Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Pethidine Hydrochloride 50 mg/ml solution for injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 ml of solution contains 50 mg pethidine hydrochloride.
Each 2 ml of solution contains 100 mg pethidine hydrochloride.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for injection (Injection)
Clear, colourless solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

As an analgesic in the relief of moderate to severe pain.
For pre-operative medication and analgesia during anaesthesia.
As an analgesic during labour.

4.2 Posology and method of administration

Pethidine Hydrochloride Injection 50 mg/ml is for administration by subcutaneous, intramuscular or slow intravenous injection.

FOR PAIN RELIEF:

Adults:
The usual dose is 25 to 100 mg intramuscularly or subcutaneously or 25 to 50 mg by slow intravenous injection. Dosage may be repeated if required every 4 hours.

Elderly:
In view of their greater sensitivity, the initial dose should not exceed 25 mg.

Paediatric patients:
The usual dose is 0.5 to 2 mg/kg body weight intramuscularly. Dosage may be repeated if required every 4 hours.

OBSTETRIC ANALGESIA

50-100 mg given by intramuscular or subcutaneous injection. Dose may be repeated after one to three hours if necessary up to a maximum of 400 mg in 24 hours.

PRE-ANAESTHETIC MEDICATION

Adults:
25 to 100 mg may be given intramuscularly or subcutaneously about one hour before surgery.

Elderly:
In view of their greater sensitivity, the initial dose should not exceed 25 mg.

Paediatric patients:
0.5 to 2 mg/kg body weight intramuscularly one hour before surgery.

The use of a small graduated syringe is recommended for the accurate administration of dosages given to children. In the absence of graduated syringes, the solution should be diluted with Water for Injections before measuring the dose.

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 psychological dependence of the morphine type, with a withdrawal syndrome on cessation of therapy.

Pethidine should only be used with extreme caution and in reduced dosage in neonates, premature infants, the elderly, the debilitated, or patients with head injuries, hypotension, hypothyroidism, adrenocortical insufficiency, severe inflammatory bowel disease, shock, prostatic hypertrophy, renal or hepatic 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 interactions

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 inhibits metabolism 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 4.3 Contraindications). 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

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 incoordination, 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. A dose of 0.4 to 2 mg is given intravenously and may be repeated at intervals of 2 to 3 minutes if necessary, up to 10 mg. 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 conjugation with glucoronic 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 further relevant information.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium hydroxide
Hydrochloric acid
Water for injections

6.2 Incompatibilities

In the absence of incompatibility studies, pethidine Hydrochloride 50 mg/ml solution for injection must not be mixed with other medicinal products.

6.3 Shelf life

Unopened: 3 years.

The product should be used immediately after opening and any unused solution must be discarded.

6.4 Special precautions for storage

Do not store above 30ºC.
Keep the ampoule in the outer carton in order to protect from light.

6.5 Nature and contents of container

Type I, neutral glass ampoules.
Pack sizes: 10 x 1 ml ampoules, 10 x 2 ml 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 only.

Discard any unused contents.
The product should be used immediately after opening.

7 MARKETING AUTHORISATION HOLDER

Accord Healthcare Ireland Ltd.
Euro House
Euro Business Park
Little Island
Cork T45 K857
Ireland

8 MARKETING AUTHORISATION NUMBER

PA2315/207/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 17 February 2006
Date of last renewal: 16th February 2011

10 DATE OF REVISION OF THE TEXT

February 2020