Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Codinex Codeine Phosphate 15mg/5ml Oral Solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml contains 15 mg codeine phosphate (equivalent to 11.8 mg codeine).
Each 5 ml also contains 75 micrograms sunset yellow (E110), 645 mg sorbitol and 0.32 micorgrams ethanol.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Oral solution
Clear, dark yellow, orange flavoured oral solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

As an anti-tussive for unproductive cough.

4.2 Posology and method of administration

Adult:
The dose is 5 to 7.5 ml (15 mg to 22.5 mg) – (equivalent to 11.8 to 17.6 mg of codeine base) up to three to four times a day.
The dose may be repeated every 4 to 6 hours if required, but with a maximum daily dose of 30 mls in any 24 hours.
The stated dose and frequency should not be exceeded.
Treatment should not exceed 3 days without medical supervision.

Elderly:
Dosage should be reduced in elderly or debilitated patients.

Paediatric population:
Children aged less than 12 years:
Codeine is contraindicated in children below the age of 12 years (see sections 4.3).

Children aged 12 years to 18 years:
As for the adult dose above.
Codeine is not recommended for use in children aged 12 years to 18 years with compromised respiratory function (see section 4.4).

Method of administration
For oral administration.

4.3 Contraindications

Hypersensitivity to the active substance(s) or to any of the excipients listed in section 6.1.
Liver disease: drug may accumulate.
Ventilatory failure: condition may be exacerbated.

In children below the age of 12 years due to an increased risk of developing serious and life-threatening adverse reactions.
In women during breastfeeding (see section 4.6).
In patients for whom it is known they are CYP2D6 ultra-rapid metabolisers.

4.4 Special warnings and precautions for use

CYP2D6

Codeine is metabolised by the liver enzyme CYP2D6 into morphine, its active metabolite. If a patient has a deficiency or is completely lacking this enzyme an adequate therapeutic effects will not be obtained. Estimates indicate that up to 7% of the caucasian population may have this deficiency. However, if the patient is an ultra-rapid metaboliser there is an increased risk of developing side effects of opioid toxicity even at commonly prescribed doses. These patients convert codeine into morphine rapidly resulting in higher than expected serum morphine levels. General symptoms of opioid toxicity include confusion, somnolence, shallow breathing, small pupils, nausea, vomiting, constipation and lack of appetite. In severe cases this may include symptoms of circulatory and respiratory depression, which may be life-threatening and very rarely fatal. Estimates of prevalence of ultra-rapid metabolisers in different populations are summarized below:

Population	Prevalence %
African/Ethiopian	29%
African American	3.4% to 6.5%
Asian	1.2% to 2%
Caucasian	3.6% to 6.5%
Greek	6.0%
Hungarian	1.9%
Northern European	1%-2%

Physical and psychological dependence

Prolonged regular use, except under medical supervision, may lead to physical and psychological dependence (addiction) and result in withdrawal symptoms such as restlessness and irritability, once the drug is stopped.

Children with compromised respiratory function

Codeine is not recommended for use in children in whom respiratory function might be compromised including neuromuscular disorders, severe cardiac or respiratory conditions, upper respiratory or lung infections, multiple trauma or extensive surgical procedures. These factors may worsen symptoms of morphine toxicity.

Risk from concomitant use of sedative medicines such as benzodiazepines or related drugs

Concomitant use of Codinex and sedative medicines such as benzodiazepines or related drugs may result in sedation, respiratory depression, coma and death. Because of these risks, concomitant prescribing with these sedative medicines should be reserved for patients for whom alternative treatment options are not possible. If a decision is made to prescribe Codinex concomitantly with sedative medicines, the lowest effective dose should be used, and the duration of treatment should be as short as possible.

The patients should be followed closely for signs and symptoms of respiratory depression and sedation. In this respect, it is strongly recommended to inform patients and their caregivers to be aware of these symptoms (see section 4.5).

Excipients:

Sunset Yellow may cause allergic reactions.

This product contains sorbitol (E420). Patients with rare hereditary problems of fructose intolerance should not take this medicine.

This product contains small amounts of ethanol (alcohol), less than 100 mg per 5ml.

4.5 Interaction with other medicinal products and other forms of interaction

CNS depressants, Anticholinergic, Hydroxyzine and Methadone - concurrent use of these medicines may result in potentiation of effects, hypotensive and CNS depressant effects may be increased. Enhances sedative effects with alcohol of antipsychotics. Metoclopramide and codeine have opposing effects on gastro-intestinal activity.

The sedative effect of hypnotics and anxiolytics may be potentiated by codeine. The concomitant use of opioids with sedative medicines such as benzodiazepines or related drugs increases the risk of sedation, respiratory depression, coma and death because of additive CNS depressant effect. The dose and duration of concomitant use should be limited (see section 4.4).

Hypertensive crisis may be caused by concurrent use of codeine and monoamine oxidase inhibitors.

4.6 Fertility, pregnancy and lactation

Risk benefit should be considered before using codeine during pregnancy and it should only be used if considered essential by the physician. Codeine crosses the placenta and is excreted in small amounts in breast milk. Regular use during pregnancy may cause physical dependency in the foetus, depression of neonatal respiration and withdrawal effects in the neonate. Teratogenic effects in humans have not been documented but controlled studies have not been done. There is a risk of gastric stasis in the mother during labour, which may lead to inhalation pneumonia.

Codeine is contraindicated in women during breastfeeding (see section 4.3).
At normal therapeutic doses codeine and its active metabolite may be present in breast milk at very low doses and is unlikely to adversely affect the breast fed infant. However, if the patient is an ultra-rapid metaboliser of codeine, higher levels of the active metabolite, morphine may be present in breast milk and on very rare occasions may result in symptoms of opioid toxicity in the infant, which may be fatal.

If symptoms of opioid toxicity develop in either the mother or the infant, then all codeine containing medicines should be stopped and alternative non-opioid analgesics prescribed. In severe cases consideration should be given to prescribing naloxone to reverse these effects.

4.7 Effects on ability to drive and use machines

Codeine may cause drowsiness. Patients receiving this medication should not drive or operate machinery unless it has been shown not to effect mental or physical ability.

This medicine can impair cognitive function and can affect a patient's ability to drive safely. When prescribing this medicine, patients should be told:
· The medicine is likely to affect your ability to drive.
· Do not drive until you know how the medicine affects you.
· It may be an offence to drive while under the influence of this medicine.

4.8 Undesirable effects

Gastrointestinal side effects, constipation, loss of appetite, flushing of face might occasionally occur; respiratory depression may be experienced; sputum retention may occur particularly, in patients with chronic bronchitis and bronchiectasis. Hypersensitivity reactions can occur (including rash, urticaria and pruritis).

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, Website: www.hpra.ie.

4.9 Overdose

In cases of overdosage supportive therapy is recommended. Gastric lavage should be carried out and a saline purgative may be given to reduce absorption from the gastro-intestinal tract. Symptomatic treatment of respiratory embarrassment should be given.

If respiratory is seriously depressed intravenous naloxone HCL may be required.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Codeine is an opium alkaloid with activity similar to but weaker than that of morphine. It is given orally in the treatment of mild to moderate pain in tablet form but is used as an antitussive in the form of linctuses. Ingestion of codeine phosphate produces peak plasma concentration in about one hour. Codeine is metabolised by O- and N-demethylation in the liver to morphine, norcodeine, and other metabolites including normorphine and hydrocodone. Codeine and its metabolites are excreted almost entirely by the kidney. Protein binding is very low. Half-life from 2.5 to 4 hours after administration by mouth.

5.2 Pharmacokinetic properties

Not applicable.

5.3 Preclinical safety data

No information provided.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium benzoate (E 211)
Citric acid monohydrate
Saccharin sodium
Sunset yellow (E 110)
Sorbitol solution 70%
Sodium carmellose
Propylene glycol
Orange flavour (contains ethanol)
Purified water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Do not store above 25°C. Store in the original container.

6.5 Nature and contents of container

Amber glass (Type III) bottles with child-resistant closures containing 100 ml and 150 ml.

Amber glass (Type III) bottles with child-resistant closures containing 200 ml or 500 ml.

High density polyethylene bottles with polypropylene tamper-evident screw caps containing 1L or 2L.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Pinewood Laboratories Ltd
Ballymacarbry
Clonmel
Co. Tipperary
Ireland

8 MARKETING AUTHORISATION NUMBER

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 25 August 1981

Date of last renewal: 25 August 2006

10 DATE OF REVISION OF THE TEXT

December 2024