CLEAN COPY OF THE PROPOSED PACKAGE INSERT

SCHEDULING STATUS: S4

PROPRIETARY NAME AND DOSAGE FORM:

Pharma-Q Betamethasone Injection 4 mg/1 ml solution for injection

COMPOSITION:

Each 1 ml ampoule contains betamethasone sodium phosphate equivalent to betamethasone 4 mg.

Excipients: Disodium edetate (dihydrate), nitrogen, sodium hydroxide, sodium metabisulphite 0,32 % *m/v* as anti-oxidant per 1 ml, sodium phosphate anhydrous and water for injections.

PHARMACOLOGICAL CLASSIFICATION:

A.21.5.1 Corticosteroids and analogues.

PHARMACOLOGICAL ACTION:

Pharmacodynamic properties:

Betamethasone sodium phosphate is a glucocorticoid (potent suppressor of inflammation) and has the general properties of corticosteroids. It acts by controlling the rate of protein-synthesis. It forms a steroid-receptor complex with receptor proteins in target tissue, moving into the nucleus where it binds the chromatin and regulates transcription of certain genes in these tissues. In most examples transcription is enhanced, however, glucocorticoids may also decrease transcription of certain genes i.e. pro-opiomelanocortin that encodes ACTH (Adrenocorticotropic hormone). This plays an important part in the negative feedback regulation

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of the HPA-axis (Hypothalamic-Pituitary-Adrenal axis).

Pharmacokinetic properties:

Absorption:

Betamethasone sodium phosphate is a soluble ester that is absorbed quickly into the tissue after injection.

Distribution:

Betamethasone sodium phosphate is rapidly distributed to all body tissues and plasma protein binding is high. It crosses the placenta and may be excreted in small amounts in breast milk.

Metabolism:

Betamethasone sodium phosphate is metabolized mainly in the liver but it is also metabolized in the kidney.

Elimination:

Betamethasone sodium phosphate is excreted in the urine.

INDICATIONS:

Pharma-Q Betamethasone Injection 4 mg/1 ml is indicated as:

- substitution therapy, for the treatment of adrenal insufficiency states in patients with a known or
- suspected adrenal insufficiency prior to surgery or if shock, severe trauma or other stressful conditions occur
- symptomatic treatment of inflammatory conditions responsive to corticosteroid therapy.

CONTRAINDICATIONS:

Pharma-Q Betamethasone Injection 4 mg/1 ml is contra-indicated in:

- patients with a known hypersensitivity to betamethasone sodium phosphate, other corticosteroids or to any of the other ingredients of this medicine
- patients with osteoporosis
- patients with psychosis or severe psychoneuroses
- patients with peptic ulcers
- patients with doubtfully quiescent or active tuberculosis
- patients suffering from acute viral infections; including herpes zoster or herpes simplex ulceration of the eye
- patients who are pregnant or lactating since the safety in pregnancy and lactation has not been established (see **PREGNANCY AND LACTATION**).

WARNINGS and SPECIAL PRECAUTIONS:

Pharma-Q Betamethasone Injection 4 mg/1 ml:

- should not be administered intrathecally or subconjunctivally.
- toxic effects may result from withdrawal or from continued use or large doses
- patients should **not** be vaccinated with live vaccines while being treated with this medicine.

Care should be taken in patients with:

- congestive heart failure
- hypertension
- diabetes mellitus
- epilepsy

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- glaucoma
- infective diseases
- ocular herpes simplex
- chronic renal failure
- uraemia
- elderly patients
- tuberculosis (Patients with quiescent tuberculosis should be observed closely and should receive chemoprophylaxis if corticosteroid therapy is prolonged).

Effects on the ability to drive and use machines:

Patients should be instructed that they should avoid potentially hazardous tasks such as driving and operating machinery until they know how **Pharma-Q Betamethasone Injection 4 mg/1 ml** affects them.

INTERACTIONS:

Pharma-Q Betamethasone Injection 4 mg/1 ml may interact with other medicines.

- **Anti-epileptic medication:**

  Simultaneous administration of barbiturates, carbamazepine, phenytoin, primidone or rifampicin may reduce the effects of corticosteroids.

- **Oestrogen therapy:**

  Concomitant use with oestrogen may cause excessive corticosteroid effects.

- **Potassium depleting diuretics:**

  Excessive potassium loss may be due to concurrent administration of corticosteroids with potassium-depleting diuretics e.g. furosemide.

- **Cardiac glycosides or Amphotericin B:**

  Concurrent use of corticosteroids with cardiac glycosides may enhance the possibility of arrhythmias or digitalis toxicity associated with hypokalaemia. Corticosteroids may enhance the potassium depletion caused by amphotericin B. In patients taking any of these medicines concurrently, serum electrolyte levels, particularly potassium levels should be closely monitored.

- **Coumarin-type anticoagulants:**

  Corticosteroids may increase or decrease the anticoagulant effects, possibly requiring adjustments in dosage.

- **Non-steroidal anti-inflammatories:**

  When corticosteroids are given with non-steroidal anti-inflammatory agents, an increase in the incidence of gastro-intestinal bleeding and ulceration may occur.

- **Anti-diabetic and antihypertensive medication:**

  Dosages of anti-diabetic and anti-hypertensive medication may need to adjusted or increased.

- **Anti-muscarinic agents:**

  Antimuscarinic effects may by decreased in myasthenia gravis.

- **Somatotropin:**

  Concomitant glucocorticosteroid therapy may inhibit the response to somatotropin.

- **Laboratory tests:**

  Corticosteroids may interfere with assay procedures for endogenous substances.

  Corticosteroids may affect the nitro-blue tetrazolium test for bacterial infection and produce false negative results.

PREGNANCY AND LACTATION:

Pharma-Q Betamethasone Injection 4 mg/1 ml:

- is contra-indicated for use in pregnancy and lactation since the safety in pregnancy and lactation has not been established (see **CONTRAINDICATIONS**)
- high doses during pregnancy may cause foetal or neonatal adrenal suppression.

DOSAGE AND DIRECTIONS FOR USE:

Pharma-Q Betamethasone Injection 4 mg/1 ml:

- may be given, intravenously, intramuscularly, intra-articularly, intralesionally or by infusion in doses equivalent to 4 mg to 20 mg of betamethasone
- it may also be given by local injection into soft tissue, in doses equivalent to 4 mg to 8 mg of betamethasone
- dosage frequency and route of administration must be adjusted to the specific requirements of the patient:
  - according to the disease
  - the severity of the condition
  - the response obtained
  - the patient's tolerance to the product.
- rapid intravenous injection of massive doses of corticosteroids may sometimes cause cardiovascular collapse and injections should therefore be given slowly or by infusion.

SIDE EFFECTS:

Pharma-Q Betamethasone Injection 4 mg/1 ml may have side effects but the frequencies are unknown:

Blood and lymphatic system disorders:

Frequency unknown:

Increased coagulability of the blood may lead to thromboembolic complications.

Immune system disorders:

Frequency unknown:

Increased susceptibility to all kinds of infection, sepsis, tuberculosis, fungal infections, viral infections and delayed wound healing.

Endocrine disorders:

Frequency unknown:

Acute adrenal insufficiency may occur during prolonged therapy or on cessation and may be precipitated by stressful situations. Growth retardation in children and amenorrhoea (in females). Reversible Cushingoid symptoms may be produced with large doses.

Metabolism and nutrition disorders:

Frequency unknown:

Electrolyte disturbances are characterized by hypertension and oedema, because of the retention of sodium and water and the increase in potassium, excretion may cause hypokalaemic alkalosis. Due to the mobilization of calcium and phosphorus, osteoporosis and spontaneous fractures, nitrogen depletion and hyperglycaemia may occur.

Nervous system disorders:

Frequency unknown:

Mental and neurological disturbances.

Eye disorders:

Frequency unknown:

Ocular changes including development of cataract.

Vascular disorders:

Frequency unknown:

Intracranial hypertension.

Hepato-biliary disorders:

Frequency unknown:

Acute pancreatitis.

Skin and subcutaneous tissue disorders:

Frequency unknown:

Hyperhidrosis and skin thinning.

Musculoskeletal, connective tissue and bone disorders:

Frequency unknown:

Muscle weakness and aseptic necrosis of bone.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

See **SIDE-EFFECTS** and **WARNINGS and SPECIAL PRECAUTIONS**.

Treatment is symptomatic and supportive and doses must be reduced and the treatment slowly withdrawn.

IDENTIFICATION:

Clear, colourless liquid in a clear ampoule.

PRESENTATION:

Ampoules of 1 ml each, boxes of 10 or 100 x 1 ml ampoules.

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STORAGE INSTRUCTIONS:

Store at or below 25 °C.

Protect from light.

Keep all medicines out of the reach of children.

REGISTRATION NUMBER:

32/21.5.1/0338

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

PHARMA-Q HOLDINGS (PTY) LTD

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DATE OF PUBLICATION OF THE PACKAGE INSERT:

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