

of response to warfarin, although there have been some conflicting reports. Therefore, coagulation indices should be monitored frequently to maintain the desired anticoagulant effect.

Antidiabetics:

Because corticosteroids may increase blood glucose concentrations, dosage adjustments of antidiabetic agents may be required.

Antitubercular Drugs:

Serum concentrations of isoniazid may be decreased.

Cholestyramine:

Cholestyramine may increase the clearance of corticosteroids.

Cyclosporine:

Increased activity of both cyclosporine and corticosteroids may occur when the two are used concurrently. Convulsions have been reported with this concurrent use.

Dexamethasone Suppression Test (DST):

False-negative results in the dexamethasone suppression test (DST) in patients being treated with indomethacin have been reported. Thus, results of the DST should be interpreted with caution in these patients.

Digitalis Glycosides:

Patients on digitalis glycosides may be at increased risk of arrhythmias due to hypokalemia.

Ephedrine:

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

Estrogens, including Oral Contraceptives:

Estrogens may decrease the hepatic metabolism of certain corticosteroids, thereby increasing their effect.

Hepatic Enzyme Inducers, Inhibitors and Substrates:

Drugs which induce cytochrome P450 3A4 (CYP 3A4) enzyme activity (*e.g., barbiturates, phenytoin, carbamazepine, rifampin*) may enhance the metabolism of corticosteroids and require that the dosage of the corticosteroid be increased. Drugs which inhibit CYP 3A4 (*e.g., ketoconazole, macrolide antibiotics such as erythromycin*) have the potential to result in increased plasma concentrations of corticosteroids. Dexamethasone is a moderate inducer of CYP 3A4. Co-administration with other drugs that are metabolized by CYP 3A4 (*e.g., indinavir, erythromycin*) may increase their clearance, resulting in decreased plasma concentration.

Ketoconazole:

Ketoconazole has been reported to decrease the metabolism of certain corticosteroids by up to 60%, leading to increased risk of corticosteroid side effects. In addition, ketoconazole alone can inhibit adrenal corticosteroid synthesis and may cause adrenal insufficiency during corticosteroid withdrawal.

Nonsteroidal Anti-Inflammatory Agents (NSAIDs):

Concomitant use of aspirin (or other nonsteroidal anti-inflammatory agents) and corticosteroids increases the risk of gastrointestinal side effects. Aspirin should be used cautiously in conjunction with corticosteroids in hypoprothrombinemia. The clearance of salicylates may be increased with concurrent use of corticosteroids.

Phenytoin:

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.

Skin Tests:

Corticosteroids may suppress reactions to skin tests.

Thalidomide:

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

Vaccines:

Patients on corticosteroid therapy may exhibit a diminished response to toxoids and live or inactivated vaccines due to inhibition of antibody response. Corticosteroids may also potentiate the replication of some organisms contained in live attenuated vaccines. Routine administration of vaccines or toxoids should be deferred until corticosteroid therapy is discontinued if possible (see **WARNINGS: Infections, Vaccination**).

Carcinogenesis, Mutagenesis, Impairment of Fertility

No adequate studies have been conducted in animals to determine whether corticosteroids have a potential for carcinogenesis or mutagenesis. Steroids may increase or decrease motility and number of spermatozoa in some patients.

Pregnancy

Teratogenic Effects: Pregnancy Category C

Corticosteroids have been shown to be teratogenic in many species when given in doses equivalent to the human dose. Animal studies in which corticosteroids have been given to pregnant mice, rats, and rabbits have yielded an increased incidence of cleft palate in the offspring. There are no adequate and well controlled studies in pregnant women. Corticosteroids should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Infants born to mothers who have received substantial doses of corticosteroids during pregnancy should be carefully observed for signs of hypoadrenalism.

Nursing Mothers:

Systemically administered corticosteroids appear in human milk and could suppress growth, interfere with endogenous corticosteroid production, or cause other untoward effects. Because of the potential for serious adverse reactions in nursing infants from corticosteroids, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use:

The efficacy and safety of corticosteroids in the pediatric population are based on the well-established course of effect of corticosteroids, which is similar in pediatric and adult populations. Published studies provide evidence of efficacy and safety in pediatric patients for the treatment of nephrotic syndrome (patients >2 years of age), and aggressive lymphomas and leukemias (patients >1 month of age). Other indications for pediatric use of corticosteroids, e.g., severe asthma and wheezing, are based on adequate and well-controlled trials conducted in adults, on the premises that the course of the diseases and their pathophysiology are considered to be substantially similar in both populations.

The adverse effects of corticosteroids in pediatric patients are similar to those in adults (see **ADVERSE REACTIONS**). Like adults, pediatric patients should be carefully observed with frequent measurements of blood pressure, weight, height, intraocular pressure, and clinical evaluation for the presence of infection, psychosocial disturbances, thromboembolism, peptic ulcers, cataracts, and osteoporosis. Pediatric patients who are treated with corticosteroids by any route, including systemically administered corticosteroids, may experience a decrease in their growth velocity. This negative impact of corticosteroids on growth has been observed at low systemic doses and in the absence of laboratory evidence of hypothalamic-pituitary-adrenal (HPA) axis suppression (i.e., cosyntropin stimulation and basal cortisol plasma levels). Growth velocity may therefore be a more sensitive indicator of systemic corticosteroid exposure in pediatric patients than some commonly used tests of HPA axis function. The linear growth of pediatric patients treated with corticosteroids should be monitored, and the potential growth effects of prolonged treatment should be weighed against clinical benefits obtained and the availability of treatment alternatives. In order to minimize the potential growth effects of corticosteroids, pediatric patients should be *titrated* to the lowest effective dose.

Geriatric Use:

Clinical studies did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy. In particular, the increased risk of diabetes mellitus, fluid retention and hypertension in elderly patients treated with corticosteroids should be considered.

ADVERSE REACTIONS

(listed alphabetically, under each subsection)

The following adverse reactions have been reported with dexamethasone or other corticosteroids:

Allergic Reactions:

Anaphylactoid reaction, anaphylaxis, angioedema.

Cardiovascular:

Bradycardia, cardiac arrest, cardiac arrhythmias, cardiac enlargement, circulatory collapse, congestive heart failure, fat embolism, hypertension, hypertrophic cardiomyopathy in premature infants, myocardial rupture following recent myocardial infarction (see **WARNINGS: Cardio-renal**), edema, pulmonary edema, syncope, tachycardia, thromboembolism, thrombophlebitis, vasculitis.

Dermatologic:

Acne, allergic dermatitis, dry scaly skin, ecchymoses and petechiae, erythema, impaired wound healing, increased sweating, rash, striae, suppression of reactions to skin tests, thin fragile skin, thinning scalp hair, urticaria.

Endocrine:

Decreased carbohydrate and glucose tolerance, development of cushingoid state, hyperglycemia, glycosuria, hirsutism, hypertrichosis, increased requirements for insulin or oral hypoglycemic agents in diabetes, manifestations of latent diabetes mellitus, menstrual irregularities, secondary adrenocortical and pituitary unresponsiveness (particularly in times of stress, as in trauma, surgery, or

illness), suppression of growth in pediatric patients.

Fluid and Electrolyte Disturbances:

Congestive heart failure in susceptible patients, fluid retention, hypokalemic alkalosis, potassium loss, sodium retention.

Gastrointestinal:

Abdominal distention, elevation in serum liver enzyme levels (usually reversible upon discontinuation), hepatomegaly, increased appetite, nausea, pancreatitis, peptic ulcer with possible perforation and hemorrhage, perforation of the small and large bowel (particularly in patients with inflammatory bowel disease), ulcerative esophagitis.

Metabolic:

Negative nitrogen balance due to protein catabolism.

Musculoskeletal:

Aseptic necrosis of femoral and humeral heads, loss of muscle mass, muscle weakness, osteoporosis, pathologic fracture of long bones, steroid myopathy, tendon rupture, vertebral compression fractures.

Neurological/Psychiatric:

Convulsions, depression, emotional instability, euphoria, headache, increased intracranial pressure with papilledema (pseudotumor cerebri) usually after treatment, insomnia, mood swings, neuritis, neuropathy, paresthesia, personality changes, psychic disorders, vertigo.

Ophthalmic:

Exophthalmos, glaucoma, increased intraocular pressure, posterior subcapsular cataracts.

Other:

Abnormal fat deposits, decreased resistance to infection, hiccups, increased or decreased motility and number of spermatozoa, malaise, moon face, weight gain.

OVERDOSAGE

Treatment of overdosage is by supportive and symptomatic therapy. In the case of acute overdosage, according to the patient's condition, supportive therapy may include gastric lavage or emesis.

DOSAGE AND ADMINISTRATION

For Oral Administration:

The initial dose varies from 0.75 to 9 mg a day depending on the disease being treated.

IT SHOULD BE EMPHASIZED THAT DOSAGE REQUIREMENTS ARE VARIABLE AND MUST BE INDIVIDUALIZED ON THE BASIS OF THE DISEASE UNDER TREATMENT AND THE RESPONSE OF THE PATIENT.

After a favorable initial response is noted, the proper maintenance dosage should be determined by decreasing the initial dosage in small decrements at appropriate time intervals until the lowest dosage that maintains an adequate clinical response is reached.

Situations which may make dosage adjustments necessary are changes in clinical status secondary to remissions or exacerbations in the disease process, the patient's individual drug responsiveness, and the effect of patient exposure to stressful situations not directly related to the disease entity under treatment. In this latter situation it may be necessary to increase the dosage of the corticosteroid for a period of time consistent with the patient's condition. If after long-term therapy the drug is to be stopped, it is recommended that it be withdrawn gradually rather than abruptly.

In the treatment of acute exacerbations of multiple sclerosis, daily doses of 30 mg of dexamethasone for a week followed by 4 to 12 mg every other day for one month have been shown to be effective (see **PRECAUTIONS: Neuro-Psychiatric**).

In pediatric patients, the initial dose of dexamethasone may vary depending on the specific disease entity being treated. The range of initial doses is 0.02 to 0.3 mg/kg/day in three or four divided doses (0.6 to 9 mg/m²bsa/day).

For the purpose of comparison, the following is the equivalent milligram dosage of the various corticosteroids:

Cortisone, 25	Triamcinolone, 4
Hydrocortisone, 20	Paramethasone, 2
Prednisolone, 5	Betamethasone, 0.75
Prednisone, 5	Dexamethasone, 0.75
Methylprednisolone, 4	

These dose relationships apply only to oral or intravenous administration of these compounds. When these substances or their derivatives are injected intramuscularly or into joint spaces, their relative properties may be greatly altered.

In acute, self-limited allergic disorders or acute exacerbations of chronic allergic disorders, the following dosage schedule combining parenteral and oral therapy is suggested:

Dexamethasone Sodium Phosphate injection, 4 mg per mL:	
First Day	1 or 2 mL, intramuscularly
Dexamethasone tablets, 0.75 mg:	
Second Day	4 tablets in two divided doses
Third Day	4 tablets in two divided doses
Fourth Day	2 tablets in two divided doses
Fifth Day	1 tablet
Sixth Day	1 tablet
Seventh Day	No treatment
Eighth Day	Follow-up visit

This schedule is designed to ensure adequate therapy during acute episodes, while minimizing the risk of overdosage in chronic cases.

In *cerebral edema*, dexamethasone sodium phosphate injection is generally administered initially in a dosage of 10 mg intravenously followed by 4 mg every six hours intramuscularly until the symptoms of cerebral edema subside. Response is usually noted within 12 to 24 hours and dosage may be reduced after two to four days and gradually discontinued over a period of five to seven days. For palliative management of patients with recurrent or inoperable brain tumors, maintenance therapy with either dexamethasone sodium phosphate injection or dexamethasone tablets in a dosage of 2 mg two or three times daily may be effective.

Dexamethasone Suppression Tests

- Tests for Cushing's syndrome

Give 1.0 mg of dexamethasone orally at 11:00 p.m. Blood is drawn for plasma cortisol determination at 8:00 a.m. the following morning. For greater accuracy, give 0.5 mg of dexamethasone orally every 6 hours for 48 hours. Twenty-four hour 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 dexamethasone orally every 6 hours for 48 hours. Twenty-four hour urine collections are made for determination of 17-hydroxycorticosteroid excretion.

HOW SUPPLIED

Decadron® tablets are available as:

0.5 mg tablets scored (yellow), debossed “Par-084” and supplied in bottles of 100, NDC 58463-014-01.
0.75 mg tablets scored (blue), debossed “Par-085” and supplied in bottles of 100, NDC 58463-015-01.
4 mg tablets scored (white), debossed “Par-087” and supplied in bottles of 100, NDC 58463-016-01.
6 mg tablets scored (white), debossed “Par-129” and supplied in bottles of 100, NDC 58463-017-01.

Store at 20° to 25°C (68° to 77°F) [See USP Controlled Room Temperature]. Dispense in a tight, light resistant container as defined in the USP/NF.

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