SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
Dihydrocodeine 30mg Tablets BP.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each tablet contains dihydrocodeine tartrate 30 mg
Also contains Lactose monohydrate 155 mg
For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM
Tablet
White, flat, circular, bevel edged plain tablet with breakline.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications
Dihydrocodeine 30mg Tablets BP (as an analgesic) are indicated for the relief of moderate to severe pain. Dihydrocodeine 30mg Tablets BP are indicated in all painful conditions where an alert patient is desired, e.g. sciatica, osteoarthritis, chronic rheumatoid arthritis, arthritis of the spine, peripheral vascular disease, post-herpetic neuralgia, Paget’s disease, malignant disease, 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:
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.

**Adults:** One tablet (30 mg) every 4 – 6 hours or at the discretion of the practitioner.

**Children under 12 years:** A more suitable dosage form is recommended for this age group (e.g. elixir)

**Elderly:** Dosage should be reduced in the elderly

**Chronic hepatic disease:** The dosage should be reduced

**Moderate to severe renal impairment:** The dosage should be reduced

For concomitant illnesses/conditions where dose reduction may be appropriate see 4.4 Special Warnings and Precautions for Use.

**Method of administration:**

Oral

It is recommended that this product should be taken during or after food.

4.3 **Contraindications**

- Hypersensitivity to dihydrocodeine or other opioid analgesics or to any of the excipients listed in section 6.1.
- Respiratory depression
- Obstructive airways disease
- Acute alcoholism.
- Risk of paralytic ileus.
- Head injuries or conditions in which intracranial pressure is raised (in addition to the risk of respiratory depression and increased intracranial pressure, may affect papillary and other responses vital for neurological assessment).
- Severe hepatic dysfunction
- Children under 4 years of age
- Dihydrocodeine should not be given to comatose patients.
- Dihydrocodeine is also contraindicated where there is a risk of paralytic ileus, or in acute diarrhoeal conditions such as acute ulcerative colitis or antibiotic associated colitis (e.g. pseudomembranous colitis) or diarrhoea caused by poisoning.

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, myasthenia gravis, hypothyroidism or convulsive disorders.

Opioid analgesics should be avoided in patients with biliary tract disorders or used in conjunction with an antispasmodic.

Administration of pethidine and possibly other opioid analgesics to patients taking a monoamine oxidase inhibitor (MAOI) has been associated with very severe and sometimes fatal reactions. If the use of codeine is considered essential then great care should be taken in patients taking MAOIs or within 14 days of stopping MAOIs (see section 4.5). However, these conditions should not necessarily be a deterrent to use in palliative care.

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

Alcohol should be avoided while under treatment with these tablets.

Discontinuation should be carried out gradually in patients who may have developed physical dependence to avoid precipitating withdrawal symptoms.

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

The risk and benefit of continued use should be assessed regularly by the doctor.

**The leaflet will state in a prominent position in the ‘before taking’ section:**
- Do not take for longer than directed by your doctor
- 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 time 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 doctor 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 (Dihydrocodeine) are enhanced by other central nervous system (CNS) depressants such as;

- Alcohol-enhanced hypotensive, sedative effect and respiratory depression
- Anaesthetics- may cause increased CNS depression and/or respiratory depression and/or hypotension
- 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- may enhance CNS depressive effects when taken with opioids

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.

Motility stimulants- Dihydrocodeine may antagonise the gastrointestinal effects metoclopramide and domperidone.

Cyclizine may counteract the haemodynamic benefits of opioids.

Mexiletine- Dihydrocodeine may delay absorption of mexiletine.

Cimetidine- may inhibit the metabolism of opioids

Quinidine - may significantly impair the analgesic activity of dihydrocodeine in extensive metabolisers of dihydrocodeine

Sodium oxybate - concomitant administration with dihydrocodeine may cause increased CNS depression and/or respiratory depression and/or hypotension

Antidiarrhoecal and antiperistaltic agents (e.g. loperamide, kaolin) - concomitant use may increase the risk of severe constipation and central nervous depression

Antihypertensives - concomitant administration of dihydrocodeine with antihypertensive agents may potentiate the hypotensive effects

Ciprofloxacin – avoidance of premedication with opioid analgesics advised by manufacturer of ciprofloxacin (reduced plasma
concentration of ciprofloxacin) when ciprofloxacin used for surgical prophylaxis

Antimuscarinics - concomitant use of antimuscarinics or medications with anti muscarinic action may result in an increased risk of severe constipation which may lead to paralytic ileus and/or urinary retention.

Interference with laboratory tests-
Opioid analgesics interfere with a number of laboratory tests including plasma amylase, lipase, bilirubin, alkaline phosphate, lactate dehydrogenase, alanine aminotransferase and aspartate aminotransferase

Opioids may interfere with gastric emptying studies as they delay gastric emptying and with hepatobiliary imaging using technetium Tc 99m disofenin as opioid treatment may cause constriction of the sphincter of Oddi and increase biliary tract pressure.

4.6 Fertility, pregnancy and lactation

**Pregnancy**

Dihydrocodeine traverses the placental barrier, regular use during pregnancy and labour may depress neonatal respiration and cause physical dependence in the foetus, leading to withdrawal symptoms, therefore administration should be avoided during the later stages of pregnancy. Gastric stasis and risk of inhalation pneumonia may occur in the mother during labour. Teratogenic effects have not been demonstrated in humans. However studies in mice have shown delayed ossification; and increased resorption has been reported in rats. Therefore risk benefit must be considered when administering during pregnancy.

**Breast-feeding:**

Dihydrocodeine is excreted in the breast milk in very small amounts which are probably insignificant however as neonates are most susceptible to its effects, especially the respiratory depressant effects, use of this product in nursing mothers is not recommended.

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 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

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.

**Immune system disorders:** Allergic reactions such as hives, itching, skin rashes, swelling of face, dyspnoea and difficulty in breathing.

**Metabolism and nutrition disorders:** Anorexia

**Skin and subcutaneous tissue disorders:** Allergic reactions such as skin rash, urticaria, pruritius, sweating, facial oedema.

**Nervous system disorders:** paraesthesia, convulsions, uncontrolled muscular movements, tremors dizziness, headache, drowsiness, Raised intracranial pressure any occur in some patients.

**Ear and labyrinth disorders:**

Vertigo

**Respiratory, thoracic and mediastinal disorders:**

Dyspnoea, Larger doses produce respiratory depression.

**Musculoskeletal, connective tissue and bone disorders:**

Uncontrolled muscle movements, Muscle rigidity has been reported after high doses especially respiratory muscles.
**Eye disorders:** visual disturbances, miosis.

**Psychiatric disorders:** Mental depression, restlessness mood changes, confusion, hallucinations, euphoria, dysphoria, unusual excitement in children, nightmares.

**Gastro-intestinal disorders:** nausea and vomiting, constipation, dry mouth, stomach cramps, abdominal pain, pancreatitis.

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

**Cardiac disorders:** Irregularities of cardiac rhythm, bradycardia, tachycardia, palpitations.

**Vascular (extra cardiac) disorders:** Postural hypotension facial flushing. Larger doses produce hypotension.

**Renal and urinary disorders:** Difficulty in micturition, urinary retention, ureteric spasm, dysuria.

**Reproductive system and breast disorders:** Sexual dysfunction, erectile dysfunction, decreased potency, decreased libido.

**General disorders and administration site conditions:** oedema, drowsiness, malaise, tiredness, hypothermia.

Dose related increased post-operative pain has been reported following dental surgery.

**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.

4.9 **Overdose**
The effects in over dosage will be potentiated by simultaneous ingestion of alcohol and psychotropic drugs.

**Symptoms:**
Toxic doses vary considerably with the individual and regular users may tolerate large doses. The triad of coma, pinpoint pupils and respiratory depression is considered indicative of opioid overdosage with dilatation of the pupils occurring as hypoxia develops. Other opioid overdose symptoms include hypothermia, confusion,
convulsions, severe dizziness, severe drowsiness, hypotension, nervousness or restlessness, hallucinations, slow heart beat, circulatory failure, slow or troubled breathing, severe weakness, convulsions, especially in infants and children. Rhabdomyolysis, progressing to renal failure, has been reported in overdosage with opioids.

**Management:**

Management 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 350mg or a child more than 5mg/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 4 hours after ingestion.

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5  PHARMACOLOGICAL PROPERTIES

5.1  Pharmacodynamic properties

Pharmacotherapeutic group: Analgesics, Natural Opium Alkaloids, ATC code: N02A A08

Dihydrocodeine is an analgesic of the opioid class. 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 and 1.8 hours after ingestion. Oral bioavailability is only about 20% possibly because of substantial pre-systemic metabolism.

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
Maize Starch
Lactose Monohydrate
Povidone
Sodium Starch Glycollate (Type A)
Magnesium Stearate
Colloidal Anhydrous Silica

6.2 Incompatibilities
Not applicable

6.3 Shelf life
3 years

6.4 Special precautions for storage
Container: Do not store above 25° C. Keep the container tightly closed. Store in the original container.
Blister packs: Do not store above 25°C. Store in the original package.

6.5 Nature and contents of container
HDPE tablet container with LDPP cap of 25, 50, 100, 250, 500, 1000 tablets.
AL/PVC blisters
Pack size: 14, 28, 30, 56, 60, 84 and 100 tablets

6.6 Special precautions for disposal
Not applicable
7  MARKETING AUTHORISATION HOLDER

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PL 17907/0010

9  DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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10  DATE OF REVISION OF THE TEXT

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