TABLETS/ELIXIR

DECADRON ®

(dexamethasone)

DECADRON ® (dexamethasone) is a synthetic glucocorticoid used primarily for its anti-inflammatory effects. It is among the most potent glucocorticoids, having about 25 to 30 times the anti-inflammatory activity of hydrocortisone. In contrast, its effect on electrolytes is slight. At equipotent anti-inflammatory doses, dexamethasone almost completely lacks the sodium-retaining property of hydrocortisone and closely related derivatives of hydrocortisone.

In addition to its anti-inflammatory properties, dexamethasone has been shown to be effective in the management of nausea and vomiting secondary to cisplatin and non-cisplatin emetogenic chemotherapy.

Glucocorticoids cause profound and varied metabolic effects. They also modify the body's immune response to diverse stimuli.

QUALITATIVE AND QUANTITATIVE COMPOSITION

Tablets

Description: Yellow, pentagonal shaped, scored tablets.
Active ingredient: Dexamethasone 0.5 mg.
Excipients: lactose, dibasic calcium phosphate, corn starch, yellow lake blend LB282, magnesium stearate.

Elixir

Active ingredient: Dexamethasone 0.5 mg/5 ml.
Excipients: Glycerin , ethyl alcohol, benzoic acid, saccharin sodium, FD&C red # 40, cherry flavor and peppermint flavor.

INDICATIONS

Conditions where the anti-inflammatory and immunosuppressive effects of the corticosteroid are desirable, especially for intensive treatment during shorter periods. (For a listing of specific indications, see SUPPLEMENTAL PRESCRIBING INFORMATION, SPECIFIC INDICATIONS.)

In addition, for the management of nausea and vomiting associated with cisplatin and non-cisplatin emetogenic chemotherapy.

DOSAGE AND ADMINISTRATION

General recommendations for oral administration

Dosage requirements are variable and must be individualized according to the severity of the disease and the response of the patient. The usual initial dosage varies from 0.75 to 15 mg a day depending on the disease being treated. (For infants and children, the recommended doses usually will have to be reduced, but dosage should be dictated by the severity of the condition rather than by age or body weight.)

Corticosteroid therapy is an adjunct to, not a replacement of, conventional therapy, which should be instituted as indicated.

Dosage must be decreased or therapy discontinued gradually when administration has been continued for more than a few days.

In acute conditions where prompt relief is urgent, large doses are permissible and may be mandatory for a short period. When symptoms have been suppressed adequately, dosage should be maintained at the minimum amount capable of providing sufficient relief without excessive hormonal effects.

Chronic conditions are subject to periods of spontaneous remission. When such periods occur, corticosteroids should be discontinued gradually.

Routine laboratory studies such as urinalysis, two-hour postprandial blood sugar, determinations of blood pressure and body weight, and a chest x-ray should be carried out at regular intervals during prolonged therapy. Periodic determinations of serum potassium are advisable if large doses are being used.

Patients may be transferred to DECADRON from any other glucocorticoid with the proper adjustment in dosage. The following milligram equivalents facilitate changing to DECADRON from other glucocorticoids:

DECADRON: 0.75 mg; Methylprednisolone and Triamcinolone: 4 mg; Prednisolone and Prednisone: 5 mg; Hydrocortisone: 20 mg; Cortisone: 25 mg

Milligram for milligram, dexamethasone is approximately equivalent to betamethasone, four to six times more potent than methylprednisolone and triamcinolone, six to eight times more potent than prednisone and prednisolone, 25 to 30 times more potent than hydrocortisone, and about 35 times more potent than cortisone. At equipotent anti-inflammatory doses, dexamethasone almost completely lacks the sodium retaining property of hydrocortisone and closely related derivatives of hydrocortisone.

Specific dosage recommendations

In chronic, usually nonfatal diseases, including endocrine and chronic rheumatic disorders, edematous states, respiratory and gastrointestinal diseases, some dermatologic diseases and hematologic disorders, start with a low dose (0.5 to 1 mg a day) and gradually increase dosage to the smallest amount that gives the desired degree of symptomatic relief.

Dosage may be administered two, three or four times a day.

In congenital adrenal hyperplasia, the **usual** daily dose is 0.5 to 1.5 mg.

In acute, nonfatal diseases, including allergic states, ophthalmic diseases, acute and subacute rheumatic disorders, dosage ranges between 2 and 3 mg a day ; however, higher doses may be necessary in some patients. Since the course of these conditions is self-limited, prolonged maintenance therapy is not usually necessary.

Antiemetic Prophylaxis During Emetogenic Chemotherapy: In clinical studies, 8-20 mg of dexamethasone was infused intravenously over 5-15 minutes just prior to chemotherapy, followed by 4 mg of dexamethasone orally every 4-6 hours, or by 8 mg orally every 8 hours, and tapered in either strength or frequency of administration over two to three days. In general, the total treatment duration for this indication should not exceed five days beyond chemotherapy. Alternatively, injectable dexamethasone was infused intravenously in lieu of an oral formulation of dexamethasone, using various schedules. (See CLINICAL STUDIES for additional information on dosage and administration.)

Use With Other Antiemetic Agents: Some patients have received dexamethasone concomitantly with ondansetron to achieve enhanced efficacy for antiemetic prophylaxis during cisplatin or non-cisplatin emetogenic chemotherapy. The dosage of dexamethasone employed in combination therapy was similar to its dosage when administered alone. (See CLINICAL STUDIES for additional information on dosage and administration.)

Concomitant administration of dexamethasone and metoclopramide has also demonstrated enhanced efficacy for antiemetic prophylaxis during emetogenic chemotherapy.

In acute, self-limited allergic disorders or acute exacerbations of chronic allergic disorders (e.g., acute allergic rhinitis, acute attacks of seasonal allergic bronchial asthma, urticaria medicamentosa, and contact dermatoses), the following dosage schedule, combining parenteral and oral therapy, is suggested:

First Day: A parenteral steroid injection IV, IM.
Second Day and Third Day: Two tablets DECADRON (0.5 mg) twice a day.
Fourth Day and Fifth Day: One tablet DECADRON (0.5 mg) twice a day.
Sixth Day and Seventh Day: One tablet DECADRON (0.5mg) daily.
Eighth Day: Follow-up visit.

In chronic, potentially fatal diseases such as systemic lupus erythematosus, pemphigus, symptomatic sarcoidosis, the recommended initial dosage is 2 to 4.5 mg a day; higher doses may be necessary in some patients.

When the disease is acute and life-threatening (e.g., acute rheumatic carditis, crisis of systemic lupus erythematosus, severe allergic reactions, pemphigus, neoplastic diseases), the initial dosage is between 4 and 10 mg a day, administered in at least four divided doses.

Epinephrine is the drug of immediate choice in severe allergic reactions. DECADRON (tablets or elixir) is useful either concurrently or as supplementary therapy.

In cerebral edema, when maintenance therapy is required, for palliative management of patients with recurrent or inoperable brain tumors, a dosage of 2 mg two or three times a day may be effective. The smallest dosage necessary to control cerebral edema should be utilized.

In the adrenogenital syndrome, daily dosages of 0.5 to 1.5 mg may keep children in remission and prevent the recurrence of abnormal excretion of 17-ketosteroids.

As massive therapy in certain conditions, such as **acute leukemia,** the **nephrotic syndrome,** and **pemphigus,** the recommended dosage is from 10 to 15 mg a day. Patients receiving such a high dosage must be observed very closely for the appearance of severe reactions.

Dexamethasone Suppression Tests.

Tests for Cushing's syndrome: Give 1.0 mg of DECADRON orally at 11 p.m. Blood is drawn for plasma cortisol determination at 8 a.m. the following morning. For greater accuracy, give 0.5 mg of DECADRON orally every 6 hours for 48 hours. Twenty-four hours urine collections are made for determination of 17-hydroxycorticosteroid excretion.

Test to distinguish Cushing's Syndrome due to pituitary ACTH Excess from Cushing's Syndrome due to Other Causes: Give 2.0 mg of DECADRON orally every 6 hours for 48 hours. Twenty-four hours urine collections are made for determination of 17-hydroxycorticosteroid excretion.

CONTRAINDICATIONS

- Systemic fungal infections.
- Hypersensitivity to any component of this drug.

Administration of live virus vaccines (see PRECAUTIONS).

PRECAUTIONS

The lowest possible dose of corticosteroid should be used to control the condition under treatment, and when reduction in dosage is possible, the reduction should be gradual.

Corticosteroids may exacerbate systemic fungal infections and therefore should not be used in the presence of such infections unless they are needed to control **life-threatening** drug reactions due to amphotericin B. Moreover, there have been cases reported in which concomitant use of amphotericin B and hydrocortisone was followed by cardiac enlargement and congestive failure. Literature reports suggest an apparent association between use of corticosteroids and left ventricular free wall rupture after a recent myocardial infarction; therefore, therapy with corticosteroids should be used with great caution in these patients.

Average and large doses of hydrocortisone or cortisone can cause elevation of blood pressure, salt and water retention, and increased excretion of potassium. These effects are less likely to occur with the synthetic derivatives except when used in large doses. Dietary salt restriction and potassium supplementation may be necessary. All corticosteroids increase calcium excretion.

Drug-induced secondary adrenocortical insufficiency may result from too rapid withdrawal of corticosteroids and may be minimized by gradual reduction of dosage. This type of relative insufficiency may persist for months after discontinuation of therapy; therefore, in any situation of stress occurring during that period, corticosteroid therapy should be reinstituted or the current dosage may have to be increased. Since mineralocorticoid secretion may be impaired, salt and/or a mineralocorticoid should be administered concurrently.(See DRUG INTERACTIONS.)

Following prolonged therapy, withdrawal of corticosteroids may result in symptoms of the corticosteroid withdrawal syndrome including fever, myalgia, arthralgia, and malaise. This may occur in patients even without evidence of adrenal insufficiency.

Administration of live virus vaccines is contraindicated in individuals receiving immunosuppressive doses of corticosteroids. If inactivated viral or bacterial vaccines are administered to individuals receiving immunosuppressive doses of corticosteroids, the expected serum antibody response may not be obtained. However, immunization procedures may be undertaken in patients who are receiving corticosteroids as replacement therapy, e.g. for Addison's disease.

The use of DECADRON tablets in active tuberculosis should be restricted to those cases of fulminating or disseminated tuberculosis in which the corticosteroid is used for the management of the disease in conjunction with an appropriate antituberculous regimen. If corticosteroids are indicated in patients with latent tuberculosis or tuberculin reactivity, close observation is necessary as reactivation of the disease may occur. During prolonged corticosteroid therapy, these patients should receive chemoprophylaxis.

Steroids should be used with caution in nonspecific ulcerative colitis, if there is a probability of impending perforation, abscess or other pyogenic infection, diverticulitis, fresh intestinal anastomoses, active or latent peptic ulcer, renal insufficiency, hypertension, osteoporosis, and myasthenia gravis. Signs of peritoneal irritation following gastrointestinal perforation in patients receiving large doses of corticosteroids may be minimal or absent. Fat embolism has been reported as a possible complication of hypercortisonism.

There is an enhanced effect of corticosteroids in patients with hypothyroidism and in those with cirrhosis. Steroids may increase or decrease motility and number of spermatozoa in some patients.

Corticosteroids may mask some signs of infection, and new infections may appear during their use.

In cerebral malaria, the use of corticosteroids is associated with prolongation of coma and a higher incidence of pneumonia and gastrointestinal bleeding.

Corticosteroids may activate latent amebiasis or strongyloidiasis or exacerbate active disease. Therefore, it is recommended that latent or active amebiasis and strongyloidiasis be ruled out before initiating corticosteroid therapy in any patient at risk or with symptoms suggestive of either condition.

Prolonged use of corticosteroids may produce subcapsular cataracts, glaucoma with possible damage to the optic nerves, and may enhance the establishment of secondary ocular infections due to fungi or viruses.

Corticosteroids should be used cautiously in patients with ocular herpes simplex because of possible corneal perforation.

Growth and development of infants and children on prolonged corticosteroid therapy should be carefully observed.

Patients who are on drugs which suppress the immune system are more susceptible to infections than healthy individuals. Chickenpox and measles, for example, can have a more serious or even fatal course in non-immune children or adults on corticosteroids. In such children or adults who have not had these diseases, particular care should be taken to avoid exposure. The risk of developing a disseminated infection varies among individuals and may be related to the dose, route and duration of corticosteroid administration as well as to the underlying disease. Exposed patients should be advised to seek medical advice without delay. If exposed to measles, prophylaxis with intramuscular pooled immunoglobulin (IG) may be indicated. If exposed to chickenpox, prophylaxis with varicella zoster immune globulin (VZIG) may be indicated. (See the respective package inserts for IG and VZIG for complete prescribing information.) If chickenpox develops, treatment with antiviral agents should be considered.

USE IN PREGNANCY AND NURSING MOTHERS Since human reproduction studies have not been done with corticosteroids, use of these drugs in pregnancy or in women of childbearing potential requires that the anticipated benefits be weighed against the possible hazards to the mother and embryo or fetus. Infants born of mothers who have received substantial doses of corticosteroids during pregnancy should be carefully observed for signs of hypoadrenalism.

Corticosteroids appear in breast milk and could suppress growth, interfere with endogenous corticosteroid production, or cause other unwanted effects in the breastfeeding infant. Mothers taking pharmacologic doses of corticosteroids should be advised not to nurse.

DRUG INTERACTIONS

Co-administration of thalidomide with DECADRON should be employed cautiously, as toxic epidermal necrolysis has been reported with concomitant use.

Acetylsalicylic acid should be used cautiously in conjunction with corticosteroids in hypoprothrombinemia.

Cytochrome P450 3A4 (CYP 3A4) enzyme inducers, such as phenytoin (diphenylhydantoin), barbiturates (e.g., phenobarbital), carbamazepine, and rifampin may enhance the metabolic clearance of corticosteroids, resulting in decreased blood levels and lessened physiologic activity, thus requiring an increase in corticosteroid dosage.

Dexamethasone is metabolized by CYP 3A4. Concomitant administration of dexamethasone with inducers of CYP 3A4 (as listed above) has the potential to result in decreased plasma concentrations of dexamethasone. In addition, concomitant administration of dexamethasone with known inhibitors of CYP 3A4 (e.g., ketoconazole, macrolide antibiotics such as erythromycin) has the potential to result in increased plasma concentrations of dexamethasone. Effects of other drugs on the metabolism of dexamethasone may interfere with dexamethasone suppression tests, which should be interpreted with caution during administration of such drugs. Dexamethasone is a moderate inducer of CYP 3A4. Co-administration of dexamethasone with other drugs that are metabolized by CYP 3A4 (e.g., indinavir, erythromycin) may increase their clearance, resulting in decreased plasma concentrations.

In post-marketing experience, there have been reports of both increases and decreases in phenytoin levels with dexamethasone co-administration, leading to alterations in seizure control.

Although ketoconazole may increase dexamethasone plasma concentrations through inhibition of CYP 3A4, ketoconazole alone can inhibit adrenal corticosteroid synthesis and may cause adrenal insufficiency during corticosteroid withdrawal (see PRECAUTIONS).

Ephedrine may enhance the metabolic clearance of corticosteroids, resulting in decreased blood levels and lessened physiologic activity, thus requiring an increase in corticosteroid dosage.

False-negative results in the dexamethasone suppression test in patients being treated with indomethacin have been reported.

The prothrombin time should be checked frequently in patients who are receiving corticosteroids and coumarin anticoagulants at the same time because of reports that corticosteroids have altered the response to these anticoagulants. Studies have shown that the usual effect produced by adding corticosteroids is inhibition of response to coumarins, although there have been some conflicting reports of potentiation not substantiated by studies.

When corticosteroids are administered concomitantly with potassium-depleting diuretics, patients should be observed closely for development of hypokalemia.

Corticosteroids may affect the nitroblue tetrazolium test for bacterial infection and produce false negative results.

SIDE EFFECTS

Fluid and electrolyte disturbances

Sodium retention; Fluid retention; Congestive heart failure in susceptible patients; Potassium loss; Hypokalemic alkalosis; Hypertension.

Musculoskeletal

Muscle weakness; Steroid myopathy; Loss of muscle mass; Osteoporosis; Vertebral compression fractures; Aseptic necrosis of femoral and humeral heads; Pathologic fracture of long bones; Tendon rupture.

Gastrointestinal

Peptic ulcer with possible perforation and hemorrhage; Perforation of the small and large bowel, particularly in patients with inflammatory bowel diseases; Pancreatitis; Abdominal distention; Ulcerative esophagitis.

Dermatologic

Impaired wound healing; Thin fragile skin; Petechiae and ecchymoses; Erythema; Increased sweating; May suppress reactions to skin tests; Other cutaneous reactions, such as allergic dermatitis, urticaria, angioneurotic edema.

Neurologic

Convulsions; Increased intracranial pressure with papilledema (pseudotumor cerebri) usually after treatment; Vertigo; Headache; Psychic disturbances.

Endocrine

Menstrual irregularities; Development of cushingoid state; Suppression of growth in children; Secondary adrenocortical and pituitary unresponsiveness, particularly in times of stress, as in trauma, surgery or illness ; Decreased carbohydrate tolerance; Manifestations of latent diabetes mellitus; Hyperglycemia; Increased requirements for insulin or oral hypoglycemic agents in diabetics; Hirsutism.

Ophthalmic

Posterior subcapsular cataracts; Increased intraocular pressure; Glaucoma; Exophthalmos.

Metabolic

Negative nitrogen balance due to protein catabolism.

Cardiovascular

Myocardial rupture following recent myocardial infarction(see PRECAUTIONS)

Other

Hypersensitivity; Thromboembolism; Weight gain; Increased appetite; Nausea; Malaise; Hiccups.

OVERDOSAGE

Reports of acute toxicity and/or death following overdosage of glucocorticoids are rare. There are no specific recommendations for the treatment of overdosage with DECADRON.

STORAGE CONDITIONS

Tablets: store in a dry place below 30˚C, protected from light. Do not refrigerate.

Elixir: store in a dry place below 30˚C, protected from light. Do not refrigerate. Keep container tightly closed.

Do not use after expiry date.

AVAILABILITY

Tablets 0.5 mg: blister pack of 30's.
Elixir 0.5 mg/5 ml: bottle of one hundred milliliters.

This is a medicament

-A medicament is a product which affects your health, and its consumption contrary to instructions is dangerous for you.
-Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who sold the medicament.
-The doctor and the pharmacist are experts in medicine, its benefits and risks.
-Do not by yourself interrupt the period of treatment prescribed.
-Do not repeat the same prescription without consulting your doctor.

Keep medicament out of reach of children.

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