PACKAGE INSERT

SCHEDULING STATUS: **S6**

PROPRIETARY NAME AND DOSAGE FORM:

Pharma-Q Morphine 10 mg Injection solution for injection

Pharma-Q Morphine 15 mg Injection solution for injection

COMPOSITION:

Pharma-Q Morphine 10 mg Injection: Each 1 ml ampoule contains 10 mg morphine sulphate, without preservative.

Pharma-Q Morphine 15 mg Injection: Each 1 ml ampoule contains 15 mg morphine sulphate, without preservative.

Excipients: nitrogen, sodium chloride, water for injections.

PHARMACOLOGICAL CLASSIFICATION:

A 2.7 Narcotic Analgesics.

PHARMACOLOGICAL ACTION:

Pharmacodynamic properties:

Pharma-Q Morphine Injection is a narcotic analgesic and produces major effects on the central nervous system and the bowel by acting as an agonist particularly at μ receptors. It also has affinity for δ and K-receptors.

Pharmacokinetic properties:

Therapeutic concentrations of morphine in plasma is about one third protein bound. The half-life of morphine is about 2 hours, the half-life of morphine-6-glucoronide is longer. Morphine is eliminated by glomerular filtration mainly as morphine-3-gluconide. The development of tolerance and physical dependence is a characteristic feature of morphine.

INDICATIONS:

Relief of intractable pain not controlled with non-narcotic analgesics.

CONTRAINDICATIONS:

Pharma-Q Morphine Injection is not usually given pre-operatively to children under 1 year of age, and it should be given with extreme care to newborn or premature infants for other conditions.

Pharma-Q Morphine Injection is generally contraindicated in:

- Patients with a hypersensitivity to morphine.
- Patients with respiratory depression and obstructive airway disease especially in the presence of cyanosis and excessive bronchial secretion.
- Patients with a presence of acute alcoholism, convulsive disorders, head injuries and in conditions in which intracranial pressure is raised.
- Patients who are suffering from an attack of bronchial asthma or in heart failure secondary to chronic lung disease.
- Patients who are comatose.
- Patients with biliary or renal colic since sphincter constriction occurs.
- Patients who are pregnant or breast-feeding unless the benefits outweigh the risk (see **PREGNANCY AND LACTATION**).

WARNINGS and SPECIAL PRECAUTIONS:

The euphoric activity of morphine sulphate may lead to abuse.

Dependence and tolerance to morphine may occur.

Special Precautions:

Pharma-Q Morphine Injection (opiod analgesic) should be used with extreme caution in patients with decreased respiratory reserve.

- It should be administered with caution and in reduced doses to patients who suffer from:
    - Hypothyroidism.

- Adrenocortical insufficiency.
- Impaired kidney or liver function.
- Prostatic hypertrophy or shock.
- Inflammatory or obstructive bowel disorders.

- It should be administered with caution:
  - To patients who suffer from myasthenia gravis.
  - To patients taking monoamine oxidase inhibitors (see **INTERACTIONS**).
- The depressant effects of **Pharma-Q Morphine Injection** are enhanced by central nervous system depressants such as alcohol, anaesthetics, hypnotics and sedatives, tricyclic anti-depressants and phenothkiazines (see **INTERACTIONS**).
- The dosage should be reduced in elderly and debilitated patients (see **DOSAGE AND DIRECTIONS**).
- The administration of **Pharma-Q Morphine Injection** (opiod analgesics) during labour may cause respiratory depression in the newborn infant (see **PREGNANCY AND LACTATION**).
- The triad of coma, pinpoint pupils and respiratory depression is considered indicative of overdosage. Dilatation of the pupils occurs as hypoxia develops. Pulmonary oedema after overdosage is a common cause of fatalities among opioid addicts.

Effects on the ability to drive and use machines:

Patients should be advised not to drive or use machines until they know how they are affected by the administration of **Pharma-Q Morphine Injection,** as drowsiness and dizziness may occur with the use of **Pharma-Q Morphine Injection and may affect** the ability to perform skilled tasks. Patients who experience such effects should be advised not drive or operate machinery.

INTERACTIONS:

The depressant effects of **Pharma-Q Morphine Injection** are enhanced by:

- Central nervous system depressants such as alcohol, anaesthetics, hypnotics and sedatives.

- Tricyclic antidepressants.
- Mono-amine oxidase inhibitors.
- Phenothiazines. (see **WARNINGS and SPECIAL PRECAUTIONS** for all above interactions).

PREGNANCY AND LACTATION:

Contraindicated during pregnancy and lactation since the safety and efficacy of **Pharma-Q Morphine Injection** has not been established (see **CONTRAINDICATIONS**).

Morphine sulphate:

- Has the potential of crossing the placenta and also of being distributed into the breast-milk.
- Regular use during pregnancy may cause physical dependencein the foetus, leading to withdrawal symptoms in the neonate.
- Use during labour may cause respiratory depression in the neonate (see **WARNINGS and SPECIAL PRECAUTIONS**).

DOSAGE AND DIRECTIONS FOR USE:

The usual dose administered by subcutaneous or intramuscular injection:

Adults:	5 to 20 mg every 4 hours.	
Children:	1 to 5 years	2,5 to 5 mg
	6 to 12 years	5 to 10 mg

Doses should generally be reduced in the elderly or debilitated patients or in patients with renal impairment.

Other dosages:

- **Slow intravenous injection or as a loading dose for continuous or patient-controlled infusion:** Adults: Doses of up to 15 mg have been given.

- **Maintenance dose for continuous intravenous administration and continuous subcutaneous infusion:** Doses have generally ranged from 0,8 mg to 80 mg per hour.
- **Intraspinal doses** are in the region of 5 mg for an initial epidural injection.
- **Intrathecal doses** ranges from 0,2 mg to 1 mg and should only involve the administration of a single dose.

SIDE EFFECTS:

The following side-effects may occur with the use of **Pharma-Q Morphine Injection**

Neurological disorders:

Frequent:	**Normal doses:** Drowsiness and dizziness.
Less frequent:	**Normal doses:** Restlessness, confusion, headache and hallucinations. **Larger doses:** Respiratory depression.
Frequency unknown:	**Normal doses:** Vertigo, raised intracranial pressure and the euphoric activity of morphine leads to abuse and dependence. **Larger doses:** Convulsions may occur, especially in infants and children.

Disorders of the eye:

Frequency unknown:	**Normal doses:** Miosis.

Cardiovascular disorders:

Frequent:	**Normal doses:** Orthostatic hypotention.
Less frequent:	**Normal doses:** Bradycardia, tachycardia and palpitation.
Frequency unknown:	**Larger doses:** Hypotension with circulatory failure and deepening coma. Death may occur from respiratory failure.

Gastrointestinal disorders:

Frequent:	**Normal doses:** Nausea, vomiting, constipation.
Less frequent*:*	**Normal doses:** Biliary spasm and dry mouth.

Frequency unknown: **Normal doses:** Anorexia.

Skin and subcutaneous tissue disorders:

Frequent: Histamine release causing urticaria, pruritus and contact dermatitis.

Less frequent: Pain and irritation may occur at the site of injection.

Histamine release:

- Due to the histamine-releasing effect, urticarial, pruritus and contact dermatitis as well as hypotension and flushing may occur.
- Anaphylactic reactions following intravenous injection may occur as well as muscle rigidity.
- Toxic doses vary considerably with the individual and regular users may tolerate large doses.

Renal and urinary disorders:

Less frequent: **Normal doses:** Ureteric spasm as well as an anti-diuretic effect may occur.

Frequency unknown: **Normal doses:** Micturition may be difficult.

Larger doses: Rhabdomyolysis progressing to renal failure may occur with overdosage.

Disorders of the reproductive system and breast:

Frequency unknown: **Normal doses:** Decreased libido or potency.

General disorders: **Frequency unknown:**

Normal doses: Sweating, facial flushing, hypothermia, changes of mood.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

Overdose with Pharma-Q Morphine Injection:

Signs and symptoms of overdose which indicate a need for medical attention:

- Cold and clammy skin.
- Confusion.
- Convulsion.
- Severe dizziness.
- Severe drowsiness.
- Low blood pressure.
- Severe nervousness or restlessness.
- Pinpoint pupils of eyes.
- Slow heartbeat.
- Slow or troubled breathing. Unconsciousness and severe weakness.
- (see **SIDE-EFFECTS**)

Medical therapy:

- 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 excesive doses of opioid analgesics.
- A dose of 0,4 mg to 2 mg is given intravenously, repeated at an interval of 2 to 3 minutes if necessary, administering up to 10 mg. For children, the initial dose is 0,01 mg/kg.
- 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.
- The use of opioid antagonists such as naloxone, nalorphine, and levallorphan in persons physically dependent on morphine or related drugs may induce withdrawal symptoms.

IDENTIFICATION:

A sealed amber ampoule containing a clear colourless to slightly yellow solution.

PRESENTATION:

1 ml amber ampoules in containers of 10 or 100

STORAGE INSTRUCTIONS:

Store at or below 25 °C.

Protect from light.

Keep out of reach of children.

REGISTRATION NUMBER:

Pharma-Q Morphine 10 mg Injection: 29/2.7/0475.

Pharma-Q Morphine 15 mg Injection: 29/2.7/0476.

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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