Millipred™

(Prednisolone Sodium Phosphate Oral Solution, 10 mg Prednisolone Base per 5 mL)

Rx only

DESCRIPTION

Millipred Oral Solution (10 mg Prednisolone per 5 mL) is a dye free, pale to light yellow solution. Each 5 mL (teaspoonful) of Millipred Oral Solution contains 13.4 mg prednisolone sodium phosphate (10 mg prednisolone base) in a palatable, aqueous vehicle.

Millipred Oral Solution (10 mg Prednisolone per 5 mL) also contains anti-bitter mask, corn syrup, edetate di-sodium, glycerin, grape flavor, hydroxyethylcellulose, methylparaben, potassium phosphate dibasic, potassium phosphate monobasic, purified water, and sodium saccharin.

Prednisolone sodium phosphate occurs as white or slightly yellow, friable granules or powder. It is freely soluble in water; soluble in methanol; slightly soluble in alcohol and in chloroform; and very slightly soluble in acetone and in dioxane. The chemical name of prednisolone sodium phosphate is pregna-1,4-diene-3,20- dione,11,17-dihydroxy-21-(phosphonooxy)- disodium salt, (11β)-. The empirical formula is $C_{21}H_{27}Na_2O_8P$; the molecular weight is 484.39.

SAFETY INFORMATION

Millipred™ oral solution is contraindicated in patients with systemic fungal infections. Administration of live or live, attenuated vaccines is contraindicated in patients receiving immunosuppressive doses of corticosteroids. Killed or inactivated vaccines may be administered, however, the response to such vaccines cannot be predicted. Immunization procedures may be undertaken in patients who are receiving corticosteroids as replacement therapy, e.g., for Addison's disease. Adverse reactions of Millipred™ oral solution include the following: 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); increased appetite; malaise; nausea; and weight gain.

DOSAGE AND ADMINISTRATION

The initial dosage of Millipred Oral Solution (10 mg Prednisolone per 5 mL) may vary from 2.5 mL to 30 mL (5 to 60 mg prednisolone base) per day depending on the specific disease entity being treated. 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, Millipred Oral Solution (10 mg Prednisolone per 5 mL) 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 Millipred Oral Solution (10 mg Prednisolone per 5 mL) 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.

In the treatment of acute exacerbations of multiple sclerosis, daily doses of 200 mg of prednisolone for a week followed by 80 mg every other day or 4 to 8 mg dexamethasone every other day for one month have been shown to be effective.

In pediatric patients, the initial dose of Millipred Oral Solution (10 mg Prednisolone per 5 mL) may vary depending on the specific disease entity being treated. The range of initial doses is 0.14 to 2 mg/kg/day in three or four divided doses (4 to 60 mg/m2bsa/day).

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.

For the purpose of comparison, 5 mL of Millipred Oral Solution (13.4 mg Prednisolone sodium phosphate) is equivalent to the following milligram dosage of the various glucocorticoids:

Cortisone	50	Triamcinolone	8
Hydrocortisone,	40	Paramethasone	4
Prednisolone,	10	Betamethasone	1.5
Prednisone	10	Dexamethasone	1.5
Methylprednisolone	8		

These dose relationships apply only to oral or intravenous administration of these compounds. When these substances or their derivatives are injected intramuscularly or into joint spaces, their relative properties may be greatly altered.

HOW SUPPLIED

Millipred™ oral solution is contraindicated in patients with systemicfungal infections. Administration of live or live, attenuatedvaccines is contraindicated in patients receiving immunosuppressivedoses of corticosteroids. Killed or inactivated vaccines may beadministered, however, the response to such vaccines cannot bepredicted. Immunization procedures may be undertaken in patientswho are receiving corticosteroids as replacement therapy, e.g.,for Addison's disease. Adverse reactions of Millipred™ oral solutioninclude the following: cardiovascular (hypertrophic cardiomyopathyin premature infants); dermatologic (facial erythema; increasedsweating; impaired wound healing; may suppress reactions to skintests; petechiae and ecchymoses; thin fragile skin; urticaria; edema);endocrine (decreased carbohydrate tolerance; development ofcushingoid state; hirsutism; increased requirements for insulin or oralhypoglycemic agents in diabetic patients; manifestations of latentdiabetes mellitus; menstrual irregularities; secondary adrenocorticaland pituitary unresponsiveness, particularly in times of stress, as intrauma, surgery or illness; suppression of growth in children); fluidand electrolyte disturbances (congestive heart failure in susceptiblepatients; fluid retention; hypertension; hypokalemic alkalosis; potassiumloss; sodium retention); gastrointestinal (abdominal distention;elevation in serum liver enzyme levels (usually reversible upondiscontinuation); pancreatitis; peptic ulcer with possible perforationand hemorrhage; ulcerative esophagitis); metabolic (negative nitrogenbalance due to protein catabolism); musculoskeletal (aseptic necrosisof 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 withpapilledema (pseudotumor cerebri) usually following discontinuationof treatment; psychic disorders; vertigo); ophthalmic (exophthalmos;glaucoma; increased intraocular pressure; posterior subcapsularcataracts); increased appetite; malaise; nausea; and weight gain.

NDC 16477-510-08 8 fl oz (237 mL) bottle

Dispense in tight, light-resistant glass or PET plastic containers as defined in the USP.

Store at 20°-25°C (68°-77°F). [See USP Controlled Room Temperature].

Keep tightly closed and out of the reach of children.

Manufactured for Laser Pharmaceuticals, LLC, Greenville, SC 29615
by Pharmaceutical Associates, Inc., Greenville, SC 29605

R 03/08

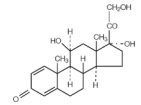
Millipred™ Tablets

(prednisolone tablets USP, 5 mg)

Rx only

DESCRIPTION

Glucocorticoids are adrenocortical steroids, both naturally occurring and synthetic, which are readily absorbed from the gastrointestinal tract. Prednisolone is a white crystalline powder, very slightly soluble in water. It is designated chemically as pregna-1,4-diene-3,20-dione,11,17,21-trihydroxy-,(11ß)-. The structural formula is represented below:



$C_{21}H_{28}O_5$ M.W. 360.45

Millipred Tablets contain the following inactive ingredients: anhydrous lactose, colloidal silicon dioxide, crospovidone, D&C Yellow No. 10, docusate sodium, FD&C Yellow No. 6, magnesium stearate and sodium benzoate.

CLINICAL PHARMACOLOGY

Naturally occurring glucocorticoids (hydrocortisone and cortisone), which also have salt-retaining properties, are used as replacement therapy in adrenocortical deficiency states.
Prednisolone is primarily used for its potent anti-inflammatory effects in disorders of many organ systems.
Glucocorticoids cause profound and varied metabolic effects.
In addition, they modify the body's immune responses to diverse stimuli.

INDICATIONS AND USAGE

1. 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; Hypercalcemia associated with cancer.
2. 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; Post-traumatic osteoarthritis; Synovitis of osteoarthritis; Epicondylitis.
3. Collagen diseases. During an exacerbation or as maintenance therapy in selected cases of: Systemic lupus erythematosus; Acute rheumatic carditis; Systemic dermatomyositis (polymyositis).
4. Dermatologic diseases. Pemphigus; Bullous dermatitis herpetiformis; Severe erythema multiforme (Stevens-Johnson syndrome); Exfoliative dermatitis; Mycosis fungoides; Severe psoriasis; Severe seborrheic dermatitis.
5. Allergic states. Control of severe or incapacitating allergic conditions intractable to adequate trials of conventional treatment: Seasonal or perennial allergic rhinitis; Serum sickness; Bronchial asthma; Contact dermatitis; Atopic dermatitis; Drug hypersensitivity reactions.
6. Ophthalmic diseases. Severe acute and chronic allergic and inflammatory processes involving the eye and its adnexa such as: Allergic conjunctivitis; Keratitis; Allergic corneal marginal ulcers; Herpes zoster ophthalmicus; Iritis and iridocyclitis; Chorioretinitis; Anterior segment inflammation; Diffuse posterior uveitis and choroiditis; Optic neuritis; Sympathetic ophthalmia.
7. Respiratory diseases. Symptomatic sarcoidosis; Loeffler's syndrome not manageable by other means; Berylliosis; Fulminating or disseminated pulmonary tuberculosis when used concurrently with appropriate antituberculous chemotherapy; Aspiration pneumonitis.
8. Hematologic disorders. Idiopathic thrombocytopenic purpura in adults; Secondary thrombocytopenia in adults; Acquired (autoimmune) hemolytic anemia; Erythroblastopenia (RBC anemia); Congenital (erythroid) hypoplastic anemia.
9. Neoplastic diseases. For palliative management of: Leukemias and lymphomas in adults; Acute leukemia of childhood.
10. 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.
11. Gastrointestinal diseases. To tide the patient over a critical period of the disease in: Ulcerative colitis; Regional enteritis.
12. Nervous system. Acute exacerbations of multiple sclerosis.
13. Miscellaneous. Tuberculous meningitis with subarachnoid block or impending block when used concurrently with appropriate antituberculous chemotherapy;
Trichinosis with neurologic or myocardial involvement.

CONTRAINDICATIONS

Systemic fungal infections

WARNINGS

Persons who are on drugs which suppress the immune system are more susceptible to infections than healthy individuals.
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 affects 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 pooled intramuscular immunoglobulin (IG) may be indicated. (See the respective package inserts for complete VZIG and IG prescribing information.) If chickenpox develops, treatment with antiviral agents may be considered.
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.

Usage in 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.
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 synthetic derivatives except when used in large doses. Dietary salt restriction and potassium supplementation may be necessary. All corticosteroids increase calcium excretion.

PRECAUTIONS

Information for Patients
Persons 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 without delay.
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. Also, 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 infection; 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.
Although controlled clinical trials have shown corticosteroids to be effective in speeding the resolution of acute exacerbations of multiple sclerosis they do not show that they affect the ultimate outcome or natural history of the disease. The studies do show that relatively high doses of corticosteroids are necessary to demonstrate a significant effect. (See DOSAGE AND ADMINISTRATION section.)
Since complications of treatment with glucocorticoids are dependent on the size of the dose and the duration of treatment, a risk/benefit decision must be made in each individual case as to dose and duration of treatment and as to whether daily or intermittent therapy should be used.

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; Pathologic fracture of long bones.

Gastrointestinal

Peptic ulcer with possible perforation and hemorrhage; Pancreatitis; Abdominal distention; Ulcerative esophagitis.

Dermatologic

Impaired wound healing; Thin fragile skin; Petechiae and ecchymoses; Facial erythema; Increased sweating; May suppress reactions to skin tests.

Neurological

Convulsions; Increased intracranial pressure with papilledema (pseudotumor cerebri) usually after treatment; Vertigo; Headache.

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 diabetics.

Ophthalmic

Posterior subcapsular cataracts; Increased intraocular pressure; Glaucoma; Exophthalmos.

Metabolic

Negative nitrogen balance due to protein catabolism.

DOSAGE AND ADMINISTRATION

The initial dosage of Millipred Tablets may vary from 5 mg to 60 mg per day depending on the specific disease entity being treated. 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 should be discontinued and the patient transferred to 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 increments 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 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.

Alternate-Day Therapy

Alternate-Day Therapy is a corticosteroid dosing regimen in which twice the usual daily dose of corticoid is administered every other morning. The purpose of this mode of therapy is to provide the patient requiring long-term pharmacologic dose treatment with the beneficial effects of corticoids while minimizing certain undesirable effects, including pituitaryadrenal suppression, the Cushingoid state, corticoid withdrawal symptoms, and growth suppression in children.
The rationale for this treatment schedule is based on two major premises: (a) the anti-inflammatory or therapeutic effect of corticoids persists longer than their physical presence and metabolic effects and (b) administration of the corticosteroid every other morning allows for re-establishment of more nearly normal hypothalamic- pituitary-adrenal (HPA) activity on the off-steroid day.

HOW SUPPLIED

Millipred Tablets (prednisolone tablets USP, 5 mg) are scored, round, peach tablets imprinted DAN DAN 5059 supplied in bottles of 100 (NDC 16477-505-01) and 1000 (NDC 16477-505-10).

Dispense in a well-closed container with child-resistant closure.
Store at 20°-25°C (68°-77°F). [See USP controlled room temperature.]

Manufactured By:
Watson Laboratories, Inc.,
Corona, CA 92880 USA

Distributed By:
LASER PHARMACEUTICALS
Greenville, SC 29615

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