CELESTAMINE® Tablets and Syrup

Betamethasone

Dexchlorpeniramine maleate

DESCRIPTION :

Each Celestamine® Tablet contains 0.25 mg betamethasone, a synthetic derivative of prednisolone, and 2 mg dexchlorpheniramine maleate. One teaspoonful (5 ml) of Celestamine® Syrup is equivalent to one Celestamine® Tablet.

ACTIONS :

Celestamine® Tablet and Syrup combine the anti-inflammatory and antiallergic effects of the corticosteroid betamethasone with the antihistaminic activity of dexchlorpheniramine maleate.

INDICATIONS AND USAGE :

Celestamine® Tablets and Syrup are recommended in the treatment of difficult cases of respiratory, dermatologic and ocular allergies, as well as ocular inflammatory disorders, where adjunctive systemic corticosteroid therapy is indicated.

DOSAGE AND ADMINISTRATION:

DOSAGE SHOULD BE INDIVIDUALIZED AND ADJUSTED ACCORDING TO THE SPECIFIC DISEASE BEING TREATED, ITS SEVERITY AND THE RESPONSE OF THE PATIENT.

The recommended initial dosage of Celestamine® Tablets and Syrup adults and children over 12 years is 1 to 2 tablets (or 1 to 2 teaspoonfuls) four times daily, after meals and at bedtime. The dose is not to exceed 8 tablets (or 8

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teaspoonfuls) per day. In younger children dosage should be adjusted according to the severity of the condition, and the response of the patient, rather than by age or body weight.

Children 6 to 12 years – The recommended dosage is ½ teaspoonful three times a day. If an additional daily dose is required, it should be taken preferable at bedtime. The dose is not to exceed 4 teaspoonful a day.

Children 2 to 6 years – The initial dosage of Celestamine® Syrup is ¼ to ½ teaspoonful three times a day with adjustment of dosage according to patient response. Daily dose is not to exceed 2 teaspoonfuls.

DRUG INTERACTIONS:

Betamethasone – Corticosteroids (including betamethasone) are metabolized by CYP3A4.

Concurrent use of Phenobarbital, phenytoin, rifampin or ephedrine 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.

Coadministration with strong CYP3A4 inhibitors, (e.g., ketoconazole, itraconazole, clarithromycin, ritonavir, cobicistat-containing products) may lead to increased exposures of corticosteroids and therefore the potential for increased risk of systemic corticosteroid side-effects. Consider the benefit of coadministration versus the potential risk of systemic corticosteroid effects, in which case patients should be monitored for systemic corticosteroid side-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-corticosteroid anti-inflammatory drugs or alcohol with glucocorticoids 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 conjuction with corticosteroids in hypoprothrombinemia.

Dosage adjustments of an antidiabetic drug may be necessary when corticosteroids are given to diabetics.

Concomitant glucocorticoid therapy may inhibit the response to somatotropin.

Dexchlorpheniramine Maleate – Monamine oxidase (MAO) inhibitors prolong and intensify the effects of antihistamines; severe hypotension may occur. Concomitant use of dexchlorpheniramine maleate with alcohol, tricyclic antidepressants, barbiturates or other central nervous system depressants may

potentiate the sedative effect of dexchlorpheniramine. The action of oral anticoagulants may be inhibited by antihistamines.

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

ADVERSE REACTIONS :

The physician should be alerted to the possibility of any adverse effects associated with the use of corticosteroids and antihistamines, especially of the sedating type.

Betamethasone: Adverse reactions to this component, which have been the same as those reported with other corticosteroids, are related to dose and duration of therapy. The small amount of corticosteroid in the combination makes the incidence of side-effects less likely.

Adverse reactions reported for corticosteroids include:

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; aggravation of myasthenic symptoms in myasthenia gravis; 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.

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; vision blurred.

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 shock-like reactions.

Dexchlorpheniramine Maleate – Adverse reactions to this component have been the same as those reported with other conventional (sedating) antihistamines, and rarely cause toxicity. Slight to moderate drowsiness is the

most frequent side-effect of dexchlorpheniramine maleate. Adverse effects of sedating antihistamines vary in incidence and severity. Among these are cardiovascular, hematologic (pancytopenia, thrombocytopenia, hemolytic anemia), neurologic (confusion, hallucinations, tremor), gastrointestinal, genitourinary (urinary retention), respiratory adverse reactions, and mood changes. The most common effects include sedation, sleepiness, dizziness, disturbed coordination, epigastric distress, rash, dry mouth and thickening of bronchial secretions.

CONTRAINDICATIONS:

Celestamine® products are contraindicated in patients with systemic fungal infections, newborn and premature infants, patients receiving MAO inhibitor therapy and in those who have shown hypersensitivity or idiosyncrasy to any component of these products or drugs of similar chemical structures.

PRECAUTIONS:

Betamethasone – 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 long-term or high-dose corticosteroid therapy.

The lowest possible dose of corticosteroid should be used to control the condition under treatment. A gradual dosage reduction is recommended.

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; diverticulitis; fresh intestinal anastomoses; active or latent peptic ulcer, renal insufficiency, hypertension, osteoporosis, and myasthenia gravis.

Since complications of glucocorticoid treatment are dependent on dosage and duration of treatment, a risk/benefit decision must be made with each patient.

Corticosterids may mask some signs of infection and new infections may appear during use. 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.

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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.

Patients who are in immunosuppressant doses of corticosteroids should be warned to avoid exposure to chicken pox 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 in conjunction with an appropriate antituberculous regimen.

If corticosteroids are indicated in patients with latent tuberculosis, close observation is necessary since reactivation of the disease may occur. During prolonged corticosteroid therapy, patients should receive chemoprophylaxis.

Growth and development of children on prolonged corticosteroid therapy should be followed carefully, since corticosteroid administration can disturb growth rates and inhibit endogenous corticosteroid production in these patients.

Corticosteroid therapy may alter the motility and number of spermatozoa.

Visual disturbance may be reported with systemic and topical (including, intranasal, inhaled and intraocular) corticosteroid use. If a patient presents with symptoms such as blurred vision or other visual disturbances, the patient should be considered for referral to an ophthalmologist for evaluation of possible causes of visual disturbances which may include cataract, glaucoma or rare diseases

such as central serous chorioretinopathy (CSCR) which have been reported after use of systemic and topical corticosteroids.

Pheochromocytoma crisis which can be fatal, has been reported after administration of systemic corticosteroids. Corticosteroids should only be administered to patients with suspected or identified pheochromocytoma after an appropriate risk/benefit evaluation.

Dexchlorpheniramine Maleate – Celestamine® products should be used with caution in patients with narrow angle glaucoma, stenosing peptic ulcer, pyloroduodenal obstruction, prostatic hypertrophy or bladder neck obstruction, cardiovascular disease including hypertension, in those with increase intraocular pressure or hyperthyroidism.

Patients should be warned about engaging in activities requiring mental alertness, such as driving a car or operating appliances, machinery, etc.

Conventional antihistamines may cause dizziness, sedation, and hypotension in patients over 60 years of age.

Safety and effectiveness of Celestamine® products have not been established in children under 2 years of age.

Usage in pregnancy and nursing mothers: The use of Celestamine® products during pregnancy, in nursing mothers or in 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: Celestamine® is a combination product and, therefore

the potential toxicity of each of its components must be considered. Toxicity from a single excessive dose of Celestamine® results primarily from thedexchlorpheniramine component. The estimated lethal dose of the antihistamine dexchlorpheniramine maleate is 2.5 to 5.0 mg/kg.

Overdosage reactions with conventional (sedating) antihistamines may vary from central nervous system depression (sedation, apnea, diminished mental alertness, *cyanosis*, *arrhythmias*, cardiovascular collapse) to stimulation (insomnia, hallucinations, tremors, convulsions) to death. Other signs and symptoms may include dizziness, tinnitus, ataxia, blurred vision and hypotension. In children, stimulation is dominant, as are atropine-like signs and symptoms (dry mouth; fixed, dilated pupils; flushing; fever, and gastrointestinal symptoms). Hallucinations, incoordination, and convulsions of the tonic-clonic type may occur. In adults, a cycle consisting of depression with drowsiness and coma, and an excitement phase leading to convulsions followed by depression may occur.

A single excessive dose of betamethasone is not expected to produce acute symptoms. Except at the most extreme dosages, a few days of excessive glucocorticosteroid dosing is unlikely to produce harmful results except in patients at particular risk due to underlying conditions or on concomitant medications likely to interact adversely with the betamethasone.

Treatment of Acute Overdosage: In the event of overdosage, emergency treatment should be started immediately. Consultation with a poison control center is recommended. Consider standard measures to remove any unabsorbed drug, e.g., activated charcoal, gastric lavage. Dialysis has not been found helpful. There is no specific antidote. Measures to enhance excretion (urinary acidification, hemodialysis) are not recommended.

Treatment of the signs and symptoms of overdosage is symptomatic and supportive.

STORAGE: Celestamine® Syrup : Store below 30° C

Celestamine® Tablets: Store below 25° C

PRESENTATION

Celestamine® Tablets, box of 15 strips @ 10 tablets; Reg. No. : DKL9106604510A1

Celestamine® Syrup, bottle of 60 ml; Reg. No.: DKL9106604137A1

Celestamine® Syrup, bottle of 30 ml; Reg. No.: DKL9106604137A1

HARUS DENGAN RESEP DOKTER

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Pasuruan, Jawa Timur

Distributed by:
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Jakarta, Indonesia

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S-PI-MK4831B-MTL-122021

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