

Celestone* Tablets

BRAND OF BETAMETHASONE

For oral administration

DESCRIPTION: CELESTONE Tablets contain betamethasone, a synthetic derivative of prednisolone. Each scored CELESTONE Tablet contains 0.5 mg betamethasone. Inactive ingredients: starch, lactose, gelatin and magnesium stearate.

ACTIONS: CELESTONE provides potent anti-inflammatory, antirheumatic and anti-allergic effects in the treatment of corticosteroid-responsive disorders. Glucocorticosteroids, such as betamethasone, cause profound and varied metabolic effects and modify the body's immune response to diverse stimuli. Betamethasone has high glucocorticosteroid activity and slight mineralocorticosteroid activity.

INDICATIONS AND USAGE: CELESTONE Tablets are indicated in the management of various endocrine, musculoskeletal, collagen, dermatologic, allergic, ophthalmic, respiratory, hematologic, neoplastic and other diseases known to be responsive to corticosteroid therapy. Corticosteroid hormone therapy is an adjunct to conventional therapy.

Endocrine Disorders: primary or secondary adrenocortical insufficiency (in conjunction with mineralocorticosteroids, if applicable); congenital adrenal hyperplasia; non-suppurative thyroiditis; and hypercalcaemia associated with cancer.

Musculoskeletal Disorders: as adjunctive therapy for short-term administration (to tide the patient over an acute episode or exacerbation) in psoriatic arthritis; rheumatoid arthritis (selected cases may require low dose maintenance therapy); ankylosing spondylitis; acute and subacute bursitis; acute nonspecific tenosynovitis; gouty arthritis; acute rheumatic fever; and synovitis.

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

Dermatologic Diseases: pemphigus; bullous dermatitis herpetiformis; severe erythema multiforme (Stevens-Johnson syndrome); exfoliative dermatitis; mycosis fungoides; severe psoriasis; allergic eczema (chronic dermatitis); and urticaria.

Allergic States: control of severe or incapacitating allergic conditions intractable to adequate trials of conventional treatment, such as seasonal or perennial allergic rhinitis, nasal polyps, bronchial asthma (including status asthmaticus), contact dermatitis, atopic dermatitis (neurodermatitis), drug and serum reactions.

Ophthalmic Disorders: acute and chronic allergic and inflammatory processes involving the eyes and their adnexae, such as allergic conjunctivitis, keratitis, allergic corneal marginal ulcers, herpes zoster ophthalmicus, iritis and iridocyclitis, chorioretinitis, diffuse posterior uveitis and chorioiditis, optic neuritis, and sympathetic ophthalmia; retinitis centralis; retrobulbar neuritis.

Respiratory Diseases: symptomatic sarcoidosis; Loeffler's syndrome not manageable by other means; bronchiolitis; fulminating or disseminated pulmonary tuberculosis without respiratory compromise; and appropriate antituberculous chemotherapy; pulmonary emphysema; pulmonary fibrosis.

Hematologic Disorders: idiopathic and secondary thrombocytopenia in adults; acquired (autoimmune) hemolytic anemia; erythroblastopenia (RBC anemia); and congenital (erythroid) hypoplastic anemia; transfusion reactions.

Neoplastic Diseases: for palliative management of leukemias and lymphomas in adults and acute leukemia in children.

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; angioedema.

Miscellaneous: tuberculous meningitis with subarachnoid block or impending block when concurrently accompanied by appropriate antituberculous chemotherapy; ulcerative colitis; Bell's palsy.

DOSE AND ADMINISTRATION: DOSING REQUIREMENTS ARE VARIABLE AND MUST BE INDIVIDUALIZED ON THE BASIS OF THE SPECIFIC DISEASE, ITS SEVERITY AND THE RESPONSE TO TREATMENT.

The initial dose of CELESTONE Tablets may vary from 0.25 mg to 8 mg per day depending on the specific disease being treated. In situations of less severity, low doses generally will suffice while in selected patients higher initial doses may be required. The initial dose should be maintained or adjusted until a satisfactory response is observed.

If after a reasonable period of time a satisfactory clinical response does not occur, CELESTONE Tablets should be discontinued and the patient transferred to other appropriate therapy.

The usual initial pediatric oral dosage varies from 175 to 250 mcg (0.017 to 0.25 mg) per kg of body weight per day or 0.5 mg to 75 mg per square meter of body surface per day. Dosages for infants and children should be governed by the same considerations as adults rather than strict adherence to ratios indicated by age or body weight.

When a favorable response is noted, the proper maintenance dose should be determined by decreasing the initial drug dose in small decrements at appropriate time intervals until the lowest dose which will maintain an adequate clinical response is reached.

If a period of spontaneous remission occurs in a chronic condition, treatment should be discontinued.

Exposure of the patient to stressful situations unrelated to the disease under treatment may necessitate an increase in the dosage of CELESTONE Tablets. If the drug is to be discontinued after long-term therapy, dosage should be decreased gradually.

DOING RECOMMENDATIONS FOR VARIOUS DISEASE ENTITIES ARE AS FOLLOWS:

Rheumatoid Arthritis and other Rheumatic Disorders: An initial daily dose of 1 to 2.5 mg is suggested until a good response is obtained, usually within three or four days or for a period of seven days. Although higher doses are generally not required, they may be used to produce the desired initial response. If no response is obtained within seven days, the diagnosis should be reevaluated. When a favorable response is obtained, the dose should be decreased by 0.25 mg every two or three days until proper maintenance dose, usually 0.5 to 1.5 mg daily, is determined. In the treatment of acute attacks of gout, therapy should be continued for only a few days after symptoms subside. Corticosteroid therapy in patients with rheumatoid arthritis does not preclude the need for supportive measures when indicated.

Acute Rheumatic Fever: The initial daily dose is between 6 and 8 mg. When adequate control is achieved, the total daily dose is decreased by 0.25 to 0.5 mg daily until a satisfactory maintenance level is reached. Therapy is continued at this level for four to five days. Once treatment is discontinued, it should be reinstated if reactivation of the disease occurs.

Bursitis: Initially, 1 to 2.5 mg daily in divided doses is recommended. A satisfactory clinical response usually is observed within two or three days, after which the dose is reduced gradually over the next few days and then discontinued. Ordinarily only a relatively short course of treatment is required. With recurrence, a second course of treatment is indicated.

Status Asthmaticus: As much as 3.5 to 4.5 mg daily may be required for one or two days to abate the attack. Then, the dose is reduced by 0.25 mg to 0.5 mg every other day until the maintenance level is reached or therapy discontinued.

Chronic Intractable Asthma: Initially, 3.5 mg daily (more may sometimes be required) is usually given until a satisfactory response is obtained or for an arbitrary period of seven days. Then, the dose is reduced by 0.25 mg to 0.5 mg per day until a satisfactory maintenance level is reached.

Pulmonary Emphysema or Fibrosis: Treatment usually begins with 2 to 3.5 mg daily in divided doses for several days until satisfactory improvement is observed. The daily dose is reduced then by 0.5 mg every two or three days until a satisfactory maintenance level, generally in the range between 1 and 2.5 mg, is reached.

Intractable Hay Fever (Pollinosis): Therapy should be directed toward adequate symptomatic relief during the peak season. On the first day, 1.5 to 2.5 mg should be administered in divided doses and then the total daily dose decreased by 0.5 mg each day until symptoms recur. Then, the dose should be adjusted and maintained at this adjusted level during the peak season (ordinarily not longer than 10 to 14 days) and discontinued thereafter. CELESTONE Tablets are intended to supplement other appropriate anti-allergic therapy only when required.

Disseminated Lupus Erythematosus: Although occasionally higher doses are required to obtain a satisfactory response, 1 to 1.5 mg administered three times daily for several days is generally adequate initial therapy. The dose is then reduced stepwise until an adequate maintenance dose (usually ranging between 1.5 and 3 mg per day) is reached.

Dermatologic Conditions: The initial dose ranges between 2.5 and 4.5 mg per day until satisfactory control is achieved, after which the daily dose is reduced by 0.25 to 0.5 mg every two or three days until a satisfactory maintenance dose is determined.

In self-limited and short-term disorders, therapy usually may be discontinued without recurrence after the process has been controlled for several days. For conditions requiring long treatment periods, dosing schedules vary. Physicians are advised to refer to the current literature for details of treatment programs in these disorders.

Inflammatory Eye Disease: Initial therapy is 2.5 to 4.5 mg daily in divided doses until satisfactory control is obtained or for an arbitrary period of seven days, whichever is shorter. The dose then is reduced by 0.5 mg daily until a maintenance level is reached for those chronic disorders requiring continuous therapy. In ordinarily self-limited or acute conditions, therapy is discontinued after the appropriate interval.

Adrenogenital Syndrome: Dosing must be individualized and adjusted to maintain the urinary 17-ketosteroid level within the normal range and is generally effective at 1 to 1.5 mg daily in divided doses.

ONCE A DAY DOSAGE: As a convenience to the patient and to insure improved compliance with dosing, the total daily maintenance dose can be administered once early in the morning.

ALTERNATE DAY THERAPY:

This corticosteroid is **not** recommended for alternate-day dosing because betamethasone has a long biological half-life (36 to 54 hours) with associated suppressive effects on the HPA axis. If oral long-term use is required for disease therapy, an alternate day dosing regimen with an intermediate acting adrenocorticosteroid (such as prednisone, prednisolone or methylprednisolone) should be considered.

DRUG AND LABORATORY TEST INTERACTIONS: Drug Interactions: Concurrent use of phenobarbital, phenytoin, rifampin or epinephrine may enhance the metabolism of corticosteroids, reducing their therapeutic effects.

Patients receiving both a corticosteroid and an estrogen should be observed for excessive corticosteroid effects.

Concurrent use of corticosteroids with potassium-depleting diuretics may enhance hypokalemia. Concurrent use of corticosteroids with cardiac glycosides may enhance the possibility of arrhythmias or digitalis toxicity associated with hypokalemia. Corticosteroids may enhance the potassium depletion caused by amphotericin B. In all patients taking any of these drug therapy combinations, serum electrolyte determinations, particularly potassium levels, should be monitored closely.

Concurrent use of corticosteroids with coumarin-type anticoagulants may increase or decrease the anticoagulant effects, possibly requiring adjustment in dosage. Combined effects of non-steroidal anti-inflammatory drugs or alcohol with glucocorticosteroids may result in an increased occurrence or increased severity of gastrointestinal ulceration.

Corticosteroids may decrease blood salicylate concentrations. Acetylsalicylic acid should be used cautiously in conjunction with corticosteroids in hypoproteinemia.

Dosage adjustments of an anti-diabetic drug may be necessary when corticosteroids are given to diabetics.

Concomitant glucocorticosteroid therapy may inhibit the response to somatotropin.

Laboratory Test Interactions: Corticosteroids may affect the nitroblue tetrazolium test for bacterial infection and produce false negative results.

ADVERSE REACTIONS: Adverse reactions to CELESTONE Tablets, which have been the same as those reported for other corticosteroids, relate both to dose and to duration of therapy. Usually these reactions can be reversed or minimized by a reduction in dosage; this is generally preferable to withdrawal of drug treatment.

Fluid and electrolyte disturbances: sodium retention, potassium loss, hypokalemic alkalosis; fluid retention; congestive heart failure in susceptible patients; hypertension.

Musculoskeletal: muscle weakness, corticosteroid myopathy, loss of muscle mass, atrophic myositis, osteoporosis, osteopenia, osteonecrosis, osteoporosis; vertebral compression fractures; aseptic necrosis of femoral and humeral heads; pathologic fracture of long bones; tendon rupture.

Gastrointestinal: peptic ulcer with possible subsequent perforation and hemorrhage; pancreatitis, abdominal distention; ulcerative esophagitis, hiatal hernia.

Dermatologic: impaired wound healing, skin atrophy, thin fragile skin; petechiae and ecchymoses; facial erythema; increased sweating; suppressed reactions to skin tests; reactions such as allergic dermatitis, urticaria, angioneurotic edema.

Neurologic: convulsions; increased intracranial pressure with papilledema (pseudotumor cerebri) usually after treatment; vertigo; headache.

Endocrine: menstrual irregularities; development of cushingoid state; suppression of fetal intrauterine or childhood growth; 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 of insulin or oral hypoglycemic agents in diabetics.

Ophthalmic: posterior subcapsular cataracts; increased intraocular pressure, glaucoma; exophthalmos.

Metabolic: negative nitrogen balance due to protein catabolism.

Psychiatric: euphoria, mood swings; severe depression to frank psychotic manifestations; personality changes; hyperirritability; insomnia.

Other: anaphylactoid or hypersensitivity and hypotensive or shocklike reactions.

CONTRAINDICATIONS: CELESTONE Tablets are contraindicated in patients with systemic fungal infections, in those with sensitivity reactions to betamethasone or other corticosteroids, or in those with active peptic ulcer.

PRECAUTIONS: Dosage adjustments may be required with remission or exacerbation of the disease process, the patient's individual response to therapy and exposure of the patient to emotional or physical stress such as serious infection, surgery or injury. Monitoring may be necessary for up to one year following cessation of longterm or high-dose corticosteroid therapy.

Corticosteroids may mask some signs of infection, and new infections may appear during therapy. When corticosteroids are used, decreased resistance and inability to localize infection may occur.

Prolonged corticosteroid use may produce posterior subcapsular cataracts (especially in children), glaucoma with possible damage to the optic nerves, and may enhance secondary ocular infections due to fungi or viruses.

Average and large doses of corticosteroids 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 considered. All corticosteroids increase calcium excretion.

While on corticosteroid therapy patients should not be vaccinated against smallpox. Other immunization procedures should not be undertaken in patients receiving corticosteroids, especially high doses, because of possible hazards of neurological complications and lack of antibody response.

However, immunization procedures may be undertaken in patients who are receiving corticosteroids for replacement therapy (e.g., hypoadrenal disease). Patients who are on immunosuppressant doses of corticosteroids should be warned to avoid exposure to chickenpox or measles and, if exposed, to obtain medical advice. This is of particular importance in children. Corticosteroid therapy in active tuberculosis should be restricted to those cases of fulminating or disseminated tuberculosis in which the corticosteroid is used for management in conjunction with an appropriate antituberculous regimen.

Corticosteroids should be used cautiously in patients with active or tubercular infection; close observation is necessary since reactivation of the disease may occur. During prolonged corticosteroid therapy, patients should receive chemoprophylaxis. If rifampin is used in a chemoprophylactic program, its enhancing effect on metabolic hepatic clearance of corticosteroids should be considered; adjustment in corticosteroid dosage may be required.

The lowest possible dose of corticosteroid should be used to control the condition under treatment; when dosage reduction is possible, it should be gradual.

Drug-induced secondary adrenocortical insufficiency may result from too rapid corticosteroid withdrawal and may be minimized by gradual dosage reduction. Such relative insufficiency may persist for months after discontinuation of therapy; therefore, if stress occurs during that period, corticotherapy should be reinstated. If the patient is receiving corticosteroids already, dosage may have to be increased. Since mineralocorticoid secretion may be impaired, salt and/or a mineralocorticosteroid should be administered concurrently.

Corticosteroid effect is enhanced in patients with hypothyroidism or in those with cirrhosis.

Cautious use of corticosteroids is advised in patients with ocular herpes simplex because of possible corneal perforation.

Psychic derangements may appear with corticosteroid therapy. Existing emotional instability or psychotic tendencies may be aggravated by corticosteroids.

Corticosteroids should be used with caution in: nonspecific ulcerative colitis, if there is a probability of impending perforation, abscess, or other pyogenic infection; acute or chronic hepatitis; fresh intestinal anastomoses; active or latent peptic ulcer; renal insufficiency; hypertension; osteoporosis; and myasthenia gravis.

Since complications of glucocorticosteroid treatment are dependent on dose, size and duration of treatment, a risk/benefit decision must be made with each patient. Since corticosteroid administration can disturb growth rates and inhibit endogenous corticosteroid production in infants and children, the growth and development of these patients receiving prolonged therapy should be followed carefully. Corticosteroids may alter the motility and number of spermatozoa in some patients.

USAGE DURING PREGNANCY AND LACTATION: Since controlled human reproduction studies have not been done with corticosteroids, the use of CELESTONE Tablets during pregnancy, in nursing mothers or women of child-bearing age requires that the possible benefits of the drug be weighed against potential hazards to mother and fetus or infant. Infants born of mothers who have received substantial doses of corticosteroids during pregnancy should be observed carefully for signs of hypoadrenalism.

OVERDOSAGE INFORMATION:

Symptoms: Acute overdosage with glucocorticosteroids, including betamethasone, is not expected to lead to a life-threatening situation. Except at the most extreme dosages, a few days of excessive glucocorticosteroid dosing is unlikely to produce harmful results in the absence of specific contraindications, such as in patients with diabetes mellitus, glaucoma, or active peptic ulcer, or in patients on medications such as digitalis, coumarin-type anti-coagulants or potassium-depleting diuretics.

Treatment: In the event of overdosage, consultation with a poison control center should be considered. Consider standard measures to remove any unabsorbed drug, e.g. gastric lavage. Otherwise complications resulting from the metabolic effects of the corticosteroid or from deleterious effects of the basic or concomitant illnesses or resulting from drug interactions should be handled as appropriate.

HOW SUPPLIED: CELESTONE Tablets, 0.5 mg, packs of 10, 30, 100 and 500 tablets.

STORAGE: Store between 2° and 30° C.

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