

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Codant 30 mg Tablets.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains Codeine Phosphate Hemihydrate 30 mg (equivalent to 23.4 mg Codeine).

Also contains 43 mg of lactose monohydrate (equivalent to 40.9 mg lactose).

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablets.

White, circular biconvex tablets.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

- 1) Management of mild to moderate pain.
- 2) As an anti-tussive for non-productive cough.

4.2 Posology and method of administration

Codant tablets are for oral administration only.

Adults

The usual dose is 30mg (one tablet), repeated 4-hourly as required.

Children

Not recommended.

4.3 Contraindications

- Hypersensitivity to codeine, other opioids or any of the excipients in the tablets.
- Conditions associated with raised intracranial pressure, and in head injury and coma

Internal obstruction.

Respiratory depression.

- Hepatic failure
- Obstructive airways disease e.g. emphysema
- Asthma – Opioids should not be administered during an asthma attack
- Acute alcoholism

- Risk of paralytic ileus
- Use of codeine containing products is contraindicated in mothers who are breastfeeding unless prescribed by a doctor.

4.4 Special warnings and precautions for use

Codeine Phosphate should be used in caution in the following conditions:

- Impaired respiratory function (avoid in chronic obstructive pulmonary disease) and asthma (avoid during an acute attack)
- There is a possible risk of CNS excitation or depression with concomitant use of opioids with MAOIs and use is not recommended (see section 4.5)
- Hepatic Impairment - avoid if severe
- Renal Impairment
- Hypothyroidism
- Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicines
- Inflammatory bowel disease – codeine reduces peristalsis, increases tone and segmentation in the bowel and can raise colonic pressure, therefore should be used with caution in diverticulitis, acute colitis, diarrhoea associated with pseudomembranous colitis or after bowel surgery.
- Convulsions - may be induced or exacerbated
- Drug abuse or dependence (including alcoholism)
- Gall bladder disease or gall stones – opioids may cause biliary obstructions

Avoid in biliary disorders

- Gastro intestinal surgery – use with caution after recent GI surgery as codeine may alter GI mobility
- Urinary tract surgery –following recent surgery patient will be more prone to urinary retention caused directly by spasm of the urethral sphincter, and via constipation caused by codeine.
- Pheochromocytoma – opioids may stimulate catecholamine release by inducing the release of endogenous histamine.
- Prostatic hypertrophy
- Adrenocortical insufficiency, e.g. Addison's Disease.
- Hypotension and shock
- Myasthenia gravis
- Elderly patients may metabolise and eliminate opioid analgesics more slowly than younger patients, a reduced dose is recommended in elderly patients.

- The risk benefit of continued use of codeine should be assessed regularly by the Prescriber

Regular or prolonged use may produce psychic and physical dependence.

Tolerance may develop with repeated administration of codeine.

Agents which inhibit intestinal motility have been reported to induce toxic megacolon in some patients with ulcerative colitis.

Codeine is partially metabolised by CYP2D6. If a patient has a deficiency or is completely lacking this enzyme they will not obtain adequate analgesic effects. Estimates indicate that up to 7% of the Caucasian population may have this deficiency. However, if the patient is an ultrarapid metaboliser there is an increased risk of developing side effects of opioid toxicity even at low doses. General symptoms of opioid toxicity include nausea, vomiting, constipation, lack of appetite and somnolence. In severe cases this may include symptoms of circulatory and respiratory depression. Estimates indicate that up to 1 to 2% of the Caucasian population may be ultra-rapid metabolisers.

4.5 Interaction with other medicinal products and other forms of interaction

Concomitant combinations not recommended (see section 4.4) :

- MAOIs (e.g. linezolid, moclobemide, selegiline) due to the possible risk of excitation or depression - avoid concomitant use and for 2 weeks after discontinuation of MAOI

Combinations to be used with caution:

Respiratory related:

- Alcohol - enhanced sedative and hypotensive effect, increased risk of respiratory depression
- Sedative antihistamines – enhanced sedative and hypotensive effect and increased risk of respiratory depression.
- Hypnotics and anxiolytics - enhanced sedative effect, increased risk of respiratory depression

Gastrointestinal related:

- Anticholinergics (e.g. atropine) - risk of severe constipation which may lead to paralytic ileus, and/or urinary retention.
- Metoclopramide and domperidone – antagonise effect on GI activity
- Antidiarrhoeal drugs (e.g. loperamide, kaolin) - increased risk of severe constipation
- CNS related:
 - Anaesthetics - enhanced sedative and hypotensive effect
 - Tricyclic antidepressants – enhanced sedative effect
 - Antipsychotics - enhanced sedative and hypotensive effect
 - Opioid antagonists e.g. buprenorphine, naltrexone, naloxone – may precipitate withdrawal symptoms
 - Quinidine - reduced analgesic effect
 - Antihypertensive drugs – enhanced hypotensive effect

- Pharmacokinetic interactions
- Ciprofloxacin - avoid premedication with opioids as they reduce plasma concentration
- Ritonavir may increase plasma levels of opioid analgesics such as codeine
- Mexiletine - delayed absorption of mexiletine
- Cimetidine inhibits the metabolism of opioid analgesics causing increased plasma concentration of codeine

4.6 Fertility, pregnancy and lactation

There is inadequate evidence of the safety of codeine in human pregnancy and administration of the drug during pregnancy should be considered only if the potential benefit justifies the potential risk to the foetus.

Opioid analgesics cross the placenta and newborn infants should be observed closely for signs of respiratory depression if the mother has received codeine during labour. Should such signs/symptoms be noted in mother or baby, the mother should immediately stop taking all codeine-containing medicines and seek medical advice.

Gastric stasis and a risk of inhalation pneumonia could occur in the mother during labour. Administration should be avoided during the late stages of labour and during the delivery of a premature infant.

At normal therapeutic doses codeine 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 CYP2D6, higher levels of the active metabolites may be present in breast milk and on very rare occasions may result in symptoms of opioid toxicity in the infant.

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 sedation and dizziness and patients should be advised not to drive or to operate machinery if affected.

4.8 Undesirable effects

- Immune system disorders: (may be caused by histamine release) – including rash, urticaria, pruritus, difficulty breathing, increased sweating, redness or flushed face.
- Nervous system disorders: confusion, drowsiness, malaise, tiredness, vertigo, dizziness, changes in mood, hallucinations, CNS excitation (restlessness/excitement), convulsions, mental depression, headache, or nightmares, raised intracranial pressure, tolerance or dependence, dysphoria hypothermia
- Eye disorders: - miosis, blurred or double vision
- Cardiac disorders: bradycardia, palpitations, hypotension, orthostatic hypotension, tachycardia.
- Respiratory, thoracic and mediastinal disorders: respiratory depression with larger doses.
- Gastrointestinal disorders: constipation (too constipating for long-term use), biliary spasm, nausea, vomiting, dry mouth.
- Musculoskeletal, connective tissue and bone density: muscle rigidity

- Renal and urinary disorders: urethral spasm, antidiuretic effect, urinary retention
- Reproductive system and breast disorders: decrease in libido and potency
- Withdrawal effects: abrupt withdrawal precipitates a withdrawal syndrome
- Symptoms may include tremor, insomnia, restlessness, irritability, anxiety, depression, anorexia, nausea, vomiting, diarrhoea, sweating, lacrimation, rhinorrhoea, sneezing, yawning, piloerection, mydriasis, weakness, pyrexia, muscle cramps, dehydration, and increase in heart rate, respiratory rate and blood pressure.

NOTE – tolerance diminishes rapidly after withdrawal so a previously tolerated dose may prove fatal.

- Regular prolonged use of codeine is known to lead to addiction and tolerance.

Symptoms of restlessness and irritability may result when treatment is then stopped.

- Prolonged use of a painkiller for headaches can make them worse

4.9 Overdose

Serious overdosage with codeine is characterised by respiratory depression, extreme somnolence progressing to stupor or coma, skeletal muscle flaccidity and sometimes bradycardia and hypotension. The triad of coma, pinpoint pupils and respiratory depression is strongly suggestive of opiate poisoning.

In cases of recent overdosage, the stomach should be emptied by aspiration and lavage. A patent airway should be maintained and assisted or controlled ventilation should be instituted if required. The narcotic antagonist naloxone hydrochloride may be administered to counteract significant respiratory depression if it occurs.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Codeine is a centrally acting analgesic. The anti-tussive activity of codeine is probably due to its depressant effect on the medullary cough centre in the brain.

5.2 Pharmacokinetic properties

Codeine phosphate is readily absorbed from the gut. The drug is metabolized in the liver and is excreted through urine as conjugates. The plasma half-life is 3-4 hours.

Codeine crosses the blood-brain and placental barriers and detectable amounts have been reported to occur in the breast milk.

5.3 Preclinical safety data

No relevant information other than that which is reported in other sections of the Summary of Product Characteristics.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Colloidal Anhydrous Silica
Lactose Monohydrate
Magnesium Stearate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

4 years.

6.4 Special precautions for storage

Do not store above 25°C.

Store in the original container in order to protect from light.

6.5 Nature and contents of container

Polypropylene tablets containers with tamper evident polyethylene caps.

Pack size: 100 tablets.

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

Antigen Pharmaceuticals Ltd
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8 MARKETING AUTHORISATION NUMBER

PA 73/29/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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Date of last renewal: 1st April 2008

10 DATE OF REVISION OF THE TEXT

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