SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Dihydrocodeine Tablets BP 30 mg

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Dihydrocodeine tartrate BP 30 mg per tablet.

Excipient with known effect: lactose

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablet

Dihydrocodeine tablets BP 30 mg are presented as white normal convex tablets engraved with company logo on one face and A435 on the other face.

4.1 Therapeutic indications

As an analgesic for the relief of moderate to severe pain. Dihydrocodeine Tablets 30mg are indicated in all painful conditions where an alert patient is desired, *eg* sciatica, osteo-arthritis, chronic rheumatoid arthritis, arthritis of the spine, peripheral vascular disease, post-herpetic neuralgia, Paget's disease, malignant disease and post-operative pain.

Because dihydrocodeine, in the recommended doses, causes little or no respiratory depression, its use in the treatment of post-operative pain may reduce the risk of chest complications.

4.2 Posology and method of administration

Posology

Adults and children over 12 years: One tablet every 4-6 hours or as recommended by the prescriber. Maximum dose in 24 hours 180mg (6 tablets).

Elderly: Dosage should be reduced in the elderly. See also sub-section 4.4 Special warnings and special precautions for use.

Paediatric population:
Not recommended for children under 12 years old.
The analgesic effect of this product is not materially enhanced by increasing the above dose: in severe cases the interval between doses should be reduced to obtain the requisite analgesic effect. Prior to starting treatment with opioids, a discussion should be help with patients to put in place a strategy for ending treatment with Dihydrocodeine Tablets 30 mg in order to minimise the risk of addiction and drug withdrawal syndrome (section 4.4).

Method of administration
For oral use.
It is recommended that this product should be taken during or after food.

Treatment goals and discontinuation
Before initiating treatment with Dihydrocodeine Tablets BP 30 mg , a treatment strategy including treatment duration and treatment goals, and a plan for end of the treatment, should be agreed together with the patient, in accordance with pain management guidelines. During treatment, there should be frequent contact between the physician and the patient to evaluate the need for continued treatment, consider discontinuation and to adjust dosages if needed. When a patient no longer requires therapy with codeine, it may be advisable to taper the dose gradually to prevent symptoms of withdrawal. In absence of adequate pain control, the possibility of hyperalgesia, tolerance and progression of underlying disease should be considered (see section 4.4).

Duration of treatment
The duration of treatment should be as short as possible, and if no effective pain relief is achieved the patients/carers should be advised to seek the views of a physician.

4.3 Contraindications

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1
- Respiratory depression
- Obstructive airways disease
- Risk of paralytic ileus.
- Head injuries or conditions in which intracranial pressure is raised
- Acute alcoholism
- As dihydrocodeine may cause the release of histamine, it should not be given during an asthma attack.

4.4 Special warnings and precautions for use

Tolerance and opioid use disorder (abuse and dependence)

Tolerance, physical and psychological dependence, and opioid use disorder (OUD) may develop upon repeated administration of opioids such as [product name]. Repeated use of [product name] can lead to OUD. A higher dose and longer duration of opioid treatment can increase the risk of developing OUD. Abuse or intentional misuse of [product name] may result in overdose and/or death. The risk of developing OUD is increased in patients with a personal or a family history (parents or siblings) of substance use disorders (including alcohol use disorder), in current tobacco users or in patients with a personal history of other mental health disorders (e.g. major depression, anxiety and personality disorders).

The patient should be made aware of the risks and signs of OUD as set out in the package leaflet. If these signs occur, patients should contact their physician.

For patients who experience signs and symptoms of OUD, and/or exibit drug seeking behaviours, review of concomitant opioids and psycho-active drugs (like benzodiazepines) and consultation with an addiction specialist may be required.

“Before initiating treatment with Dihydrocodeine Tablets BP 30 mg, and during the treatment, treatment goals and a discontinuation plan should be agreed with the patient (see section 4.2).”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 Tablets 30mg.

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

As with other opioids, in case of insufficient pain control in response to an increased dose of codeine, the possibility of opioid-induced hyperalgesia should be considered. A dose reduction or treatment review may be indicated.

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 elderly patients, debilitated patients, adrenocortical insufficiency, prostatic hyperplasia, urethral stricture, hypotension, shock, inflammatory or obstructive bowel disorders, hypothyroidism or convulsive disorders, reduced level of consciousness of uncertain origin, biliary tract disorders, pancreatitis, constipation, cor pulmonale.
However, these conditions should not necessarily be a deterrent to use in palliative care. Alcohol should be avoided whilst under treatment with dihydrocodeine.

Opioids may cause sleep-related breathing disorders including central sleep apnoea (CSA) and sleep-related hypoxemia. Opioid use may increase the risk of CSA in a dose-dependent manner in some patients. Opioids may also cause worsening of pre-existing sleep apnoea (see section 4.8). In patients who present with CSA, consider decreasing the total opioid dosage.

Hepatobiliary disorders
Codeine may cause dysfunction and spasm of the sphincter of Oddi, thus increasing the risk of biliary tract symptoms and pancreatitis. Therefore, codeine has to be administered with caution in patients with pancreatitis and diseases of the biliary tract.

Sleep-related breathing disorders including central sleep apnoea
Opioids can cause sleep-related breathing disorders including central sleep apnoea (CSA) and sleep-related hypoxemia. Opioid use increases the risk of CSA in a dose-dependent fashion. In patients who present with CSA, consider decreasing the total opioid dosage.

Risk from concomitant use of sedative medicines such as benzodiazepines or related drugs:
Concomitant use of Dihydrocodeine Tablets 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 Tablets 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).
Opioids, such as dihydrocodeine, may influence the hypothalamic-pituitary-adrenal or -gonadal axes. Some changes that can be seen include an increase in serum prolactin, and decrease in plasma cortisol and testosterone. Clinical symptoms may manifest from these hormonal changes.
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 1mmol sodium (23mg) per tablet, that is to say essentially 'sodium-free'.

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

The leaflet will state in a prominent position in ’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

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:

- Anaesthetics- may increase anaesthetic and sedative effect.
- Alcohol – enhanced hypotensive, sedative effect and respiratory depression.
- 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 of 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 gabapentinoids (gabapentin and pregabalin), sedative medicines such as benzodiazepines or related drugs increases the risk of profound sedation,may result in respiratory depression, hypotension, coma and or 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

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 cause respiratory depression in the new-born infant, therefore administration should be avoided during the later stages of pregnancy 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.

May cause drowsiness, paraesthesia, dizziness, vertigo, muscle rigidity, visual disturbances, confusion, syncope and hallucinations, if affected, do 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 drug reactions listed below are classified by system organ class according to their frequency using the following convention: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000), not known (cannot be estimated from the available data).

System Organ Class	**Frequency**		
	Common	**Uncommon**	**Not Known**
Skin and subcutaneous tissue disorders		Hyperhidrosis, pruritus, rash, urticaria	
Immunes system disorders		Angioedema	
Psychiatric disorders		Confusional state, hallucinations, mood altered, dysphoria	Drowsiness, , , sexual dysfunction, , euphoria, Drug dependence (see section 4.4)
Nervous system disorders	Somnolence	Convulsions, dizziness, headache, paraesthesia, sedation	, vertigo, respiratory depression. Muscle rigidity has been reported after high doses, sleep apnoea syndrome
Eye disorders		Blurred vision	, miosis
Cardiac disorders			Bradycardia, tachycardia, palpitations
Vascular disorders		Hypotension, flushing	, syncope,

Respiratory, thoracic and mediastinal disorders		Dyspnoea, respiratory depression	
Gastrointestinal disorders	Abdominal pain, constipation, dry mouth, nausea, vomiting	Diarrhoea, paralytic ileus	
Hepatobiliary disorders		Biliary colic, hepatic enzymes increased	sphincter of Oddi dysfunction
Renal and urinary disorders		Urinary retention, ureteric spasm	Micturition may be difficult and there may be ureteric spasm
Reproductive system and breast disorders		Decreased libido	
General disorders and administration site conditions		Drug withdrawal Syndrome, Asthenia, fatigue, malaise, drug tolerance	Oedema, Drug withdrawal Syndrome neonatal
Ear and labyrinth disorders		Vertigo	

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.

Drug dependence
Repeated use of Dihydrocodeine Tablets BP 30 mg , can lead to drug dependence, even at therapeutic doses. The risk of drug dependence may vary depending on a patient's individual risk factors, dosage, and duration of opioid treatment (see section 4.4).

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 overdose 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.

Acute overdosage with dihydrocodeine can be manifested by somnolence progressing to stupor or coma, rhabdomyolysis, non-cardiac pulmonary oedema, bradycardia, hypotension and respiratory depression or apnoea, which may in severe cases result in a fatal outcome.

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. In the case of massive overdosage, administer naloxone hydrochloride intravenously (0.4mg to 2mg 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 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. Naloxone is a competitive antagonist and has a short

half-life so large (4 mg) doses may be required in a seriously poisoned patient. For less severe overdosage, administer naloxone 0.2 mg intravenously followed by increments of 0.1 mg every 2 minutes if required. Observe for at least four hours after ingestion, or eight hours if a sustained release preparation has been taken.

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Analgesics, Natural opium alkaloids, ATC code N02AA08

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

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

Absorption
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 0- and N-demethylation.

Biotransformation
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.

Elimination

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

There are no preclinical safety data of relevance to the prescriber.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose BP
Maize starch BP
Pregelatinised maize starch BP
Sodium starch glycollate BP
Stearic acid BP
Magnesium stearate BP

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

6.4 Special precautions for storage

Store in the original package in order to protect from light and moisture.

6.5 Nature and contents of container

The product is packed in opaque plastic containers composed of either, high density polypropylene or high density polyethylene with caps composed of high density polyethylene in pack sizes of 28, 30, 42, 50, 56, 84, 100, 112, 250, 500 and 1000 tablets.

Blister packs of aluminium /opaque PVC. It is subsequently packed in printed boxboard cartons in pack sizes of 28, 30, 42, 56, 84, 100 and 112 tablets.

6.6 Special precautions for disposal

No special requirements for handling.
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

SUMMARY OF PRODUCT CHARACTERISTICS

7 MARKETING AUTHORISATION HOLDER

Crescent Pharma Ltd,Key House, Sarum Hill, Basingstoke, RG21 8SR, UK

8 MARKETING AUTHORISATION NUMBER(S)

PL 20416/0065

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 09 January 2009

10 DATE OF REVISION OF THE TEXT

05/05/2026