CONTRAINDICATIONS

Systemic fungal infections (see WARNINGS: Fungal Infections). Dexamethasone tablets are contraindicated in patients who are hypersensitive to any components of this product.

WARNINGS

General:
Rare instances of anaphylactic reactions have occurred in patients receiving corticosteroid therapy (see ADVERSE REACTIONS). Increased dosage of rapidly acting corticosteroids is indicated in patients on corticosteroid therapy subjected to any unusual stress before, during, and after the stressful situation.

Cardio-Renal:
Large doses of corticosteroids can cause elevation of blood pressure, sodium 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. Diuretic salt restriction and potassium supplementation may be necessary. All corticosteroids increase calcium excretion.

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.

Endocrine:
Corticosteroids can produce reversible hypothalamic-pituitary-adrenal (HPA) axis suppression with the potential for corticosteroid insufficiency following withdrawal of treatment. 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 the drug, therefore, in any situation of stress occurring during that period, hormone therapy should be reinstituted. If the patient is receiving steroids already, dosage may have to be increased.

Metabolic clearance of corticosteroids is decreased in hypothyroid patients and increased in hyperthyroid patients. Changes in thyroid status of the patient may necessitate adjustment in dose.

Infections General:
Patients who are on corticosteroids are more susceptible to infections than healthy individuals. There may be decreased resistance and inability to localize infection when corticosteroids are used. Infection with any pathogen (viral, bacterial, fungal, protistan or helminthic) in any location of the body may be associated with the use of corticosteroids alone or in combination with other immunosuppressive agents. When the use of corticosteroids is necessary for the management of severe infections, concomitant use of antibiotics or antifungal medications is desirable. In unusual situations when simultaneous administration of corticosteroids and anticoagulants is necessary, prevention of thrombosis must be considered.

Fungal Infections:
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. There have been cases reported in which concomitant use of amphotericin B and hydrocortisone was followed by cardiac enlargement and congestive heart failure (see PRECAUTIONS: Drug Interactions: Amphotericin B injection and potassium-depleting agents).

Special Pathologies:
Latent disease may be activated or there may be an exacerbation of intercurrent infections due to pathogenic organisms for which the patient is susceptible (e.g., Candida, Cryptococcus, Mycobacterium, Nocardia, Pneumocystis, Toxoplasma).

It is recommended that latent meningitis or active meningoencephalitis be ruled out before initiating corticosteroid therapy in any patient who has spent time in the tropics or any patient with unexplained meningitis.

Similarly, corticosteroids should be used with great care in patients with known or suspected Strongyloides (threadworm) infection. In such patients, corticosteroid-induced immunosuppression may lead to Strongyloides hyperinfection and dissemination with widespread larval invasion, often accompanied by severe enterocolitis and potentially fatal gran-negative sepsis.

Corticosteroids should not be used in cerebral malaria.

Tuberculosis:
The use of corticosteroids in active tuberculosis should be restricted to those cases of Fluorinated 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 tuberculosis reactively, close observation is necessary as reactivation of the disease may occur. During prolonged corticosteroid therapy, these patients should receive chemoprophylaxis.

Vaccination:
Administration of live or live, attenuated vaccines is contraindicated in patients receiving immunosuppressive doses of corticosteroids. Killed or inactivated vaccines may be administered. However, the response to such vaccines cannot be predicted. Immunization procedures may be undertaken in patients who are receiving corticosteroids as replacement therapy. e.g., Addison's disease.

Viral infections:
Chickenpox and measles can have a more serious or even fatal course in pediatric and adult patients on corticosteroids. In pediatric and adult patients who have not had these diseases, particular care should be taken to avoid exposure. The possibility of worsening and precipitating infection and/or unusual severe reactions and of abnormally rapid development of Herpes zoster has been reported in chicken-pox and herpes zoster patients who are receiving immunosuppressant drugs (see WARNINGS: Infectious Disease).

If chickenpox develops, treatment with antiviral agents should be considered.

Opthalmic:
Use of corticosteroids may produce a more serious or even fatal course in patients receiving immunosuppressive doses of corticosteroids. Killed or inactivated vaccines may be administered. However, the response to such vaccines cannot be predicted. Immunization procedures may be undertaken in patients who are receiving corticosteroids as replacement therapy. e.g., Addison's disease.

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Antisepsis, Oral
Co-administration of corticosteroids and warfarin usually results in inhibition of response to warfarin, although there have been some conflicting reports. Therefore, coagulation indices should be monitored frequently to maintain the desired anticoagulant effect.

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

Antibacterial Drugs:
Serum concentrations of isoniazid may be decreased.

Chlorothiazide:
Chlorothiazide may increase the clearance of corticosteroids.

Cyclosporine:
Increased activity of both cyclosporine and corticosteroids may occur when the two are used concurrently. Concomitant use of aspirin (or other nonsteroidal anti-inflammatory agents) and corticosteroids should be used cautiously in conjunction with corticosteroids in hypoprothrombinemia.

Dexamethasone is a moderate inducer of CYP 3A4. Co-administration with corticosteroids and potentially increase the risk for systemic corticosteroid side effects. In addition, ketoconazole alone can cause the decreased hepatic metabolism of the corticosteroid and potentially increase the risk of systemic corticosteroid side effects. Consider the benefit of co-administration versus the potential risk of systemic corticosteroid side effects, in which case patients should be monitored for systemic corticosteroid side effects.

CYP 3A4 Substrates:
Dexamethasone is a moderate inducer of CYP 3A4. Co-administration with other drugs that are metabolized by CYP 3A4 (e.g., indinavir, ritonavir, cyclosporine, felodipine, midazolam, triazolam) may increase the clearance, resulting in decreased plasma concentration.

Nonsteroidal Anti-Inflammatory Agents (NSAIDs):
Concomitant use of aspirin (or other nonsteroidal anti-inflammatory agents) and corticosteroids may increase the risk of gastrointestinal side effects. Aspirin should be used cautiously in conjunction with corticosteroids in hydroxypropionibutyrinemia. 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 effects may be additive.

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 in vivo in the absence of protective antibody. 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 produce a potential for carcinogenesis or mutagenesis. Steroids may increase or decrease motility and number of spermatozoa in some patients. Pregnancy:
Therapeutic Effects:
Corticosteroids have proven to be teratogenic in many species when given in doses equivalent to or greater than 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 safety and efficacy in pediatric and adult populations. Pediatrists should carefully observe children on corticosteroids and 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 increased sensitivity to these drugs in these patients. In particular, the increased risk of systemic corticosteroid side effects, in which case patients should be monitored for systemic corticosteroid side effects.

Pharmacology:
Antistress: Antistress: dexamethasone may be effective.

Tests for Cushing's syndrome

1. Test to distinguish Cushing's syndrome due to pituitary ACTH excess from Cushing's syndrome due to other causes. For this test, give 0.5 mg dexamethasone orally every 6 hours for 24 hours. Twenty-four hour urine collections are made for determination of 17-hydroxycorticosteroids.

2. Test to distinguish Cushing's syndrome due to pituitary AACTH 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-hydroxycorticosteroids.

HOW SUPPLIED:
Dexamethasone tablets are available as:

- 0.5 mg tablets scored (yellow), debossed “F 085” and supplied in:
  - Bottles of 100, NDC 48102-048-00
  - Bottles of 500, NDC 48102-048-40

- 0.75 mg tablets scored (white), debossed “F 085” and supplied in:
  - Bottles of 100, NDC 48102-049-00

- 1 mg tablets scored (white), debossed “F 085” and supplied in:
  - Bottles of 100, NDC 48102-049-40

- 0.5 mg tablets scored (white), debossed “F 129” and supplied in:
  - Bottles of 100, NDC 48102-049-50

- 0.75 mg tablets scored (white), debossed “F 129” and supplied in:
  - Bottles of 100, NDC 48102-049-50

- 1 mg tablets scored (white), debossed “F 129” and supplied in:
  - Bottles of 100, NDC 48102-049-50

- 2 mg tablets scored (white), debossed “F 129” and supplied in:
  - Bottles of 100, NDC 48102-049-50

- 4 mg tablets scored (white), debossed “F 129” and supplied in:
  - Bottles of 100, NDC 48102-049-50

- 8 mg tablets scored (white), debossed “F 129” and supplied in:
  - Bottles of 100, NDC 48102-049-50

- 16 mg tablets scored (white), debossed “F 129” and supplied in:
  - Bottles of 100, NDC 48102-049-50

- 32 mg tablets scored (white), debossed “F 129” and supplied in:
  - Bottles of 100, NDC 48102-049-50

In the treatment of acute exacerbations of multiple sclerosis, daily doses of 30 mg of dexamethasone for a week followed by 4 to 8 mg every other day for one month after the initial dose is completed at the appropriate time intervals until the lowest dosage that maintains an adequate clinical response is reached.

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/m²/24 hours).

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

<table>
<thead>
<tr>
<th>Corticosterone</th>
<th>Intramuscular</th>
<th>Bemethasone</th>
<th>0.75</th>
<th>Dexamethasone</th>
<th>0.75</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cortisone, 25</td>
<td>1 or 2 ml, intramuscular</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Hydrocortisone, 20</td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td>Prednisone, 5</td>
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<tr>
<td>Prednisone, 5</td>
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<td></td>
</tr>
<tr>
<td>Methylprednisolone, 4</td>
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</tbody>
</table>

These dose relationships apply only to oral or intravenous administration of these compounds. When these substances or their derivatives are injected intraocularly 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, intramuscular

- 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 subsist. (Dexamethasone Sodium Phosphate injection, 4 mg per mL) continued for 10 to 14 days. 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.