PACKAGE LEAFLET: INFORMATION FOR THE USER

Pethidine 50mg/ml & 100mg/2ml Solution for Injection

Pethidine Hydrochloride

Read all of this leaflet carefully before you are given this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, nurse or midwife.
- If you get any side effects, talk to your doctor or pharmacist . This includes any possible side effects not listed in this leaflet. See section 4.

D04963 00000

What is in this leaflet

1. What Pethidine Injection is and what it is used for

Pethidine is a drug with powerful pain relieving properties.

Pethidine Injection is used for the relief of moderate to severe pain and is used for pain relief during labour. It may also be used to stop you from feeling pain before and during an operation and to provide continuous pain relief if needed

2. Before you are given Pethidine Injection

You should not be given Pethidine Injection if:
- you are allergic (hypersensitive) to Pethidine Hydrochloride or to any of the ingredients of this medicine (listed in section 6)
- you suffer from asthma, shallow breathing or other breathing difficulties
- you are suffering from severe headaches or have suffered a head injury
- you suffer from alcoholism
- you suffer from a convulsive disorder (fits) such as epilepsy
- you have any liver or kidney problems
- you are suffering from a condition known as delirium tremens, caused by withdrawal from alcohol
- your heartbeat is faster than usual
- you suffer from a tumour of the adrenal gland known as phaeochromocytoma
- you suffer from diabetes
- you are taking or have recently taken any drugs used to treat depression known as Monoamine Oxidase Inhibitors (MAOI's) (see 'Taking other medicines)

Patients in a coma should not be given this medicine

Warnings and precautions
Talk to your doctor or pharmacist before being given Pethidine Injection if:
- are in shock, the symptoms of which include sweating, a fast pulse and cold, clammy skin
- suffer from thyroid problems
- suffer from problems related to your adrenal gland (the organ responsible for stress levels), including adrenocortical insufficiency (a lack of the hormones produced by the adrenal gland)
- suffer from low blood pressure
- suffer from problems with your prostate
- suffer from problems with your gallbladder
- suffer from problems with your bowel
- you have weak muscular movement
- you have lung problems

If you are elderly or ill, or your baby or child is being given Pethidine Injection, special care will be taken.

If any of the above apply to you or your child, please tell your doctor before being given Pethidine Injection.

Other medicines and Pethidine Injection
Tell your doctor, nurse or midwife if you are taking, have recently taken or might take any other medicines including medicines obtained without a prescription.

Pethidine Injection **must not** be used with drugs used to treat severe depression, such as rasagiline or moclobemide, or if you are within 2 weeks of discontinuing them.
These drugs are known as Monoamine Oxidase Inhibitors (MAOI's),

Other medicines which may interact with Pethidine Injection include:
- selegiline, a medicine used to treat Parkinson's disease
- ritonavir, a medicine used to treat HIV
- cimetidine, a medicine used to treat stomach ulcers
- medicines used to reduce anxiety (anxiolytics) (eg. benzodiazepines such as diazepam)
- medicines used to help you to sleep (hypnotics)
- CNS depressants (drugs that act on the brain and make you feel drowsy or faint). These include sleeping pills, anti-histamines (medicines used to treat allergies) that make you drowsy, medicines used to treat certain mental disorders.
- phenytoin, a medicine used to treat fits
- medicines used to treat serious mental disorders (phenothiazines)
- citalopram, a medicine used to treat depression
- medicines for depression (eg. tricyclic antidepressants such as amitriptyline)
- sedatives, sleeping tablets or barbiturates (eg. phenobarbitone for epilepsy)
- domperidone and metoclopramide (used for disorders of the gastrointestinal tract)
- pain relievers and other opioid medicines
- ciprofloxacin, an antibiotic used to treat a number of bacterial infections
- mexiletine, a medicine used to treat seriously irregular heartbeats

Concomitant use of Pethidine Injection and sedative medicines such as benzodiazepines or related drugs increases the risk of drowsiness, difficulties in breathing (respiratory depression), coma and may be life-threatening. Because of this, concomitant use should only be considered when other treatment options are not possible.

However, if your doctor does prescribe Pethidine together with sedative medicines the dose and duration of concomitant treatment should be limited by your doctor.

Please tell your doctor about all sedative medicines you are taking and follow your doctor's dose recommendation closely. It could be helpful to inform friends or relatives to be aware of the signs and symptoms stated above. Contact your doctor when experiencing such symptoms.

If you are in any doubt please tell your doctor of any medication you are taking.

Pregnancy, breast-feeding and fertility
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before using this medicine.

Pethidine can pass into your baby either through your blood (during pregnancy and labour) or through your breast milk. This can cause breathing problems in newborn babies. Your doctor will be aware of this and will correct the problem and discuss feeding with you.

Driving and using machines:
This medicine can affect your ability to drive and operate machinery. Do not drive or operate machinery if you feel drowsy or cannot think clearly.

This medicine can affect your ability to drive and operate machinery as it may make you sleepy or dizzy.
- Do not drive while taking this medicine until you know how it affects you.
- It is an offence to drive if this medicine affects your ability to drive.
- However, you would not be committing an offence 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 or in the information provided with the medicine and
  - It was not affecting your ability to drive safely

Continued overleaf

TECHNICAL PRESCRIBING INFORMATION

Pethidine 50mg/ml & 100mg/2ml Solution for Injection

Composition/excipients:
Pethidine injection is a sterile aqueous solution of 5% w/v Pethidine Hydrochloride. It also contains Water for Injections and may contain Sodium Hydroxide as a pH adjuster.

Indications:
Relief of moderate to severe pain, as a premedication, obstetric analgesia and enhancement of analgesia.

Dose:

Adults.
For moderate or severe pain.
Normal single dose (usually not to be repeated more often than 4 hourly)

By intramuscular or subcutaneous injection	25 - 100 mg.
By slow intravenous injection	25 - 50 mg.

For obstetric analgesia.

By intramuscular or subcutaneous injection repeated 1 – 3 hours later. Maximum of 400mg in 24 hours.	50 - 100 mg.

As a premedication.

By intramuscular injection one hour prior to the operation.	50 - 100mg

For the enhancement of analgesia.

By slow intravenous injection.	10 -25mg as required.

Elderly or debilitated patients.
Initial doses should not exceed 25mg as this group of patients may be specially sensitive to the central depressant effect of the drug.

Children
For moderate or severe pain.

By intramuscular injection	0.5 - 2 mg per Kg of body weight.

As a premedication.

By intramuscular injection one hour prior to the operation	1 - 2 mg per Kg of body weight.

Method of administration
Intramuscular, intravenous or subcutaneous injection.

Contraindications:

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

Severe respiratory depression, severe obstructive airways disease or acute asthma.

It should not be administered to patients with severe renal impairment or severe hepatic impairment.

Should be avoided in patients with acute alcoholism, delirium tremens, raised intracranial pressure or in those with convulsive states such as status epilepticus.

It should not be administered to patients receiving monoamine oxidase inhibitors (including moclobemide, and the monoamine B inhibitors selegiline and rasagiline) or within two weeks of their withdrawal. Pethidine should not be administered to patients receiving ritonavir.

Use of pethidine should be avoided in patients with supraventricular tachycardia.

Use of pethidine in patients with phaechromocytoma may result in hypertensive crisis.

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

In comatose patients

In patients with a risk of paralytic ileus

In patients with head injuries.

Warnings :

Repeated use may result in dependence of the morphine type.
Pethidine should be used with caution in patients with acute or chronic airflow obstruction including asthma.

Pethidine should be used with caution or in reduced doses in patients with myasthenia gravis.

Pethidine should only be given with caution and in reduced doses to neonates, premature infants, patients who are elderly or debilitated or those with impaired hepatic or renal function.

Renal impairment may result in accumulation of the potentially toxic metabolite norpethidine, particularly with repeat dosing All of these patient groups may experience increased or prolonged effects of the product.

Pethidine should be used with caution in patients with shock, hypothyrodism,adreno-corticol insufficiency and a history of convulsive disorders.

Although less spasmogenic than morphine, pethidine may precipitate spasm of the ureter or Sphincter of Oddi. Subsequently it should be used with caution in patients with prostatic hypertrophy and biliary tract disorders including those with pain secondary to gallbladder pathology.

Pethidine should be used with caution in patients with existing hypotension as it may reduce the blood pressure further.

In addition it should be avoided in patients with severe inflammatory bowel disease due to its effects on the gastrointestinal tract where it may precipitate toxic megacolon.

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

Concomitant use of methadone 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.

Interactions :

Pethidine should not be administered to patients receiving:
Monoamine Oxidase Inhibitors
The concurrent use of MAOIs (including moclobemide) is contra-indicated as they may result in CNS excitation or depression. Pethidine should not be administered to patients receiving monoamine oxidase inhibitors or moclobemide or within two weeks of their withdrawal.

CNS depressants
CNS depressants such as alcohol, hypnotics, anxiolytics and sedatives, barbiturates and tricyclic antidepressants may increase the general depressant effects of pethidine and should therefore be used with caution.

Opioid agonists
Additive effects on CNS depression, respiratory depression and hypotension can occur with concomitant use of opioid agonist analgesics.

MAO-B inhibitors
Concomitant use of MAO-B inhibitors such as selegiline or rasagiline is contraindicated as this may lead to hyperpyrexia and CNS toxicity. Rasagiline should not be given with pethidine as there is risk of CNS toxicity, its use should be avoided for two weeks after taking rasagiline.

Anticonvulsants
Administration of phenytoin may cause an increase in hepatic metabolism of pethidine and subsequently increased levels of norpethidine (a toxic metabolite).

Antipsychotics
Concomitant use of phenothiazines and pethidine can induce severe hypotension.

Anti-virals
Plasma concentrations of pethidine may be decreased by concomitant administration of ritonavir, however levels of norpethidine (a toxic metabolite) may rise. Concomitant administration of ritanovir and pethidine should be avoided.

Histamine H2 antagonists
Cimetidine can reduce the metabolism of pethidine resulting in increased plasma concentration.

Effects of pethidine on other drugs
Pethidine may have an effect on the activities of other drugs, for example domperidone, as a consequence of reduced gastro-intestinal motility.

Continued overleaf

100mm Measurement Verification Bar

The plasma levels of ciprofloxacin may be reduced in the presence of opiate premedicants.

Plasma levels of mexiletine may also be reduced in the presence of opioid analgesics.
Possible increased serotonergic effects when pethidine is given with SSRI's.

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.

Pregnancy and Lactation:

Pregnancy
There is inadequate evidence of safety in human pregnancy, but the drug has been in widely use for many years without apparent ill consequence. Animal studies have not shown any hazard.
As with all drugs during pregnancy care should be taken in assessing the risk to benefit ratio. Administration during labour may cause respiratory depression in the new-born infant.

Lactation:
Pethidine crosses the placental barrier and is excreted in breast milk. Patients should be advised to discontinue breast-feeding during treatment with pethidine

Side Effects:

There are no modern clinical studies available that can be used to determine the frequency of undesirable effects. Therefore, all the undesirable effects listed are classified as "frequency unknown" (cannot be estimated from the available data).
The undesirable effects listed below include class effects for opioid analgesics and effects related to the pharmacologically active metabolite, norpethidine.

Immune system disorders:
General hypersensitivity reactions

Psychiatric disorders:
Dependence, confusion, mood altered, mild euphoria, hallucinations, dysphoria

Nervous system disorders:
Drowsiness, dizziness, tremor, convulsions, headache, fainting, CNS excitation

Eye disorders:
Dry eye, miosis, corneal reflex decreased

Ear and labyrinth disorders:
Vertigo

Cardiac disorders:
Tachycardia, bradycardia, palpitations

Vascular disorders:
Orthostatic hypotension, flushing, hypotension, hypertension, vasodilation

Respiratory, thoracic and mediastinal disorders:
Respiratory depression

Gastrointestinal disorders:
Nausea, vomiting, dry mouth, constipation

Hepatobiliary disorders:
Biliary spasm or Ureteric spasm

Skin & subcutaneous tissue disorders:
Sweating, rash, urticaria, pruritus

Musculoskeletal and connective tissue disorders:
Muscle twitching

Renal & urinary disorders:
Difficulty in micturition, renal colic

Reproductive system and breast disorders:
Sexual dysfunction

General disorders & administration site conditions:
Hypothermia, weakness, injection site reactions including induration and irritation

Overdose:

Symptoms:
Respiratory depression, CNS depression with extreme somnolence progressing to incoordination, stupor or coma, convulsions, CNS stimulation, cyanosis, miosis, skeletal muscle flaccidity or tremors, cold, clammy skin, hypothermia, bradycardia and hypotension. In severe overdosage, apnoea, circulatory collapse, pulmonary oedema, mydriasis, cardiac arrest and death may occur.

Management:
Treatment is supportive. A patent airway must be established with assisted or controlled ventilation. If signs of CNS toxicity are exhibited the use of pethidine should be discontinued. Narcotic antagonists may be required if there is evidence of significant respiratory or cardiovascular depression.
Naloxone should be given intravenously as soon as possible and repeated every 2-3 minutes if necessary (refer to naloxone product literature for details).
Anti-convulsive therapy, oxygen, intravenous fluids, vasopressors and other supportive measures should be employed as indicated.

Incompatibilities:

Pethidine is incompatible with barbiturate salts and with other drugs including aminophylline, heparin sodium, methicillin sodium, morphine sulphate, nitrofurantoin sodium, phenytoin sodium, sulphadiazine sodium, sodium iodide, sulphafurazole diethanolamine. Incompatibility has also been observed between pethidine hydrochloride and acyclovir sodium, imipenem, frusemide and idarubicin.

Colour changes or precipitation have been observed on mixing pethidine with the following drugs, minocycline hydrochloride, tetracycline hydrochloride, cefoperazone sodium, mezlocillin sodium, nafcillin sodium and liposomal doxorubicin hydrochloride.

Pharmacodynamics:

Pethidine is a synthetic opioid analgesic similar to morphine although less potent and shorter acting. Its analgesic effect usually lasts for 2 to 4 hours. The analgesic effect occurs after about 10 minutes following parenteral administration. It acts on the CNS system and smooth muscles via the peripheral nervous system. However, it has a weaker action on smooth muscle than morphine and therefore has less effect on cough, bowel motility, biliary tone and secretion of pituitary hormones. Pethidine also causes the release of histamine from mast cells resulting in a number of allergic-type reactions.

Pethidine is a narcotic analgesic with similar actions to morphine.

Pharmacokinetics:

Pethidine is rapidly absorbed following intramuscular or subcutaneous injection, however, there are wide inter-individual variations. It is widely distributed in the tissues with a volume of distribution of 200-300 litres and is extensively protein bound (60-80%).
Pethidine is metabolised in the liver and excreted via the urine (70% in 24hours). One of the metabolites, norpethidine, is pharmacologically active and its accumulation can result in toxicity. Urinary excretion is pH-dependent, the lower the pH the greater the clearance. At normal urinary pH only a small amount of pethidine is excreted unchanged.
Pethidine has a plasma elimination half-life of about 3 to 6 hours. The metabolite norpethidine is eliminated more slowly with a half-life of up to 20 hours and may accumulate with chronic use, especially in the presence of renal impairment.
Pethidine crosses the placenta and is excreted in breast milk.
Both pethidine and norpethidine cross the blood/brain barrier and are found in the cerebrospinal fluid.

Shelf Life: 36 months.

Storage: Store below 25°C.
Keep the ampoules in the outer carton. Protect from light.

Product licence numbers: PL 01883/6150R
This leaflet was last revised in June 2019

MARTINDALE PHARMA
Bampton Road, Harold Hill, Romford, RM3 8UG, UK

Talk to your doctor or pharmacist if you are not sure whether it is safe for you to drive while taking this medicine.

Having Pethidine Injection with food, drink and alcohol
You are advised not to drink alcohol during your treatment with this medicine.

3. How Pethidine Injection will be given

Your doctor will give Pethidine Injection to you as an injection into a vein (intravenously), under the skin (subcutaneously) or into a muscle (intramuscularly). Your doctor will determine how much you need.

Adults
For the relief of moderate to severe pain:
The usual initial dose is 25-100mg either into a muscle or under the skin, or 25-50mg if given into a vein. The dose is given at a minimum of four hourly intervals if needed.

For pain relief during labour:
The usual dose is 50-100mg either into a muscle or under the skin every 1-3 hours during labour up to a maximum of 400mg in 24 hours.

For pain relief before and during an operation:
The usual dose is 50-100mg into a muscle one hour before the operation.

For continuous pain relief:
The usual dose is 10-25mg by slow injection into the vein as needed.

The elderly and ill
It is recommended that a reduced dose be used. The usual initial dose is up to a maximum of 25mg.

Children
For the relief of moderate to severe pain:
The usual dose is 0.5-2mg per kilogram of body weight by intramuscular injection.

For pain relief before and during an operation:
The usual dose is 1-2mg per kilogram of body weight into the muscle one hour before the operation.

If you are given too much of Pethidine Injection:
The symptoms and signs of taking too much of this medicine include shallow breathing, drowsiness, incoordination, coma, seizures, blue skin and lips, eye closure (miosis), shaking, cold, clammy skin, drop in body temperature, slow heartbeat and low blood pressure.
This medicine will be given to you in hospital so it is unlikely you will receive too much. Your doctor has information on how to recognise and treat an overdose.
If you feel unwell after being given this medicine, or are at all concerned you have been given too much, tell your doctor or nurse.
If you have any further questions on the use of this product, ask your doctor or nurse.

4. Possible Side Effects

Like all medicines this medicine can cause side effects, although not everybody gets them.

Repeated use of pethidine can result in tolerance and addiction
If any of the following symptoms occur, contact your doctor or nearest accident and emergency department **immediately**. These are symptoms of a serious allergic reaction.
Not known (frequency cannot be estimated from the available data):
- sudden wheeziness and tightness of chest
- swelling of eyelids, face or lips
- skin lumps or hives
- skin rash (red spots), itchiness, fever
- collapse

Other side effects that may occur include:
Not known (frequency cannot be estimated from the available data):
- restlessness
- drowsiness
- constipation
- dry mouth
- feeling sick (nausea)
- being sick (vomiting)
- facial flushing
- sweating
- a fast or slow heartbeat
- palpitations (an irregular heart rhythm or missed beats)
- low blood pressure, the symptoms of which include feeling dizzy or light-headed, feeling weak and fainting.
- high blood pressure
- pin-point pupils
- a feeling of dizziness or spinning
- fainting
- feeling weak
- hallucinations (seeing or hearing things that aren't real)
- mood changes (symptoms include feeling tense and restless)
- headache
- feeling faint on standing up from a seated position
- slowed breathing
- a red, itchy rash
- reduced sex drive
- difficulty achieving or maintaining an erection
- pain, redness or itching at the injection site
- hypothermia, the symptoms of which include shivering, drowsiness and feeling weak
- feeling of intense happiness (euphoria)
- difficulty in passing urine
- spasms in the lower abdomen
- addiction
- confusion
- tremor or involuntary shaking
- convulsions
- dry eye
- dizziness
- muscle twitching

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via Yellow Card Scheme. Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to Store Pethidine Injection

Keep this medicine out of the sight and reach of children.

You should not be given Pethidine Injection after the expiry date which is stated on the ampoule and carton label. The expiry date refers to the last day of that month. The doctor or nurse will check that the product has not passed this date.

Do not store above 25°C.
Keep the ampoules in the outer carton. Protect from light.

6. Contents of the pack and other information

What Pethidine Injection contains
Active Ingredient: Pethidine Hydrochloride 5%w/v
Other Ingredients: sodium hydroxide and water for injections.

What Pethidine Injection looks like and contents of the pack:
Pethidine Injection is a sterile solution, supplied in clear glass ampoules. Each ampoule contains 1ml or 2ml of the solution.

Marketing Authorisation Holder:
Martindale Pharma, Bampton Road, Harold Hill,
Romford, RM3 8UG, United Kingdom.

Manufacturers:
Macarthys Laboratories Limited, T/A Martindale Pharma,
Bampton Road, Harold Hill, Romford, RM3 8UG, United Kingdom.

Rotexmedica GmbH Arzneimittelwerk
Bunsenstraße 4
D-22946 Trittau
Germany

Product Licence Number:
PL 01883/6150R

This leaflet was last revised in: June 2019

MARTINDALE PHARMA
Bampton Road, Harold Hill, Romford, RM3 8UG, UK

D04963 00000

4963-B

100mm Measurement Verification Bar