PACKAGE INSERT

SCHEDULING STATUS: S6

PROPRIETARY NAME AND DOSAGE FORM:

Pharma-Q Pethidine Injection 25 mg/1 ml solution for injection.

Pharma-Q Pethidine Injection 50 mg/1 ml solution for injection.

Pharma-Q Pehtidine Injection 100 mg/2 ml solution for injection.

COMPOSITION:

Pharma-Q Pethidine Injection 25 mg/1 ml: 1 ml Ampoules containing 25 mg pethidine hydrochloride.

Pharma-Q Pethidine Injection 50 mg/1 ml: 1 ml Ampoules containing 50 mg pethidine hydrochloride.

Pharma-Q Pethidine Injection 100 mg/2 ml: 2 ml Ampoules containing 100 mg pethidine hydrochloride.

Excipients: nitrogen, hydrochloric acid, water for injections.

PHARMACOLOGICAL CLASSIFICATION:

A 2.9 Other Analgesics.

PHARMACOLOGICAL ACTION:

Pharmacodynamic properties:

Pethidine hydrochloride is predominantly a mu (μ) receptor agonist. It binds to the opioid receptors and exerts its main pharmacological action on the central nervous system and the neutral elements in the bowel.

Pharmacokinetic properties:

The analgesic potency of pethidine hydrochloride is approximately equal to one-fifth that of morphine but it has a more rapid onset of action and shorter duration. Pethidine hydrochloride is absorbed by all routes but the rate of absorption may be erratic after intramuscular injection. Peak plasma concentration is usually reached in 1-2 hours. Pethidine hydrochloride is metabolised mainly in the liver with a half life of about 3 hours.

INDICATIONS:

- **Pharma-Q Pethidine Injection** is indicated for the relief of severe pain.
- It is particularly useful for the relief of post-operative pain.
- It may be used to relieve labour pain.

CONTRAINDICATIONS:

Pharma-Q Pethidine Injection is contraindicated in:

- Patients with a hypersensitivity to pethidine hydrochloride.
- Patients who suffer from respiratory depression, especially in the presence of cyanosis and excessive bronchial secretion, chronic lung disease, renal and hepatic insufficiency.
- Patients who display a presence of acute alcoholism, head injuries, and conditions in which intracranial pressure is raised.
- Patients who are being treated with monoamine oxidase inhibitors, or within 2 weeks of the discontinuation of such treatment (see Interactions).
- Patients suffering from an attack of bronchial asthma or in heart failure secondary to chronic lung disease.
- Patients who are comatose.
- Patients who are pregnant or breast-feeding as safety has not been established (see **PREGNANCY AND LACTATION**).

WARNINGS and SPECIAL PRECAUTIONS:

Prolonged use of **Pharma-Q Pethidine Injection** may lead to dependence. Cross-tolerance and cross-dependence can be expected between opioids acting at the same receptors.

Pharma-Q Pethidine Injection should be administered with **caution** to:

- Patients with supraventricular tachycardia or a history of convulsive disorder.
- Patients who suffer from phaeochromocytoma as it may provoke episodes of hypertension.

Pharma-Q Pethidine Injection should be administered with **caution or in reduced doses** to patients with:

- Hypothyroidism.
- Adrenocortical insufficiency.
- Asthma.
- Decreased respiratory reserve.
- Impaired kidney or liver function.
- Prostatic hyperplasia.
- Hypotension.
- Shock.
- Inflammatory or obstructive bowel disorders.
- Myasthenia gravis.

Pharma-Q Pethidine Injection should be given with **great care** to:

- Infants, more especially neonates.
- The use of **Pharma-Q Pethidine Injection** during labour may cause respiratory depression in the neonate

Special precautions:

Pharma-Q Pethidine Injection:

- The dosage should be reduced in elderly and debilitated patients.
- The depressant effects are enhanced by depressants of the central nervous system such as alcohol, anaesthetics, hypnotics and sedatives, tricyclic antidepressants, and phenothiazines.
- Hypotension may develop if used in conjunction with meprobamate and phenothiazines.
- Hypotension and vasodilation may occur with intravenous injection.
- Extreme vigilance and appropriate monitoring are required for all patients receiving intraspinal narcotics.
- Is regarded as a medicine of addiction.

Effects on the ability to drive and use machines:

Pharma-Q Pethidine Injection may cause drowsiness that may affect the ability to perform skilled tasks. Patients who experience such effects should be advised not drive or operate machinery.

INTERACTIONS:

- **MAOI (mono-amine oxidase inhibitors):**
- **Pharma-Q Pethidine Injection** should not be given to patients receiving MAOI or within 14 days of their discontinuation as very severe reactions, including coma, respiratory depression, cyanosis and hypotension may occur (see **CONTRAINDICATIONS**). MAOI enhances the effects of **Pharma-Q Pethidine Injection.**

- **Barbiturates and other opioid analgesics:**
- Opioid analgesics (including **Pharma-Q Pethidine Injection**) and barbiturates can be expected to have additive central nervous system (CNS) depressant effects when used concomitantly with alcohol, anaesthetics, anxiolytics, hypnotics, tricyclic anti-depressants and anti-psychotics.

- **Histamine H_2antogonists:**
- Cimetidine reduces the clearance and volume of distribution of **Pharma-Q Pethidine Injection.**

- **Phenothiazines:**
- Prochlorperazine prolongs the respiratory depressant effect of **Pharma-Q Pethidine Injection.**

PREGNANCY AND LACTATION:

Pharma-Q Pethidine Injection:

- Safety in pregnancy and lactation has not been established (see **CONTRAINDICATIONS**).
- The administration during labour may cause respiratory depression in the newborn infant.
- Respiratory depression varies according to the timing and size of the maternal dose.
- Foetal depression is not apparent immediately when delivery occurs and may occur 1-3 hours after delivery.
- Crosses the placenta and is excreted in breast milk.

DOSAGE AND DIRECTIONS FOR USE:

Pharma-Q Pethidine Injection dosages:

- **Children:**
- **Intramuscular injection:**
- 0,5 mg to 2 mg per kg body-mass, but not exceeding the adult dose.

- **Adults:**
- **Subcutaneous or Intramuscular injection:**
- 25 mg to 100 mg.
- **Slow intravenous injection:**
- In doses of 25 mg to 50 mg.

Obstetric Analgesia:

Intramuscular or subcutaneous injection:

50 mg to 100 mg may be give as soon as contractions occur at regular intervals. This dose may be repeated after 1 to 3 hours if necessary.

Epidural Administration:

Slow injection:

- Proper placement of needle or catheter in the epidural space should be verified before **Pharma-Q Pethidine Injection** is injected to assure that unintentional intravascular or intrathecal administration does not occur.
- Unintentional intrathecal injection of the full epidural doses could produce effects of high spinal anaesthesia including prolonged paralysis and delayed recovery.
- If analgesia is inadequate, the placement and integrity of the catheter should be verified prior to administration of any additional epidural medications.

- **Pharma-Q Pethidine Injection** should be administered by slow injection.
- With epidural administration, caution should be exercised in the presence of respiratory depression and in the presence of foetal distress.
- Epidural administration requires that the patient should be in a high care environment with continuous supervision.
- The patient should be closely monitored for at least 2 hours after each dose, as early respiratory depression may occur.

In addition to conventional routes of administration **Pharma-Q Pethidine Injection** may be given epidurally and intrathecally.

Intraspinal doses are in the region of 20 mg to 150 mg for initial epidural injection or at an infusion rate of 5 mg to 20 mg per hour. Onset of action is around 5 minutes. The duration of effect of a single dose is 4 to 8 hours.

SIDE EFFECTS:

Nervous system disorders:

Frequency unknown: Dysphoria, confusion, drowsiness, dizziness, raised intracranial pressure, headache, vertigo, restlessness, changes in mood and hallucinations.

Eye disorders:

Frequency unknown: Miosis may occur more frequently in ambulant patients than in those at rest in bed.

Cardiovascular disorders:

Frequency unknown: Intravenous injection may produce vasodilation and hypotension, bradycardia, tachycardia, palpitations and orthostatic hypotension.

Gastrointestinal disorders:

Frequency unknown: Nausea, vomiting, constipation and dry mouth.

Hepatobiliary disorders:

Frequency unknown: Biliary spasm.

Skin and subcutaneous tissue disorders:

Frequency unknown: Sweating, facial flushing, hypothermia and anaphylactic reactions following IV administration.

Due to histamine releasing effect, reactions such as urticaria and pruritus.

Musculoskeletal, connective tissue and bone disorders:

Frequency unknown: Muscle rigidity following high doses

Renal and urinary disorders:

Frequency unknown: Urinary retention (anti-diuretic effect), difficulty in micturition, uretic or biliary spasm.

Reproductive system and breast disorders:

Frequency unknown: Decreased libido or potency.

General disorders and administrative site disorders:

Frequency unknown: Local reactions often follow injections of pethidine and general hypersensitivity reactions.

Larger doses of **Pharma-Q Pethidine Injection** may produce:

- Respiratory depression and hypotension, with circulatory failure and deepening coma.
- Convulsions may occur in infants and children.
- Death may occur from respiratory failure.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

Overdose with **Pharma-Q Pethidine Injection** may cause:

- Muscular twitching.
- Tremors.
- Hyperactive reflexes.
- Dilated pupils and convulsions followed by repiratory depression.
- Hypotension with circulatory failure and deepening coma.
- Death may occur from respiratory failure.
- Rhabdomyolysis progressing to renal failure may occur.

Treatment of toxic effects:

- The stomach should be emptied by aspiration and lavage if oral ingestion occurs.
- Intensive supportive therapy may be required to correct respiratory failure and shock.
- In addition, the specific antagonist naloxone hydrochloride is used to counteract very rapidly the severe respiratory depression and coma produced by excessive doses of opioid analgesics.
- In adults a dose of 0,4 mg to 2 mg is given intravenously, repeated at interval of 2 to 3 minutes if necessary, up to 10 mg.

- In children a dose of 5 mcg to 10 mcg/kg body-mass may be given, repeated at intervals of 2-3 minutes.
- Naloxone may also be given by subcutaneous or intramuscular injection.
- The effect of naloxone may be of shorter duration than that of the opioid analgesic and additional doses may be required to prevent relapses. Respiration assistance may be necessary.
- Circulation should be maintained with infusions of dextrose injection and suitable electrolyte solutions.
- Further treatment is supportive and symptomatic.

IDENTIFICATION:

Clear, colourless solution in clear, colourless glass ampoules.

PRESENTATION:

Pharma-Q Pethidine Injection 25 mg/1 ml: Containers of 10 or 100 x 1 ml ampoules

Pharma-Q Pethidine Injection 50 mg/1 ml: Containers of 10 or 100 x 1 ml ampoules

Pharma-Q Pethidine Injection 100 mg/2 ml: Containers of 10 or 100 x 2 ml ampoules

STORAGE INSTRUCTIONS:

Store at or below 25 °C.

Protect from light.

Store all medicines out of the reach of children.

REGISTRATION NUMBERS:

Pharma-Q Pethidine Injection 25 mg/1 ml: 31/2.9/0083.

Pharma-Q Pethidine Injection 50 mg/1 ml: 31/2.9/0084.

Pharma-Q Pethidine Injection 100 mg/2 ml: 31/2.9/0085.

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:

PHARMA-Q HOLDINGS (PTY) LTD

50 Commando Road

Industria West, 2093

Johannesburg.

DATE OF PUBLICATION OF THE PACKAGE INSERT:

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