Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Pethidine Injection BP 50mg/ml

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 ml ampoule contains 50 mg of pethidine hydrochloride.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection.
A clear, colourless to pale yellow solution, free from visible particles.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Pethidine is a narcotic analgesic with similar actions to morphine.

Relief of moderate to severe pain.
As a premedication.
Obstetric analgesia.
Enhancement of analgesia.

4.2 Posology and method of administration

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.
50 - 100 mg.
Maximum of 400mg in 24 hours.

As a premedication.
By intramuscular or subcutaneous injection 25 - 100mg
(one hour prior to the operation)

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 especially 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 or subcutaneous injection 0.5 –2 mg per Kg of body weight.
(one hour prior to the operation)

4.3 Contraindications

Known hypersensitivity to pethidine or any of the excipients used.

Respiratory depression, obstructive airways disease, coma.

Use in patients who are receiving, or have within two weeks received, monoamine oxidase inhibitors, including moclobemide.

Patients taking selegiline should not be given pethidine as hyperpyrexia and CNS toxicity may result.

4.4 Special warnings and precautions for use

Repeated use will induce physical and psychology dependence of the morphine type, with a withdrawal syndrome on cessation of therapy.

Pethidine should only be used with extreme caution and in reduced doses to neonates, premature infants, the elderly, the debilitated or patients with head injuries, hypotension, hypothyroidism, adrenocortical insufficiency, severe inflammatory bowel disease, shock, prostatic hypertrophy, hepatic or renal dysfunction, or biliary tract disorders.

Excessive dosage (relative or absolute) may induce convulsions.

Pethidine should only be administered with great caution to patients with supraventricular tachycardia, respiratory dysfunction, convulsive disorders, increased intracranial pressure, acute alcoholism or phaeochromocytoma.

Repeated use will result in the development of tolerance and cross tolerance with other opioid analgesics, requiring increases in dosage to achieve the required effect.

If the intravenous route is being used, pethidine should be given slowly in order to reduce the risk of adverse reactions.

Use of pethidine in prolonged dosage may result in neurotoxicity in patients with renal failure, cancer and sickle cell anaemia.

Severe hypotension may occur when pethidine is administered to patients whose ability to maintain blood pressure has been compromised by a depleted blood volume.

4.5 Interaction with other medicinal products and other forms of interaction

The central depressant effects of pethidine may be potentiated by the concurrent use of other central nervous system depressants including sedatives, phenothiazine neuroleptics, anxiolytics, antidepressants, other analgesics, alcohol and general anaesthetics; respiratory depression, hypotension and profound sedation or coma may occur.

Severe hypotension may occur when pethidine is administered to patients whose ability to maintain blood pressure has been compromised by the administration of drugs such as phenothiazines.

Cimetidine potentiates the effect of pethidine and therefore increases plasma concentration.

Very severe reactions including coma, respiratory depression, cyanosis and hypotension have occurred in patients administered monoamine oxidase inhibitors (MAOIs). Pethidine should not be administered to patients taking MAOIs or to those who have taken MAOIs within 14 days (see section 4.3). Patients taking selegiline should not be given pethidine as hyperpyrexia and CNS toxicity may result.

Use of pethidine concomitantly with anticholinergics may result in neurotoxicity in patients with renal failure, cancer, and sickle cell anaemia. Administration of phenytoin may cause an increase in the hepatic metabolism of pethidine. Plasma concentrations of pethidine may be increased by concomitant administration of ritonavir.

4.6 Fertility, pregnancy and lactation

Pethidine should not be administered in pregnancy prior to the period of labour, unless the potential benefits outweigh the possible hazards, because the safe use of pethidine in pregnancy prior to labour has not been established relative to possible adverse effects on foetal development.

Like other opioid analgesics pethidine traverses the placenta and is excreted in milk. This should be borne in mind when considering use in patients during pregnancy or lactation. Administration during labour may cause respiratory depression in the newborn.

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable effects

The most serious adverse effects of pethidine are respiratory depression and hypotension. Rapid intravenous administration of pethidine increases the incidence of these effects and may result in serious respiratory depression and hypotension with tachycardia. Dependence may occur as a result of continued use.

The most frequently observed adverse effects included lightheadedness, dizziness, sedation, nausea, vomiting and sweating.

Other adverse effects include:
Psychiatric disorders: euphoria, dysphoria, hallucinations.
Nervous system disorders: weakness, headache, agitation, tremor, uncoordinated muscle movements, convulsions, confusion, mood changes.
Eye disorders: visual disturbances, pupil constriction.
Cardiac disorders: tachycardia, bradycardia, palpitation.
Vascular disorders: flushing of the face, hypotension, syncope.
Gastrointestinal disorders: dry mouth, constipation.
Hepatobiliary disorders: biliary tract spasm.
Skin and subcutaneous disorders: pruritis, urticaria, other skin rashes.
Renal and urinary disorders: urinary retention
General disorders and administration site conditions: pain at the site of injection, local tissue irritation, wheal and flare over the vein with intravenous injection.

There have been reports of decreased libido or potency.

The development of hypothermia has been reported.

4.9 Overdose

Possible manifestations of overdosage include in-coordination, tremors, muscle twitching, hallucinations, pinpoint pupils, convulsions, hypotension followed by respiratory depression and coma.

Intensive supportive therapy may be required to correct respiratory failure and shock. A patent airway must be maintained and assisted respiration may be required. The specific opioid antagonist naloxone hydrochloride is used to counteract respiratory depression and coma. Intravenous fluids and other supportive measures may be required in the management of shock. An anticonvulsant drug may be required to control seizures.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC code: N02AB02

Pethidine is an opioid analgesic. It binds to opioid receptors and exerts its principal pharmacological actions on the central nervous system where its analgesic and sedative effects are of particular therapeutic value.

Pethidine has a spasmogenic effect on certain smooth muscles which is qualitatively similar to that of morphine. In equianalgesic doses, pethidine appears to cause less constipation and biliary tract spasm than does morphine.

Pethidine, like other opioids, dilates resistance and capacitance vessels and may thereby decrease the capacity of the cardiovascular system to respond to gravitational shifts. In therapeutic doses, the effects of pethidine on the cardiovascular system are generally not of clinical significance, especially when the patient is recumbent. However, rapid intravenous administration, or administration of pethidine to patients with depleted blood volume or in other situations where ability to maintain blood pressure has been compromised, may result in severe hypotension.

5.2 Pharmacokinetic properties

Pethidine hydrochloride is well absorbed by all recommended routes of administration. It is metabolised in the liver by hydrolysis. Following intravenous injection, a rapid decline in plasma concentration occurs due to distribution and this is followed by a slower phase with a half-life of approximately 3 hours. In patients with cirrhosis, the half-life is increased to 6 hours.

Approximately 60% of pethidine in plasma is protein-bound. Older patients have decreased binding to plasma proteins and have higher concentrations in plasma, both of which may account for their increased response to therapeutic 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. About 1/3 of administered pethidine may be accounted for in the urine as N-demethylated derivatives. The accumulation of norpethidine may result in toxicity. The T½ of norpethidine is reported to be up to 20 hours.

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 (may be added to adjust the pH.)
Water for injections.

6.2 Incompatibilities

Pethidine is incompatible with barbiturate salts and with drugs like aminophylline, heparin sodium, methicillin sodium, morphine sulphate, nitrofurantoin sodium, phenytoin sodium, sulfadiazine sodium, sodium iodide, sulphafurazole diethanolamine. Incompatibility has also been observed between pethidine hydrochloride and aciclovir sodium, imipenem, furosemide 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

Unopened: 3 years.
Product should be used immediately after opening and any remaining contents discarded.

6.4 Special precautions for storage

Store below 25°C. Keep the ampoule in the outer carton in order to protect from light.

6.5 Nature and contents of container

Type I glass ampoule, 1 ml in volume, in cardboard cartons of 10 ampoules.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

For single use. Discard any remaining contents immediately after use.

7 MARKETING AUTHORISATION HOLDER

Martindale Pharmaceuticals Limited
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8 MARKETING AUTHORISATION NUMBER

PA 361/8/2

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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Date of last renewal: 13 December 2006

10 DATE OF REVISION OF THE TEXT

October 2010