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 Pregna-1,4-diene-3,20-dione, 9-fluoro 11,17-dihydroxy-16-methyl-21-(phosphonooxy)-disodium salt, (11 β , 16 α).

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:

C22H28FNa2O8P

M.W. 516.41

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 hydrox ide, if necessary. pH: 7.0 to 8.5.
Each mL 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 (hydrocorti-sone and cortisone), 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

FRESENIUS

45955E/Revised: May 2014

INJECTION, USP

Rx only

DEXAMETHASONE SODIUM PHOSPHATE

For Intravenous or Intramuscular Use Only

Primary or secondary adrenocortical insufficiency (hydrocortisone or cortisone is the drug of choice; synthetic analogs may be used in conjunction with mineralocorticoids where applicable; in infancy, mineralocorticoid supplementation is of particular importance).

Acute adrenocortical insufficiency (hydro cortisone or cortisone 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

Shock unresponsive to conventional therapy if adrenocortical insufficiency exists or is

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

Synovitis of 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

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

Pemphiaus Severe erythema multiforme (Stevens-Johnson syndrome) Exfoliative dermatitis Bullous dermatitis herpetiformis Severe seborrheic dermatitis Severe psoriasis

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 (epineph-

rine 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

Iritis, iridocyclitis Chorioretinitis

Keratitis

Diffuse posterior uveitis and choroiditis Optic neuritis

Sympathetic ophthalmia Anterior segment inflammation Allergic conjunctivitis

Allergic corneal marginal ulcers

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

Berylliosis
Fulminating or disseminated pulmonary tuberculosis when used concurrently with appropriate antituberculous chemotherapy.

Loeffler's syndrome not manageable by other means.

Aspiration pneumonitis

9. Hematologic Disorders

Acquired (autoimmune) hemolytic anemia. Idiopathic thrombocytopenic purpura in adults (IV only; IM administration is contraindicated). Secondary thrombocytopenia in adults Erythroblastopenia (RBC anemia) Congenital (erythroid) hypoplastic anemia

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

Trichinosis with neurologic or myocardial involvement

13. Diagnostic testing of adrenocortical hyper-

14. Cerebral Edema associated with primary or

metastatic brain tumor, craniotomy, 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 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, hormone therapy should be reinstituted. If the patient is receiving steroids already, dosage may have to be increased. Since mineralocorticoid secretion may be impaired, salt and/or a mineralocorticoid should be administered

Corticosteroids may mask some signs of infection, and new infections may appear during their use. There may be decreased resistance and inability to localize infection when corticosteroids are used. 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 prolongation of coma and a higher incidence of pneumonia and gastrointestinal bleeding.

Corticosteroids may activate latent amebiasis. Therefore, it is recommended that latent or active amebiasis be ruled out before initiating corticosteroid therapy in any patient who has spent time in the tropics or in any patient with unexplained

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 hydro-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.

Administration of live virus vaccines, including smallpox, 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.

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 can be related to the dose, route and duration of corticosteroid administration as well as to the underlying disease. If exposed to chickenpox, prophylaxis with varicella zoster immune globulin (VZIG) may be indicated. If chickenpox develops, treatment with antiviral agents may be considered. If exposed to measles, prophylaxis with immune globulin (IG) may be indicated. (See the respective package inserts for VZIG and IG for complete prescribing information).

The use of dexamethasone sodium phosphate injection 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.

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

Serious Neurologic Adverse Reactions with Epidural Administration

Serious neurologic events, some resulting in death, have been reported with epidural injection of corticosteroids. Specific events reported include, but are not limited to, spinal cord infarction, paraplegia, quadriplegia, cortical blindness, and stroke. These serious neurologic events have been reported with and without use of fluoroscopy. The safety and effectiveness of epidural administration of corticosteroids has not been established. and corticosteroids are not approved for this use.

Usage in Pregnancy

Since adequate 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. Mothers taking pharmacologic doses of corticosteroids should be advised not to nurse

PRECAUTIONS:

This product, like many other steroid formulations, is sensitive to heat. Therefore, it should not be autoclaved when it is desirable to sterilize the exterior of the vial.

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

in patients with hypothyroidism and in those with

patients with ocular herpes simplex for fear of corneal perforation.

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

Psychic derangements may appear when corticosteroids are used, ranging from euphoria, insomnia mood swings, personality changes, and severe depression to frank psychotic manifestations. Also, existing emotional instability or psychotic tenden-

tion with corticosteroids in hypoprothrombinemia. Steroids should be used with caution in non-

specific ulcerative colitis, if there is a probability of impending perforation, abscess, or other pyogénic infection, also in diverticulitis, fresh intestinal anastomoses, active or latent peptic ulcer, renal insufficiency, hypertension, osteoporosis, and myasthenia gravis. Signs of peritoneal irritation following gas-

advise that antacids be administered between meals to help prevent peptic ulcer. Steroids may increase or decrease motility and

number of spermatozoa in some patients.

Phenytoin, phenobarbital, ephedrine, and rifampin

steroids resulting in decreased blood levels and lessened physiologic activity, thus requiring adjustment in corticosteroid dosage. These interactions may interfere with dexamethasone suppression tests which should be interpreted with caution during

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

quently 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

comitantly 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 immunosuppressant 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

Fluid and electrolyte disturbances:

Fluid retention Congestive heart failure in susceptible patients Potassium loss Hypokalemic alkalosis

Muscle weakness Steroid myopathy Loss of muscle mass Osteoporosis

Vertebral compression fractures

Tendon rupture Pathologic fracture of long bones

Peptic ulcer with possible subsequent perforation

larly in patients with inflammatory bowel disease Abdominal distention

Ervthema

Increased sweating
May suppress reactions to skin tests
Burning or tingling, especially in the perineal area (after IV injection)

Other cutaneous reactions, such as allergic dermatitis, urticaria, angioneurotic edema

Increased intracranial pressure with papilledema

Neurologic: Convulsions

(pseudotumor cerebri) usually after treatment Headache

Psychic disturbances Endocrine:

Menstrual irregularities

Development of cushingoid state Suppression of growth in pediatric patients Secondary adrenocortical and pituitary unre-

sponsiveness, particularly in times of stress, as in trauma, surgery, or illness Decreased carbohydrate tolerance

Manifestations of latent diabetes mellitus Increased requirements for insulin or oral hypoglycemic agents in diabetics Hirsutism

Ophthalmic:

Posterior subcapsular cataracts Increased intraocular pressure Glaucoma

Retinopathy of prematurity

Negative nitrogen balance due to protein catabolism

Cardiovascular:

Exophthalmos

Myocardial rupture following recent myocardial infarction (see WARNINGS) Hypertrophic cardiomyopathy in low birth weight

Malaise

Anaphylactoid or hypersensitivity reactions

Weight gain Increased appetite Nausea

Hiccups The following additional adverse reactions are related

to parenteral corticosteroid therapy: Hyperpigmentation or hypopigmentation Subcutaneous and cutaneous atrophy

Sterile abscess Charcot-like arthropathy

OVERDOSAGE:

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

The oral LD50 of dexamethasone in female mice was 6.5 g/kg. The intravenous 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 iniection only.

Dexamethasone sodium phosphate injection can be given directly from the vial, or it can be added to Sodium Chloride Injection or Dextrose Injection 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

DOSAGE REQUIREMENTS ARE VARIABLE AND MUST BE INDIVIDUALIZED ON THE BASIS OF THE DISEASE AND THE RESPONSE OF THE

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 until 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.

After 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.

Dermatologic: Impaired wound healing Thin fragile skin

There is an enhanced effect of corticosteroids

Corticosteroids should be used cautiously in

reduction must be gradual.

cies may be aggravated by corticosteroids.
Aspirin should be used within caution in conjunc-

trointestinal perforation in patients receiving large doses of corticosteroids may be minimal or absent. Fat embolism has been reported as a possible complication of hypercortisonism.

When large doses are given, some authorities

may enhance the metabolic clearance of cortico

administration of these drugs.
False negative results in the dexamethasone

The prothrombin time should be checked fre

When corticosteroids are administered con-

be carefully followed

ADVERSE REACTIONS:

Sodium retention

Hypertension Musculoskeletal

Aseptic necrosis of femoral and humeral heads

Gastrointestinal:

and hemorrhage Perforation of the small and large bowel; particu-

Ulcerative esophagitis

Petechiae and ecchymoses

Patients should be observed closely for signs that might require dosage adjustment, 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 the same as 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.

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:

Cavanagh¹

Dosage 3 mg/kg of body weight per 24 hours by constant intravenous infusion after an initial intravenous injection of 20 mg 2 to 6 mg/kg of body weight as a single intravenous injection

Dietzman² Frank³

Schumer⁵

40 mg initially followed by repeat intravenous injection every 4 to 6 hours while shock persists 40 mg initially followed by repeat

Oaks⁶

intravenous injection every 2 to 6 hours while shock persists 1 mg/kg of body weight as a single intravenous injection

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

HOW SUPPLIED:

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

Product NDC

500601

63323-506-01 10 mg per mL

Strength Vial Size packaged in twenty-

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

Product NDC

Strength Vial Size 63323-516-10 100 mg 10 mL vial, per 10 mL packaged 501610

(10 mg This container closure is not made with natural

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 con-

- 1. Cavanagh, D.; Singh, K.B.: Endotoxin shock in pregnancy and abortion, in: "Corticosteroids in the Treatment of Shock", Schumer, W.; Nyhus, L.M., Editors, Urbana, University of Illinois Press, 1970. pp. 86-96.
- Dietzman, R.H.; Ersek, R.A.; Bloch, J.M.; Lilleheir R.C.: High-output, low-resistance gram-negative septic shock in man, Angiology 20: 691-700,
- Frank, E.: Clinical observations in shock and management (in: Shields, T.F., ed.: Symposium on current concepts and management of shock)
 J. Maine Med. Ass. 59: 195-200, Oct. 1968.
- 4. Oaks, W. W.; Cohen, H.E.: Endotoxin shock in the geriatric patient, Geriat. 22: 120-130, Mar. 1967. 5. Schumer, W.; Nyhus, L.M.: Corticosteroid effect
- on biochemical parameters of human oligemic shock, Arch. Surg. 100: 405-408, Apr. 1970.



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