SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

DF118 FORTE 40mg

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains Dihydrocodeine Tartrate 40mg

Excipients with known effect:
Each tablet contains 177.80mg lactose.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

White circular biconvex tablets engraved DF118 on one side and Forte on the other.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

For the relief of severe and chronic pain

Dihydrocodeine Tablets are indicated in all painful conditions where an alert patient is desired, e.g. sciatica, osteo-arthritis, 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

Prior to starting treatment with opioids, a discussion should be held with patients to put in place a strategy for ending treatment with DF118 tablets in order to minimise the risk of addiction and drug withdrawal syndrome (see section 4.4).

Route of Administration
Oral
DF118 tablets should be administered with or after food.
Adults and elderly and children over 12 years

One or two tablets three times daily. The maximum daily dose is 240mg.

Children under 12 years

Not recommended.

4.3 Contraindications

- Hypersensitivity to any of the products ingredients.
- Acute respiratory depression or Chronic Obstructive Airways Disease.
- Asthma attack.
- Acute alcoholism.
- Biliary colic.
- Head injuries or increased intracranial pressure.
- Heart failure secondary to lung disease.
- Concurrent use with Monoamine Oxidase Inhibitors (including moclobemide), or within two weeks of their withdrawal.
- Risk of paralytic ileus.
- Phaeochromocytoma.

4.4 Special warnings and precautions for use

As dihydrocodeine may cause the release of histamine it should be given 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 dihydrocodeine.

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

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

Concomitant use of Dihydrocodeine Tartrate 40mg 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

Tartrate 40mg 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).

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 DF118 FORTE.
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

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 effect of opioids analgesics are enhanced by other CNS depressants such as;

Alcohol: Enhanced sedative and hypertensive effects and respiratory depression.

Anaesthetics: may increase anaesthetic and sedative effect.

Sedating Antihistamines: may enhance the CNS depressive effects when taken with opioids.

Tricyclic Antidepressants: may enhance CNS depressive effects when taken with opioids.

Antipsychotics: Enhanced hypotensive, sedative effect.

Anxiolytics and Hypnotics: 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.

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

Ciprofloxacin: If dihydrocodeine is used prior to surgery and ciprofloxacin is used for surgical prophylaxis then serum levels of ciprofloxacin are reduced and adequate cover may not be obtained during surgery.

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

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 cause drowsiness, 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

- 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.
- 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.
- Body as a whole, general; oedema.
- General disorders and administration site conditions: Uncommon: Drug withdrawal syndrome
- 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.

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; website: 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 is a semi-synthetic 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.

5.2 Pharmacokinetic properties

Absorption

Dihydrocodeine is well absorbed after oral administration. Peak plasma levels occur 1.6 - 1.8 hours after ingestion.

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 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

Lactose
Maize Starch
Pregelatinised Maize Starch
Magnesium Stearate

6.2 Incompatibilities

None known

6.3 Shelf life

Three years

6.4 Special precautions for storage

Store below 25ºC

Store in a dry place and protect from light

6.5 Nature and contents of container

28, 56, 100 and 500 tablet packs
Polypropylene container fitted with polyethylene lid or PVdC coated PVC blister packs with aluminium backing foil.

10, 28 and 56 tablet pack
Polypropylene container fitted with polyethylene lid.

6.6 Special precautions for disposal

None stated

7 MARKETING AUTHORISATION HOLDER

Martindale Pharmaceuticals Ltd.

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RM3 8UG

United Kingdom

8 MARKETING AUTHORISATION NUMBER(S)

PL 00156/0093

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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Date of latest renewal: 13th September 2005

10 DATE OF REVISION OF THE TEXT

11/06/2020