

Data Sheet

DEXAMETHASONE

Dexamethasone 1mg and 4mg tablets

Presentation

Dexamethasone 1mg tablets: Biconvex, circular, white tablets of 7.94mm diameter with the DP logo on one face and two bisecting scores at right angles to each other on the opposite face.

Dexamethasone 4mg tablets: Biconvex, circular, white tablets of 7.94mm with a break-line on one face and "4" on the other.

Uses

Actions

Dexamethasone is a synthetic corticosteroid exhibiting both anti-inflammatory and immuno-suppressant properties. The anti-inflammatory potency of dexamethasone has been estimated as 25x that of hydrocortisone. It has little mineralocorticoid activity.

Pharmacokinetics

Dexamethasone is readily absorbed after oral administration achieving peak plasma concentrations after one hour. Binding to plasma proteins is less than for most other corticosteroids.

The biological half-life is approximately 190 minutes. Dexamethasone penetrates tissue and cerebrospinal fluid.

Elimination occurs via metabolism and renal excretion.

Indications

Dexamethasone is indicated for replacement therapy in secondary adrenal insufficiency arising from insufficient corticotrophin secretion. It is not indicated for primary adrenal insufficiency states, such as Addison's disease or after adrenalectomy. In such cases hydrocortisone and fludrocortisone in combination is more appropriate.

Dexamethasone is also indicated for allergic disorders such as bronchial asthma and allergic skin reactions, blood disorders such as leukaemia,

thrombocytopenia and haemolytic anaemias, selected collagen and rheumatic disorders (only rarely in rheumatoid arthritis), gastrointestinal disorders such as inflammatory bowel disease, connective tissue disorders such as arteritis, systemic lupus erythematosus (but not scleroderma), some skin diseases such as pemphigus, oedema, some eye disorders, certain neoplastic disorders such as cerebral neoplasm, secondary hypercalcaemia, and acute leukaemia in children. It may also be used to prevent neonatal respiratory distress syndrome and in the diagnosis of Cushing's syndrome.

Dosage and administration

The dose of dexamethasone varies according to the condition being treated. The tablets are for oral administration in a dose of 4mg-20mg daily.

The duration of therapy is dependent on the clinical response of the patient and as soon as improvement is indicated, the dosage should be adjusted to the minimum required to maintain the desired response. Withdrawal of dexamethasone at completion of treatment should be gradual.

Contraindications

- Hypersensitivity to any ingredient
 - Systemic infections unless specific anti-infective therapy is given
 - Live virus immunisation
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Warnings and precautions

General Precautions

Caution is necessary when oral corticosteroids are used in patients with the following conditions and frequent monitoring is necessary:

- Hypertension
- Hypothyroidism
- Congestive Heart failure or recent myocardial infarction
- Liver failure
- Renal insufficiency
- Diabetes mellitus or in those with a family history of diabetes
- Osteoporosis
- Glaucoma
- Patients with a history of severe affective disorders particularly of steroid induced psychoses
- Epilepsy and/or seizure disorder
- Peptic ulceration
- Previous steroid myopathy
- Tuberculosis

- Patients with myasthenia gravis receiving anticholinesterase therapy since corticosteroid use may decrease plasma anticholinesterase activity
- Patients with thromboembolic disorders
- Patients with Duchenne's muscular dystrophy since transient rhabdomyolysis and myoglobinuria have been reported following strenuous physical activity
- Patients with Cushing's disease

Adrenocortical Insufficiency

Pharmacologic doses of corticosteroids administered for prolonged periods may result in hypothalamic-pituitary-adrenal (HPA) suppression (secondary adrenocortical insufficiency). The degree and duration of adrenocortical insufficiency produced is variable among patients and depends on the dose, frequency, time of administration and duration of therapy.

Symptoms of adrenal insufficiency include: malaise, muscle weakness, mental changes, muscle and joint pain, desquamation of the skin, dyspnoea, anorexia, nausea and vomiting, fever, hypoglycaemia, hypotension and dehydration.

During prolonged courses of corticosteroid therapy sodium intake may need to be reduced and calcium and potassium supplements may be necessary. Monitoring of fluid intake and output and daily weight records may give an early warning of fluid retention.

Acute adrenal insufficiency leading to a fatal outcome may occur if glucocorticoids are withdrawn abruptly, therefore withdrawal of corticosteroids should always be gradual. A degree of adrenal insufficiency may persist for 6 to 12 months; therefore in any situation of stress occurring during that period steroid therapy may need to be reinstated. Since mineralocorticoid secretion may be impaired treatment with salt and/or a mineralocorticoid may also be needed.

During prolonged therapy, any intercurrent illness, trauma or surgical procedure will require a temporary increase in dosage.

Anti-inflammatory/ Immunosuppressive effects and Infection

Suppression of the inflammatory response and immune function increases susceptibility to infections and their severity. The clinical presentation may often be atypical and serious infections such as septicaemia and tuberculosis may be masked and may reach an advanced stage before being recognized when corticosteroids are used. The immunosuppressive effects of glucocorticoids may result in activation of latent infection or exacerbation of intercurrent infections.

Chickenpox is of particular concern since this may be fatal in immunosuppressed patients. Patients without a definite history of chickenpox should be advised to avoid close personal contact with chickenpox or herpes zoster and if exposed they should seek urgent medical attention. Passive immunization is recommended for non-immune patients who do come into

contact with chickenpox. If a diagnosis of chickenpox is confirmed the illness warrants specialist care and urgent treatment.

Live vaccines are contraindicated in individuals on high doses of corticosteroids and should be postponed until at least 3 months after stopping corticosteroid therapy.

Ocular Effects

Prolonged use of corticosteroids may produce subcapsular cataracts and nuclear cataracts (particularly in children), exophthalmos or increased intraocular pressure, which may result in glaucoma with possible damage to the optic nerves.

Corticosteroids should only be initiated in patients with ocular herpes simplex with appropriate viral cover by ophthalmologists because of the risk of corneal scarring loss of vision and corneal perforation.

Psychiatric effects

Patients and/or carers should be warned that potentially severe psychiatric reactions may occur. Symptoms typically emerge within a few days or weeks of starting treatment. Most reactions recover after either dose reduction or withdrawal, although specific treatment may be necessary. Patients and/or carers should be encouraged to seek medical advice if worrying psychological symptoms develop, especially if depressed mood or suicidal ideation is suspected.

Particular care is required when considering the use of corticosteroids in patients with existing or previous history of severe affective disorders.

Psychic derangements range from euphoria, insomnia, mood swings, personality changes and severe depression to frank psychotic manifestations.

Use in Children

Corticosteroids cause growth retardation in infancy, childhood and adolescence, which may be irreversible and therefore long-term administration of pharmacological doses should be avoided. If prolonged therapy is necessary, treatment should be limited to the minimum suppression of the hypothalamo-pituitary adrenal axis and growth retardation, the growth and development of infants and children should be closely monitored. Treatment should be administered where possible as a single dose on alternate days.

Children are at special risk from raised intracranial pressure.

Use in the elderly

Long-term use in the elderly should be planned bearing in mind the more serious consequences of the common side-effects of corticosteroids in old age, especially osteoporosis, diabetes, hypertension, hypokalaemia, susceptibility to infection and thinning of the skin. Close medical supervision is required to avoid life threatening reactions.

Adverse effects

Body as a whole:

Leucocytosis, hypersensitivity including anaphylaxis, thromboembolism, fatigue, malaise

Cardiovascular:

Congestive heart failure in susceptible patients, hypertension

Gastro-intestinal:

Dyspepsia, nausea, peptic ulceration with perforation and haemorrhage, abdominal distension, abdominal pain, increased appetite which may result in weight gain, diarrhoea, oesophageal ulceration, oesophageal candidiasis, acute pancreatitis

Musculoskeletal:

Proximal myopathy, osteoporosis, vertebral and long bone fractures, avascular osteonecrosis, tendon rupture, myalgia

Metabolic/Nutritional:

Sodium and water retention, hypokalaemic alkalosis, potassium loss, negative nitrogen and calcium balance

Skin:

Impaired healing, hirsutism, skin atrophy, bruising, striae, telangiectasia, acne, increased sweating, may suppress reactions to skin tests, pruritis, rash, urticaria

Endocrine:

Suppression of the hypothalamo-pituitary adrenal axis particularly in times of stress as in trauma surgery or illness, growth suppression in infancy, childhood and adolescence, menstrual irregularity and amenorrhoea. Cushingoid facies, weight gain, impaired carbohydrate tolerance with increased requirement for antidiabetic therapy, manifestation of latent diabetes mellitus, increased appetite.

Nervous system:

Euphoria, psychological dependence, depression, insomnia, dizziness, headache, vertigo, raised intracranial pressure with papilloedema in children, usually after treatment withdrawal. Aggravation of schizophrenia, Aggravation of epilepsy suicidal ideation, mania, delusions, hallucinations, irritability anxiety, insomnia and cognitive dysfunction. In adults the frequency of severe psychiatric reactions has been estimated to be 5-6%.

Eye disorders:

Increased intra-ocular pressure, glaucoma, papilloedema, posterior subcapsular cataracts, exophthalmos, corneal or scleral thinning, exacerbation of ophthalmic viral or fungal disease

Anti-inflammatory and Immunosuppressive effects:

Increased susceptibility to and severity of infections with suppression of clinical symptoms and signs. Opportunistic infections, recurrence of dormant tuberculosis.

Withdrawal symptoms:

Too rapid a reduction of corticosteroids following prolonged treatment can lead to acute adrenal insufficiency, hypotension and death. A steroid withdrawal syndrome seemingly unrelated to adrenocortical insufficiency may also occur and include symptoms such as anorexia, nausea, vomiting, lethargy, headache, fever, weight loss, and/or hypotension.

Drug interactions

Hepatic microsomal enzyme inducers

Medicines that induce hepatic enzyme cytochrome P-450 isozyme 3A4 such as Phenobarbital, phenytoin, rifampicin, rifabutin, carbamazepine, primidone and aminogluethimide may reduce the therapeutic efficacy of corticosteroids by increasing the rate of metabolism.

Hepatic microsomal enzyme inhibitors

Medicines that inhibit hepatic enzyme cytochrome P-450 isozyme 3A4 such as ketoconazole, ciclosporin or ritonavir may decrease glucocorticoid clearance. A reduction in corticosteroid dose may be needed to reduce the risk of adverse effects.

Antidiabetic Agents

Corticosteroids may increase blood glucose levels. Patients may need dosage adjustment of any concurrent antidiabetic therapy.

Non-steroidal anti-inflammatory drugs (NSAIDs)

Concomitant administration may increase the risk of GI ulceration. Aspirin should be used cautiously in conjunction with corticosteroids in patients with hypothyroidism. The renal clearance of salicylates is increased by corticosteroids and steroid withdrawal may result in salicylate intoxication. Patients should be observed closely for adverse effects of either medicine.

Anticoagulants

Response to anticoagulants may be reduced or less often enhanced by corticosteroids. Close monitoring of the INR or prothrombin time is recommended.

Antifungals

The risk of hypokalaemia may be increased with amphotericin.

Cardiac glycosides

There is a risk of toxicity if hypokalaemia occurs due to corticosteroid treatment.

Mifepristone

The effect of corticosteroids may be reduced for 3-4 days after mifepristone.

Vaccines

Live vaccines should not be given to individuals with impaired immune responsiveness. The antibody response to other vaccines may be diminished.

Oestrogens

Oestrogens may potentiate the effects of glucocorticoids. The dose of corticosteroid may need to be adjusted if oestrogen therapy is commenced or stopped.

Somatropin

The growth promoting effect may be inhibited.

Sympathomimetics

There is an increased risk of hypokalaemia if high doses of corticosteroids are given with high doses of salbutamol, salmeterol, terbutaline or formoterol.

Diuretics

Excessive potassium loss may be experienced if glucocorticoids and potassium-depleting diuretics (such as frusemide and thiazides) or carbonic anhydrase inhibitors (such as acetazolamide) are given together.

Antacids

Concurrent use of antacids may decrease absorption of corticosteroids – efficacy may be decreased sufficiently to require dosage adjustments in patients receiving small doses of corticosteroids.

Overdosage

Adverse effects related to dexamethasone normally develop only after prolonged use. Treatment is symptomatic and where possible the dexamethasone dose should be reduced gradually.

Pharmaceutical precautions

Store at or below 30°C, protected from light and moisture and kept out of reach of children.

Medicine classification

Prescription Medicine

Package quantities

Dexamethasone 1mg and 4mg tablets: Packs of 100 tablets.

Further information

Dexamethasone is (11 β ,16 α)-9-Fluoro-11, 17, 21-trihydroxy-16-methylpregna-1, 4-diene-3, 20-dione. Its molecular formula is C₂₂H₂₉FO₅ and its molecular weight is 392.5.

Other ingredients of the tablets are: Magnesium Stearate, Talc, Lactose, Maize Cornflour, Polyvinylpyrrolidinone, and Sodium Starch Glycolate.

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