

# SUMMARY OF PRODUCT CHARACTERISTICS

## 1 NAME OF THE MEDICINAL PRODUCT

Dihydrocodeine Tablets BP 30mg

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 30mg Dihydrocodeine Tartrate

## 3 PHARMACEUTICAL FORM

Tablet

## 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

The analgesic effect is not materially enhanced by increasing the dose above that recommended below; in severe cases the interval between doses should be reduced to obtain the requisite analgesic cover.

Dihydrocodeine tablets are best taken with or after food.

Adults and children over 12 years:

1 tablet every four to six hours or at the discretion of the practitioner. Maximum dose in 24 hours 180mg (6 tablets).

Elderly:

A reduced adult dose is recommended, at the advice 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

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).

### **4.3 Contraindications**

- Hypersensitivity to dihydrocodeine or any of the excipients
- Respiratory depression
- Obstructive airways disease
- Acute alcoholism
- Risk of paralytic ileus
- Head injuries or conditions in which intracranial pressure is raised.

### **4.4 Special warnings and precautions for use**

Dihydrocodeine should be given in reduced doses or with caution to patients with asthma and decreased respiratory reserve. Avoid use during an acute asthma attack.

Dihydrocodeine should be avoided, or the dose reduced in patients with hepatic or renal impairment.

Dihydrocodeine should be given in reduced doses or with caution to; debilitated patients, adrenocortical insufficiency, prostatic hyperplasia, urethral stricture, hypotension, shock, inflammatory or obstructive bowel disorders, hypothyroidism or convulsive disorders.

However, these conditions should not necessarily be a deterrent to use in palliative care.

Use in caution in those with a history of drug abuse.

Alcohol should be avoided whilst under treatment with these tablets.

Risk from concomitant use of sedative medicines such as benzodiazepines or related drugs:

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).

Contains lactose monohydrate. Patients with rare hereditary problems of galactose

intolerance, the Lapp lactose deficiency or glucose-galactose malabsorption should not take this medicine.

The risk-benefit of continued use should be assessed regularly by the prescriber.

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

- Do not take for longer than directed by your prescriber
- Taking dihydrocodeine (DHC) 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 DHC 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.

The depressant effects of opioid analgesics are enhanced by other CNS depressants such as:

- Alcohol-enhanced hypotensive, sedative effect and respiratory depression
- Anaesthetics - may increase anaesthetic and sedative effect
- Sedating antihistamines - may enhance the CNS depressive effects when taken with opioids.
- Anxiolytics or Hypnotics - may enhance CNS depressive effects when taken with opioids
- Tricyclic antidepressants - may enhance CNS depressive effects when taken with opioids
- Antipsychotics - enhanced hypotensive, sedative effect
- 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. Therefore, the use of dihydrocodeine should be avoided while the patient is taking MAOIs and for 2 weeks after MAOI discontinuation.
- • When dihydrocodeine is taken concomitantly with antipsychotics there may be an increased sedative and hypotensive effect. Concomitant use of dihydrocodeine and ritonavir should be avoided due to the risk of toxicity.

Dihydrocodeine may antagonise the gastrointestinal effects metoclopramide and domperidone.

Cyclizine may counteract the haemodynamic benefits of opioids.

Dihydrocodeine may delay absorption of mexiletine.

Cimetidine may inhibit the metabolism of opioids

Sedative medicines such as benzodiazepines or related drugs: 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).

#### **4.6 Fertility, pregnancy and lactation**

Whilst there is no adequate evidence of safety in human pregnancy, dihydrocodeine has been widely used without apparent ill-effect for many years and studies in animals have not yet demonstrated any hazard. 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.

Dihydrocodeine passes into breast milk in very small amounts which are probably insignificant, however, it is recommended that administration should be avoided if the mother is breast feeding. Administration to nursing women is not recommended as codeine 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.

Effects such as paraesthesia, dizziness, vertigo, muscle rigidity, visual disturbances, drowsiness, confusion and hallucinations may occur. Do not drive or operate machinery if affected.

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 information below lists reported adverse reactions, using the following frequency classification:

Very common ( $\geq 1/10$ ); common ( $\geq 1/100$  to  $< 1/10$ ); uncommon ( $\geq 1/1,000$  to  $< 1/100$ ); rare ( $\geq 1/10,000$  to  $< 1/1,000$ ); very rare ( $< 1/10,000$ ), not known (cannot be estimated from the available data).

*Skin disorders:* rash, urticaria, pruritus, sweating.

*Central and peripheral nervous system disorders:* paraesthesia, dizziness, headache, vertigo, respiratory depression. Muscle rigidity has been reported after high doses.

*Vision disorders:* visual disturbances, miosis.

*Psychiatric disorders:* drowsiness, changes of mood, confusion, sexual dysfunction, hallucinations, euphoria; Frequency unknown: Drug dependence (see section 4.4).

*Gastro-intestinal system disorders:* dry mouth, nausea, vomiting, abdominal pain, constipation.

*Liver and biliary system disorders:* biliary spasm which may be associated with alterations in liver enzyme values.

*Cardiovascular disorders general:* hypotension, syncope

*Heart rate and rhythm disorders:* bradycardia, tachycardia, palpitations.

*Vascular (extracardiac) disorders:* facial flushing.

*Urinary systems disorders:* Micturition may be difficult and there may be ureteric spasm.

*General disorders and administration site conditions:* uncommon: drug withdrawal syndrome

*Body as a whole, general:* oedema.

Regular prolonged use of DHC 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.

#### **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](http://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**

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. The pupils may be pin-point in size; nausea and vomiting are common. Hypotension and tachycardia are possible but unlikely.

### **Management**

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 seriously poisoned patient. Observe for at least four hours after ingestion, or eight hours if a sustained release preparation has been taken.

## **5 PHARMACOLOGICAL PROPERTIES**

### **5.1 Pharmacodynamic properties**

ATC code N02A A08

Dihydrocodeine tartrate is an analgesic with uses similar to those of morphine but it is much less potent as an analgesic and has only mild sedative effects.

### **5.2 Pharmacokinetic properties**

Dihydrocodeine is well absorbed after oral administration. Peak plasma levels occur 1.6 - 1.8 hours after ingestion. Plasma half-life has been reported to be 34 hours after oral ingestion.

Dihydrocodeine is metabolised in the liver by O- and N- demethylation.

After oral administration the bioavailability of the drug is approximately 20%, indicating that the pre-systemic metabolism plays a substantial role in reducing the bioavailability of dihydrocodeine.

Dihydrocodeine is excreted in the urine as unchanged drug and metabolites. The mean elimination half life ranges between 3.5 – 5 hours.

### **5.3 Preclinical safety data**

Not applicable.

## **6 PHARMACEUTICAL PARTICULARS**

### **6.1 List of excipients**

The tablet contains Maize Starch, Lactose Monohydrate, Polyvinylpyrrolidone, Sodium Starch Glycollate (Type A), Magnesium Stearate and Colloidal Silicon Dioxide.

### **6.2 Incompatibilities**

None stated

### **6.3 Shelf life**

36 months

### **6.4 Special precautions for storage**

Do not store above 25°C. For containers, keep tightly closed, store in the original container. For strip packaging, store in the original package, keep in the outer carton.

### **6.5 Nature and contents of container**

HDPE containers with LDPE lids or polypropylene containers with polyethylene lids (Securitainers) in packs of 25, 50, 100, 250, 500 and 1000 tablets.

PVDC coated PVC film with hard temper aluminium foil (strips) in packs of 7, 10, 14, 21, 28, 30, 56, 60, 84, 90, 100, 110, 112, 120, 150, 160 and 168 tablets.

**6.6 Special precautions for disposal**

Not applicable

**7 MARKETING AUTHORISATION HOLDER**

Palla Pharma (UK) Holding Limited,  
10 Norwich Street,  
London,  
EC4A 1BD

**8 MARKETING AUTHORISATION NUMBER(S)**

PL 52635/0007

**9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

27/09/2005

**10 DATE OF REVISION OF THE TEXT**

13/07/2021