PROPOSED PACKAGE INSERT FOR DEXONA INJECTION 4 mg/1 ml

SCHEDULING STATUS:

S4

PROPRIETARY NAME (and dosage form):

DEXONA INJECTION 4 mg/1 ml

COMPOSITION:

Each 1 ml contains dexamethasone sodium phosphate equivalent to 4,0 mg dexamethasone phosphate, 1,0 mg sodium metabisulfite (antioxidant), 0,15 % *m/v* methyl hydroxybenzoate and 0,02 % *m/v* propyl hydroxybenzoate (preservatives).

PHARMACOLOGICAL CLASSIFICATION:

A 21.5.1 Corticosteroids and analogues

PHARMACOLOGICAL ACTION:

Dexamethasone is a corticosteroid with mainly glucocorticoid activity. It acts by controlling the rate of protein-synthesis. Corticosteroids interact with specific receptor proteins in target tissues to regulate the expression of corticosteroid-responsive genes, thereby changing the levels and array of pt\protein synthesized by the various target tissues.

Pharmacokinetics

Dexamethasone has a biological half-life in plasma of about 190 minutes and 77 % of the agent is bind to plasma proteins.

INDICATIONS:

Conditions where the anti-inflammatory and immunosuppressive effects of a corticosteroid are desirable, including intensive treatment during shorter periods.

CONTRAINDICATIONS:

- Hypersensitivity to corticosteroids
- Patients with active or doubtfully quiescent tuberculosis
- Ocular herpes simplex
- Primary glaucoma
- Acute psychosis and psychoneurosis
- Acute, uncontrolled infection
- Peptic ulcer
- Osteoporosis

For intra-articular injection

- Arthroplasty of joint (increased risk of infection)
- Blood clotting disorders (risk of intra and extra-articular hemorrhage)
- Intra-articular fracture (healing may be retarded)
- Current or a history of periarticular infection (may be exacerbated or reactivated)
- Osteoporosis (may be exacerbated)
- Unstable joint

WARNINGS:

Too rapid withdrawal of therapy with DEXONA INJECTION 4 mg/1 ml, especially after prolonged used, may cause acute, possibly life-threatening, adrenal insufficiency and /or a withdrawal syndrome not related to hypothalamic-pituitary-adrenal (HPA) axis suppression.

DEXONA INJECTION 4 mg/1 ml should not be administered intrathecally or subconjunctivally.

DEXONA INJECTION 4 mg/1 ml should be used with extreme caution in immunosuppressed patients e.g. with HIV and AIDS, intestinal anastomoses, cardiac disease, congestive heart failure, renal function impairment, existing or recent chickenpox and measles, esophagitis, gastritis, diabetes mellitus, myasthenia gravis, myocardial infection, hypertension, epilepsy, uraemia and in elderly patients.

INTERACTIONS:

Aminoglutethimide suppresses adrenal function so that glucocorticoid supplementation may be required; however aminoglutethimide accelerates the metabolism of DEXONA INJECTION 4 mg/1 ml so that the half-life may be reduced twofold.

Co-administration of DEXONA INJECTION 4 mg/1 ml and amphotericin B (parenteral) may result in severe hypokalaemia and should be undertaken with caution.

Macrolide antibiotics cause a significant decrease in corticosteroid clearance.

Concomitant use of anticholinesterases and DEXONA INJECTION 4 mg/1 ml may produce severe weakness in patients with myasthenia gravis.

DEXONA INJECTION 4 mg/1 ml may increase blood glucose concentrations and dosage adjustments of oral antidiabetic agents or insulin may be required.

Concurrent use of digitalis glycosides and DEXONA INJECTION 4 mg/1 ml may increase the possibility of arrhythmias or digitalis toxicity.

Ketoconazole may decrease the metabolism of certain corticosteroids by up to 60 % and dosage adjustments may be required.

Inhibition of the growth response to somatrem or somatropin may occur with chronic therapeutic use of daily dose in excess of 187,5 – 281,5 µg DEXONA INJECTION 4 mg/1 ml per square meter of body surface.

Concurrent administration of DEXONA INJECTION 4 mg/1 ml with the potassium-depleting diuretics, such as the thiazides or furosemide, may cause excessive potassium loss. Co-administration of barbiturates, carbamazepine, phenytoin, primidone, or rifampicin may enhance the metabolism and reduce the effects of DEXONA INJECTION 4 mg/1 ml.
There may be an increased incidence of gastrointestinal bleeding and ulceration when DEXONA INJECTION 4 mg/1 ml is given with non-steroidal anti-inflammatory agents.
Response to anticoagulants may be altered by DEXONA INJECTION 4 mg/1 ml and requirements of antihypertensives may be increased.

DEXONA INJECTION 4 mg/1 ml may interfere with or alter the results of assays for some endogenous substances or other medicines.

PREGNANCY AND LACTATION:

Safety during pregnancy and lactation has not been established.

DOSAGE AND DIRECTIONS FOR USE:

Usual adult dosage ranges form 0,5 mg to 20 mg daily depending on the severity of the disorder.

DEXONA INJECTION 4 mg/1 ml (dexamethasone phosphate) may be administered intravenously or intramuscularly.

The parenteral administration must be reserved for administration in emergencies or intensive therapy.

Intra-articular, intralesional, intra-muscular or soft-tissue injection: 0,8 mg to 4 mg (depending on the size of the joint).

SIDE EFFECTS AND SPECIAL PRECAUTIONS:

<u>General disorders and administration site conditions</u>

Less frequent: Generalized anaphylaxis; flushing of face and cheeks; seizures; burning, numbness, pain or tingling at or near injection site.

Cardiac disorders

Less frequent: Cardiac arrhythmias and congestive heart failure.

Nervous system disorders

Less frequent: Psychic disturbances such as delirium, disorientation, euphoria, hallucinations, manic-depressive episodes and mental depression or paranoia.

Endocrine disorders

Less frequent: Diabetes mellitus.

Those occurring principally during long term use

General disorders and administration site conditions

Frequent: Trouble in sleeping.

Less frequent: Cushing's syndrome (filling or rounding of the face, hirsutism, hypertension, menstrual irregularities, muscle weakness, striae), growth suppression and scarring at injection site.

Skin and subcutaneous tissue disorder

Less frequent: Acne; cutaneous or subcutaneous tissue atrophy; ecchymosis; impaired wound healing; thin, fragile skin.

Endocrine disorders

Less frequent: Adrenal suppression and pancreatitis, Cushing's syndrome (see General disorders and administration site conditions).

Musculoskeletal, connective tissue and bone disorders

Less frequent: Avascular necrosis (hip or shoulder pain); osteoporosis or bone fracture; steroid myopathy; tendon rupture.

Eye disorders

Less frequent: Cataracts; glaucoma with possible damage to the optic nerves and ocular infections.

Renal and urinary disorders

Less frequent: Fluid and sodium retention; hypokalaemic syndrome.

Gastrointestinal disorders

Frequent: Gastrointestinal perforation; increased appetite resulting in weight gain and indigestion.

Less frequent: Peptic ulceration or intestinal perforation.

Nervous system disorders

Frequent: Nervousness or restlessness.

Special Precautions

Patients on DEXONA INJECTION 4 mg/1 ml treatment are more susceptible to infection, the symptoms of which may be masked until an advanced stage has been reached. Live vaccines should not be given to patients receiving high-dose systemic DEXONA INJECTION 4 mg/1 ml therapy because of the risk of precipitating a serious infection. People living with the patient receiving DEXONA INJECTION 4 mg/1 ml should also not receive the oral polio

vaccine and close contact should be avoided with people who have recently received the oral polio vaccine or any other live attenuated virus vaccinations. Killed vaccines or toxoids may be given although the response may be attenuated. Immunoglobulin may need to be administered to children since they are at special risk of infection.

Close contact with anyone who has chickenpox or measles should be avoided. This is especially important for children.

Hypertension, glycosuria, hypokalaemia, gastric discomfort, and mental changes should be monitored in patients receiving long courses of DEXONA INJECTION 4 mg/1 ml.

Monitoring of the fluid intake and output and daily weight records may give early warning of fluid retention. To prevent the above mentioned, sodium intake may need to be reduced and potassium supplements taken. Children are at special risk from raised intracranial pressure.

Infections should be treated as an emergency.

Patients should carry cards – and preferably also wear bracelets – giving full details of their therapy; they and their relatives should be fully conversant with the implications of their therapy and the precautions to be taken.

In order to prevent cardiovascular collapse large doses should be given slowly or by infusion. High doses should not be used for prolonged treatment.

Patients on long-term treatment may require potassium supplementation, sodium restriction, increased protein intake and calorie restriction in their diet.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

See **SIDE EFFECTS AND SPECIAL PRECAUTIONS**.

Treatment is symptomatic and supportive.

IDENTIFICATION:

Clear, colourless to light yellow solution free from visible particulate matter and fibres, filled in 1 ml amber, USP type-1 glass ampoule (OPC with blue dot).

Clear, colourless to light yellow solution free from visible particulate matter and fibres, filled in 2 ml USP type-1 glass vial.

PRESENTATION:

1 ml amber, USP type-1 glass ampoule (OPC with blue dot).

2 ml 13 mm flint USP type-1 tubular vials with 13 mm grey butyl rubber stoppers packed into non-toxic PCV film (amber) / printed aluminium foil blister.

STORAGE INSTRUCTIONS:

Store below 25 °C.

Protect from light.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER:

41/21.5.1/0225

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

Zydus Healthcare S.A. (Pty) Ltd

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