SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Codeine Linctus Bell's Healthcare 15 mg per 5 ml Oral Solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5 ml dose contains:

Codeine Phosphate BP 15 mg

Each 5 ml solution contains Sucrose 4g

Each 5 ml solution contains 2 vol% ethanol (alcohol)

For a full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

Oral solution.

4 CLINICAL PARTICULARS

4.1. Therapeutic indications

Codeine linctus is indicated for a dry or painful cough.

4.2 Posology and method of administration

Adults and the elderly: 5 – 10 ml three to four times a day. 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: Codeine is not recommended for use in children aged 12 years to 18 years with compromised respiratory function (see section 4.4)

4.3 Contraindications

- Hypersensitivity to codeine or to any of the excipients listed in section 6.1
- Ventilatory failure condition may be exacerbated.
- Liver disease: drug may accumulate
- In women during breastfeeding (see section 4.6)
- In patients for whom it is known they are CYP2D6 ultra-rapid metabolisers
- In children below the age of 12 years due to an increased risk of developing serious and life threatening adverse reactions.

4.4 Special warnings and precautions for use

Geriatric patients should be supervised while on this medication, and consideration of reduced dosage should be based on response. Codeine should only be used with caution in patients with kidney or liver impairment. Care should be taken in patients with asthma, hypothyroidism, and in patients with a history of drug abuse. Tolerance and dependency may occur with prolonged use.

CYP2D6 metabolism

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 effect will not be obtained. Estimates indicate that up to 7% of the Caucasian population may have this deficiency. However, if the patient is an extensive or 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 summarised 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%

The leaflet will state, under “Pregnancy and breast-feeding”: Do not take codeine while you are breastfeeding. Codeine and morphine passes into breast milk.

Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.
It contains 4 of sucrose per 5ml. To be taken into account in people with diabetes mellitus. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.

This medicinal product contains 2% vol% ethanol (alcohol) i.e. up to 156 mg per 10 ml dose, equivalent to 4 ml of beer or 1.6 ml of wine per 10 ml dose. Harmful for those suffering from alcoholism. To be taken into account in pregnant or breast-feeding women, children and high risk groups such as patient with liver disease or epilepsy.

This product contains sunset yellow which may cause allergic reaction.

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.

4.5 Interaction with other medicinal products and other forms of interaction

CNS depressants, anticholinergics, hydroxyzine and methadone – concurrent use of these medicines may result in potentiation of effects and hypotensive effects and CNS depressant effects may be increased; levallorphan is a morphine antagonist; the respiratory effects of neuromuscular blocking agents may be addictive to the central respiratory effects of the opioid analgesics; metoclopramide and codeine have opposing effects on gastro – intestinal activity; codeine causes delayed absorption of mexiletine; the effects of hypnotics and sedatives may be potentiated by codeine; hypertensive crisis may be caused by concurrent use of codeine and monoamine – oxidase inhibitors.

4.6 Fertility, pregnancy and lactation

Risk – benefit must be considered before using codeine during pregnancy. Codeine crosses the placenta and is excreted in small amounts in breast milk.

Pregnancy
As with all medications caution should be exercised during pregnancy, especially in the third trimester when codeine may depress respiration in the neonate. Regular use during pregnancy may cause physical dependency in the foetus, depression of neonatal respiration, 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.

Breastfeeding
Codeine should not be used 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 ultrarapid metaboliser of CYP2D6, 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 nonopioid 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 affect mental or physical ability.

This medicine can impair cognitive function and can affect a patient's ability to drive safely. This class of medicine is in the list of drugs included in regulations under 5a of the Road Traffic Act 1988. 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 is an offence to drive while under the influence of this medicine
• However, you would not be committing an offence (called 'statutory defence') if:
o The medicine has been prescribed to treat a medical or dental problem and
o You have taken it according to the instructions given by the prescriber and in the information provided with the medicine and
o It was not affecting your ability to drive safely

4.8 Undesirable effects

Side effects include tolerance and dependence, dizziness, nausea, 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.
In therapeutic doses, codeine is much less liable than morphine to produce adverse effects.

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 the Yellow Card Scheme at: www.yellowcard.mhra.gov.uk.

4.9 Overdose

Symptoms are:
Respiratory depression, dry mouth, sweating and facial flushing. High doses of Codeine may produce sedation or excitement, and in children convulsions may occur. Respiratory depression may be reversed with naloxone using one of the following dose regimens:

Intravenous injection
Adults:
0.8 – 2 mg repeated at intervals of two to three minutes to a maximum of 10 mg.
Children:
10 micrograms/kg and, if no response, subsequent doses of 100 micrograms/kg.

Subcutaneous or Intramuscular Injection
As for intravenous injection but only if the intravenous route is not feasible. The onset of action is slower with subcutaneous or intramuscular injection.

Continuous Intravenous Infusion
2 mg diluted in 500 ml of intravenous infusion solution at a rate adjusted according to the patient's response.

In cases of overdosage supportive therapy is recommended. Gastric lavage should be carried out and a saline purgative may then be given to reduce absorption from gastro – intestinal tract. Symptomatic treatment of respiratory embarrassment should be given. If respiration is seriously depressed intravenous naloxone HCl may be required.

5.1 Pharmacodynamic properties

Morphine derivative. Antitussive – suppresses the cough reflex by a direct central action, probably in the medulla or pons.

Codeine is a centrally acting weak analgesic. Codeine exerts its effect through μ opioid receptors, although codeine has low affinity for these receptors, and its analgesic effect is due to its conversion to morphine. Codeine, particularly in combination with other analgesics such as paracetamol, has been shown to be effective in acute nociceptive pain.

5.2 Pharmacokinetic properties

Codeine is well absorbed after oral administration. It is metabolised in the liver to morphine and norcodeine which are both excreted in the urine, partly as conjugates with glucuronic acid. Protein binding is very low. Half-life is from 2.5 to 4 hours. Duration of action is approximately 4 hours. Onset of action after oral administration is 30 to 45 minutes.
Most of the excretion products appear in the urine within 6 hours and up to 86% of the dose is excreted in 24 hours. About 70% of the dose is excreted as free codeine, 10% as free and conjugated morphine and a further 10% as free or conjugated norcodeine. Only traces are found in the faeces.

5.3. Preclinical safety data

There are no preclinical data of relevance to the prescriber which are additional to those already included in other sections.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Anhydrous Citric Acid BP

Sunset yellow E110

Quinoline yellow E104

Glycerol BP

Invert Syrup BP

Benzoic Acid BP

Propylene Glycol BP

Ethanol 90% BP

Terpeneless Lemon Oil BP

Sucrose BP

Methyl Hydroxybenzoate Sodium BP

Purified Water BP

6.2. Incompatibilities

None known.

6.3. Shelf Life

Three years.

6.4. Special Precautions for Storage

Do not store above 25°C.
Protect from light.

6.5 Nature and contents of container

100 ml, 200 ml and 500 ml glass bottles, child resistant cap with EPE liner.

Not all packs may be marketed.

6.6. Instructions for Use, Handling and Disposal

None.

7 MARKETING AUTHORISATION HOLDER

Bell, Sons and Co (Druggists) Ltd [Trading Style – Bell's Healthcare]
Gifford House,
Slaidburn Crescent
Southport
Merseyside
PR9 9AL

8. MARKETING AUTHORISATION NUMBER

PL 03105/0063

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

21st May 1998 / 15th December 1998

10 DATE OF REVISION OF THE TEXT

03/03/2017