SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Dihydrocodeine 30 mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 30 mg of Dihydrocodeine Tartrate BP. For excipients, see 6.1.

3 PHARMACEUTICAL FORM

Tablet
White, flat, bevel edged tablets, engraved 5B4 with a breakline.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Dihydrocodeine tablets are indicated for the relief of moderate to severe pain.

4.2 Posology and method of administration

For oral administration
Dihydrocodeine tablets are best administered after food.

Adults
1 tablet (30 mg) every 4 to 6 hours or at the discretion of the physician.

Children 4 to 12 years of age
0.5 to 1 mg/kg body weight, every 4 to 6 hours.

Children under 4 years of age
Dihydrocodeine is not recommended.

4.3 Contraindications

Hypersensitivity to dihydrocodeine or any of the tablet constituents; respiratory depression; obstructive airways disease; where there is a risk of paralytic ileus; acute alcoholism. Dihydrocodeine should also be avoided in patients with raised intracranial pressure or with significant head injury (in addition to interfering with respiration, it affects papillary response vital for neurological assessment). Dihydrocodeine may cause the release of histamine,
it should not be given during an asthma attack and should be given with caution to asthmatics.

Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose galactose malabsorption should not take this medicine.

4.4 Special warnings and precautions for use

Dosage should be reduced in the elderly, debilitated in hypothyroidism, chronic hepatic disease and renal insufficiency.

Dihydrocodeine should be administered with caution to patients with a history of opioid abuse, biliary tract disorders, hypotension, prostatic hypertrophy, convulsive disorders, pancreatitis, constipation, obstructive bowel disorder and severe cor pulmonale.

The patient may develop tolerance to the drug with chronic use and require progressively higher doses to maintain pain control. Prolonged use of this product may lead to physical dependence and a withdrawal syndrome may occur upon abrupt cessation of therapy. When a patient no longer requires therapy with dihydrocodeine, it may be advisable to taper the dose gradually to prevent symptoms of withdrawal.

Dihydrocodeine has an abuse profile similar to other agonist opioids. Dihydrocodeine tablets may be sought and abused by people with latent or manifest addiction disorders. The product should be used with particular care in patients with a history of alcohol and drug abuse.

The risk-benefit of continued use should be assessed regularly by the prescriber, and in particular the prescriber should take care to avoid any unnecessary increase in dosage especially where there is evidence of a previous history of drug dependence or abuse.

Dihydrocodeine should not be given during an attack of asthma, and should be administered with due care to persons liable to such attacks. Dihydrocodeine should be avoided, or the dose reduced in hepatic impairment. Alcohol should be avoided whilst under treatment with these tablets.

The leaflet will state in a prominent position in the ‘before taking’ section:

- Do not take for longer than directed by your prescriber.
- Taking dihydrocodeine regularly for a long time can lead to addiction, which might cause you to feel restless and irritable when you stop the tablets.
- Taking a painkiller for headaches too often or for too long can make them worse.
The label will state (To be displayed prominently on outer pack - not boxed):

- Do not take for longer than directed by your prescriber as taking dihydrocodeine regularly for a long time can lead to addiction.

4.5 Interaction with other medicinal products and other forms of interaction

Other central nervous system depressants, including sedatives or hypnotics, phenothiazines, other tranquillisers and alcohol, may result in respiratory depression or sedation. Dihydrocodeine should be used with caution in patients taking monoamine oxidase inhibitors or within two weeks of such therapy.

Dihydrocodeine tartrate causes delayed absorption of mexiletine, CNS excitation and hypertension by interacting with monoamine-oxidase inhibitors. Increased sedation may occur with tricyclic antidepressants.

Opiod analgesics may reduce the plasma concentration of ciprofloxacin when taken concomitantly.

An enhanced sedative and hypotensive effect may occur if antipsychotics are taken concomitantly with opioid analgesics.

The plasma concentration of some opioid analgesics may be increased by ritonavir.

Cimetidine may inhibit the metabolism of opioid analgesics.

Gastrointestinal effects of metoclopramide and domperidone may be antagonised.

4.6 Pregnancy and lactation

There are no or limited amount of data from the use of dihydrocodeine in pregnant women. Dihydrocodeine should not be used during pregnancy and labour due to the risk of neonatal respiratory depression. Infants born to mothers who have received opioids during pregnancy should be monitored for respiratory depression. Withdrawal symptoms may be observed in the newborn of mothers undergoing treatment with dihydrocodeine.

Dihydrocodeine has not been reported to be excreted in breast milk. However, it is advisable that dihydrocodeine only be administered to breast-feeding mothers if considered essential.

4.7 Effects on ability to drive and use machines

Dihydrocodeine may cause drowsiness and, if affected, patients should not drive or operate machinery.
## 4.8 Undesirable effects

The adverse experiences listed below are classified by body system according to their incidence.

Adverse effects have been ranked under headings of frequency using the following convention: common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); not known (cannot be estimated from the available data).

<table>
<thead>
<tr>
<th>Undesirable Effects</th>
<th>Common (≥1/100 to &lt;1/10)</th>
<th>Uncommon (≥1/1,000 to &lt;1/100)</th>
<th>Not known (cannot be estimated from the available data)</th>
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<td>Immune system disorders</td>
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<td>Angioedema</td>
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<td>Psychiatric disorders</td>
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<td>Confusional state</td>
<td>Dysphoria</td>
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<td>Drug dependence</td>
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<td>Hallucination</td>
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<td>Mood altered</td>
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<td>Nervous system disorders</td>
<td>Somnolence</td>
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<td>Dizziness</td>
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<td>Paraesthesia</td>
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<td>Eye disorders</td>
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<td>Blurred vision</td>
<td>Miosis</td>
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<td>Ear and labyrinth disorders</td>
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<td>Cardiac disorders</td>
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<td>Palpitations</td>
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<td>Vascular disorders</td>
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<td>Hypotension</td>
<td>Facial flushing</td>
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<td>Flushing</td>
<td>Larger dose may produce hypotension</td>
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<td>Postural hypotension</td>
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<td>Respiratory, thoracic</td>
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<td>Dyspnoea</td>
<td>Larger dose may</td>
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and mediastinal disorders | Respiratory depression | produce respiratory depression
---|---|---
Gastrointestinal disorders | Abdominal pain | Diarrhoea
Constipation | Ileus paralytic
Dry mouth | Nausea, Vomiting |
Hepato-biliary disorders | Biliary colic | Biliary spasm
Hepatic enzymes increased |
Skin and subcutaneous tissue disorders | Hyperhidrosis | Difficulty with micturition
Pruritus | Rash | Urticaria
Renal and urinary disorders | Urinary retention | Ureteric spasm
Decreased libido or potency |
Reproductive system and breast disorders | General disorders and administration site conditions | Asthenic conditions
Withdrawal syndrome | Drug tolerance | Hypothermia

Dependence may occur. Regular prolonged use of dihydrocodeine 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.
Paediatric population

Neonatal respiratory depression and withdrawal symptoms may occur in the newborn of mothers undergoing treatment with dihydrocodeine (see Section 4.6).

4.9 Overdose

The effects in overdosage will be potentiated by simultaneous ingestion of alcohol and psychotropic drugs.

Symptoms

Acute overdosage with dihydrocodeine can be manifested by somnolence progressing to stupor or coma, miotic pupils, rhabdomyolysis, non-cardiac pulmonary oedema, bradycardia, hypotension and respiratory depression or apnoea, which may in severe cases result in a fatal outcome. Central nervous system depression, including respiratory depression, may develop but is unlikely to be severe unless other sedative agents have been co-ingested, including alcohol, or the overdose is very large. Nausea and vomiting are common. Hypotension and tachycardia are possible but unlikely.

Management

Primary attention should be given to the establishment of a patent airway and institution of assisted or controlled ventilation. This should include general symptomatic and supportive measures including a clear airway and monitoring of vital signs until stable. Consider activated charcoal if an adult presents within one hour of ingestion of more than 350 mg or a child more than 5 mg/kg.

Give naloxone if coma or respiratory depression is present. Naloxone is a competitive antagonist and has a short half-life so large and repeated doses may be required in a serious poisoned patient. Observe for at least four hours after ingestion, or eight hours if a sustained release preparation has been taken.

In the case of massive overdose, administer naloxone intravenously (0.4 to 2 mg for an adult and 0.01 mg/kg body weight for children) if the patient is in coma or respiratory depression is present. Repeat the dose at 2 minute intervals if there is no response, or by an infusion. An infusion of 60% of the initial dose per hour is a useful starting point. A solution of 10 mg made up in 50 ml dextrose will produce 200 micrograms/ml for infusion using an IV pump (dose adjusted to the clinical response). Infusions are not a substitute for frequent review of the patient's clinical state. Intramuscular naloxone is an alternative in the event that IV access is not possible.

As the duration of action of naloxone is relatively short, the patient must be carefully monitored until spontaneous respiration is reliably re-established. Naloxone is a competitive antagonist and large doses (4 mg) may be required in seriously poisoned patients. For less severe overdosage, administer
Naloxone 0.2 mg intravenously followed by increments of 0.1 mg every 2 minutes if required.

Naloxone should not be administered in the absence of clinically significant respiratory or circulatory depression secondary to dihydrocodeine overdosage. Naloxone should be administered cautiously to persons who are known, or suspected, to be physically dependent on dihydrocodeine. In such cases, an abrupt or complete reversal of opioid effects may precipitate pain and an acute withdrawal syndrome.

Additional/other considerations:
• Consider activated charcoal (50 g for adults, 10-15 g for children), if a substantial amount has been ingested within 1 hour, provided the airway can be protected. It may be reasonable to assume that late administration of activated charcoal may be beneficial for prolonged release preparations but there is no evidence to support this.

• Dihydrocodeine tablets will continue to release and add to the dihydrocodeine load for up to 12 hours after administration and the management of overdosage should be modified accordingly. Gastric contents may therefore need to be emptied, as this can be useful in removing unabsorbed drug, particularly when a prolonged release formulation has been taken.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC Code: NO2A AO8

Dihydrocodeine tartrate is a potent analgesic. It also has well-defined antitussive activity.

Pharmacotherapeutic group: opioids, Natural opium alkaloids

Dihydrocodeine is a semisynthetic narcotic analgesic with a potency between morphine and codeine. It acts on opioid receptors in the brain to reduce the patient's perception of pain and improve the psychological reaction to pain by reducing the associated anxiety.

Central Nervous System
The principal actions of therapeutic value of dihydrocodeine are analgesia and an antitussive effect (depression of the cough reflex by direct effect on the cough centre in the medulla). Antitussive effects may occur with doses lower than those usually required for analgesia.

Dihydrocodeine may produce respiratory depression by direct action on brain stem respiratory centres.
Gastrointestinal Tract and Other Smooth Muscle
Dihydrocodeine causes a reduction in motility associated with an increase in smooth muscle tone in the antrum of the stomach and duodenum. Digestion of food in the small intestine is delayed and propulsive contractions are decreased. Propulsive peristaltic waves in the colon are decreased, while tone is increased to the point of spasm resulting in constipation.

5.2 Pharmacokinetic properties
Dihydrocodeine is well absorbed from the gastrointestinal tract following administration of dihydrocodeine tablets.

Like other phenanthrene derivatives, dihydrocodeine is mainly metabolised in the liver with the resultant metabolites being excreted mainly in the urine.

Metabolism of dihydrocodeine includes o-demethylation, n-demethylation and 6-keto reduction.

5.3 Preclinical safety data
There are no pre-clinical data of relevance to the prescriber which are additional to that already included in other sections of the SPC.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Maize Starch
Lactose Monohydrate
Povidone (E1201)
Sodium Starch Glycolate (Type A)
Magnesium Stearate (E572)
Colloidal Silicon Dioxide

6.2 Incompatibilities
Not applicable

6.3 Shelf life
36 months.

6.4 Special precautions for storage
Store in a dry place below 20ºC, and protect from light.
6.5 Nature and contents of container

HDPE or polypropylene containers with caps in packs of 25, 50, 100, 250, 500 and 1000 tablets.
PVDC coated PVC film with hard temper aluminium foil (blister packs) in packs of 7, 10, 14, 21, 28, 30, 56, 60, 84, 90, 100, 110, 112, 120, 150, 160, and 168 tablets.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal

Not applicable

7 MARKETING AUTHORISATION HOLDER

TEVA UK Limited
Brampton Road
Hampden Park
Eastbourne
BN22 9AG

8 MARKETING AUTHORISATION NUMBER(S)

PL 00289/0228

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10 March 1997

10 DATE OF REVISION OF THE TEXT

12.04.2011