

PRODUCT INFORMATION

Bis-Pectin oral suspension

Product description

The product is a pale green, milky liquid containing codeine phosphate 0.54mg/mL, aluminium hydroxide dried 25mg/mL, kaolin light 125mg/mL, pectin 8mg/mL, propylene glycol, chloroform, emerald green C109, methyl hydroxybenzoate, propyl hydroxybenzoate, sodium benzoate, xanthan gum, purified water, sucrose, spearmint oil, tartrazine.

Pharmacology

Pharmacokinetics:

Codeine: Codeine and its salts are well absorbed from the gastrointestinal tract: peak plasma-codeine concentrations occur at about one hour after ingestion of codeine phosphate.

Codeine is metabolised by *O*- and *N*-demethylation in the liver (via the cytochrome P450 system) to morphine (about ten per cent of a codeine dose is demethylated to morphine), norcodeine and other metabolites including normorphine and hydrocodone. Codeine and its metabolites are excreted almost entirely by the kidney, mainly as conjugates with glucuronic acid. Approximately 3% to 16% of a dose is eliminated unchanged in the urine.

About 8% of people metabolise drugs poorly via CYP2D6, and are likely to obtain reduced benefit from codeine due to reduced formation of the active metabolite, morphine.

The plasma half-life of codeine has been reported to be between 3 and 4 hours after oral administration.

Kaolin light: Kaolin light is an adsorbent antidiarrhoeal agent that has been used as an adjunct to rehydration therapy in the management of diarrhoea. It is often combined with other antidiarrhoeals, especially pectin.

Pectin: Pectin is an adsorbent and bulk-forming agent and is present in multi-ingredient preparations such as for the management of diarrhoea.

Aluminium hydroxide dried: Aluminium hydroxide, given by mouth, slowly reacts with the hydrochloric acid in the stomach to form soluble aluminium chloride, some of which is absorbed. The presence of food or other factors that decrease gastric emptying prolongs the availability of aluminium hydroxide to react and may increase the amount of aluminium chloride formed. About 100 to 500 micrograms of the cation is reported to be absorbed from standard daily doses of an aluminium-containing antacid, leading to about a doubling of usual aluminium concentrations in the plasma of patients with normal renal function. Absorbed aluminium is eliminated in the urine, and patients with renal failure are therefore at particular risk of accumulation (especially in bone and the CNS), and aluminium toxicity. The aluminium compounds remaining in the

gastrointestinal tract, which account for most of a dose, form insoluble, poorly absorbed aluminium salts in the intestines including hydroxides, carbonates, phosphates and fatty acid derivatives, which are excreted in the faeces.

Pharmacodynamics/Mechanism of action:

Bis-pectin contains codeine which reduces intestinal motility, kaolin and pectin which are both adsorbents and aluminium hydroxide, an antacid.

Codeine:

Codeine has an exceptionally low affinity for opioid receptors. The antidiarrhoeal effect of codeine is thought to be due to its conversion to morphine which acts by several different mechanisms, mediated principally through either the mu- or delta- opioid receptors on enteric nerves, epithelial cells and muscle. Activation of opioid receptors in the gut wall decreases bowel motility, decreases intestinal secretions and increases fluid absorption. This in turn increases the viscosity of the bowel contents.

Aluminium hydroxide: Aluminium hydroxide is an antacid.

Kaolin light: Kaolin light is an adsorbent agent.

Pectin: Pectin is an adsorbent and bulk-forming agent.

Indications

For the treatment of diarrhoea, nausea, vomiting, gastroenteritis and nervous dyspepsia.

Contraindications

Bis-pectin is contraindicated for use in patients with known hypersensitivity or idiosyncratic reaction to codeine or other opiates, aluminium hydroxide, kaolin, pectin or any of the other ingredients in the product (see 'Product description' above).

It is also contraindicated for use in patients:

- with acute respiratory depression
- with chronic constipation
- during labour when delivery of a premature infant is anticipated as it may produce codeine withdrawal symptoms in the neonate
- with active alcoholism
- with diarrhoea caused by pseudomembranous colitis or poisoning (until the causative organism or toxin has been eliminated from the gastrointestinal tract, since codeine may slow down the elimination, thereby prolonging the diarrhoea)
- with renal failure (absorbed aluminium is eliminated in the urine, and patients with renal failure are therefore at particular risk of accumulation (especially in bone and the CNS), and aluminium toxicity)
- with intestinal obstruction.

Refer to 'Interactions with other medicines' for additional information.

Bis-pectin should not be used in children under 8 years of age.

Precautions

Bis-pectin should be used with caution in patients with:

- impaired hepatic function
- impaired renal function
- decreased respiratory reserve e.g. asthma or chronic obstructive pulmonary disease (COPD)
- pre-existing respiratory depression
- raised intracranial pressure or head injury
- prostatic hypertrophy
- hypotension
- hypothyroidism.

It should also be used with caution in patients who:

- have a history of drug abuse
- are taking other respiratory depressants or sedatives, including alcohol
- have had recent gastrointestinal tract surgery

Codeine may obscure the diagnosis or the course of gastrointestinal diseases.

Prolonged use of codeine may produce physical and psychological dependence.

Codeine may cause drowsiness. Those affected should not drive or operate machinery.

Aluminium hydroxide may be unsafe in patients with porphyria because it has been shown to be porphyrinogenic in *animals*.

Refer to 'Interactions with other medicines' for additional information.

Use in pregnancy

Opioid analgesics may cause respiratory depression in the newborn infant. Prolonged high-dose use of codeine prior to delivery may produce codeine withdrawal symptoms in the neonate. Kaolin is a hydrated aluminium silicate clay. Aluminium load may occur with the use of kaolin, especially during pregnancy. Therefore, Bis-pectin is not recommended for use in pregnancy.

Use in lactation

Aluminium absorbed from maternal ingestion of aluminium-containing antacids is believed to be low when taken in usual antacid doses by patients with normal renal function. Thus, concentrations in breast milk are likely low, if present at all. Premature infants and those born with renal insufficiency may be at increased risk of aluminium accumulation. Kaolin and pectin are not absorbed into the systemic circulation.

Codeine appears in breast milk in low concentrations and may cause respiratory depression in newborn infants.

In breastfeeding mothers, who are ultra rapid metabolisers of codeine, higher than expected serum and breast milk morphine levels can occur. Morphine toxicity in babies can cause excessive somnolence, hypotonia and difficulty breastfeeding or breathing. In severe cases of respiratory depression death can occur.

Breastfeeding mothers should be informed about carefully monitoring the infant during treatment for any sign and symptom of morphine toxicity such as increased drowsiness or sedation, difficulty breastfeeding, breathing difficulties and decreased tone and seeking immediate medical care if such symptoms or signs are noticed

Bis-pectin is therefore not recommended for breastfeeding mothers unless the potential benefits to the patient outweigh the possible risk to the infant.

Use in the elderly

The elderly are more likely to have age related renal impairment and may be more susceptible to the respiratory depressant effects of codeine.

Interaction with other medicines

The following interactions have been noted:

- CNS depressants – concomitant use of codeine with central nervous system depressants (e.g. barbiturates, chloral hydrate, sedatives, alcohol and centrally acting muscle relaxants) can cause additive CNS depression
- Anticholinergics – concurrent use of codeine with anticholinergic agents may increase the risk of severe constipation and/or urinary retention
- Antihypertensives – hypotensive effects may be potentiated when used concurrently with codeine and lead to orthostatic hypotension
- Antiperistaltic antidiarrhoeals (e.g. loperamide) – concurrent use with codeine may increase the risk of severe constipation
- Metoclopramide – codeine may antagonise the effects of metoclopramide on gastrointestinal activity
- Monoamine oxidase inhibitors (MAOIs) – concurrent administration or use within 14 days of ceasing MAOIs may enhance the potential respiratory depressant effects of codeine
- Opioid analgesics – concurrent use of codeine and other opioid receptor antagonists is usually inappropriate as additive CNS depression, respiratory depression and hypotensive effects may occur
- Substances that inhibit CYP2D6 such as quinidine, phenothiazines and antipsychotic agents can interfere with the metabolism of codeine to morphine, reducing the effect of codeine
- Tranquillisers, sedatives and hypnotics – codeine may potentiate the effects of these substances
- Kaolin can form insoluble complexes with a number of other drugs in the gastrointestinal tract and reduce their absorption; oral doses should not be taken at the same time as other drugs
- As a bulk-forming agent, pectin may lower the transit time through the gut and may affect the absorption of other drugs
- By alterations in gastric pH and emptying and by direct adsorption of complexes that are not absorbed, aluminium hydroxide interacts with many other medicines.

Adverse reactions

The most common adverse effects associated with codeine are nausea, vomiting, drowsiness, dizziness and constipation.

Other side effects include: cough suppression, respiratory depression, euphoria, dysphoria, skin rashes, histamine release (hypotension, flushing of the face, tachycardia, breathlessness) and other allergic reactions.

Aluminium salts are not, in general, well absorbed from the gastrointestinal tract, and systemic effects are therefore rare in patients with normal renal function. Aluminium hydroxide, like other aluminium compounds, is astringent and may cause constipation; large doses can cause intestinal obstruction. Excessive doses, or even normal doses in patients with low-phosphate diets, may lead to phosphate depletion accompanied by increased bone resorption and hypercalciuria with the risk of osteomalacia.

Dosage

Shake the bottle well before use. Adults and children 12 years and over: 15mL hourly for 3 doses, then at 3 hourly intervals. Children 8 – 11 years: 11mL every 4 hours. Medical advice should be sought if symptoms persist for more than 48 hours. Not to be used in children under 8 years of age.

Overdosage

If an overdose is taken or suspected, contact the Poisons Information Centre (in Australia, call 131 126; in New Zealand call 0800 764 766) for advice.

Presentation

Bis-pectin is presented in a 200mL bottle with a child-resistant closure. It is a pale green milky liquid.

Poisons schedule: Bis-pectin is included in Schedule 3 (pharmacist only) of the *Standard for the Scheduling of Drugs and Poisons* (SUSDP)

Sponsor details:

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