# 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.

For the full list of excipients, see section 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

Posology

Prior to starting treatment with opioids, a discussion should be held with patients to put in place a strategy for ending treatment with dihydrocodeine in order to minimise the risk of addiction and drug withdrawal syndrome (see section 4.4).

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.

Method of administration
For oral administration

## 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

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.

Dihydrocodeine should be given in reduced doses or with caution to the elderly, debilitated in hypothyroidism, chronic hepatic disease, adrenocortical insufficiency, urethral stricture, shock, inflammatory or obstructive bowel disorder 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 and severe cor pulmonale.
However, these conditions should not necessarily be a deterrent to use in palliative care.

Concomitant use of Dihydrocodeine and sedative medicines such as benzodiazepines or related drugs may result in sedation, respiratory depression, coma and death. Because of these risks, concomitant prescribing with these sedative medicines should be reserved for patients for whom alternative treatment options are not possible. If a decision is made to prescribe Dihydrocodeine concomitantly with sedative medicines, the lowest effective dose should be used, and the duration of treatment should be as short as possible.

The patients should be followed closely for signs and symptoms of respiratory depression and sedation. In this respect, it is strongly recommended to inform patients and their caregivers to be aware of these symptoms (see section 4.5).

Alcohol should be avoided whilst under treatment with these tablets

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

This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially ‘sodium-free’.

Drug dependence, tolerance and potential for abuse

For all patients, prolonged use of this product may lead to drug dependence (addiction), even at therapeutic doses. The risks are increased in individuals with current or past history of substance misuse disorder (including alcohol misuse) or mental health disorder (e.g., major depression).

Additional support and monitoring may be necessary when prescribing for patients at risk of opioid misuse.

A comprehensive patient history should be taken to document concomitant medications, including over- the-counter medicines and medicines obtained on-line, and past and present medical and psychiatric conditions.

Patients may find that treatment is less effective with chronic use and express a need to increase the dose to obtain the same level of pain control as initially experienced. Patients may also supplement their treatment with additional pain relievers. These could be signs that the patient is developing tolerance. The risks of developing tolerance should be explained to the patient.

Overuse or misuse may result in overdose and/or death. It is important that patients only use medicines that are prescribed for them at the dose they have been prescribed and do not give this medicine to anyone else.

Patients should be closely monitored for signs of misuse, abuse, or addiction. The clinical need for analgesic treatment should be reviewed regularly.

Drug withdrawal syndrome

Prior to starting treatment with any opioids, a discussion should be held with patients to put in place a withdrawal strategy for ending treatment with dihydrocodeine.

Drug withdrawal syndrome may occur upon abrupt cessation of therapy or dose reduction. When a patient no longer requires therapy, it is advisable to taper the dose gradually to minimise symptoms of withdrawal. Tapering from a high dose may take weeks to months.

The opioid drug withdrawal syndrome is characterised by some or all of the following: restlessness, lacrimation, rhinorrhoea, yawning, perspiration, chills, myalgia, mydriasis and palpitations. Other symptoms may also develop including irritability, agitation, anxiety, hyperkinesia, tremor, weakness, insomnia, anorexia, abdominal cramps, nausea, vomiting, diarrhoea, increased blood pressure, increased respiratory rate or heart rate.

If women take this drug during pregnancy, there is a risk that their newborn infants will experience neonatal withdrawal syndrome.

Hyperalgesia

Hyperalgesia may be diagnosed if the patient on long-term opioid therapy presents with increased pain. This might be qualitatively and anatomically distinct from pain related to disease progression or to breakthrough pain resulting from development of opioid tolerance. Pain associated with hyperalgesia tends to be more diffuse than the pre-existing pain and less defined in quality. Symptoms of hyperalgesia may resolve with a reduction of opioid dose.

**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

Dihydrocodeine may cause the release of histamine; hence this product should not be administered during an asthmatic attack and should be administered with caution in patients with allergic disorders.

Alcohol enhanced hypotensive, sedative effect and respiratory depression.

Anaesthetics may increase anaesthetic and sedative effect.

Hypnotic or sedative, phenothiazines and tranquillisers may result in sedation or respiratory depression or enhance CNS depressive effect when taken with opioids.

Increased sedation may occur with tricyclic antidepressants or tricyclic antidepressant may enhance CNS depressive effect when taken with opioids.

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

The concomitant use of opioids with sedative medicines such as benzodiazepines or related drugs increases the risk of sedation, respiratory depression, coma and death because of additive CNS depressant effect. The dose and duration of concomitant use should be limited (see section 4.4).

Dihydrocodeine should be used with caution in patients taking monoamine oxidase inhibitors (MAOI) or within two weeks of such therapy. MAOIs taken with pethidine have been associated with severe CNS excitation or depression. Although this has not been documented with dihydrocodeine, it is possible that a similar interaction may occur with other opioid analgesics.

Gastrointestinal effects of metoclopramide and domperidone may be antagonised

Cyclizine may counteract the haemodynamic benefits of opioids.

Dihydrocodeine tartrate causes delayed absorption of mexiletine, CNS excitation and hypertension by interacting with monoamine-oxidase inhibitors.

Cimetidine may inhibit the metabolism of opioid analgesics.

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

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

## 4.6 Fertility, pregnancy and lactation

Pregnancy
Regular use during pregnancy may cause drug dependence in the foetus, leading to withdrawal symptoms in the neonate.

If opioid use is required for a prolonged period in a pregnant woman, advise the patient of the risk of neonatal opioid withdrawal syndrome and ensure that appropriate treatment will be available.

Administration during labour may depress respiration in the neonate and an antidote for the child should be readily available.

Breast-feeding
Administration to nursing women is not recommended as dihydrocodeine may be secreted in breast milk and may cause respiratory depression in the infant.

## 4.7 Effects on ability to drive and use machines

Dihydrocodeine may impair the mental and/or physical abilities required for the performance of potentially hazardous tasks such as driving a car or operating machinery.

Dihydrocodeine may cause drowsiness, paraesthesia, dizziness, vertigo, muscle rigidity, visual disturbances, confusion and hallucinations and, if affected, patients should not drive or operate machinery.

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:

- The medicine has been prescribed to treat a medical or dental problem and
- You have taken it according to the instructions given by the prescriber and in the information provided with the medicine and
- It was not affecting your ability to drive safely.

## 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).

| **Undesirable Effects** | **Common** (≥1/100 to <1/10) | **Uncommon** (≥1/1,000 to <1/100) | **Not known** (cannot be estimated from the available data) |
|---|---|---|---|
| Immune system disorders | | Angioedema | |
| Psychiatric disorders | | Confusional state<br>Hallucination<br>Mood altered | Dysphoria<br>Drug dependence (see section 4.4) |
| Nervous system disorders | Somnolence | Convulsions<br>Dizziness<br>Headache<br>Paraesthesia | |
| Eye disorders | | Blurred vision | Miosis |
| Ear and labyrinth disorders | | Vertigo | |
| Cardiac disorders | | | Bradycardia,<br>Tachycardia,<br>Palpitations |
| Vascular disorders | | Hypotension<br>Flushing | Facial flushing<br>Larger dose may produce hypotension<br>Postural hypotension |
| Respiratory, thoracic and mediastinal disorders | | Dyspnoea<br>Respiratory depression | Larger dose may produce respiratory depression |
| Gastrointestinal disorders | Abdominal pain<br>Constipation<br>Dry mouth<br>Nausea,<br>Vomiting | Diarrhoea<br>Ileus paralytic | |
| Hepato-biliary disorders | | Biliary colic<br>Hepatic enzymes increased | Biliary spasm |
| Skin and subcutaneous tissue disorders | | Hyperhidrosis<br>Pruritus<br>Rash<br>Urticaria | |
| Musculoskeletal and connective tissue disorders | | | Muscle rigidity* |
| Renal and urinary disorders | | Urinary retention<br>Ureteric spasm | Difficulty with micturition |
| Reproductive system | | Decreased libido | |

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|---|---|---|---|
| and breast disorders | | or potency | |
| General disorders and administration site conditions | | Asthenic conditions<br>Drug withdrawal syndrome<br>Drug tolerance | Hypothermia, oedema |

*reported after high doses.

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).

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.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

## 4.9 Overdose

Patients should be informed of the signs and symptoms of overdose and to ensure that family and friends are also aware of these signs and to seek immediate medical help if they occur.

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 over dosage, 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 anti-tussive 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 25ºC, 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,
Ridings Point,
Whistler Drive,
Castleford,
WF10 5HX,
United Kingdom.

## 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

07/03/2022