PRODUCT INFORMATION

DEXMETHSONE®
(dexamethasone)

NAME OF THE MEDICINE:

DEXMETHSONE® (dexamethasone).

The structure of dexamethasone is shown below:

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HO
CH3
CH3
CH3
F
O
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Chemical formula: C22H29FO5
Molecular weight: 392.5
CAS Number: 50-02-2

DESCRIPTION:

Dexamethasone is a white or almost white, crystalline powder. It is practically insoluble in water, sparingly soluble in anhydrous ethanol, slightly soluble in methylene chloride.

Dexamethasone is a glucocorticoid.

Each DEXMETHSONE tablet contains either 0.5 mg or 4 mg of dexamethasone as the active ingredient. Excipients include lactose, magnesium stearate, povidone and starch-wheat (0.5 mg tablet) or starch-maize (4 mg tablet).

INDICATIONS:

Wherever corticosteroid therapy is indicated such as: pemphigus vulgaris, allergic dermatitis, eczema, exfoliative dermatitis, dermatitis herpetiformis, dermatitis medicamentosa, erythema multiforme; disseminated lupus erythematosus, dermatomyositis, polyarteritis nodosa; severe bronchial asthma and status asthmaticus, emphysema, pulmonary fibrosis; adrenal hyperplasia (adrenogenital syndrome); idiopathic thrombocytopenic purpura, acquired haemolytic anaemia, acute leukaemia; nephrotic syndrome; iridochoroiditis; ulcerative colitis; rheumatoid arthritis; ankylosing spondylitis, rheumatic fever, gout, periarthritis of the shoulder.

CONTRAINDICATIONS:

Uncontrolled infections. Known hypersensitivity to dexamethasone.
WARNINGS:

Stress and Intercurrent Illness
In patients on corticosteroid therapy subjected to unusual stress (from trauma or infection), increased dosage of rapidly acting corticosteroids before, during & after the stressful situation is indicated.

Adrenocortical Insufficiency
Drug induced secondary adrenocortical insufficiency may result from too rapid withdrawal of corticosteroids and may be minimised by gradual reduction of dosage (see PRECAUTIONS). This type of relative insufficiency may persist for months after discontinuation of therapy; therefore, in any situation of stress occurring during that period, hormone therapy may need to be reinstituted. If the patient is receiving steroids already, dosage may have to be increased.

Infection
Corticosteroids may mask some signs of infection (such as fever and inflammation), and new infections may appear during their use. There may be decreased resistance and inability to localise infection when corticosteroids are used. Susceptibility to infection is not specific for any particular bacterial or fungal pathogen.

Ophthalmological Complications
Prolonged use of corticosteroids may produce posterior subcapsular cataracts or glaucoma with possible damage to optic nerves, and may enhance the establishment of secondary ocular infections due to fungi or viruses (see ADVERSE REACTIONS).

Children who are on immunosuppressant drugs are more susceptible to infections than healthy children. Chickenpox and measles, for example, can have a more serious or even fatal course in children on immunosuppressant corticosteroids. In such children, or in adults who have not had these diseases, particular care should be taken to avoid exposure. If exposed, therapy with varicella zoster immune globulin (VZIG) or pooled intravenous immunoglobulin (IVIG), as appropriate, may be indicated. If chickenpox develops, treatment with antiviral agents may be considered.

PRECAUTIONS:

During prolonged corticosteroid therapy, adrenal suppression and atrophy may occur and secretion of corticotrophin may be suppressed. Abrupt withdrawal of corticosteroid therapy may precipitate acute adrenal insufficiency with muscle weakness, hypotension, hypoglycaemia, headache, nausea, vomiting, restlessness and muscle and joint pain. Muscle weakness and stiff joints may persist for three to six months after discontinuation of treatment. In some cases, withdrawal symptoms may simulate a clinical relapse of the disease for which the patient has been under treatment.

Duration of treatment and dosage appear to be important factors in determining suppression of the pituitary adrenal axis and response to stress on cessation of steroid treatment. The patient's liability to suppression is also variable. Some patients may recover normal function rapidly. In others, the production of hydrocortisone in response to the stress of infections, surgical operations or accident may be insufficient, and death results. Therefore, withdrawal of corticosteroids should always be gradual. If sudden withdrawal is necessary, corticotrophin (20 units) given daily by IV infusion during 8 hours for three to five successive days is usually sufficient to prevent withdrawal symptoms.

During long courses of treatment, laboratory and metabolic studies should be made. Fluid retention should be watched for via a fluid balance chart and daily weighing. Sodium intake may need to be reduced to less than 1 g daily and potassium supplements may be necessary.

Use with caution in patients with impaired hepatic function, a reduction of dosage may be necessary. In treating chronic active liver disease with the drug, major adverse reactions such as vertebral collapse, diabetes, hypertension, cataracts and Cushing's syndrome occur in about 30% of patients.

Caution is recommended for elderly patients as they are more susceptible to adverse reactions.
The possibility of development of osteoporosis should be an important consideration in initiating and managing corticosteroid therapy, especially in post menopausal women (see ADVERSE REACTIONS). Caution should be taken in patients with diabetes mellitus (see ADVERSE REACTIONS).

Patients should not be vaccinated with live vaccines while on corticosteroid therapy. Other immunisation procedures should not be undertaken in patients on corticosteroid therapy, especially on high doses, because of possible hazards of neurological complications and lack of antibody response. Immunisation procedures may be undertaken in patients receiving corticosteroids as replacement therapy.

Close observation is necessary in patients with latent tuberculosis or tuberculin reactivity as reactivation of the disease may occur. Chemoprophylaxis is indicated during prolonged corticosteroid therapy.

**Use in Pregnancy:**
Category A of Australian Categorisation of Risk of Drug Use in Pregnancy.

In animal experiments, corticosteroids have been found to cause malformations of various kinds (cleft palate, skeletal malformations) and abortion. These findings do not seem to be relevant to humans. Reduced placental and birth weight have been recorded in animals and humans after long-term treatment. Since the possibility of suppression of the adrenal cortex in the newborn baby after long-term treatment must be considered, the needs of the mother must be carefully weighed against the risk to the foetus when prescribing corticosteroids. The short-term use of corticosteroids antepartum for the prevention of respiratory distress syndrome does not seem to pose a risk to the fetus or the newborn infant. Maternal pulmonary oedema has been reported with tocolysis and fluid overload.

**Use in Lactation:**
Glucocorticoids appear in breast milk in small quantities. Mothers taking high doses of glucocorticoids should be advised against breast feeding.

**Use in Children:**
Children on long term steroids must be carefully observed for potential serious adverse reactions such as obesity, growth retardation, osteoporosis and adrenal suppression.

**Interactions with other medicines:**
Drugs which induce hepatic microsomal enzymes, such as barbiturates, phenytoin and rifampicin, administered before or during treatment may shorten the elimination half-life of the drug. Long term corticosteroid therapy may also reduce the half-life.

Oral contraceptives have been reported to increase the volume of distribution.

**ADVERSE REACTIONS:**

Adverse reactions from corticosteroids are those resulting from withdrawal or from prolonged use of high doses.

**More Common Reactions Cardiovascular:**
The mineralocorticoid activity of a steroid may lead to salt and water retention which can also result in hypertension. Hypokalaemia can lead to arrhythmias and cardiac arrest.

**Central Nervous System:**
Large doses can cause behavioural and personality changes ranging from nervousness, insomnia, euphoria, or mood swings to psychotic episodes which can include both manic and depressive states, paranoid states and acute toxic psychoses.

It is no longer believed that previous psychiatric problems predispose to behavioural disturbances during therapy with glucocorticoids. Conversely, the absence of a history of psychiatric illness is no guarantee against the occurrence of psychosis during hormonal therapy.
**Dermatologic:**
Impaired wound healing. Facial plethora. An acneiform eruption on the face, chest and back, red striae on the thighs, buttocks and shoulders. Several months of high dose therapy often result in thinning of skin.

Corticosteroid induced purpura resembles senile purpura. This purpura usually occurs on extensor surfaces, dorsum of the hand, and radial aspect of the forearm.

**Endocrine:**
The endocrine effects of the glucocorticoids involve variously the hypothalamic pituitary adrenal axis; the genitals, the parathyroid and thyroid; there are also metabolic effects, primarily involving the carbohydrates. Suppression of growth may occur in children.

Cushing's syndrome may result from prolonged elevation of plasma glucocorticoid levels.

Disorders of menstruation are common.

Antagonism occurs between the parathyroids and hypercorticism. The phosphate retention occurring in renal failure caused by adrenal insufficiency may also make hypoparathyroidism manifest.

**Biochemical:**
All glucocorticoids increase gluconeogenesis. Glucose tolerance and sensitivity to insulin are decreased but, provided pancreatic islet function is normal, carbohydrate metabolism will not be noticeably deranged. Steroid diabetes has been reported to develop in one fifth of patients treated with high glucocorticoid dosage.

High dose corticosteroid therapy may induce marked hypertriglyceridaemia with milky plasma.

**General:**
Retardation of growth by long term corticosteroid treatment in children.

**Haematological:**
Corticosteroids will increase the total white blood cell count, with an increase in neutrophils and a decrease in monocytes, lymphocytes and eosinophils.

**Immunological:**
The frequency and severity of clinical infections increase during glucocorticoid therapy.

**Musculoskeletal:**
Osteoporosis and vertebral compression fractures in patients of all ages. Osteoporosis is an indication for withdrawal of therapy.

Myopathy, characterised by weakness of the proximal musculature of arms and legs of their associated shoulder and pelvic muscles, is occasionally reported in patients taking large doses of corticosteroids. It may occur soon after treatment is begun and be sufficiently severe to prevent ambulation. It is an indication for withdrawal of therapy.

Avascular aseptic necrosis of bone has often been described and preferentially involves the femoral and humeral head.

**Ocular:**
The incidence of posterior subcapsular cataract in patients undergoing long term therapy with corticosteroids is approximately 10%. A correlation with duration of treatment and the total dose is clear.

**Less Common Reactions Gastrointestinal:**
Pancreatitis. Peptic ulceration is an occasional complication. The high incidence of haemorrhage and perforation in these ulcers and the insidious nature of their development make them severe therapeutic problems. Some investigators believe the available evidence does not support the conclusion that steroids cause ulcers. Others feel that only patients with rheumatoid arthritis have an increased incidence of ulcers. It has been proposed that the glucocorticoids alter the mucosal defence mechanism.
Neurological:
Latent epilepsy can be rendered manifest by corticosteroid treatment. Long term treatment may result in benign intracranial hypertension.

Ophthalmological:
Increased intraocular pressure and glaucoma may occur with corticosteroid treatment. The rise in intraocular pressure may lead to blindness.

Serious or Life Threatening Reactions
Suppression of the hypothalamic pituitary adrenal axis is one of the consequences of repeated administration of glucocorticoids; after termination of treatment a withdrawal syndrome may be experienced (see PRECAUTIONS).

In some cases, acute adrenal insufficiency after a period of glucocorticoid treatment has proved fatal.

**DOSAGE AND ADMINISTRATION:**

Adults: 0.5 to 10 mg daily in divided doses, gradually reduced after good effect is achieved to a maintenance dosage of 0.5 to 1 mg daily. In potentially fatal conditions, much larger doses may be given for acute rheumatic carditis, acute leukaemia, the nephrotic syndrome and pemphigus.

**OVERDOSAGE:**

Treatment is symptomatic with the dosage being reduced or the drug withdrawn.

Contact the Poisons Information Centre on 131126 for management of overdose.

**PRESENTATION:**

0.5 mg: Round, slightly biconvex, white tablets plain on one side and 'DS/0.5' with breakline on the other side.
Pack sizes of 30's, 100's* and 1000's*.

4 mg: Round, white tablets plain on one side and 'DS/4' with breakline on the other side.
Pack sizes of 30's, 100's* and 1000's*.

(* not currently distributed in Australia)

**INSTRUCTIONS TO PATIENTS:**

Patients should be warned of the long term adverse effects of corticosteroids.

The necessity for increasing dosage in situations of intercurrent stress or infection should be advised. The patient should seek medical advice for any but the most minor infections. The danger of interrupting steroid therapy should be explained and the need to inform medical personnel that corticosteroid medication is being taken.

Patients on a dose reduction regime should be advised of the symptoms of acute glucocorticoid deficiency (faintness, weakness, vomiting).

Patients who are on immunosuppressant doses of corticosteroids should be warned to avoid exposure to chickenpox or measles and, if exposed, to obtain medical advice.
STORAGE:
Store below 30°C. Protect from light.

POISON SCHEDULE:
S4.

SPONSOR:
Aspen Pharmacare Australia Pty Ltd
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St Leonards NSW 2065
Australia

DATE OF TGA APPROVAL:
Approved by the Therapeutic Goods Administration: 26 August 1992
Date of most recent amendment: 10 August 2010