SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Pethidine 50 mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 50mg pethidine hydrochloride
Excipients with known effect
Each tablet also contains lactose monohydrate(66.70 mg) and sucrose(4.30mg)

For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

White or almost white tablet for oral use, with a score line on one side and an imprint of M50 on the reverse side.
The score line is only to facilitate breaking for ease of swallowing and not to divide into equal doses.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

1. Obstetric analgesia.
2. Moderate to severe pain.
3. Premedication and analgesia during anaesthesia.

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 pethidine in order to minimise the risk of addiction and drug withdrawal syndrome (see section 4.4)

Posology

Adults:

The normal single dose, usually not to be repeated more often than four hourly, is as follows: Orally: 50 - 150 mg.

Elderly and debilitated patients

The initial dose should not exceed 50 mg orally as such patients are likely to be particularly sensitive to the central depressant effects of the drug.

Paediatric population:

A single dose of 0.5 - 2 mg / kg body weight orally. This dose may be repeated if clinically necessary but it should not be repeated more often than four hourly.
(As the tablet may not be cut, a child requiring 2mg/kg will need to weigh 25kg, and any child requiring a lower dose will need to be given Pethidine Solution for Injection.)

Method of administration

For oral administration

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1

Not to be given to comatose patients or to patients with respiratory depression, obstructive airways disease or acute asthma. It should not be given to patients who are receiving monoamine oxidase inhibitors or moclobemide, or within two weeks of their withdrawal. For full list of interactions with other medicinal products, see section 4.5. Not to be given to patients with a history of hypersensitivity or idiosyncratic response to the drug or any of its constituents.

Pethidine should be avoided in patients exhibiting acute alcoholism, delirium tremens or convulsive disorders, and paralytic ileus. Pethidine depresses respiratory function and should be avoided in patients with respiratory insufficiency and in patients with head injuries, raised intracranial pressure severe hepatic or renal impairment. Patients with phaechromocytoma should not be treated with pethidine

Use of pethidine should be avoided in patients with diabetic acidosis where there is a danger of coma.

4.4 Special warnings and precautions for use

Pethidine should only be given with caution, and in reduced dosage, to neonates and premature infants, elderly or debilitated patients, hypotension, decreased respiratory reserve, biliary tract disorders, hypothyroidism, adrenal

cortical insufficiency, shock, prostatic hypertrophy, and supraventricular tachycardia. Use of cough suppressants containing opioid analgesics is not generally recommended in children and should be avoided altogether in those under at least 1 year.

Repeated administration may induce tolerance to the drug, with a tendency to psychological dependence of the morphine type, with withdrawal symptoms after abrupt cessation of therapy. Cross tolerance between narcotic analgesics can occur. In the case of severe continuing pain it may be advisable to try other treatments. A reduction in dose is advisable in cases of renal disease and chronic hepatic disease.

Pethidine hydrochloride tablets contain lactose and sucrose. Patients with rare hereditary problems of galactose intolerance, fructose intolerance, the Lapp lactase deficiency, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

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

Concomitant use of Pethidine 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 methadone 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 pethidine.

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: Enhanced sedative and hypotensive effects.

Antidepressants, SSRI and Tricyclic: The use of pethidine should be avoided in patients receiving monoamine oxidase inhibitors (including moclobemide), or within two weeks of their withdrawal. Increased risk of CNS toxicity.

Pethidine may increase potential for both selective serotonin re-uptake inhibitors (SSRIs) and tricyclic antidepressants (TCAs) to cause convulsions.

Anxiolytics and Hypnotics: Sedative effects may be enhanced by simultaneous use of pethidine.
Antipsychotics: Increased risk of convulsions with pethidine

Carbamazepine: Reduces the effects of Pethidine.

Coumarins: Pethidine enhances anticoagulant effects of coumarins.

Digoxin: Risk of digoxin toxicity increased.

Duloxetine: Possible increased serotonergic effects when administered with pethidine.

Selegiline: Caution with pethidine advised by manufacturer of selegiline.

Ciprofloxacin: The manufacturer of ciprofloxacin advises that, if it is used for surgical prophylaxis, opiates should not be used for premedication as this may reduce the plasma concentration of ciprofloxacin.

Cimetidine: The metabolism of pethidine is inhibited (plasma concentrations of pethidine are increased).

Domperidone and metoclopramide: Pethidine antagonises the gastro-intestinal activity of these drugs.

Mexilitine: Pethidine delays the absorption of mexilitine.

Ritonavir: Plasma concentration of pethidine may be increased by ritonavir.

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

There is inadequate evidence of safety of pethidine in human pregnancy, but the drug has been widely used for many years without apparent ill-

consequence, and animal studies have not shown any hazard. Nevertheless the established medical practice of prescribing medicaments in early pregnancy should be observed.

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 pethidine may be secreted in breast milk and may cause respiratory depression in the infant.

Fertility
There are insufficient fertility data available to indicate whether pethidine hydrochloride has any effect on fertility.

4.7 Effects on ability to drive and use machines

Pethidine may modify the patient's reactions to a varying extent, depending on dosage, administration and individual susceptibility. If affected or if you are in any doubt that you may be affected do not drive or operate machinery until any effects have worn off.

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 table below presents adverse drug reactions by System Organ Class. Within each System Organ Class, the adverse drug reactions are presented by incidence, using the following convention:

Not known (cannot be estimated from the available data).

System Organ Class	**Frequency**	**Adverse Event**
Psychiatric disorders	Unknown	Euphoria, hallucinations, dysphoria, mood changes, drug dependence (see section 4.4)
Nervous system disorders	Unknown	Central Nervous System excitation, dizziness, vertigo, drowsiness, headache
Eye disorders	Unknown	Obtund or abolish the corneal reflex, miosis (pupillary constriction)
Cardiac disorders	Unknown	Bradycardia, tachycardia, palpitations
Vascular disorders	Unknown	Hypotension, facial flushing,
Respiratory, thoracic and mediastinal disorders	Unknown	Respiratory depression
Gastrointestinal disorders	Unknown	Nausea,vomiting, constipation, dry mouth
Hepatobiliary disorders	Unknown	Biliary spasm
Skin and subcutaneous tissue disorders	Unknown	Rashes, urticaria, pruritis
Musculoskeletal and connective tissue disorders	Unknown	Muscle rigidity
Renal and urinary disorders	Unknown	Difficulty in micturition, ureteral spasm
Reproductive system and breast disorders	Unknown	Decreased libido or potency
General disorders and administration site conditions	Unknown Uncommon	Sweating, hypothermia, drug withdrawal syndrome

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.

Symptoms

In acute overdose the signs may be incoordination, tremors and convulsions followed by respiratory depression and coma.

Management

Gastric lavage should be performed soon after ingestion, and intensive supportive therapy carried out. Naloxone is the preferred antidote. The urinary excretion can be increased by rendering the urine acid by the administration of ammonium chloride. Patients exhibiting symptoms of CNS toxicity should be treated by immediate discontinuation of pethidine, substituting an alternative narcotic for pain, supporting respiratory function and administering an anticonvulsant if seizures occur.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Phenylpiperidine derivatives

ATC code: N02A B02

Pethidine binds to opioid receptors and exerts its chief pharmacological action on the CNS and the neural elements of the bowel. The analgesic effects of pethidine are detectable about 15 minutes after oral administration, reaching a peak in about 2 hours and subsiding gradually over several hours. In equianalgesic doses pethidine depresses respiration to a similar extent to morphine. Pethidine has a spasmogenic effect on certain smooth muscles similar to that observed for other opioids.

Ambulatory patients given pethidine may experience syncope associated with hypotension but symptoms rapidly clear on lying down. Otherwise in therapeutic doses pethidine has no significant untoward effects on the cardiovascular systems, especially if patients are lying down. Pethidine combines analgesic and antispasmodic properties; it is relatively short acting and has little soporific effect. These properties make pethidine particularly useful for pain relief in labour and as an adjunct to nitrous oxide-oxygen anaesthesia.

5.2 Pharmacokinetic properties

Peak plasma concentrations are normally observed between 1 and 2 hours after oral administration. However, only about 50% of the drug escapes first pass metabolism to enter the circulation. About 60% is protein bound in plasma.

Heavy alcohol drinkers have an increased apparent volume of distribution with consequent initially lower pethidine plasma concentrations. Older Patients have higher plasma concentrations and reduced protein binding which may account for the increased response in therapeutic dosages. Pethidine is mainly metabolised in the liver by hydrolysis to pethidinic acid, or by N-demethylation to norpethidine, followed by hydrolysis to norpethidinic acid. Subsequent, partial conjugation with glucuronic acid may also occur.

5.3 Preclinical safety data

None stated

6.1 List of excipients

Maize starch
Lactose monohydrate
Sucrose
Purified talc
Magnesium Stearate
Acacia

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

2 years (24 months).

6.4 Special precautions for storage

Store in the original packaging.
Do not store above 25°C.

6.5 Nature and contents of container

A blister strip of 25 tablets, 2blisters per pack.

Pack size of 50 tablets

6.6 Special precautions for disposal

No special requirement.

7 MARKETING AUTHORISATION HOLDER

Martindale Pharma
Bampton Road
Romford
RM3 8UG
England.

8 MARKETING AUTHORISATION NUMBER(S)

PL 00156/0031

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 07/08/2008

10 DATE OF REVISION OF THE TEXT

28/01/2025