# PROLADONE
# (oxycodone) 30 mg suppository

**WARNINGS**

***Limitations of use***
Because of the risks associated with the use of opioids, Proladone suppositories should only be used in patients for whom other treatment options, including non-opioid analgesics, are ineffective, not tolerated or otherwise inadequate to provide appropriate management of pain (see section 4.4 Special Warnings and Precautions for Use).

***Hazardous and harmful use***
Proladone suppositories poses risks of hazardous and harmful use which can lead to overdose and death. Assess the patient's risk of hazardous and harmful use before prescribing and monitor the patient regularly during treatment (see section 4.4. Special Warnings and Precautions for Use).

***Life threatening respiratory depression***
Serious, life-threatening or fatal respiratory depression may occur with the use of Proladone suppositories. Be aware of situations which increase the risk of respiratory depression, modify dosing in patients at risk and monitor patients closely, especially on initiation or following a dose increase (see section 4.4 Special Warnings and Precautions for Use).

***Concomitant use of benzodiazepines and other central nervous system (CNS) depressants, including alcohol***
Concomitant use of opioids with benzodiazepines, gabapentinoids, antihistamines, tricyclic antidepressants, antipsychotics, cannabis or other central nervous system (CNS) depressants, including alcohol, may result in profound sedation, respiratory depression, coma, and death. Limit dosages and durations to the minimum required; and monitor patients for signs and symptoms of respiratory depression and sedation. Caution patients not to drink alcohol while taking Proladone suppositories.

## 1 NAME OF THE MEDICINE

Oxycodone

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Proladone suppositories contain oxycodone 30 mg per suppository as the active ingredient.

Proladone suppositories also contain lactose monohydrate.

For the full list of excipients, see Section 6.1 List of Excipients.

## 3 PHARMACEUTICAL FORM

Proladone suppositories consist of an oval, 22 mm x 10 mm compressed cone, which will dissolve in use and which is covered by a wax coating to aid insertion, presented as a smooth, mottled, off-white product.

## 4 CLINICAL PARTICULARS

### 4.1 THERAPEUTIC INDICATIONS

Semisynthetic narcotic analgesic. Relief of post-operative pain following a wide range of major operative procedures such as major orthopaedic, abdominal, gynaecological and thoracic surgery and for the relief of pain in malignant disease.

### 4.2 DOSE AND METHOD OF ADMINISTRATION

One suppository every six to eight hours; in case of terminal disease, one suppository as required to control pain.

### 4.3 CONTRAINDICATIONS

Hypersensitivity to opiate narcotics, severe respiratory disease, acute respiratory disease, acute respiratory depression, cor pulmonale, cardiac arrhythmias, bronchial asthma, acute alcoholism, brain tumour, head injuries, increased cerebrospinal or intracranial pressure, severe central nervous system (CNS) depression, convulsive disorders, delirium tremens, suspected surgical abdomen and concomitant monoamine oxidase inhibitors (MAOIs) or within 14 days of such therapy.

The use of Proladone suppositories is contraindicated in chronic (long-term) non-cancer pain.

### 4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Oxycodone can produce drug dependence and therefore has the potential of being abused. Psychological dependence, physical dependence and tolerance may develop upon repeated administration. Abrupt withdrawal of oxycodone in those physically dependent may precipitate withdrawal symptoms. Therefore, patients on prolonged therapy should be withdrawn gradually from the drug if it is no longer required for pain control.

Oxycodone should be used with extreme caution in patients with head injuries and raised intracranial pressure as respiratory depression and ability to increase cerebrospinal fluid (CSF) pressure may be exaggerated, thereby complicating the clinical course.

Therapeutic doses of oxycodone may decrease respiratory drive and increase airways resistance in patients with acute asthma, chronic obstructive airways disease or those with substantially decreased pulmonary reserve or respiratory depression.

Oxycodone should be used only with caution and in reduced dosage during concomitant administration of other narcotic analgesics, general anaesthetics, phenothiazines and other tranquillisers, sedative/hypnotics, some tricyclic antidepressants and other CNS depressants (including alcohol). Respiratory depression, hypotension and profound sedation or coma may result.

Administration of oxycodone may result in severe hypotension in patients whose ability to maintain adequate blood pressure is compromised by reduced blood volume, or concurrent administration of such drugs as phenothiazines or certain anaesthetics. Oxycodone may obscure the diagnosis or clinical course of patients with acute abdominal conditions. Opioid analgesics should be used with caution in patients with myasthenia gravis.

The euphoric activity of opioid compounds has led to their abuse. It should be given with caution or in reduced doses to patients with hypothyroidism, adrenocortical insufficiency, impaired kidney or liver function, prostatic hypertrophy or shock. It should be used with caution in patients with obstructive bowel disorders.

**Hazardous and harmful use**

Proladone suppositories contains the opioid oxycodone and is a potential drug of abuse, misuse and addiction. Addiction can occur in patients appropriately prescribed Proladone suppositories at recommended doses.

The risk of addiction is increased in patients with a personal or family history of substance abuse (including alcohol and prescription and illicit drugs) or mental illness. The risk also increases the longer the drug is used and with higher doses. Patients should be assessed for their risks for opioid abuse or addiction prior to being prescribed Proladone suppositories.

All patients receiving opioids should be routinely monitored for signs of misuse and abuse. Opioids are sought by people with addiction and may be subject to diversion. Strategies to reduce these risks include prescribing the drug in the smallest appropriate quantity and advising the patient on the safe storage and proper disposal of any unused drug (see Section 6.4 Special precautions for storage and Section 6.6 Special precautions for disposal). Caution patients that abuse of oral or transdermal forms of opioids by parenteral administration can result in serious adverse events, which may be fatal.

Patients should be advised not to share Proladone suppositories with anyone else.

**Respiratory depression**

Serious, life-threatening or fatal respiratory depression can occur with the use of opioids even when used as recommended. It can occur at any time during the use of Proladone suppositories but the risk is greatest during initiation of therapy or following an increase in dose. Patients should be monitored closely for respiratory depression at these times.

The risk of life-threatening respiratory depression is also higher in elderly, frail, or debilitated patients and in patients with existing impairment of respiratory function (e.g. chronic obstructive pulmonary disease; asthma) and in patients with hepatic or renal impairment (see Use in hepatic impairment and Use in renal impairment). Opioids should be used with caution and with close monitoring in these patients (see Section 4.2 Dose and Method of Administration). The use of opioids is contraindicated in patients with severe respiratory disease, acute respiratory disease and respiratory depression (see Section 4.3 Contraindications).

The risk of respiratory depression is greater with the use of high doses of opioids, especially high potency and modified release formulations, and in opioid naïve patients. Initiation of opioid treatment should be at the lower end of the dosage recommendations with careful titration of doses to achieve effective pain relief. Careful calculation of equianalgesic doses is required when changing opioids or switching from immediate release to modified release formulations, (see section 4.2 Dose and Method of Administration), together with consideration of pharmacological differences between opioids. Consider starting the new opioid at a reduced dose to account for individual variation in response.

**Risks from concomitant use of benzodiazepines or other CNS depressants, including alcohol**

Concomitant use of opioids and benzodiazepines or other CNS depressants, including alcohol, may result in sedation, respiratory depression, coma and death. Because of these risks, concomitant prescribing of Proladone suppositories with CNS depressant medicines, such as other opioid analgesics, benzodiazepines, gabapentinoids,

cannabis, sedatives, hypnotics, tricyclic antidepressants, antipsychotics, antihistamines, centrally-active anti-emetics and other CNS depressants, should be reserved for patients for whom other treatment options are not possible. If a decision is made to prescribe Proladone suppositories concomitantly with any of the medicines, the lowest effective dose should be used, and the duration of treatment should be as short as possible. Patients should be followed closely for signs and symptoms of respiratory depression and sedation. Patients and their caregivers should be made aware of these symptoms. Patients and their caregivers should also be informed of the potential harms of consuming alcohol while taking Proladone suppositories.

**Tolerance, dependence and withdrawal**

Neuroadaptation of the opioid receptors to repeated administration of opioids can produce tolerance and physical dependence. Tolerance is the need for increasing doses to maintain analgesia. Tolerance may occur to both the desired and undesired effects of the opioid.

Physical dependence, which can occur after several days to weeks of continued opioid usage, results in withdrawal symptoms if the opioid is ceased abruptly or the dose is significantly reduced. Withdrawal symptoms can also occur following the administration of an opioid antagonist (e.g. naloxone) or partial agonist (e.g. buprenorphine). Withdrawal can result in some or all of the following symptoms: dysphoria, restlessness/agitation, lacrimation, rhinorrhoea, yawning, sweating, chills, myalgia, mydriasis, irritability, anxiety, increasing pain, backache, joint pain, weakness, abdominal cramps, insomnia, nausea, anorexia, vomiting, diarrhoea, increased blood pressure, increased respiratory rate and increased heart rate.

When discontinuing Proladone suppositories in a person who may be physically-dependent, the drug should not be ceased abruptly but withdrawn by tapering the dose gradually (see Ceasing opioids and section 4.2 Dose and Method of Administration).

**Accidental ingestion/exposure**

Accidental ingestion or exposure of Proladone suppositories, especially by children, can result in a fatal overdose of oxycodone. Patients and their caregivers should be given information on safe storage and disposal of unused Proladone suppositories (see section 6.4 Special precautions for storage and section 6.6 Special precautions for disposal).

**Hyperalgesia**

Hyperalgesia may occur with the use of opioids, particularly at high doses. Hyperalgesia may manifest as an unexplained increase in pain, increased levels of pain with increasing opioid dosages or diffuse sensitivity not associated with the original pain. Hyperalgesia should not be confused with tolerance (see Tolerance, dependence and withdrawal). If opioid induced hyperalgesia is suspected, the dose should be reduced and tapered off if possible. A change to a different opioid may be required.

**Ceasing opioids**

Abrupt discontinuation or rapid decreasing of the dose in a person physically dependent on an opioid may result in serious withdrawal symptoms and uncontrolled pain (see Tolerance, dependence and withdrawal). Such symptoms may lead the patient to seek other sources of licit or illicit opioids. Opioids should not be ceased abruptly in a patient who is physically dependent but withdrawn by tapering the dose slowly. Factors to take into account when deciding how to discontinue or decrease therapy include the dose and duration of the opioid the patient has been taking, the type of pain being treated and the physical and psychological attributes of the patient. A multimodal approach to pain management should be in place before initiating an opioid analgesic taper. During tapering,

patients require regular review and support to manage any increase in pain, psychological distress and withdrawal symptoms.

There are no standard tapering schedules suitable for all patients and an individualised plan is necessary. In general, tapering should involve a dose reduction of no more than 10 percent to 25 percent every 2 to 4 weeks (see section 4.2 Dose and Method of Administration). If the patient is experiencing increased pain or serious withdrawal symptoms, it may be necessary to go back to the previous dose until stable before proceeding with a more gradual taper.

When ceasing opioids in a patient who has a suspected opioid use disorder, the need for medication assisted treatment and/or referral to a specialist should be considered.

**Use in hepatic impairment**

Oxycodone should be given with caution or in reduced doses to patients with impaired liver function.

**Use in renal impairment**

Oxycodone should be given with caution or in reduced doses to patients with impaired kidney function.

**Use in the elderly**

Oxycodone should be administered with caution and in reduced dosages to elderly patients.

**Paediatric use**

Oxycodone should not be administered to children.

**Effects on laboratory tests**

No data available.

## 4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

Generally, the effects of oxycodone may be antagonised by acidifying agents and potentiated by alkalising agents.

The analgesic effect of oxycodone is potentiated by amphetamines, chlorpromazine and methocarbol. CNS depressants, such as other opioids, alcohol, anaesthetics, sedatives, benzodiazepines, hypnotics, barbiturates, phenothiazines, chloral hydrate glutethimide, gabapentinoids, cannabis, tricyclic antidepressants, antipsychotics, antihistamines, centrally-active anti-emetics and other CNS depressants may enhance the depressant effects of oxycodone (see Section 4.4 Special Warnings and Precautions for Use: Risks from concomitant use of benzodiazepines or other CNS depressants, including alcohol). MAOIs (including procarbazine hydrochloride), pyrazolidone antihistamines, β-blockers and alcohol may also enhance the depressant effect of oxycodone.

Oxycodone may increase the anticoagulant activity of coumarin derivatives.

## 4.6 FERTILITY, PREGNANCY AND LACTATION

**Effects on fertility**

No data available.

### Use in pregnancy

Oxycodone is Pregnancy Category C - *Drugs which, owing to their pharmacological effects, have caused or may be suspected of causing, harmful effects on the human fetus or neonate without causing malformations. These effects may be reversible. Accompanying texts should be consulted for further details.*

The only concern with oxycodone in pregnancy is with its use during labour when narcotic analgesics may cause respiratory depression in the newborn infant.

### Use in lactation

It is not known whether oxycodone is excreted in breast milk nor whether it has a harmful effect on the newborn. Therefore, oxycodone is not recommended for nursing mothers unless the expected benefits outweigh the potential risk.

## 4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Oxycodone may impair the mental and/or physical abilities needed for certain potentially hazardous activities, such as driving a car or operating machinery. Patients should be cautioned accordingly.

## 4.8 ADVERSE EFFECTS (UNDESIRABLE EFFECTS)

In normal doses, the most common side effects of opioid analgesics are nausea, vomiting, constipation, drowsiness and confusion. Micturition may be difficult and there may be ureteric or biliary spasm; there is also an antidiuretic effect. Dry mouth, sweating, facial flushing, anorexia, faintness, vertigo, bradycardia, supraventricular tachycardia, syncope, palpitations, orthostatic hypotension, hypothermia, restlessness, changes of mood and miosis also occur. Raised intracranial pressure occurs in some patients. Due to the histamine-releasing effect, reactions such as urticaria and pruritus occur in some individuals. Muscle rigidity has been reported following the administration of opioids. Larger doses produce respiratory depression and hypotension, with circulatory failure and deepening coma. Convulsions may occur in infants and children. Death may occur from respiratory failure. Toxic doses vary considerably with the individual and regular users may tolerate large doses.

In long term use, physical dependence and tolerance may develop.

The following withdrawal symptoms may be observed after narcotics are discontinued: body aches, diarrhoea, gooseflesh, loss of appetite, nervousness, restlessness, runny nose, sneezing, tremors or shivering, stomach cramps, nausea, trouble with sleeping, unusual increase in sweating and yawning, weakness, tachycardia and unexplained fever. With appropriate medical use of narcotics and gradual withdrawal from the drug, these symptoms are usually mild.

### Reporting suspected adverse reactions

Reporting suspected adverse reactions after registration 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 at www.tga.gov.au/reporting-problems.

## 4.9 OVERDOSE

### Symptoms

Serious overdosage with oxycodone is characterised by respiratory depression and somnolence progressing to coma and skeletal muscle flaccidity. Cardiac arrest and death may occur.

**Treatment**

Primary attention should be given to the re-establishment of adequate respiratory exchange through provision of a patent airway and the institution of assisted or controlled ventilation. The narcotic antagonist naloxone is a specific antidote against respiratory depression which may result from overdosage or unusual sensitivity to narcotics, including oxycodone. Therefore, an appropriate dose of naloxone (usual adult dose: 0.4 mg) should be administered, preferably by the intravenous route, simultaneously with efforts at respiratory resuscitation. Since the duration of action of oxycodone may exceed that of the antagonist, the patient should be kept under continued surveillance and repeated doses of the antagonist should be administered as needed to maintain adequate respiration.

An antagonist should not be administered in the absence of clinically significant respiratory or cardiovascular depression.

Oxygen, intravenous fluids, vasopressors and other supportive measures should be used as indicated.

Gastric emptying may be useful in removing unabsorbed drug.

In an individual physically dependent on narcotics, the administration of the usual dose of a narcotic antagonist will precipitate an acute withdrawal syndrome. The severity of this syndrome will depend on the degree of physical dependence and the dose of antagonist administered. The use of narcotic antagonists in such individuals should be avoided if possible. If a narcotic antagonist must be used to treat serious respiratory depression in the physically dependent patient, only 10 to 20% of the usual initial dose of the antagonist should be administered.

In severe toxicity, the cardiovascular system is usually depressed and requires supportive treatment. If hypotension is due to vasodilatation, plasma expansion, or even vasopressors may be required. Additional measures include support of electrolyte balance, maintenance of normal temperature, catheterisation of the bladder to avoid distension and symptomatic treatment of itching, nausea, vomiting, headache and confusion during the recovery period.

For information on the management of overdose, contact the Poisons Information Centre on 131126 (Australia).

## 5 PHARMACOLOGICAL PROPERTIES

### 5.1 PHARMACODYNAMIC PROPERTIES

**Mechanism of action**

The effects of oxycodone when combined with pectin are of longer duration than those of oxycodone hydrochloride.

The suppository has been found to reduce the severity of intractable pain due to carcinomatosis for up to 8 hours.

**Clinical trials**

No data available.

### 5.2 PHARMACOKINETIC PROPERTIES

**Absorption**

No data available.

### Distribution

No data available.

### Metabolism

No data available.

### Excretion

No data available.

## 5.3 PRECLINICAL SAFETY DATA

### Genotoxicity

No data available.

### Carcinogenicity

No data available.

# 6 PHARMACEUTICAL PARTICULARS

## 6.1 LIST OF EXCIPIENTS

Proladone suppositories also contain lactose monohydrate, maize starch, pectin, povidone, magnesium stearate and hard fat.

## 6.2 INCOMPATIBILITIES

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

## 6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG)[1]. The expiry date can be found on the packaging.

## 6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 25ºC.

## 6.5 NATURE AND CONTENTS OF CONTAINER

Proladone is presented as a strip pack of 12 suppositories.

Phebra product code - TAB007

## 6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy.

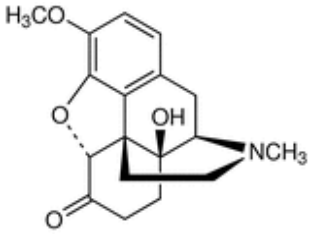
## 6.7 PHYSICOCHEMICAL PROPERTIES

[1] AUST R 14965

Chemical name: 6-deoxy-7, 8-dihydro-14-hydroxy-3-*O*-methyl-6-oxomorphine.

The molecular weight of oxycodone is 315.4. The molecular formula is $C_{18}H_{21}NO_4$.

**Chemical structure**




**CAS number**

76-42-6

## 7 MEDICINE SCHEDULE (POISONS STANDARD)

S8 - Controlled Drug

## 8 SPONSOR

Phebra[2] Pty Ltd, 19 Orion Road, Lane Cove West, NSW 2066, Australia.
Telephone: 1800 720 020

## 9 DATE OF FIRST APPROVAL

9 Sep 1991

## 10 DATE OF REVISION

24 Apr 2020

**SUMMARY TABLE OF CHANGES**

| Section Changed | Summary of new information |
|---|---|
| **All** | PI reformatted to align with new form |
| **-** | Added boxed warning per opioid reforms |
| **4.3** | Add contraindication per opioid reforms |
| **4.4** | Add warnings related to opioid reforms |
| **4.5** | Update text related to opioid reforms |

[2] Phebra and the Phi symbol are trademarks of Phebra Pty Ltd, 19 Orion Road, Lane Cove West, NSW 2066, Australia.