SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Dihydrocodeine 30mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Dihydrocodeine tartrate 30mg

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet - Oral use

4.1. Therapeutic indications

Dihydrocodeine is used to relieve moderate to severe pain.

4.2 Posology and method of administration

Posology

Adults:

1 tablet (30mg) every four to six hours or at the discretion of the physician.

Elderly:

Dosage should be reduced

Children aged 4 to 12 years:

0.5 to 1mg/kg bodyweight every four to six hours.

Children under 4 years:

Not recommended

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.

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).

Method of administration

For oral use.

4.3 Contraindications

Acute respiratory depression.
Obstructive airways disease
Known hypersensitivity to dihydrocodeine, or other opioid analgesics, or to any of the excipients
Acute alcoholism
Severe hepatic dysfunction
Head injury or raised intracranial pressure (in addition to the risk of respiratory depression and increased intracranial pressure, may affect papillary and other responses vital for neurological assessment).
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 (see 4.3 Contraindication). Dihydrocodeine should be given in reduced doses or with caution to elderly or debilitated patients (see 4.2 Posology) and in patients with adrenocortical insufficiency, prostatic hyperplasia, urethral stricture, hypotension, shock, inflammatory or obstructive bowel disorders, myasthenia gravis, hypothyroidism or convulsive disorders. It should be avoided or the dose reduced in patients with hepatic or renal impairment. 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.

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).

Alcohol should be avoided whilst under treatment with dihydrocodeine.

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

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

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.

4.5 Interaction with other medicinal products and other forms of interaction

Alcohol: The hypotensive, sedative and respiratory depressive effects of alcohol may be enhanced; alcohol should be avoided.

Anaesthetics: concomitant administration of dihydrocodeine and anaesthetics may cause increased CNS depression and/or respiratory depression and/or hypotension.

Anti-arrhythmics: Dihydrocodeine may delay absorption of mexiletine. The analgesic activity of dihydrocodeine may be significantly impaired by quinidine which impairs codeine metabolism.

Antidepressants, anxiolytics, hypnotics and antipsychotics: Opiates potentiate the effects of CNS depressants, including anxiolytics (e.g.: chlordiazepoxide, diazepam), hypnotics, antipsychotics and tricyclic antidepressants.

Antihistamines: concomitant administration of dihydrocodeine and antihistamines with sedative properties may cause increased CNS depression and/or respiratory depression and/or hypotension.

MAOIs taken with pethidine have been associated with severe CNS excitation or depression (including hypertension or hypotension). Although this has not been documented with dihydrocodeine, it is possible that a similar interaction may occur and therefore the use of dihydrocodeine should be avoided while the patient is taking MAOIs and for 2 weeks after MAOI discontinuation.

Antidiarrhoeal and antiperistaltic agents (e.g. loperamide, kaolin): concurrent use may increase the risk of severe constipation.

Motility stimulants: Dihydrocodeine has an antagonistic effect on cisapride, metoclopramide and domperidone.

Ulcer-healing drugs: Cimetidine may inhibit the metabolism of dihydrocodeine resulting in increased plasma concentrations.

Sodium oxybate: concomitant administration of dihydrocodeine and sodium oxybate may cause increased CNS depression and/or respiratory depression and/or hypotension.

Interference with laboratory tests: Opioid analgesics interfere with a number of laboratory tests including plasma amylase, lipase, bilirubin, alkaline phosphatase,

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

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.

A possible association with respiratory and cardiac malformations has been reported following first trimester exposure to codeine.

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 produces sedation and may also cause changes in vision, including blurred or double vision. If affected, patients should not drive or operate machinery. The effects of alcohol are enhanced by opioid analgesics.

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 of 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.

Tolerance and some of the most common side effects – drowsiness, nausea, and vomiting, and confusion – generally develops with long term use.

Immune system disorders: maculopapular rash has been seen as part of a hypersensitivity syndrome associated with oral codeine phosphate; fever, splenomegaly and lymphadenopathy also occurred.

Endocrine disorders: hyperglycaemia

Metabolism and nutrition disorders: anorexia.

Psychiatric disorders: mental depression, hallucinations and nightmares, restlessness, confusion, mood changes, euphoria, dysphoria, drug dependence (see section 4.4)

Nervous System disorders: convulsions (especially in infants and children), dizziness, drowsiness, headache, (prolonged use of a painkiller for headaches can make them worse). Raised intracranial pressure may occur in some patients.

Eye disorders: blurred or double vision or other changes in vision. Miosis.

Ear and labyrinth disorders: vertigo.

Cardiac disorders: tachycardia, palpitations and bradycardia.

Vascular disorders: postural hypotension, facial flushing. Large doses produce hypotension.

Respiratory, thoracic and mediastinal disorders: Dyspnoea. Larger doses produce respiratory depression.

Gastrointestinal disorders: nausea, vomiting, constipation, dry mouth, stomach cramps, pancreatitis.

Hepatobiliary disorders: Biliary spasm (may be associated with altered liver enzyme values).

Skin and subcutaneous tissue disorders: allergic reactions, such as skin rash, pruritus, urticaria, sweating, facial oedema.

Musculoskeletal and connective tissue disorders: Uncontrolled muscle movements. Muscle rigidity may occur after high doses.

Renal and urinary disorders: urinary retention, difficulty with micturition, ureteric spasm, dysuria. An antidiuretic effect may also occur with codeine.

Reproductive system and breast disorders: sexual dysfunction, erectile dysfunction, decreased potency. Decreased libido.

General disorders and administration site conditions: malaise, tiredness, hypothermia, drug withdrawal syndrome.

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 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.

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.

Conservative management is recommended. In acute overdosage with respiratory depression or coma, the specific opioid antagonist naloxone is indicated, using one of the recommended dosage regimens. Patients should be observed closely.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Natural opium alkaloids, ATC code: N02AA08

Dihydrocodeine is a narcotic analgesic similar in potency to codeine, and is used in the relief of moderate to severe pain.

5.2. Pharmacokinetic properties

Dihydrocodeine is well absorbed after oral administration. Peak plasma levels are attained approximately 1.6 - 1.8 hours after ingestion. The half life is of the order of 3.5 hours. 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.

5.3. Pre-clinical safety data

There are no pre-clinical data of relevance to the prescriber which are additional to those already included in other sections.

6.1. List of excipients

Lactose
Maize starch
Magnesium stearate
Purified water
Ethanol with 5% methanol (IMS)
Povidone

6.2 Incompatibilities

Not applicable.

6.3. Shelf life

Two years.

6.4. Special precautions for storage

Protect from light.
Do not store above 25°C.

6.5 Nature and contents of container

Polypropylene or polyethylene tablet containers of 30 or 100 tablets
Strip packs of 10 or 14 tablets in multiple pack sizes
Not all pack sizes may be marketed.

6.6. Instructions for use/handling

None.

7 MARKETING AUTHORISATION HOLDER

Wockhardt UK Ltd

Ash Road North
Wrexham
LL13 9UF
United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 29831/0069

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

01 / 11 / 2006

10 DATE OF REVISION OF THE TEXT

15/05/2020