

# DATA SHEET

## **Pethidine Hydrochloride**

Pethidine Hydrochloride 50mg and 100mg Tablets.

## **Presentation**

**Pethidine hydrochloride 50mg and 100mg tablets** are white, circular, film-coated tablets embossed with DP on one side and '50' or '100' respectively on the other.

## **Uses**

### ***Actions***

Pethidine is a synthetic narcotic pharmacologically similar to morphine and may be used clinically in place of morphine. It exerts agonist activity at the opioid receptors located in the central and peripheral nervous systems. Its main effects are on the central nervous system resulting in analgesia, sedation, euphoria and respiratory depression. Pethidine also increases smooth muscle tone, causing spasm. Clinically pethidine is used for the relief of moderate to severe pain (including the pain of labour) and in other dosage forms as a pre-operative medication and as an adjunct to anaesthesia. It has little effect on cough or diarrhoea.

The analgesic effect of pethidine hydrochloride is shorter than for morphine and usually lasts for 2 to 4 hours with a rapid onset of action at 15 minutes. Peak effect is obtained orally within 60 to 90 minutes.

10mg of morphine is equivalent in analgesic effect to approximately 100mg of pethidine.

### ***Pharmacokinetics***

Pethidine hydrochloride is absorbed from the gastro-intestinal tract, but availability is less with the oral than the parenteral routes. It is highly bound to plasma proteins.

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 glucuronic acid. Norpethidine is both active and toxic. The half life of pethidine is 2.4 to 4 hours.

Elimination is renal and negligible unchanged pethidine is excreted into the urine (5%). Acidification of the urine enhances excretion of both pethidine and norpethidine. In subjects with cirrhosis, excretion of pethidine is delayed.

Pethidine crosses the placenta and appears in breast milk.

Pethidine produces prompt but short-lasting analgesia, even in high doses it is a less potent analgesic than morphine.

## **Indications**

Pethidine hydrochloride given orally is indicated for the relief of most types of moderate to severe pain.

As it has some antispasmodic activity, it may be the analgesic of choice in renal colic, biliary colic and acute pancreatitis.

## **Dosage and Administration**

**Adults:** For the relief of pain, pethidine hydrochloride is given in doses of 50 to 150mg by mouth every 4 hours.

**Children:** For the relief of pain, 1.1 to 1.76mg per kg of body weight, not to exceed 100mg every 3 to 4 hours as needed. (See Warnings and Precautions)

Opioid agonist analgesics may suppress respiration, especially in the very young, elderly, very ill or debilitated patients and those with respiratory problems. Lower doses may be required for these patients.

Tolerance to many of the effects of opioid analgesics may develop with repeated administration. The first sign of tolerance is a decrease in the duration of adequate analgesia. Careful dosage adjustment is required to maintain analgesic effect.

Psychological and physical dependence may occur with chronic administration of opioid analgesics; an abstinence syndrome may occur when these drugs are discontinued. Physical dependence in patients receiving prolonged therapy for severe chronic pain rarely leads to true addiction. Gradual withdrawal may minimise the development of withdrawal symptoms following prolonged use.

## **Contraindications**

Pethidine hydrochloride is contraindicated in the following:

- respiratory depression
- raised intracranial pressure
- acute bronchial asthma
- supraventricular tachycardias
- concurrent use of monoamine oxidase inhibitors or within 14 days of ceasing MAOI therapy
- convulsive states such as status epilepticus, tetanus and strychnine poisoning
- diabetic acidosis where there is danger of coma
- acute alcoholism or delirium tremens
- severe liver disease
- hypersensitivity to pethidine

## **Warnings and Precautions**

Pethidine should be given cautiously to patients with supraventricular tachycardia.

Prolonged use of pethidine may lead to dependence and tolerance (*see Dosage and Administration*). Doses as large as 3 or 4g daily may be taken by addicts. As tolerance to the central nervous system stimulant and anticholinergic effects is not complete with these very

large doses, muscle twitching, tremor, mental confusion, dilated pupils and sometimes convulsions may be present. Withdrawal symptoms appear more rapidly than with morphine and are of shorter duration.

**Use in Pregnancy:** Risk-benefit must be considered as opioid analgesics cross the placenta. Regular use during pregnancy may cause physical dependence in the foetus, leading to withdrawal symptoms (convulsions, irritability, excessive crying, tremors, hyperactive reflexes, fever, vomiting, diarrhoea, sneezing and yawning) in the neonate.

Although teratogenic effects in humans have not been documented with pethidine, controlled studies have not been done.

**Use in Labour:** Opioid analgesics readily enter the foetal circulation when used during labour and may cause respiratory depression in the neonate, especially the premature neonate.

**Use in Lactation:** Problems in humans with most opioid analgesics have not been documented. Pethidine is excreted into breastmilk however with usual analgesic doses, concentrations are generally low.

**Use in Children:** Children up to 2 years of age may be more susceptible to the effects, especially the respiratory depressant effects of these drugs. Paradoxical excitation is especially likely to occur in paediatric patients receiving opioid analgesics.

**Use in the Elderly:** Geriatric patients may be more susceptible to the effects, especially the respiratory depressant effects of the opioid analgesics.

Also geriatric patients are more likely to have prostatic hypertrophy or obstruction and age-related renal function impairment, and are therefore more likely to be adversely affected by opioid-induced urinary retention. In addition, geriatric patients may metabolise or eliminate opioid analgesics more slowly than younger adults. Lower doses or longer dosing intervals than those usually recommended for adults may be required, and are usually therapeutically effective for these patients.

## **Adverse Effects**

Pethidine may cause dizziness, nausea and vomiting, dry mouth, tachycardia, bradycardia, palpitations, syncope, perspiration, euphoria, dysphoria, hallucinations, headache, weakness, sedation, visual disturbance, constipation and urinary retention. Constipation occurs less frequently than with morphine. Pethidine is more likely than most other opioids to cause side effects associated with histamine release.

## **Interactions**

Very severe reactions including coma, severe respiratory depression, cyanosis and hypotension have occurred in patients receiving monoamine oxidase inhibitors and given pethidine. There are also reports of hyperexcitability, convulsions, tachycardia, hyperpyrexia and hypertension when these agents have been used simultaneously. Pethidine should not be given to patients receiving monoamine oxidase inhibitors or within fourteen days of their discontinuation.

Concurrent administration of pethidine and phenothiazines has produced severe hypotensive episodes and may prolong the respiratory depression due to pethidine. Narcotic analgesics may interact with alcohol, butyrophenones and phenothiazines to enhance CNS depressant effects.

## Overdosage

**Symptoms:** Symptoms of overdose are generally similar to those of morphine poisoning, however stimulation of the central nervous system as well as convulsions may also occur, especially in tolerant individuals or following toxic doses by mouth. Respiratory depression and coma may follow.

**Treatment:** The stomach should be washed out, a 0.02% solution of potassium permanganate is commonly used for this purpose. A saline purgative may then be administered to reduce absorption from the gastro-intestinal tract. The most important aspect of treatment is to guard the patient from respiratory failure; for this naloxone or levallorphan should be used only when respiration is dangerously depressed. Artificial respiration may be required.

## Pharmaceutical Precautions

Protect from light and moisture. Store below 30°C. Keep out of reach of children.

## Medicine Classification

Controlled Drug B3.

## Package Quantities

Pethidine hydrochloride 50mg tablets:	10's
Pethidine hydrochloride 100mg tablets:	10's

## Further Information

Pethidine hydrochloride is a fine white odourless crystalline powder with a slightly acid and bitter taste. It has a molecular formula and weight of  $C_{15}H_{21}NO_2.HCl$  and 283.8 respectively.

Other ingredients of the tablets are: Lactose, Maize cornflour, Microcrystalline cellulose, Sodium starch glycolate, Polyvinylpyrrolidinone, Magnesium stearate and Opadry white Y-1-7000B.

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