DESCRIPTION:
Dexamethasone Sodium Phosphate Injection, USP, is a water-soluble inorganic ester of dexamethasone which produces a rapid response even when injected intramuscularly.

Dexamethasone Sodium Phosphate, USP chemically is 3α,21-dihydroxy-16,17-diyn-11-yl (phosphonooxy)-, disodium salt, (1β,16β).

It occurs as a white to creamy white powder, is exceedingly hygroscopic, is soluble in water and its solutions have a pH between 7.0 and 8.5. It has the following structural formula:

\[ \text{C}_{22}\text{H}_{28}\text{FNa}_2\text{O}_8\text{P} \]

Each mL of Dexamethasone Sodium Phosphate Injection, USP (Preservative Free) contains dexamethasone sodium phosphate, USP equivalent to 10 mg dexamethasone phosphate; 24.75 mg sodium citrate, dihydrate; and water for Injection, q.s. pH adjusted with citric acid or sodium hydroxide, if necessary, pH 7.0 to 8.5.

Each mL of Dexamethasone Sodium Phosphate Injection, USP (Preserved) contains dexamethasone sodium phosphate, USP equivalent to 10 mg dexamethasone phosphate; 13.5 mg sodium citrate, dihydrate; 10 mg benzyl alcohol; and water for Injection, q.s. pH adjusted with citric acid or sodium hydroxide, if necessary, pH 7.0 to 8.5.

CLINICAL PHARMACOLOGY:
Dexamethasone sodium phosphate injection has a rapid onset but short duration of action when compared with less soluble preparations. Because of this, it is suitable for the treatment of acute disorders responsive to adrenocortical steroid therapy.

Naturally occurring glucocorticoids (hydrocortisone and cortisol), which also have salt-retaining properties, are used as replacement therapy in adrenocortical deficiency states. Their synthetic analogs, including dexamethasone, are primarily used for their potent anti-inflammatory effects in disorders of many organ systems.

Glucocorticoids cause profound and varied metabolic effects. In addition, they modify the body's immune responses to diverse stimuli. At equipotent anti-inflammatory doses, dexamethasone almost completely lacks the sodium-retaining property of hydrocortisone and closely related derivatives of hydrocortisone.

INDICATIONS AND USAGE:
By intravenous or intramuscular injection when oral therapy is not feasible:

1. Endocrine Disorders
   - Primary or secondary adrenocortical insufficiency (hydrocortisone or cortisol is the drug of choice; synthetic analogs may be used in conjunction with mineralocorticoids where applicable; in adrenal insufficiency, mineralocorticoid supplementation is of particular importance).
   - Acute adrenocortical insufficiency (hydrocortisone or cortisol is the drug of choice; mineralocorticoid supplementation may be necessary, particularly when synthetic analogs are used).
   - Preoperatively, and in the event of serious trauma or illness, in patients with known adrenal insufficiency or when adrenocortical reserve is doubtful.
   - Shock unresponsive to conventional therapy if adrenocortical insufficiency exists or is suspected.
   - Congenital adrenal hyperplasia
   - Nonsuppurative thyroiditis
   - Hypercalcemia associated with cancer

2. Rheumatic Disorders
   - As adjunctive therapy for short-term administration (to tide the patient over an acute episode or exacerbation) in:
     - Post-traumatic osteoarthritis
     - Rheumatoid arthritis, including juvenile rheumatoid arthritis (selected cases may require low-dose maintenance therapy).
     - Acute and subacute bursitis
     - Epicondylitis
     - Acute nonspecific tenosynovitis
     - Acute gouty arthritis
     - Psoriatic arthritis
     - Ankylosing spondylitis

3. Collagen Diseases
   - During an exacerbation or as maintenance therapy in selected cases of:
     - Systemic lupus erythematosus
     - Acute rheumatic carditis

4. Dermatologic Diseases
   - Periphisis
   - Severe erythema multiforme (Stevens-Johnson syndrome)
   - Exfoliative dermatitis
   - Bullous dermatitis herpetiformis
   - Severe seborrheic dermatitis
   - Severe pityriasis rosea
   - Mycosis fungoides

5. Allergic States
   - Control of severe or incapacitating allergic conditions intractable to adequate trials of conventional treatment in:
     - Bronchial asthma
     - Contact dermatitis
     - Atopic dermatitis
     - Serum sickness
     - Seasonal or perennial allergic rhinitis
     - Drug hypersensitivity reactions
     - Urticarial transfusion reactions
     - Acute noninfectious laryngeal edema (epinephrine is the drug of first choice).

6. Ophthalmic Diseases
   - Severe acute and chronic allergic and inflammatory processes involving the eye, such as:
     - Herpes zoster ophthalmicus
     - Uveitis, iridocyclitis
     - Cholesterolosis
     - Diffuse posterior uveitis and choroiditis
     - Optic neuritis
     - Sympathetic ophthalmia
     - Idiopathic thrombocytopenic purpura in adults (IV only; IM administration is contraindicated).
     - Idiopathic thrombocytopenic purpura in children (IM administration is contraindicated).

7. Gastrointestinal Diseases
   - To tide the patient over a critical period of the disease in:
     - Ulcerative colitis (systemic therapy)
     - Regional enteritis (systemic therapy)

8. Respiratory Diseases
   - Symptomatic sarcoidosis
   - Bronchitis or emphysema with paroxysmal nocturnal dyspnea
   - Cholesterolosis
   - Optic neuritis
   - Sympathetic ophthalmia
   - Acute Granulocytic Leukemia
   - Myelogenous leukemia (selected cases may require low-dose maintenance therapy).

9. Hematologic Disorders
   - Acquired (autoimmune) hemolytic anemia
   - Idiopathic thrombocytopenic purpura
   - Acute leukemia of childhood
   - Acute lymphocytic leukemia
   - Leukemias and lymphomas in adults
   - Myelogenous leukemia in adults
   - Myelogenous leukemia in children
   - Myelogenous leukemia in infants

10. Neoplastic Diseases
    - For palliative management of:
        - Leukemias and lymphomas in adults
        - Acute leukemia of childhood

11. Edematous States
    - To induce diuresis or remission of proteinuria in the nephrotic syndrome, without uremia, of the idiopathic type or that due to lupus erythematosus.

12. Miscellaneous
    - Tuberculous meningitis with subarachnoid block or impending block when used concurrently with appropriate antituberculous chemotherapy.
    - Loeffler’s syndrome not manageable by other means.
    - Aspiration pneumonitis

13. Diagnostic testing of adrenocortical hyperfunction.

14. Cerebral Edema associated with primary or metastatic brain tumor, cranialotomy, or head injury. Use in cerebral edema is not a substitute for careful neurosurgical evaluation and definitive management such as neurosurgery or other specific therapy.

CONTRAINDICATIONS:
Systemic fungal infections (see WARNINGS regarding amphotericin B).

Hypersensitivity to any component of this product (see WARNINGS).

WARNINGS:
Because rare instances of anaphylactoid reactions have occurred in patients receiving parenteral corticosteroid therapy, appropriate precautionary measures should be taken prior to administration, especially when the patient has a history of allergy to any drug. Anaphylactoid and hypersensitivity reactions have been reported for dexamethasone sodium phosphate injection (see ADVERSE REACTIONS).

Corticosteroids may exacerbate systemic fungal infections and, therefore, should not be used in the presence of such infections unless they are needed to control 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.

In patients on corticosteroid therapy subjected to any unusual stress, increased dosage of rapidly acting corticosteroids before, during, and after the stressful situation is indicated.
Drug-induced secondary adrenal insufficiency may result from too rapid withdrawal of corticosteroids, or be minimized by gradual reduction of dosage. This type of relative insufficiency may last for months after discontinuation of therapy, therefore, in any situation of stress occurring during that period hormone therapy should be instituted. In patients receiving corticosteroids, dosage may have to be increased. Since mineralocorticoid secretion may be impaired, salt and/or a mineralocorticoid should be administered concurrently.

Corticosteroids may mask signs of infection, and delay or prevent the appearance of sequelae during their use. There may be decreased resistance and inability to localize infection, and subclinical gram-negative infections may be exaggerated.

Moreover, corticosteroids may affect the nitroblue- tetrazolium test for bacterial infection and produce false negative results.

In cerebral malaria, a double-blind trial has shown that the use of corticosteroids is associated with a higher percentage and a higher incidence of pneumonia and gastrointestinal bleeding. Therefore, it is recommended that patients with malaria who exhibit clinical evidence of meningitis be treated with corticosteroids. Therefore, it is recommended that patients with malaria who exhibit clinical evidence of meningitis be treated with corticosteroids.

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

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

Administration of live virus vaccines, including some varicella-zoster virus vaccines, in children receiving immuno suppressive doses of corticosteroids, if inactivated viral or bacterial vaccines are administered to patients receiving immuno suppressive doses of corticosteroids, the expected serum antibody response may be subnormal. However, immunization procedures may be undertaken in patients who are receiving corticosteroids as replacement therapy for Addison’s disease.

Patients who are on drugs which suppress the immune system may be more susceptible to infection than healthy individuals. Chickenpox and measles, for example, can have a more serious or even fatal course in children and adults on corticosteroids.

In such children or adults who have not had these diseases, particular care should be taken to avoid exposure to chickenpox or measles. Patients should also be advised that if they are exposed, medical advice should be sought without delay.

Susceptible patients who are on immunosuppressive doses of corticosteroids or are receiving corticosteroids and concomitant anticoagulants at the same time because of reports of acute or fatal reactions, have coagulopathy with decreased bleeding time.

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

The slower rate of absorption by intramuscular administration should be recognized.

Information for Patients

Susceptible patients who are on immunosuppressive doses of corticosteroids should be warned to avoid exposure to chickenpox or measles. Patients should also be advised that if they are exposed, medical advice should be sought without delay.

Pediatric Use

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

ADVERSE REACTIONS:

Fluid and electrolyte disturbances: Sodium retention, fluid retention

Congestive heart failure in susceptible patients

Potassium loss

Hypocalcemia

Hypertension

Musculoskeletal:

Muscle weakness

Steroid myopathy

Loss of muscle mass

Osteoporosis

Vertebral compression fractures

Aseptic necrosis of femoral and humeral heads

Tendon rupture

Pathologic fracture of long bones

Gastrointestinal:

Peptic ulceration

Perforation of the small and large bowel

Pancreatitis

Abdominal distention

Ulcerative esophagitis

Dermatologic:

Impaired wound healing

Thin fragile skin

Petechiae and ecchymoses

Thickening of skin

Hirsutism

Increased sweating

Thin fragile skin

Acne

Hair loss

Increased appetite

Glycemic agents in diabetics

Manifestations of latent diabetes mellitus

Increased intraocular pressure

Posterior subcapsular cataracts

Glaucoma

Hypertension

Increased intracranial pressure with papilledema

Headache

Psychic disturbances

Endocrine:

Menstrual irregularities

Development of cushingoid state

Suppression of the hypothalamic-pituitary-adrenal axis

Secondary adrenal and pituitary unre sponsiveness, particularly in times of stress, as in trauma, surgery, or illness

Decreased carbohydrate tolerance

Manifestations of latent diabetes mellitus

Increased requirement for insulin or oral hypoglycemic agents in diabetics

Hirsutism

Ophthalmic:

Posterior subcapsular cataracts

Increased intraocular pressure

Glaucoma

Exophthalmos

Retinopathy of prematurity

Metabolic:

Negative nitrogen balance due to protein catabolism

Cardiovascular:

Myocardial rupture following recent myocardial infarction (see WARNINGS)

Hypertrophic cardiomyopathy in low birth weight infants

Other:

Anaphylactoid or hypersensitivity reactions

Thromboembolism

Weight gain

Increased appetite

Nausea

Malaise

Hiccups

The following additional adverse reactions are related to parenteral corticosteroid therapy:

Hyperpigmentation or hypertrophy

Subcutaneous and cutaneous atrophy

Sterile abscess

Charcot-like arthropathy

OVERDOSE:

Reversal of toxicity and/or death following overdose of glucocorticoids is rare. In the event of overdosage, no specific antidote is available; treatment is primarily supportive and symptomatic.

The oral LD₅₀ of dexamethasone sodium phosphate in female mice was 794 mg/kg.

DOSAGE AND ADMINISTRATION:

Dexamethasone sodium phosphate injection, 10 mg/mL—For intravenous and intramuscular injection only.

Dexamethasone sodium phosphate injection can be given directly from the vial, or it can be added to a solution containing dextran 40 or polyvinylpyrrolidone and administered by intravenous drip.

Solutions used for intravenous administration or further dilution of this product should be preservative free when used in the neonate, especially the premature infant.

When it is mixed with an infusion solution, sterile precautions should be observed. Since infusion solutions generally do not contain preservatives, mixtures should be used within 24 hours.

DOSE REQUIREMENTS AND CHANGES MUST BE INDIVIDUALIZED ON THE BASIS OF THE DISEASE AND THE RESPONSE OF THE PATIENT.

Intravenous and Intramuscular Injection

The initial dosage of dexamethasone sodium phosphate injection varies from 0.5 to 9 mg a day depending on the disease being treated. In less severe diseases doses lower than 0.5 mg may suffice, while in severe diseases doses higher than 9 mg may be required.

The initial dosage should be maintained or adjusted under the patient’s response is satisfactory. If a satisfactory clinical response does not occur after a reasonable period of time, discontinue dexamethasone sodium phosphate injection and transfer the patient to other therapy.

A favorable initial response, the proper maintenance dosage should be determined by decreasing the initial dosage in small amounts to the lowest dosage that maintains an adequate clinical response.

Patients should be observed closely for signs that might require dosage adjustments, including changes in clinical status resulting from remissions or exacerbations of the disease, individual drug responsiveness, and the effect of stress (e.g., surgery, infection, trauma). During stress it may be necessary to increase dosage temporarily.

If the drug is to be stopped after more than a few days of treatment, it usually should be withdrawn gradually.

When the intravenous route of administration is used, dosage usually should be up to the oral dosage. In certain overwhelming, acute, life-threatening situations, however, administration in dosages exceeding the usual dosages may be justified and may be in multiples of the oral dosages.
The slower rate of absorption by intramuscular administration should be recognized.

**Shock**

There is a tendency in current medical practice to use high (pharmacologic) doses of corticosteroids for the treatment of unresponsive shock. The following dosages of dexamethasone sodium phosphate injection have been suggested by various authors:

<table>
<thead>
<tr>
<th>Author</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cavanagh</td>
<td>3 mg/kg of body weight per 24 hours by constant intravenous infusion after an initial intravenous injection of 20 mg</td>
</tr>
<tr>
<td>Dietzman</td>
<td>2 to 6 mg/kg of body weight as a single intravenous injection</td>
</tr>
<tr>
<td>Frank</td>
<td>40 mg initially followed by repeat intravenous injection every 4 to 6 hours while shock persists</td>
</tr>
<tr>
<td>Oaks</td>
<td>40 mg initially followed by repeat intravenous injection every 2 to 6 hours while shock persists</td>
</tr>
<tr>
<td>Schumer</td>
<td>1 mg/kg of body weight as a single intravenous injection</td>
</tr>
</tbody>
</table>

Administration of high dose corticosteroid therapy should be continued only until the patient’s condition has stabilized and usually not longer than 48 to 72 hours.

Although adverse reactions associated with high dose, short term corticosteroid therapy are uncommon, peptic ulceration may occur.

**Cerebral Edema**

Dexamethasone sodium phosphate injection is generally administered initially in a dosage of 10 mg intravenously followed by four 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 2 mg two or three times a day may be effective.

**Acute Allergic Disorders**

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, first day, 4 or 8 mg intramuscularly.

Dexamethasone tablets, 0.75 mg: second and third days, 4 tablets in two divided doses each day; fourth day, 2 tablets in two divided doses; fifth and sixth days, 1 tablet each day; 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.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever the solution and container permit.

**HOW SUPPLIED:**

Dexamethasone Sodium Phosphate Injection, USP (Preservative Free) equivalent to 10 mg dexamethasone phosphate, is supplied in a single dose vial as follows:

<table>
<thead>
<tr>
<th>Product NDC No.</th>
<th>Strength</th>
<th>Vial Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>500601 63323-506-01</td>
<td>10 mg/mL</td>
<td>1 mL</td>
</tr>
</tbody>
</table>

Packaged in twenty-fives.

Dexamethasone Sodium Phosphate Injection, USP (Preserved) equivalent to 10 mg dexamethasone phosphate, is supplied in a multiple dose vial as follows:

<table>
<thead>
<tr>
<th>Product NDC No.</th>
<th>Strength</th>
<th>Vial Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>501610 63323-516-10</td>
<td>10 mg/mL</td>
<td>10 mL</td>
</tr>
</tbody>
</table>

Packaged in tens. Vial stoppers do not contain natural rubber latex.

**Storage**

Store at 20° to 25°C (68° to 77°F) [see USP Controlled Room Temperature]. Sensitive to heat. Do not autoclave.

Protect from freezing.

Protect from light.

Single dose vials—Store in container until time of use. Discard unused portion.

Multiple dose vials—Store in container until contents are used.

**REFERENCES:**