CHAPHA

PREDOXONE
Oral solution

1. QUALITATIVE AND QUANTITATIVE COMPOSITION

- Active ingredients: Each 5 mL (teaspoonful) of prednisolone sodium phosphate oral solution contains 20.16 mg /5ml equivalent to Prednisolone 15mg/5ml

- Excipients: Sorbitol, Propylene glycol, Glycerol, Methyl p-hydroxybenzoate, Strawberry flavor, Disodium edetate, Sucralose, Propyl p-hydroxybenzoate, Purified water.

2. PHARMACEUTICAL FORM

Oral solution, bottle of 100ml

3. CLINICAL PARTICULARS

3.1. Therapeutic indications and Usage for Prednisolone Oral Solution

Prednisolone sodium phosphate oral solution is indicated in the following conditions:

- **Allergic States:** Control of severe or incapacitating allergic conditions intractable to adequate trials of conventional treatment in adult and pediatric populations with: seasonal or perennial allergic rhinitis; asthma; contact dermatitis; atopic dermatitis; serum sickness; drug hypersensitivity reactions; dermatitis herpetiformis; severe erythema multiforme (Stevens-Johnson syndrome); exfoliative erythroderma; mycosis fungoides.

- Edematous States: To induce diuresis or remission of proteinuria in nephrotic syndrome in adults with lupus erythematosus and in adults and pediatric populations, with idiopathic nephrotic syndrome, without uremia.

- Endocrine Disorders: Primary or secondary adrenocortical insufficiency (hydrocortisone or cortisone is the first choice; synthetic analogs may be used in conjunction with mineralocorticoids where applicable; in infancy mineralocorticoid supplementation is of particular importance); congenital adrenal hyperplasia; hypercalcemia associated with cancer; non suppurative thyroiditis.

- Gastrointestinal Diseases: To tide the patient ove a critical period of the disease in: ulcerative colitis; regional enteritis.

- Hematologic Disorders: Idiopathic thrombocytopenic purpura in adults; selected cases of secondary thrombocytopenia; acquired (autoimmune) hemolytic anemia; pure red cell aplasia; Diamond-Blackfan anemia.

- Neoplastic Diseases: For the treatment of acute leukemia and aggressive lymphomas in adults and children.

- Nervous System: Acute exacerbations of multiple sclerosis.

- Ophthalmic Diseases: Uveitis and ocular inflammatory conditions unresponsive to topical corticosteroids; temporal arteritis; sympathetic ophthalmia.

- Respiratory Diseases: Symptomatic sarcoidosis; idiopathic eosinophilic pneumonias; fulminating or disseminated pulmonary tuberculosis when used concurrently with appropriate antituberculous chemotherapy; asthma (as distinct from allergic asthma listed above under "Allergic States"), hypersensitivity pneumonitis, idiopathic pulmonary fibrosis, acute exacerbations of chronic obstructive pulmonary disease (COPD), and Pneumocystis carinii pneumonia (PCP) associated with hypoxemia occurring in an HIV (+) individual who is also under treatment with appropriate anti-PCP antibiotics. Studies support the efficacy of systemic corticosteroids for the treatment of these conditions: allergic bronchopulmonary aspergillosis, idiopathic bronchiolitis obliterans with organizing pneumonia.

- Rheumatic Disorders: As adjunctive therapy for short term administration (to tide the patient over an acute episode or exacerbation) in: psoriatic arthritis; rheumatoid arthritis, including juvenile rheumatoid arthritis (selected cases may require low dose maintenance therapy); ankylosing spondylitis; acute and subacute bursitis; acute nonspecific tenosynovitis; acute gouty arthritis; epicondylitis. For the treatment of systemic lupus erythematosus, dermatomyositis (polymyositis), polymyalgia rheumatica, Sjogren's syndrome, relapsing polychrondritis, and certain cases of vasculitis.

- Miscellaneous: Tuberculous meningitis with subarachnoid block or impending block, tuberculosis with enlarged mediastinal lymph nodes causing respiratory difficulty, and tuberculosis with pleural or pericardial effusion (appropriate antituberculous chemotherapy must be used concurrently when treating any tuberculosis complications); Trichinosis with neurologic or myocardial involvement; acute or chronic solid organ rejection (with or without other agents).

3.2. Posology and method of administration

The initial dose of prednisolone sodium phosphate oral solution, (15 mg prednisolone base/5ml) may vary depending on the specific disease entity being treated:

- In adults: from 1.67 mL to 20 mL (5 to 60 mg prednisolone base) per day.

- In Pediatric Patients: from 0.14 to 2 mg/kg/day or 4 to 60 mg/m2/day given in 3 to 4 divided doses.
In situations of less severity, lower doses will generally suffice while in selected patients higher initial doses may be required. The initial dosage should be maintained or adjusted until a satisfactory response is noted. If after a reasonable period of time, there is a lack of satisfactory clinical response, prednisolone sodium phosphate oral solution should be discontinued and the patient placed on other appropriate therapy.

IT SHOULD BE EMPHASIZED THAT DOSAGE REQUIREMENTS ARE VARIABLE AND MUST BE INDIVIDUALIZED ON THE BASIS OF THE DISEASE UNDER TREATMENT AND THE RESPONSE OF THE PATIENT.

After a favorable response is noted, the proper maintenance dosage should be determined by decreasing the initial drug dosage in small decrements at appropriate time intervals until the lowest dosage, which will maintain an adequate clinical response is reached. It should be kept in mind that constant monitoring is needed in regard to drug dosage. Included in the situations which may make dosage adjustments necessary are changes in clinical status secondary to remissions or exacerbations in the disease process, the patient's individual drug responsiveness, and the effect of patient exposure to stressful situations not directly related to the disease entity under treatment; in this latter situation it may be necessary to increase the dosage of prednisolone sodium phosphate oral solution for a period of time consistent with the patient's condition.
If after long-term therapy the drug is to be stopped, it is recommended that it be withdrawn gradually rather than abruptly.

The standard regimen used to treat nephrotic syndrome in pediatric patients is 60 mg/m2/day given in three divided doses for 4 weeks, followed by 4 weeks of single dose alternate-day therapy at 40 mg/m2 /day.

The National Heart, Lung, and Blood Institute (NHLBI) recommended dosing for systemic prednisone, prednisolone or methylprednisolone in children whose asthma is uncontrolled by inhaled corticosteroids and long-acting bronchodilators is 1-2 mg/kg/day in single or divided doses. It is further recommended that short course, or "burst" therapy, be continued
until a child achieves a peak expiratory flow rate of 80% of his or her personal best or symptoms resolve. This usually requires 3 to 10 days of treatment, although it can take longer. There is no evidence that tapering the dose after improvement will prevent a relapse.

3.3. Contraindications

Systemic fungal infections. Hypersensitivity to the drug or any of its components.

3.4. Special warnings and precautions for use

Cardio-renal

Average and large doses of hydrocortisone or 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.

Endocrine

Corticosteroids can produce reversible hypothalamic -pituitary adrenal (HPA) axis suppression with the potential for glucocorticosteroid insufficiency after withdrawal of treatment.
Metabolic clearance of corticosteroids is decreased in hypothyroid patients and increased in hyperthyroid patients. Changes in thyroid status of the patient may necessitate adjustment in dosage.

Infections (General)

Persons who are on drugs which suppress the immune system are more susceptible to infections than healthy individuals. There may be decreased resistance and inability to localize infection when

corticosteroids are used.
Infection with any pathogen including viral, bacterial, fungal, protozoan or helminthic infection, in any location of the body, may be associated with the use of corticosteroids alone or in combination with other immunosuppressive agents that affect humoral or cellular immunity, or neutrophil function.
These infections may be mild to severe, and, with increasing doses of corticosteroids, the rate of occurrence of infectious complications increases. Corticosteroids may also mask some signs of infection after it has already started.

Infections (Viral)

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.
How the dose, route and duration of corticosteroid administration affect the risk of developing a disseminated infection is not known. The contribution of the underlying disease and/or prior corticosteroid treatment to the risk is also not known. If exposed to chickenpox, prophylaxis with varicella zoster immune globulin (VZIG) may be indicated. If exposed to measles, prophylaxis with immunoglobulin (IG) may be indicated. (See the respective package inserts for complete VZIG and IG prescribing information). If chickenpox develops, treatment with antiviral agents should be considered.

Ophthalmic

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 bacteria, fungi or viruses.
The use of oral corticosteroids is not recommended in the treatment of optic neuritis and may lead to an increase in the risk of new episodes. Corticosteroids should not be used in active ocular herpes simplex.

Special pathogens

Latent disease may be activated or there may be an exacerbation of intercurrent infections due to pathogens, including those caused by Candida, Mycobacterium, Ameba, Toxoplasma, Pneumocystis, Cryptococcus, Nocardia, etc.
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 diarrhea. Similarly, corticosteroids should be used with great care in patients with known or suspected Strongyloides (threadworm) infestation.
In such patients, corticosteroid-induced immunosuppression may lead to Strongyloides hyperinfection and dissemination with widespread larval migration, often accompanied by severe enterocolitis and potentially fatal gram-negative septicemia. Corticosteroids should not be used in cerebral malaria.

Tuberculosis

The use of prednisolone 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.

4. Drug Interactions

Drugs such as barbiturates, phenytoin, ephedrine, and rifampin, which induce hepatic microsomal drug metabolizing enzyme activity may enhance metabolism of prednisolone and require that the dosage of prednisolone sodium phosphate oral solution be increased.
Increased activity of both cyclosporin and corticosteroids may occur when the two are used concurrently. Convulsions have been reported with this concurrent use.
Estrogens may decrease the hepatic metabolism of certain corticosteroids thereby increasing their effect. Ketoconazole has been reported to decrease the metabolism of certain corticosteroids by up to 60% leading to an increased risk of corticosteroid side effects.
Coadministration of corticosteroids and warfarin usually results in inhibition of response to warfarin, although there have been some conflicting reports. Therefore, coagulation indices should be monitored frequently to maintain the desired anticoagulant effect. Concomitant use of aspirin (or other non-steroidal anti-inflammatory agents) and corticosteroids increases the risk of gastrointestinal side effects. Aspirin should be used cautiously in conjunction with corticosteroids in hypoprothrombinemia. The clearance of salicylates may be increased with concurrent use of corticosteroids.
When corticosteroids are administered concomitantly with potassium-depleting agents (i.e., diuretics, amphotericin-B), patients should be observed closely for development of hypokalemia. Patients on digitalis glycosides may be at increased risk of arrhythmias due to hypokalemia.
Concomitant use of anticholinesterase agents and corticosteroids may produce severe weakness in patients with myasthenia gravis. If possible, anticholinesterase agents should be withdrawn at least 24 hours before initiating corticosteroid therapy.
Due to inhibition of antibody response, patients on prolonged corticosteroid therapy may exhibit a diminished response to toxoids and live or inactivated vaccines. Corticosteroids may also potentiate the replication of some organisms contained in live attenuated vaccines. If possible, routine administration of vaccines or toxoids should be deferred until corticosteroid therapy is discontinued.
Because corticosteroids may increase blood glucose concentrations, dosage adjustments of antidiabetic agents may be required. Corticosteroids may suppress reactions to skin tests.

Pregnancy

Teratogenic Effects
Pregnancy Category C

5. ADVERSE REACTIONS

- Cardiovascular: Hypertrophic cardiomyopathy in premature infants.

- Dermatologic: Facial erythema; increased sweating; impaired wound healing; may suppress reactions to skin tests; petechiae and ecchymoses; thin fragile skin; urticaria; edema.

- Endocrine: Decreased carbohydrate tolerance; development of cushingoid state; hirsutism; increased requirements for insulin or oral hypoglycemic agents in diabetic patients; manifestations of latent diabetes mellitus; menstrual irregularities; secondary adrenocortical and pituitary unresponsiveness, particularly in times of stress, as in trauma, surgery or illness; suppression of growth in children.

- Fluid and Electrolyte Disturbances:
Congestive heart failure in susceptible patients; fluid retention; hypertension; hypokalemic alkalosis; potassium loss; sodium retention.

- Gastrointestinal: Abdominal distention; elevation in serum liver enzyme levels (usually reversible upon discontinuation); pancreatitis; peptic ulcer with possible perforation and hemorrhage; ulcerative esophagitis.

- Metabolic: Negative nitrogen balance due to protein catabolism.

- Musculoskeletal: Aseptic necrosis of femoral and humeral heads; loss of muscle mass; muscle weakness; osteoporosis; pathologic fracture of long bones; steroid myopathy; tendon rupture; vertebral compression fractures.

- Neurological: Convulsions; headache; increased intracranial pressure with papilledema (pseudotumor cerebri) usually following discontinuation of treatment; psychic disorders; vertigo.

-Ophthalmic: Exophthalmos; glaucoma; increased intraocular pressure; posterior subcapsular cataracts.

-Other: Increased appetite; malaise; nausea; weight gain.

Storage Conditions

Store at 20° to 25°C.

Keep tightly closed and out of the reach of children.

Manufactured by Chaoul Pharmaceuticals (CHA-PHA) S.A.L - Lebanon

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