PRESCRIBING INFORMATION

[Pr] DEXAMETHASONE OMEGA UNIDOSE

(Dexamethasone Sodium Phosphate Injection USP)

(10 mg/mL)

Sterile

Corticosteroid

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ACTION AND PHARMACOLOGY

Dexamethasone is a synthetic glucocorticoid used principally as an anti-inflammatory or immunosuppressant drug. After administration of the injection, dexamethasone sodium phosphate is rapidly converted into dexamethasone. Dexamethasone is a synthetic glucocorticoid which has 7 times the anti-inflammatory potency of prednisolone. Like other glucocorticoids, dexamethasone also has antiallergic, antitoxic, antishock, antipyretic and immunosuppressive properties. Dexamethasone has practically no water and salt-retaining properties and is, therefore, particularly suitable for use in patients with cardiac decompensation or hypertension. Because of the long biological half-life (36 to 54 hours), dexamethasone is especially suitable in conditions where a continuous glucocorticoid action is desired.

INDICATIONS AND CLINICAL USE

DEXAMETHASONE OMEGA UNIDOSE may be given by IV or IM injection when oral therapy is not feasible in the following conditions:

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

Acute adrenocortical insufficiency (hydrocortisone or cortisone is the drug of choice; mineralocorticoid supplementation may be necessary, particularly when synthetic glucocorticoids 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.

Rheumatic Disorders: As adjunctive therapy for short-term administration (to support the patient during an acute episode of exacerbation) in post-traumatic osteoarthritis, synovitis of osteoarthritis, rheumatoid arthritis, acute gouty arthritis, psoriatic arthritis, ankylosing spondylitis, juvenile rheumatoid arthritis.

Collagen Diseases: During an exacerbation or as maintenance therapy in selected cases of systemic lupus erythematosus, acute rheumatic carditis.

Dermatologic Diseases: Pemphigus, bullous dermatitis herpetiformis, severe erythema multiforme (Stevens-Johnson syndrome), exfoliative dermatitis, severe psoriasis, severe seborrheic dermatitis.

Allergic States: Initial control of severe allergic conditions: seasonal or perennial allergic rhinitis, bronchial asthma (including *status asthmaticus*), contact dermatitis, atopic dermatitis, serum sickness, drug hypersensitivity reactions, urticarial transfusion reactions, acute noninfectious laryngeal edema (epinephrine is the drug of first choice).

Ophthalmic Diseases: Severe acute and chronic allergic and inflammatory processes involving the eye and its adnexa, such as: herpes zoster ophthalmicus (but **not** herpes simplex), iritis, iridocylitis, chorioretinitis, anterior segment inflammation, diffuse posterior uveitis and choroiditis, optic neuritis, retrobulbar neuritis, sympathetic ophthalmia.

Gastrointestinal Diseases: To support the patient during a critical period of the disease in ulcerative colitis (systemic therapy), regional enteritis (systemic therapy).

Respiratory Diseases: Sarcoidosis, berylliosis, fulminating or disseminated pulmonary tuberculosis when concurrently accompanied by appropriate antituberculous chemotherapy, aspiration pneumonitis.

Hematologic Disorders: Idiopathic thrombocytopenic purpura in adults (IV only; IM administration is contraindicated), acquired (autoimmune) hemolytic anemia.

Neoplastic Disorders: For palliative management of leukemias and lymphomas in adults, acute childhood leukemia, hypercalcemia associated with cancer.

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.

Cerebral Edema: May be used to treat patients with cerebral edema of diverse etiologies in conjunction with adequate neurological evaluation and management.

It may be used also in the preoperative preparation of patients with increased intracranial pressure secondary to brain tumours or for palliation of patients with inoperable or recurrent brain neoplasms.

Use of Dexamethasone Sodium Phosphate Injection in cerebral edema is not a substitute for careful neurological evaluation and definitive management such as neurosurgery or other specific therapy.

Miscellaneous: Tuberculous meningitis with subarachnoid block or impending block when concurrently accompanied by appropriate antituberculous chemotherapy.

Diagnostic testing of adrenocortical hyperfunction.

When given intrasynovially or locally into soft tissue sites, this product may provide relief of symptoms in: traumatic arthritis, ganglia, bursitis, tendonitis, fibrositis, localized myositis, heloma.

CONTRAINDICATIONS

Bacteremia and systemic fungal infections, glaucoma, hypersensitivity to any of the product's components, Cushing's syndrome, gastric and duodenal ulcers, certain viral infections, i.e. varicella, herpes genitalis.

Administration to live virus vaccines (see **WARNINGS AND PRECAUTIONS**).

WARNINGS AND PRECAUTIONS

Warnings

In patients on corticosteroid therapy subjected to unusual stress, increased dosage of rapidly acting corticosteroids before, during and after the stressful situation is indicated.

While on corticosteroid therapy patients should not be vaccinated against smallpox because of potential complications. Conversely, patients with vaccinia should not receive corticosteroid therapy. Other immunization procedures should not be undertaken in patients who are on corticosteroids, especially on high doses, because of possible hazards of neurological complications and a lack of antibody response. However, immunization procedures may be undertaken in patients who are receiving corticosteroids as replacement therapy, e.g. for Addison's disease.

Pregnancy: Since adequate human reproduction studies have not been done with corticosteroids, the use of these drugs in pregnancy, nursing mothers or women of childbearing potential requires that the possible benefits of the drug be weighed against the potential 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.

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

The use of corticosteroids 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.

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, viruses, or tuberculosis.

Corticosteroids should be used cautiously in patients with ocular herpes simplex for fear of corneal ulcerations and perforation.

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. If corticosteroids have to be used in the presence of bacterial infections, institute appropriate vigorous anti-infective therapy. Patients with latent or overt cardiac failure, renal dysfunction, hypertension or migraine, certain parasitic infections, particularly amebiasis, should be monitored.

Average and large doses of corticosteroids can cause elevation of blood pressure, salt and water retention, and increased excretion of potassium. The 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.

Because rare instances of serious anaphylactoid reactions such as glottis edema and bronchospasm 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.

Idiopathic thrombocytopenic purpura in adults should be treated by IV injection.

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.

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 any patient with unexplained diarrhea.

Precautions

Drug induced secondary adrenocortical insufficiency may result from too rapid a 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. If the patient is receiving steroids already, the dosage may have to be increased. Since mineralocorticoid secretion may be impaired, salt and/or a mineral corticoid should be administered concurrently.

When large doses are given, some authorities advise that antacids be administered between meals to help prevent peptic ulcer.

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

Average and large doses of corticosteroids can cause elevation of blood pressure, salt and water retention and increased potassium excretion. 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.

Use corticosteroids 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.

There is an enhanced effect of corticosteroids in patients with hypothyroidism and in those with cirrhosis.

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

Psychological and/or physiological dependency may develop with long-term use of corticosteroids. Discontinuance of therapy may lead to the development of withdrawal symptoms, including anorexia, vague pain, weakness and lethargy.

Corticosteroids may increase or decrease motility and number of spermatozoa in some patients.

Advise patients to inform subsequent physicians of the prior use of corticosteroids.

Corticosteroids may suppress reactions to skin tests and decrease responsiveness to vaccination.

Intra-articular corticosteroid injection may produce systemic as well as local effects. Frequent intra-articular injection may result in damage to joint tissues. Avoid overdistension of the joint capsule and deposition of steroid along the needle track in intra-articular injection, since this may lead to tissue atrophy.

Intra-articular injections should be given under strictly aseptic conditions as glucocorticoids decrease the resistance to infection.

Appropriate examination of any joint fluid present is necessary to exclude a septic process. Avoid local injection of a corticosteroid into an infected site (septic arthritis).

The slower rate of absorption by IM administration must be recognized.

A marked increase in pain accompanied by local swelling, further restriction of joint motion, fever, and malaise are suggestive of septic arthritis. If this complication occurs and the diagnosis of sepsis is confirmed, institute appropriate antimicrobial therapy.

Do not inject corticosteroids into unstable joints.

Avoid injection in the deltoid muscle because of high incidence of tissue atrophy.

Patients should be impressed strongly with the importance of not overusing joints in which symptomatic benefit has been obtained as long as the inflammatory process remains active.

DEXAMETHASONE OMEGA UNIDOSE contains 8 mg/mL of creatinine, which can complicate the evaluation of creatinine clearance.

Pregnancy and Lactation: (see **WARNINGS AND PRECAUTIONS, Warnings**)
Growth and development of infants and children on prolonged corticosteroid therapy should be carefully observed.

DRUG INTERACTIONS

Phenytoin (diphenylhydantoin), phenobarbital, ephedrine and rifampin may enhance the metabolic clearance of corticosteroids, resulting in decreased blood levels and lessened physiologic activity, and thus require corticosteroid dosage adjustment. These interactions may interfere with the dexamethasone suppression tests which should be interpreted with caution during administration of these drugs.

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

The prothrombin time should be checked frequently in patients receiving corticosteroids and coumarin anticoagulants concomitantly 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.

ADVERSE REACTIONS

Fluid and Electrolyte Disturbances: Sodium retention; fluid retention; congestive heart failure in susceptible patients; potassium loss; hypokalemic alkalosis; hypertension; hypotension or shock-like reaction.

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.

Gastrointestinal: Nausea; gastric and peptic ulcer with possible subsequent perforation and hemorrhage; pancreatitis; abdominal distention; ulcerative esophagitis.

Dermatologic: Impaired wound healing; thin fragile skin; petechiae and ecchymoses; facial erythema; striae; increased sweating; burning or tingling, especially in the perineal area (after IV injection); may suppress reactions to skin tests; other cutaneous reactions such as allergic dermatitis, urticaria, angioneurotic edema.

Neurological: 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; increased requirements for insulin or oral hypoglycemic agents in diabetes; hirsutism.

Ophthalmic: Posterior subcapsular cataracts; increased intraocular pressure; glaucoma; exophthalmos.

Metabolic: Negative nitrogen balance due to protein catabolism.

Other: Anaphylactoid or hypersensitivity reactions; thromboembolism; weight gain; increased appetite; malaise; psychological or physiological dependence.

The following additional adverse reactions are related to parenteral corticosteroid therapy: hyperpigmentation or hypopigmentation; subcutaneous and cutaneous atrophy; sterile abscess; postinjection flare (following intra-articular use); Charcot-like arthropathy.

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- **Report online at www.healthcanada.gc.ca/medeffect**
- **Call toll-free to 1-866-234-2345**
- **Complete a Canada Vigilance Reporting Form and:**
  - **Fax toll-free to 1-866-678-6789, or**
  - **Mail to: Canada Vigilance Program**
    Health Canada
    Postal Locator 0701E
    Ottawa, Ontario
    K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at www.healthcanada.gc.ca/medeffect.

NOTE: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.

OVERDOSAGE

Symptoms: Hypertension, edema.

Treatment: Anaphylactic and hypersensitivity reactions may be treated with epinephrine, positive pressure artificial respiration, and aminophylline. Keep the patient warm and quiet. Treatment probably is not indicated for reactions due to chronic overdosage.

For management of a suspected drug overdose, contact your regional Poison Control Centre.

DOSAGE AND ADMINISTRATION

The dose for IM or IV administration varies from 4 to 20 mg depending on the nature and severity of the disease being treated. Give IV doses exceeding 8 mg slowly over a period of several minutes. Repeat the initial dose as necessary until the desired response is

noted. Maintenance doses average 2 to 4 mg daily. After achieving satisfactory control, switch the patient to oral therapy as soon as feasible.

In the treatment of unresponsive shock, high pharmacologic doses of glucocorticoids are recommended currently. Various dosage regiments have been suggested in the literature. These include (1) the use of a single IV injection of 1 to 6 mg/kg; (2) continuous infusion of 3 mg/kg/24 hours after initial IV bolus of 20 mg; and (3) initial IV bolus of 40 mg followed by repeat IV injections every 2 to 6 hours while the state of shock persists.

Administration of high dose corticosteroid therapy should be continued only until the patient's condition has stabilized and usually no longer than 48 to 72 hours.

Whenever possible use IV route for the initial and for as many subsequent doses as are given while the patient is in shock (because of irregular absorption by other routes in such patients). When the blood pressure responds, use the IM route until oral therapy can be substituted.

For the treatment of cerebral edema in adults an initial IV dose of 10 mg is recommended, followed by 4 mg IV or IM every 6 hours until maximum response has been noted. The regimen may then be tapered over several days using either parenteral or oral dexamethasone. Nonoperative cases of cerebral edema may require continuous therapy to remain free of symptoms of increased intracranial pressure. The smallest effective dose may be used in children, preferably orally. This may approximate 0.2 mg/kg/24 hours in divided doses.

There is a tendency in current medical practice to use high doses of parenteral Dexamethasone Sodium Phosphate Injection in the short term therapy of selected cases of life-threatening cerebral edema. The following dosage regimens have been suggested:

Adults: 48 mg as a single dose, then 8 mg every 2 hours on days 1 and 3; 4 mg every 2 hours on days 2 and 4; 4 mg every 4 hours on days 5 through 8. All doses are to be given parenterally.

Alternatively: 100 mg IV followed by 100 mg IM 6 hours later; then, 4 mg IM every 6 hours for 8 days. Thereafter, taper daily by 4 mg.

Children: 10 to 14 years of age: 50% of the adult dose; less than 10 years of age: 25% of the adult dose.

Alternatively: Adults and children: 1.5 mg/kg as a loading dose followed by 1.5 mg/kg/day for the first 5 days. Then taper slowly over the following 5 days and discontinue. All doses are to be given parenterally.

The dose for intrasynovial administration is usually 4 mg for large joints and 0.8 to 1 mg for small joints. For soft tissue and bursal injections a dose of 2 to 4 mg is recommended.

Ganglia require a dose of 1 to 2 mg. A dose of 0.4 to 1 mg is used for injection into tendon sheaths and helomata. Injection into intervertebral joints should not be attempted at any time and hip joint injection cannot be recommended as an office procedure.

Employ intrasynovial and soft tissue injections only when affected areas are limited to 1 or 2 sites. Corticosteroids provide palliation only and other conventional or curative methods of therapy should be employed when indicated.

Dosage Equivalency: Patients currently being treated with other glucocorticoids may be conveniently transferred to this agent using the following dosage equivalents:

Dexamethasone	0.75 mg
Methylprednisolone	4.0 mg
Triamcinolone	4.0 mg
Prednisone	5.0 mg
Prednisolone	5.0 mg
Hydrocortisone	20 mg
Cortisone	25 mg

Special Instructions: This preparation can be given directly from the vial without mixing or dilution. If preferred, it can be added to Sodium Chloride Injection, or Dextrose Injection, or compatible blood for transfusion, without loss of potency, and administered by IV drip.

Do not use product if solution shows haziness, particulate matter or discoloration. Discard unused portion.

When DEXAMETHASONE OMEGA UNIDOSE is added to an infusion solution, the mixture must be used within 24 hours since infusion solutions do not contain preservatives.

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

The usual aseptic techniques governing injections should be observed.

DOSAGE FORMS, COMPOSITION AND PACKAGING

DEXAMETHASONE OMEGA UNIDOSE (Dexamethasone Sodium Phosphate Injection USP), 10 mg/mL:
Each mL contains Dexamethasone Sodium Phosphate equivalent to Dexamethasone Phosphate 10 mg, Creatinine 8 mg, Sodium Citrate 10 mg, Citric Acid and/or Sodium Hydroxide to adjust the pH and Water for Injection. Sulfite-free. Available in single-use vials of 1 mL, boxes of 10.

Store between 15°C and 30°C. Protect from light. Protect from freezing. Do not autoclave.