SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Pethidine Injection BP

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Pethidine Hydrochloride BP 1% w/v

3 PHARMACEUTICAL FORM

Injection

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Relief of moderate to severe pain.

Premedication and analgesia during anaesthesia.

Obstetric analgesia.

Pethidine is a narcotic analgesic with similar actions to morphine

4.2 Posology and method of administration

Adults.
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.
50 - 100 mg up to a maximum of 400mg in 24 hours.

As a premedication.
By intramuscular injection one hour prior to the operation. 25 – 100mg

For postoperative pain:
By subcutaneous or intramuscular injection 25-100mg, every 2-3 hours if necessary.

Elderly or debilitated patients

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

Children

As a single dose

0.5 - 2mg/kg/body weight by intramuscular injection

As a premedication:
By intramuscular injection one hour prior to the operation 0.5 –2 mg per kg of body weight.

For Postoperative pain:
By intramuscular injection 0.5-2 mg per kg of body weight.

Dose adjustment should be made for patients with impaired hepatic or impaired renal function (See Section 4.4)
4.3 Contraindications

Respiratory depression, 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 or moclobemide, or within two weeks of their withdrawal. Pethidine should not be administered to patients receiving ritonavir or selegiline.

Not to be given to patients with a history of hypersensitivity or idiosyncratic response to the drug or its excipients.

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

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

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

4.4 Special warnings and precautions for use

Repeated use may result in dependence of the morphine type.

The use of pethidine should be avoided in patients with head injuries where administration may affect both the respiratory function and pupillary responses required for neurological assessment.

Pethidine should be avoided in patients with low respiratory reserve due to the respiratory effects of the drug.

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. All of these patient groups may experience increased or prolonged effects of the product.
Pethidine should be used with caution in patients with shock, hypothyroidism, adrenocorticol 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.

4.5 Interaction with other medicinal products and other forms of interaction

Pethidine should not be administered to patients receiving monoamine oxidase inhibitors or moclobemide, or within two weeks of their withdrawal (see Section 4.3).

Patients receiving selegiline should not be given pethidine as hyperpyrexia and CNS toxicity may result (see Section 4.3).

Plasma concentrations of pethidine may be decreased by concomitant administration of ritonavir, however levels of norpethidine (a toxic metabolite) may rise. Concomitant administration of ritonavir and pethidine should be avoided (see Section 4.3).

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.

Cimetidine potentiates the effect of pethidine.

Duloxetine when given with pethidine can increase the serotonergic effects.

The effects of pethidine may also be potentiated by concurrent administration with other CNS depressants including anaesthetics, anxiolytics, hypnotics, and alcohol (see Section 4.3).

Administration of phenytoin may cause an increase in the hepatic metabolism of pethidine and subsequently increased levels of norpethidine (a toxic metabolite).
Concomitant administration with phenothiazines may induce severe hypotension.

4.6 Fertility, pregnancy and lactation

Pregnancy
There is inadequate evidence of safety in human pregnancy, but the drug has been widely used for many years without apparent ill consequence. Animal studies have not shown any hazard.

Breastfeeding
As with all drugs during pregnancy care should be taken in assessing the risk to benefit ratio. Pethidine crosses the placental barrier and is excreted in breast milk. This should be taken into account when considering its use in patients during pregnancy or breast feeding. Administration during labour may cause respiratory depression in the new-born infant.

4.7 Effects on ability to drive and use machines

Pethidine may cause drowsiness. If affected patients should not drive or operate machinery.

4.8 Undesirable effects

General hypersensitivity reactions occur rarely.

Mild euphoria may occur and CNS excitation has been reported in some patients. Following administration of pethidine dizziness, fainting, drowsiness, weakness, hallucinations, dysphoria, mood changes, vertigo, sweating, and headache have been reported. Dependence may occur as a result of continued use.

Pethidine may obtund or abolish the corneal reflex and cause pupillary constriction.

Other undesirable effects include hypotension, hypertension, vasodilatation, dry mouth, facial flushing, bradycardia, tachycardia, palpitations, and postural hypotension.
Administration of pethidine may cause respiratory depression.

Nausea, vomiting, and constipation have all been reported following administration of pethidine.

Rashes, urticaria and pruritus may occur due to the release of histamine.

Ureteric or biliary spasm may be experienced, as may difficulty with micturition.

There have been reports of decreased libido or potency.

Local reactions at the injection site may be experienced. These include induration and local irritation.

The development of hypothermia has been reported.

4.9 Overdose

Symptoms

Incoordination, tremors, muscle twitching, hallucinations, constricted pupils and convulsions followed by dilated pupils, respiratory depression and coma.

Treatment

If respiration is dangerously depressed the use of naloxone is recommended. Artificial respiration may be necessary. If signs of CNS toxicity are exhibited the use of pethidine should be discontinued. Respiratory support and, if necessary, anticonvulsive therapy should be provided.

5 PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties

Pethidine is a narcotic analgesic with similar actions to morphine.

5.2 Pharmacokinetic properties

Pethidine is absorbed from the gastrointestinal tract, but only about 50% of the drug reaches the systemic circulation because of first-pass metabolism. Absorption following intramuscular injection is variable. Peak plasma concentrations have been reported 1 to 2 hours after oral doses.

Pethidine is metabolised in the liver by hydrolysis to pethidinic acid or by demethylation to norpethidine and hydrolysis to norpethidinic acid, followed by partial conjugation with glucuronic acid. Norpethidine is pharmacologically active and its accumulation may result in toxicity. Pethidine is reported to have a plasma elimination half-life of about 3 to 6 hours in healthy individuals, the metabolite norpethidine is eliminated more slowly, with a half-life reported to be up to about 20 hours. Both pethidine and norpethidine appear in the CSF. If the urine is alkaline, only a small amount of pethidine is excreted unchanged, urinary excretion of pethidine and norpethidine is enhanced by acidification of the urine.

Pethidine is extensively distributed throughout the body with a volume of distribution of 200 - 300L. It is 60 - 80% plasma bound, can cross the placenta and is found in breast milk. 70% of a dose is excreted in the urine in 24 hours. 5 - 30% is unchanged depending on the pH of the urine.

5.3 Preclinical safety data

No additional pre-clinical data of relevance to the prescriber.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium Hydroxide BP (q.s)
Water for Injection BP to 100%
6.2 **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.

6.3 **Shelf life**

36 months.

6.4 **Special precautions for storage**

None stated.

6.5 **Nature and contents of container**

Clear, colourless ampoules of Ph. Eu. type 1 glass in 10's in a cardboard outer. Ampoule sizes are 5ml and 10ml.

6.6 **Special precautions for disposal**

None stated.
7 MARKETING AUTHORISATION HOLDER

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8 MARKETING AUTHORISATION NUMBER(S)

PL 01883/6183R

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18/03/2008

10 DATE OF REVISION OF THE TEXT

03/01/2012