SUMMARY OF PRODUCT CHARACTERISTICS

Product Summary

1. Trade Name of the Medicinal Product

Pethidine injection B.P. 50mg/ml, 1ml & 2ml.

2. Qualitative and Quantitative Composition

Each 1ml of solution contains 50mg of Pethidine Hydrochloride B.P.

3. Pharmaceutical Form

Clear, colourless, sterile solution intended for parenteral administration to human beings.

Clinical Particulars

4.1. Therapeutic Indications

Pethidine hydrochloride may be used as an analgesic for the relief of moderate to severe pain including: obstetric analgesia; pre-operative medication and analgesia during anaesthesia; post-operative analgesia.

4.2. Posology and Method of Administration

Pethidine Injection may be administered by subcutaneous, intramuscular or slow intravenous injection.

Adults: The following single doses may be used and should not usually be repeated more frequently than four hourly; Subcutaneous or intramuscular injection: 25 - 100mg. Intravenous injection: 25 - 50mg.

Elderly or debilitated patients: The initial dose should not exceed 25mg, because of the particular sensitivity among elderly or debilitated patients to the central depressant effects of pethidine.

Children: The usual single dose is 0.5 to 2mg/kg body weight by intramuscular injection. If necessary, this dose may be repeated, allowing a minimum of four hours between doses. Use of a small graduated syringe is recommended for the accurate administration of dosages in

children. In the absence of graduated syringes, the solution should be diluted with Water for Injections before measuring the dose.

4.3. Contra-indications

History of hypersensitivity to pethidine.
Coma.
Respiratory depression or obstructive airways disease.
Use in patients receiving monoamine oxidase inhibitors or within two weeks following their withdrawal.

4.4. Special Warnings and Precautions for Use

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

Extreme care is required when administering pethidine to patients with reduced respiratory function.

Pethidine should only be used with caution and in reduced dosage in neonates and premature infants, elderly and debilitated patients and in patients with head injuries, severe hepatic or renal impairment, biliary tract disorders, hypothyroidism, adrenocortical insufficiency, shock, prostatic hypertrophy and supraventricular tachycardia.

Caution is also required in patients with acute alcoholism, raised intracranial pressure or convulsive disorders.

Repeated administration of pethidine may produce physical and psychological dependence of the morphine type, with the development of withdrawal symptoms on abrupt cessation of therapy or on administration of a narcotic antagonist. Repeated administration may also induce tolerance, with a tendency to increase the dose in order to obtain the desired effect.

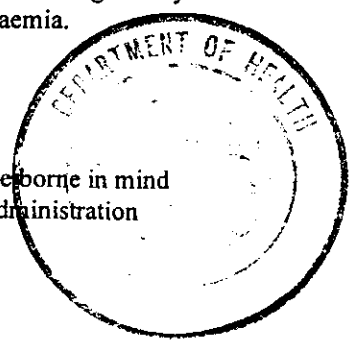
4.5. Interactions with other Medicaments and other forms of Interaction

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

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

Cimetidine inhibits metabolism of pethidine and therefore increases plasma concentration.

Use of pethidine in prolonged increasing dosage or concomitantly with anticholinergics may result in neurotoxicity in patients with renal failure, cancer or sickle cell anaemia.



4.6. Pregnancy and Lactation

Pethidine crosses the placenta and is excreted in breast milk. This should be borne in mind when considering its use in patients during pregnancy or breast feeding. Administration during labour may cause respiratory depression in the newborn.

4.7. Effects on Ability to Drive and Use Machines

Pethidine may impair the mental and/or physical abilities required for driving or for operating machinery; patients should be advised accordingly and warned not to drive or to operate machines if affected.

4.8. Undesirable Effects

Pethidine may cause drowsiness, dizziness, euphoria or visual disturbances, nausea and vomiting. Constipation, biliary tract spasm and urinary retention may occur. Urticaria and other skin reactions have been reported.

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.

4.9. Overdose

Signs of acute overdosage may include convulsions, respiratory depression, hypotension, shock and coma.

Primary attention should be directed at correcting respiratory failure and shock. A patent airway should be established and assisted or controlled ventilation should be provided. Naloxone is a specific antidote used to counteract respiratory depression and coma resulting from opioid overdosage. Intravenous fluids and other supportive measures may be required in the management of shock. An anticonvulsant may be required if seizures occur.

Pharmacological Properties

5.1. Pharmacodynamic Properties

Like other opioids, pethidine 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. The respiratory depression produced by pethidine can be antagonised by naloxone and nalorphine.

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-time 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 conjugation with glucoronic acid. About 1/3 of administered pethidine may be accounted for in the urine as N-demethylated derivatives.

5.3. Preclinical Safety Data

No further relevant information other than that which is included with other sections of the Summary of Product Characteristics.

Pharmaceutical Particulars

6.1. List of Excipients

Sodium Hydroxide B.P.
Dilute Hydrochloric Acid B.P.
Water for Injections B.P.

6.2. Incompatibilities

There was loss of clarity when intravenous solutions of pethidine hydrochloride were mixed with those of aminophylline, amylobarbitone sodium, heparin sodium, methicillin sodium, morphine sulphate, nitrofurantoin sodium, pentobarbitone sodium, phenobarbitone sodium, phenytoin sodium, sodium bicarbonate, sodium iodide, sulphadiazine sodium, sulphafurazole diethanolamine or thiopentone sodium.

6.3. Shelf Life

4 years.
If only part used, discard the remaining solution.

6.4. Special Precautions for Storage

Keep in outer carton
Do not store above 25°C

6.5. Nature and Contents of Container

1ml and 2ml clear glass ampoules, glass type 1 Ph. Eur. packed in cardboard cartons to contain 10 x 1ml or 10 x 2ml ampoules.

6.6. Instruction for Use/Handling

CD (2)

Dated 24/10/2001 in substitution for SPC page 4 dated 21/8/1997
Signed: C.A. Kennedy

For S/C., I/M., or I/V injection.
Use as directed by the physician.

Administrative Data

7. Marketing Authorisation Holder

Antigen International Limited
Roscrea
Co. Tipperary
Ireland.

8. Marketing Authorisation Number

PL 2848/0016R.

9. Date of First Authorisation/Renewal of Authorisation

10 May 1982 / 13 March 1992

10. Date of (Partial) Revision of the Text

Not applicable.