PREDNILET

Syrup

Composition
Each 5 ml contains Prednisolone 15 mg

Action
Prednisolone is a synthetic glucocorticoid with the general properties of the corticosteroids. Prednisolone exceeds hydrocortisone in glucocorticoid and anti-inflammatory activity, being about three times more potent on a weight basis than the parent hormone, but is considerably less active than hydrocortisone in mineralocorticoid activity.
Prednisolone, like hydrocortisone, is a potent therapeutic agent influencing the biochemical behavior of most tissues of the body. The mechanism of action of corticosteroids is thought to be by control of protein synthesis. Corticosteroids react with receptor proteins in the cytoplasm of sensitive cells in many tissues to form a steroid-receptor complex.
Corticosteroids are palliative symptomatic treatment of virtue of their anti-inflammatory effects; they are never curative.

Pharmacokinetics
Absorption
Prednisolone is readily absorbed from the gastrointestinal tract with peak plasma concentrations achieved by 1-2 hours after an oral dose. Plasma prednisolone is mainly protein bound (70-90%), with binding to albumin and corticosteroid-binding globulin. The plasma half-life of prednisolone, after a single dose, is between 2.5-3.5 hours.

Distribution
The volume of distribution and clearance of total and unbound prednisolone are concentration dependent, and this has been attributed to saturable protein binding over the therapeutic plasma concentration range.

Metabolism
Prednisolone is extensively metabolised, mainly in the liver, but the metabolic pathways are not clearly defined.

Excretion
Over 90% of the prednisolone dose is excreted in the urine, with 7-30% as free prednisolone, and the remainder being recovered as a variety of metabolites.

Indications
Prednilet is indicated in the following conditions:

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, nonsuppurative thyroiditis, hypocalcaemia associated with cancer.

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 gouty arthritis, acute and subacute bursitis, post-traumatic osteoarthritis, acute nonspecific tenosynovitis, synovitis of osteoarthritis, epicondylitis.

Collagen Diseases
During an exacerbation or as maintenance therapy in selected cases of: Systemic lupus erythematosus, acute rheumatic carditis and systemic dermatomyositis (polymyositis).

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

Allergic States
Control of severe or incapacitating allergic conditions intractable to adequate trials of conventional treatment: Seasonal or perennial allergic rhinitis, contact dermatitis, atopic dermatitis, serum sickness, drug hypersensitivity reactions, bronchial asthma

Ophthalmic Diseases
Severe acute and chronic allergic and inflammatory processes involving the eye and its adnexa such as: Allergic conjunctivitis, chorioretinitis, keratitis, anterior segment inflammation, allergic corneal marginal ulcers, diffuse posterior uveitis and choroiditis, herpes zoster ophthalmicus, optic neuritis, iritis and iridocyclitis, sympathetic ophthalmia.

Respiratory Diseases
Symptomatic sarcoidosis, Loeffler's syndrome not manageable by other means, berylliosis, fulminating or disseminated pulmonary tuberculosis when used concurrently with appropriate chemotherapy, aspiration pneumonitis.

Hematologic Disorders
Idiopathic thrombocytopenic purpura in adults, secondary thrombocytopenia in adults, acquired (autoimmune) hemolytic anemia, erythroblastopenia (RBC anemia), and congenital (erythroid) hypoplastic anemia.

Neoplastic Diseases
For palliative management of: leukemias and lymphomas in adults, acute leukemia of childhood.

Edematous States
To induce a diuresis or remission of proteinuria in the nephrotic syndrome, without uremia, of the idiopathic type or that due to lupus erythematosus.

Gastrointestinal Diseases
To tide the patient over a critical period of the disease in ulcerative colitis, regional enteritis.

Miscellaneous
Tuberculous meningitis with subarachnoid block or impending block used concurrently with appropriate antituberculous chemotherapy, trichinosis with neurologic or myocardial involvement.
In addition to the above indications, prednisolone is indicated for systemic dermatomyositis (polymyositis).

Contraindications

- Prednisolone is contra-indicated in pregnancy and lactation.
- Prednisolone is contra-indicated in patients with systemic fungal infections, sensitivity to prednisolone, or other corticosteroids.
- Contraindicated in patients with peptic ulceration, osteoporosis, psychoses, or severe psychoneuroses.
- Patients with active or doubtfully quiescent tuberculosis should not be given corticosteroids except, very rarely, as adjuncts to treatment with anti-tubercular medication.
- Contra-indicated in the presence of acute viral infections including herpes zoster or herpes simplex ulceration of the eye. Vaccination with live vaccine is contra-indicated with the use of prednisolone.

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.

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.

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 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.

WHILE ON CORTICOSTEROID THERAPY, PATIENTS SHOULD NOT BE VACCINATED AGAINST SMALLPOX. OTHER IMMUNIZATION PROCEDURES SHOULD NOT BE UNDERTAKEN IN PATIENTS WHO ARE ON CORTICOSTEROIDS, ESPECIALLY ON HIGH DOSE, BECAUSE OF POSSIBLE HAZARDS OF NEUROLOGICAL COMPLICATIONS AND A LACK OF ANTIBODY RESPONSE.

Persons who are on drugs that suppress the immune system are more susceptible to infections than healthy individuals are. Chickenpox and measles, for example, can have a more serious or even fatal course in nonimmune 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 unknown. The contribution of the underlying disease and/or prior corticosteroid treatment to the risk is also unknown. If exposed to chickenpox, prophylaxis with varicella zoster immune globulin (VZIG) may be indicated. If exposed to measles, prophylaxis with pooled intravenous immunoglobulin (IVIG) may be indicated. If chickenpox develops, treatment with antiviral agents may be considered.

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.

If corticosteroids are indicated in patients with latent tuberculosis or tuberculin reactivity, dose observation is necessary as reactivation of the disease may occur. During prolonged corticosteroid therapy, these patients should receive chemoprophylaxis.

Pregnancy
Category B
Animal reproduction studies have failed to demonstrate a risk to the fetus and there are no adequate and well-controlled studies in pregnant women.

Adverse Reactions

Fluid and Electrolyte Disturbances
Sodium retention, fluid retention, congestive heart failure in susceptible patients, potassium loss, hypokalemic alkalosis, hypertension

Musculoskeletal
Muscle weakness, steroid myopathy, loss of muscle mass, osteoporosis, vertebral compression fractures, aseptic necrosis of femoral and humeral heads, pathological fracture of long bones.

Gastrointestinal
Peptic ulcer with possible perforation and hemorrhage, pancreatitis, abdominal distention, ulcerative esophagitis.

Dermatologic
Impaired wound healing, thin and fragile skin, petechiae and ecchymoses, facial erythema, increased sweating, may suppress reactions to skin tests.

Metabolic
Negative nitrogen balance due to protein catabolism.

Neurological
Increased intracranial pressure with papilledema (pseudotumor cerebri) usually after treatment, convulsions, vertigo, and headache.

Endocrine
Menstrual irregularities, development of Cushingoid state, secondary adrenocortical and pituitary unresponsiveness (particularly in times of stress, as in trauma, surgery, or illness), suppression of growth in pediatric patients, decreased carbohydrate tolerance, manifestations of latent diabetes mellitus, increased requirements for insulin or oral hypoglycemic agents in diabetics.

Ophthalmic
Posterior subscapular cataracts, increased intraocular pressure, glaucoma, exophthalmos.

Precautions

General
Drug-induced secondary adrenocortical insufficiency 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. Since mineralocorticoid, secretion may be impaired, salt and/or a mineralocorticoid should be administered concurrently.
There is an enhanced effect of corticosteroids on patients with hypothyroidism and in those with cirrhosis. Corticosteroids should be used cautiously in patients with ocular herpes simplex because of possible 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 reduction should be gradual.
Psychic derangements may appear when corticosteroids are used, ranging from euphoria, insomnia, mood swings, personality changes, and severe depression, to frank psychotic manifestations. In addition, existing emotional instability or psychotic tendencies may be aggravated by corticosteroids.

Aspirin should be used cautiously in conjunction with corticosteroids in hypoprothrombinemia.
Steroids should be used with caution in nonspecific ulcerative colitis if there is a probability of impending perforation, abscess or other pyogenic infections, diverticulitis, fresh intestinal anastomoses, active or latent peptic ulcer, renal insufficiency, hypertension, osteoporosis, and myasthenia gravis.
Growth and development of infants and children on prolonged corticosteroid therapy should be carefully observed.

Information for the Patient
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 immediately.

Dosage and Administration

DOSING REQUIREMENTS ARE VARIABLE AND MUST BE INDIVIDUALIZED BASED ON THE SPECIFIC DISEASE, ITS SEVERITY AND THE RESPONSE OF THE PATIENT.

Prednilet has a usual dose range of 5 mg to 60 mg daily in divided doses 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. 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.

The initial dose should be maintained or adjusted until a satisfactory response is observed.
If a period of spontaneous remission occurs in a chronic condition, treatment should be gradually discontinued.

Once a day dosage
The total daily maintenance dose can be administered once early in the morning or as a double dose on alternative days.

The following should be kept in mind when considering alternate-day therapy (ADT):

- Basic principles and indications for corticosteroid therapy should apply. The benefits of ADT should not encourage the indiscriminate use of steroids.
- ADT is a therapeutic technique primarily designed for patients in whom long-term pharmacologic corticoid therapy is anticipated.
- In less severe disease processes in which corticoid therapy is indicated, it may be possible to initiate treatment with ADT. More severe disease states usually will require daily divided high dose therapy for initial control of the disease process. The initial suppressive dose level should be continued until satisfactory clinical response is obtained, usually 4-10 days in the case of many allergic and collagen diseases.
- It is important to keep the period of initial suppressive dose as brief as possible particularly when subsequent use of alternate-day therapy is intended.
- Because of the advantages of ADT, is may be desirable to try patients on this form of therapy who have been on daily corticoids for long periods of time (*e.g.,* patients with rheumatoid arthritis). Since these patients may already have a suppressed HPA axis, establishing them on ADT may be difficult and not always successful; however, it is recommended that regular attempts be made to change them over. It may be helpful to triple or even quadruple the daily maintenance dose and administer this every other day rather than just doubling the daily dose if difficulty is encountered. Once the patient is again controlled, an attempt should be made to reduce this dose to a minimum.
- As indicated above, certain corticosteroids, because of their prolonged suppressive effect on adrenal activity, are not recommended for alternate-day therapy (*e.g.,* dexamethasone and betamethasone).
- The maximal activity of the adrenal cortex is between 2 AM and 8 AM and it is minimal between 4 PM and midnight. Exogenous corticosteroids suppress adrenocortical activity the least when given at the time of maximal activity (am).
- In using ADT it is important, as in all therapeutic situations, to individualize and tailor the therapy to each patient. Complete control of symptoms will not be possible in all patients. An explanation of the benefits of ADT will help the patient to understand and tolerate the possible flare-up in symptoms that may occur in the latter part of the off-steroid day. Other symptomatic therapy may be added or increased at this time if needed.
- In the event of an acute flare-up of the disease process, it may be necessary to return to a full suppressive daily divided corticoid dose for control. Once control is again established alternate-day, therapy may be reinstituted.
- Although many of the undesirable features of corticosteroid therapy can be minimized by ADT, as in any therapeutic situation, the physician must carefully weigh the benefit-risk ratio for each patient in whom corticoid therapy is being considered.

Presentation

Prednilet syrup
Bottle of 60 ml