available on the actual incidence of psychological dependence in chronic pain patients.

Chronic use of Dancex SR can cause physical dependence. Withdrawal symptoms may occur following abrupt discontinuation of therapy. If therapy with oxycodone is no longer required it may be advisable to reduce the daily dose gradually in order to avoid the occurrence of a withdrawal syndrome (see also section 4.8). Withdrawal symptoms may include yawning, mydriasis, lacrimation, rhinorrhoea, tremor, hyperhidrosis, anxiety, agitation, convulsions and insomnia.

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.

#### Abuse

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. Dancex SR should be used with particular care in patients with a history of alcohol and drug abuse.

In case of abusive parenteral injection the tablet excipients may lead to necrosis of the local tissue, granulomas of the lung or other serious, potentially fatal events. 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 (see section 4.9) due to the damage of the prolonged-release properties.

#### Surgical procedures

The use of oxycodone prolonged-release tablets is not recommended prior and during the first 12-24 hours after surgical procedures. If further treatment with oxycodone is indicated, the dose should be adjusted to the new post-operative requirements.

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 undergoing additional pain-relieving procedures (e.g. surgery, plexus blockade) should not receive oxycodone for 12 hours prior to the intervention.

#### Children

Dancex SR have not been studied in children and adolescents below 12 years of age. The safety and efficacy of the tablets have not been demonstrated and the use in children and adolescents younger than 12 years of age is therefore not recommended.

#### Patients with severe hepatic impairment

Patients with severe hepatic impairment should be closely monitored.

#### Paralytic ileus

Dancex SR should not be used where there is a possibility of paralytic ileus occurring. Should paralytic ileus be suspected or occur during use, Dancex SR should be discontinued immediately.

#### Alcohol

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

#### Anti-Doping Warning

Athletes must be aware that this medicine may cause a positive reaction to 'anti-doping' tests.

**Use of Dancex SR as a doping agent may become a health hazard.**

This medicinal product contains lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take Dancex SR prolonged-release tablets.

## 4.5 Interaction with other medicinal products and other forms of interaction

- Alcohol may enhance the pharmacodynamic effects of oxycodone; concomitant use should be avoided.
- Medicinal products inducing respiratory depression such as benzodiazepines, phenobarbital and other opioids (analgesic, antitussive or substitution treatments) can enhance the risk of respiratory arrest, notably in case of overdose and/or in the elderly.
- **Central nervous system depressants** (e.g. benzodiazepines, be they anxiolytics or hypnotics, antipsychotics, some antidepressants, H<sub>1</sub>-antihistamines, other opioids, alcohol...) can enhance the sedative effect of oxycodone and impair vigilance.
- **Anticholinergics** (phenothiazine, antipsychotics, tricyclic antidepressants, most non-recent H<sub>1</sub> antihistamines, certain antiparkinson medicines) can enhance the anticholinergic undesirable effects of oxycodone (such as constipation, dry mouth or micturition disorders).
- Care should be taken if Dancex SR prolonged-release tablets should be used concomitantly with mixed mu-opioid agonist/antagonists (like pentazocine, nalbuphine) or partial mu-opioid agonists (like buprenorphine). In patients maintained on buprenorphine for the treatment of opioid dependence, alternative treatment options (like e.g. temporary buprenorphine discontinuation) should be considered, if administration of full  $\mu$ -agonists (like oxycodone) becomes necessary in acute pain situations. On combined use with buprenorphine, higher dose requirements for full  $\mu$ -receptor agonists have been reported and close monitoring of adverse events such as respiratory depression is required in such circumstances (see also section 4.4).
- The concomitant use of oxycodone and naltrexone may result in the need for increased oxycodone doses.
- 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 prolonged-release tablets.

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 and quinidine, may cause decreased clearance of oxycodone which could lead to an increase in oxycodone plasma concentrations.

## 4.6 Fertility, pregnancy and lactation

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

### Pregnancy

There are limited data from the use of oxycodone in pregnant women. Infants born to mothers who have received opioids during the last 3 to 4 weeks before giving birth should be monitored for respiratory depression. Withdrawal symptoms may be observed in the 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. This is particularly likely at the initiation of treatment with Dancex SR, after dose increase or product rotation and if Dancex SR is combined with alcohol or other CNS depressant agents. 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 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 ( $\geq 1/10$ )

Common ( $\geq 1/100$  to  $< 1/10$ )

Uncommon ( $\geq 1/1,000$  to  $< 1/100$ )

Rare ( $\geq 1/10,000$  to  $< 1/1,000$ )

Very rare ( $< 1/10,000$ )

Not known (cannot be estimated from the available data)

### 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

*Uncommon:* dehydration

### Psychiatric disorders

*Common:* anxiety, depression, nervousness, insomnia, abnormal thinking, confusional state

*Uncommon:* agitation, affect lability, euphoric mood, hallucinations, decreased libido, drug dependence (see section 4.4), hyperacusis

*Not known:* aggression

### Nervous system disorders

*Very common:* somnolence, dizziness, headache

*Common:* tremor,

*Uncommon:* amnesia, convulsion, increased or decreased muscle tone, involuntary muscle contractions, speech disorder, syncope, paraesthesia, dysgeusia, hypaesthesia, coordination disturbances,

*Rare:* muscle spasm

*Not known:* hyperalgesia

### Eye disorders

*Uncommon:* visual impairment, lacrimation disorder, miosis

### Ear and labyrinth disorders

*Uncommon:* vertigo

### Cardiac disorders

*Uncommon:* palpitations (in the context of withdrawal syndrome), supraventricular tachycardia

### Vascular disorders

*Uncommon:* vasodilatation

*Rare:* hypotension, orthostatic hypotension

### Respiratory, thoracic and mediastinal disorders

*Common:* dyspnoea, bronchospasm

*Uncommon:* respiratory depression, increased coughing, pharyngitis, rhinitis, voice changes

### Gastrointestinal disorders

*Very common:* constipation, nausea, vomiting

*Common:* dry mouth, gastrointestinal disorders such as abdominal pain, diarrhoea, dyspepsia, loss of appetite

*Uncommon:* dysphagia, eructation, ileus, oral ulcers, gingivitis, stomatitis, flatulence

*Rare:* gingival bleeding, increased appetite, tarry stool, tooth staining and damage

*Not known:* dental caries

### Hepatobiliary disorders

*Uncommon:* increased hepatic enzymes

*Not known:* cholestasis, biliary colic

### Skin and subcutaneous tissue disorders

*Very common:* pruritus

*Common:* rash, hyperhidrosis

*Uncommon:* dry skin

*Rare:* manifestations of herpes simplex, increased photosensitivity, urticaria

*Very rare:* exfoliative dermatitis

Renal and urinary disorders*Common:* increased urge to urinate*Uncommon:* urinary retention*Rare:* haematuriaReproductive system and breast disorders*Uncommon:* erectile dysfunction*Not known:* amenorrhoeaGeneral disorders and administration site conditions*Common:* asthenic conditions, *Uncommon:* chills, accidental injuries, pain (e.g. chest pain), oedema, peripheral oedema, migraine, drug withdrawal syndrome, drug tolerance, thirst*Rare:* weight changes (increase or decrease), cellulitis

Prolonged use of Dancex SR 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, rhinorrhea, 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.

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 preferably through the online reporting option accessible from the IMB homepage. A downloadable report form is also accessible from the IMB website, which may be completed manually and submitted to the IMB via 'freepost', in addition to the traditional post-paid 'yellow card' option.

**FREEPOST**

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Miosis, respiratory depression, somnolence, reduced skeletal muscle tone and drop in blood pressure. In severe cases circulatory collapse, stupor, coma, 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 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.

Naloxone should not be administered in the absence of clinically significant respiratory or circulatory depression secondary to oxycodone overdose. Naloxone should be administered cautiously to patients 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.

Gastric lavage can be taken into consideration. The administration 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 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: 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. 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.

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 semi-synthetic opioid, has immunological effects similar to morphine is unknown.

### 5.2 Pharmacokinetic properties

#### Absorption

The relative bioavailability of Dancex SR Prolonged-Release Tablets is comparable to that of rapid-release oxycodone with maximum plasma concentrations being achieved after 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.

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. The elimination half-life of oxycodone from prolonged-release tablets is 4-5 hours with steady state values being achieved after a mean of 1 day.

#### Metabolism

Oxycodone is metabolised in the intestine and liver via the P450 cytochrome 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

Across the 5-80 mg dose range of prolonged release oxycodone tablets linearity of plasma concentrations was demonstrated in terms of rate and extent of absorption.

## 5.3 Preclinical safety data

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

Long-term studies on carcinogenicity have not been performed.

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

## 6 PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

#### Tablet core

Hydrogenated castor oil  
Copovidone  
Behenoyl polyoxylglycerides  
Lactose monohydrate  
Magnesium stearate  
Maize starch  
Colloidal anhydrous silica  
Triglycerides, medium-chain

#### Tablet coating

Microcrystalline cellulose  
Hypromellose  
Stearic acid  
Titanium dioxide (E 171)  
Iron oxide yellow (E 172)

### 6.2 Incompatibilities

Not applicable

### **6.3 Shelf life**

5 years

HDPE-bottle:

Shelf life after first opening: 6 months

### **6.4 Special precautions for storage**

This medicinal product does not require any special storage conditions.

### **6.5 Nature and contents of container**

PVC/PE/PVDC-aluminium blister

HDPE –bottles, closed with child resistant closure cap of polypropylene (PP) or HDPE, with or without a desiccant capsule of polyethylene (PE), containing silica gel as desiccant.

Pack sizes:

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

HDPE bottle: 50 and 100 prolonged-release tablets

Not all pack sizes may be marketed.

### **6.6 Special precautions for disposal**

No special requirements

## **7 MARKETING AUTHORISATION HOLDER**

Rowex Ltd  
Bantry  
Co. Cork  
Ireland

## **8 MARKETING AUTHORISATION NUMBER**

PA0711/143/004

## **9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

Date of first authorisation: 24th September 2012

## **10 DATE OF REVISION OF THE TEXT**

September 2013