

# PRODUCT INFORMATION

## ACTACODE

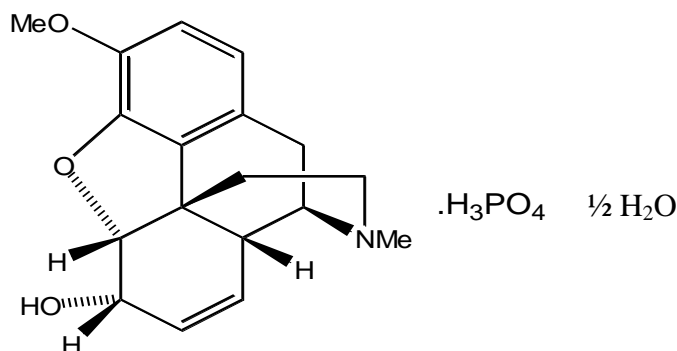
### NAME OF THE DRUG

Actacode codeine linctus contains codeine phosphate 5 mg/mL.

### DESCRIPTION

Codeine phosphate is a small, colourless, odourless crystal or a white, odourless crystalline powder. Codeine phosphate is soluble in 4 parts of water, slightly soluble in ethanol (96%), practically insoluble in chloroform and ether.

Codeine phosphate is (5*R*,6*S*)-7,8-didehydro-4,5-epoxy-3-methoxy-*N*-methylmorphinan-6-ol dihydrogen orthophosphate hemihydrate. It has the following chemical structure:



The molecular formula is  $\text{C}_{18}\text{H}_{21}\text{NO}_3 \cdot \text{H}_3\text{PO}_4 \cdot \frac{1}{2}\text{H}_2\text{O}$ . The molecular weight is 406.4. (CAS - 41444-62-6)

Actacode codeine linctus contains the following excipients: Propylene glycol, sucrose, glycerol, hydroxybenzoic acid esters (present in Nipastat), potassium sorbate, hydrochloric acid, sodium hydroxide and water - purified.

### PHARMACOLOGY

#### Actions:

Codeine causes suppression of the cough reflex by a direct effect on the cough centre in the medulla of the brain and appears to exert a drying effect on the respiratory tract mucosa and to increase viscosity of bronchial secretions.

On a weight basis, antitussive activity of codeine is less than that of morphine. Codeine also has mild analgesic and sedative effects.

#### Pharmacokinetics

Codeine is well absorbed after administration by mouth. It is metabolised in the liver to morphine and norcodeine, which with codeine are excreted in the urine, partly as conjugates with glucuronic acid. Patients who metabolise drugs poorly via CYP2D6 are likely to obtain

reduced benefit from codeine due to reduced formation of the active metabolite. Most of the excretion products appear in the urine within 6 hours and excretion of up to 86% of the dose is almost complete in 24 hours. About 70% of the codeine is excreted free or conjugated, about 10% as free and conjugated morphine, and about 10% as free and conjugated norcodeine. Only traces are excreted in the faeces.

## INDICATIONS

Relief of unproductive, dry and intractable coughs associated with colds and flu.

## CONTRAINDICATIONS

- Acute respiratory depression, especially in the presence of cyanosis and excessive bronchial secretion, since codeine may exacerbate the condition.
- After operations on the biliary tract as codeine may cause biliary contraction.
- In the presence of acute alcohol intoxication, head injuries and conditions in which intracranial pressure is raised.
- Bronchial asthma attack or in heart failure secondary to chronic lung disease.
- Codeine is contraindicated in patients taking MAOI's or within ten days of stopping such treatment.
- Due to codeine's structural similarity to morphine and oxycodone, patients experiencing systemic allergy (generalised rash, shortness of breath) to these drugs should not receive codeine.
- Codeine is contraindicated in patients with diarrhoea caused by poisoning, until the toxic substance has been eliminated from the gastrointestinal tract, or diarrhoea associated with pseudomembranous colitis caused by antibiotic administration since codeine may slow the elimination of the toxic material or antibiotic.
- Actacode is contraindicated in patients with a past history of allergic reactions to codeine.

## PRECAUTIONS

Codeine should be used with caution in elderly or debilitated patients because of the danger of respiratory or cardiac depression.

Codeine should be given with caution or in reduced doses to patients with hypothyroidism, adrenocortical insufficiency, impaired hepatic function, or shock.

Codeine should be administered with caution in patients with prostatic hypertrophy, urethral stricture or recent urinary tract surgery since codeine may cause urinary retention.

Patients should be warned that codeine might impair their ability to perform activities requiring mental alertness or physical coordination (eg operating machinery, driving a motor vehicle).

Codeine should be used with caution in patients with a history of drug abuse or dependence, including alcoholism.

Prolonged use of high doses of codeine has produced dependence of the morphine type in a very small proportion of users. Codeine produces less euphoria and sedation than morphine and is not a completely satisfactory substitute for morphine in morphine addicts. Withdrawal symptoms develop more slowly than with morphine and are milder.

### **Use in Pregnancy:** Category A.

Opioid analgesics cross the placenta. Regular use during pregnancy may cause physical dependence in the foetus, leading to withdrawal symptoms in the neonate.

### **Use in Lactation:**

Limited evidence suggests that individuals who are ultra-rapid metabolisers (those with a specific CYP2D6 genotype) may convert codeine to its active metabolite, morphine, more rapidly and completely than other people. In nursing mothers, this metabolism can result in higher than expected serum and breast milk morphine levels. One published case report of an infant death raises concern that nursing babies may be at increased risk of morphine overdose if their mothers are taking codeine and are ultra-rapid metabolisers of the drug. Actacode codeine linctus should be avoided in breastfeeding women.

### **Paediatric Use:**

Codeine is not recommended for use in children without medical supervision.

### **Use in the Elderly:**

The elderly are more likely to have age-related renal impairment and may be more susceptible to the respiratory effects of opioid analgesics. Dose reduction may be required.

### **Carcinogenicity, Mutagenicity, Effects on Fertility:**

No significant effects have been reported.

### **Interactions with Other Drugs**

#### *General anaesthetics:*

Codeine may potentiate the effects of general anaesthetics.

#### *Tranquillisers, sedatives and hypnotics:*

Codeine may potentiate the effects of these drugs.

#### *CNS depressants:*

Codeine may potentiate the effects of CNS depressants.

#### *Alcohol:*

Codeine may potentiate the effects of alcohol.

#### *Opioid analgesics:*

Codeine may potentiate the effects of opioid agonists.

#### *Antihistamines:*

Concomitant use of codeine and antihistamines with anticholinergic effects may result in an increased risk of severe constipation and/or urinary retention. Codeine may potentiate the CNS depressant effects of certain antihistamines.

#### *Monoamine Oxidase Inhibitors:*

Serious and sometimes fatal reactions have occurred in patients concurrently administered MAO inhibitors and pethidine. Codeine should not be given to patients taking non-selective MAO inhibitors or within 10 days of stopping such treatment. Caution is advised with the combination of codeine and selective MAO inhibitors (reversible inhibitors of Monoamine Oxidase A).

#### *Quinidine:*

Quinidine interferes with the metabolism of codeine to morphine lowering the analgesic effect of codeine.

#### *Cimetidine:*

Cimetidine may reduce the metabolism of codeine, enhancing the possibility of codeine toxicity.

### **Effects on laboratory tests**

#### *Plasma amylase and lipase activity:*

Codeine may cause increased biliary tract pressure, thus increasing plasma amylase and/or lipase concentrations.

*Gastric emptying studies:*

Gastric emptying is delayed by codeine so gastric emptying studies will not be valid.

## **ADVERSE REACTIONS**

### ***Gastrointestinal***

*Common*

- Constipation

*Uncommon*

- Nausea
- Vomiting
- Dry mouth

### ***Neurological***

*Common*

- Dizziness
- Drowsiness

*Uncommon*

- Euphoria, dysphoria, nervousness, restlessness
- Paradoxical CNS stimulation (especially in children)
- Confusion
- Headache
- Blurred or double vision

### ***Hypersensitive***

*Uncommon*

- Skin rashes and other allergic reactions (pruritus, urticaria)
- Histamine release (hypotension, sweating, flushing of the face, tachycardia, breathlessness)

### ***Genitourinary***

*Uncommon*

- Urinary retention or hesitance

### ***Withdrawal syndrome***

A withdrawal syndrome may be precipitated when chronic administration of codeine is discontinued or opioid antagonists administered. The following symptoms may be observed: body aches, diarrhoea, gooseflesh, loss of appetite, nervousness or restlessness, runny nose, sneezing, tremors, shivering, stomach cramps, nausea, sleep disturbance, increased sweating and yawning, weakness, tachycardia, fever, irritability, vomiting, mydriasis.

## **DOSAGE AND ADMINISTRATION**

*Adults:* 5 mL every four to six hours.

## **OVERDOSAGE**

### ***Symptoms:***

Symptoms of codeine overdose include vomiting, hypotension, sweating, central stimulation with exhilaration and convulsions in children, drowsiness, respiratory depression, cyanosis, miosis and coma.

### ***Treatment:***

Treatment of overdose involves the following measures:

- Support respiratory and cardiovascular function. Assisted ventilation may be necessary.

- Activated charcoal may reduce absorption of the drug if given within one or two hours after ingestion. In patients who are not fully conscious or have impaired gag reflex, consideration should be given to administering activated charcoal via a nasogastric tube, once the airway is protected.
- If clinically significant respiratory or cardiac depression is present, give naloxone. The usual adult dose is 0.4 – 2.0 mg intravenously (or subcutaneously), repeated every 2 to 3 minutes if necessary. The use of naloxone in physically dependent patients may precipitate withdrawal symptoms.

## **PRESENTATION**

Bottle, linctus containing codeine phosphate 5 mg/mL, 100 mL.

## **STORAGE**

Store below 30°C. Protect from light.

## **POISONS SCHEDULE**

CONTROLLED DRUG – SCHEDULE 8

## **NAME AND ADDRESS OF SPONSOR**

Aspen Pharma Pty Ltd  
34-36 Chandos Street,  
St. Leonards NSW 2065  
Australia

**Approved by the Therapeutic Goods Administration on 8<sup>th</sup> March 2006.**

Safety-related change notification dated 06 September 2001.

Change to Scheduling of product from S4 to S8 to conform with new legislation (September 2006)

Safety-related change notification dated 20 February 2008

**Last revision approved by the Therapeutic Goods Administration on 19<sup>th</sup> September 2006.**