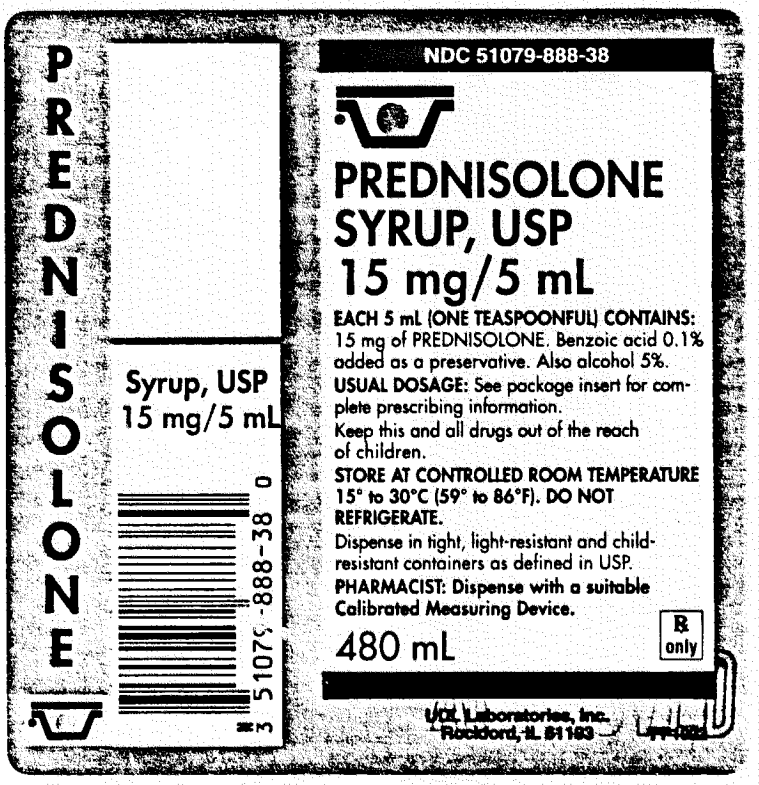
CENTER FOR DRUG EVALUATION AND RESEARCH

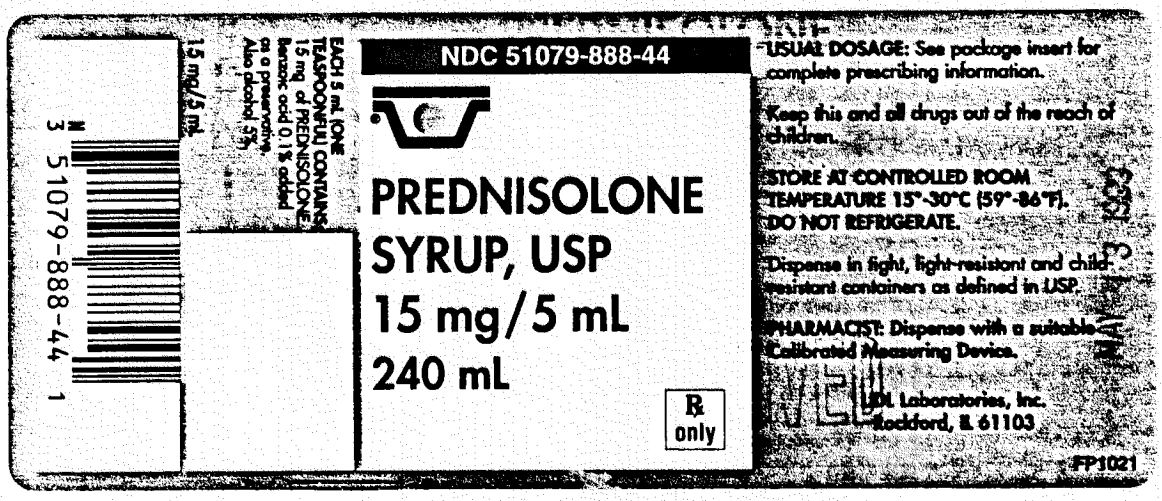
APPLICATION NUMBER: 40-323

PRINTED LABELING



BOTTLE LABEL
480 mL

Margo



BOTTLE LABEL
240 mL

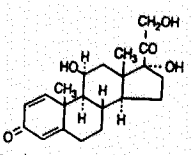
FP1023

PREDNISOLONE SYRUP, USP
15 mg per 5 mL

℞ only

DESCRIPTION: Prednisolone syrup contains prednisolone which is a glucocorticoid. Glucocorticoids are adrenocortical steroids, both naturally occurring and synthetic, which are readily absorbed from the gastrointestinal tract. Prednisolone is a white to practically white, odorless, crystalline powder. It is very slightly soluble in water, soluble in methanol and in dioxane; sparingly soluble in acetone and alcohol, slightly soluble in chloroform.

The chemical name for Prednisolone is 11β,17,21-Trihydroxypregna-1,4-diene-3,20-dione (anhydrous). Its molecular weight is 360.45. The molecular formula is $C_{21}H_{28}O_5$, and the structural formula is:



Each 5 mL (teaspoonful) contains 15 mg of Prednisolone Syrup, USP. In addition, each 5 mL (teaspoonful) contains the following inactive ingredients: Benzoic acid 0.1% added as a preservative. It also contains alcohol 5%, citric acid, edetate disodium, FD&C red #40, flavor wild cherry, glycerin, propylene glycol, purified water, sodium saccharin and sucrose.

CLINICAL PHARMACOLOGY: Naturally occurring glucocorticoids (hydrocortisone and cortisone), which also have salt-retaining properties, are used as replacement therapy in adrenocortical deficiency states. Synthetic analogs such as prednisolone are primarily used for their potent anti-inflammatory effects in disorders of many organ systems.

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Glucocorticoids such as prednisolone cause profound and varied metabolic effects. In addition, they modify the body's immune responses to diverse stimuli.

INDICATIONS AND USAGE: Prednisolone syrup is indicated in the following conditions:

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

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:

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
Bronchial asthma
Contact dermatitis
Atopic dermatitis
Serum sickness
Drug hypersensitivity reactions

6. **Ophthalmic Diseases**
Severe acute and chronic allergic and inflammatory processes involving the eye and its adnexa such as:
Allergic corneal marginal ulcers
Herpes zoster ophthalmicus
Anterior segment inflammation
Diffuse posterior uveitis and choroiditis
Sympathetic ophthalmia
Allergic conjunctivitis
Keratitis
Chorioretinitis
Optic neuritis
Iritis and Iridocyclitis

7. **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

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. **Miscellaneous**
Tuberculous meningitis

...leukemia of childhood

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Ulcerative colitis
Regional enteritis

12. 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 syrup is indicated for systemic dermatomyositis (polymyositis).

CONTRAINDICATIONS. Systemic fungal infections.

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 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...

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The use of prednisolone syrup 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.

Use in pregnancy: Since adequate human reproduction studies have not been done with corticosteroids, the use of these drugs in pregnancies, 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.

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. 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 infections, diverticulitis, fresh intestinal anastomoses, active or latent peptic ulcer, renal insufficiency, hypertension, osteoporosis, and myasthe-

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Growth and development of infants and children on prolonged corticosteroid therapy should be carefully observed.

Information for patients: 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 without delay.

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 (pseudo-tumor cerebri) usually after treatment
- Vertigo
- Headache

Endocrine
- Menstrual irregularities
- Development of Cushingoid state
- Suppression of growth in pediatric patients
- 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

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Ophthalmic
- Posterior subcapsular cataracts
- Increased intraocular pressure
- Glaucoma
- Exophthalmos

Metabolic
- Negative nitrogen balance due to protein catabolism

DOSAGE AND ADMINISTRATION: Dosage of prednisolone syrup should be individualized according to the severity of the disease and the response of the patient. For pediatric patients, the recommended dosage should be governed by the same considerations rather than strict adherence to the ratio indicated by age or body weight.

Hormone therapy is an adjunct to and not a replacement for conventional therapy.

Dosage should be decreased or discontinued gradually when the drug has been administered for more than a few days.

The severity, prognosis, expected duration of the disease, and the reaction of the patient to medication are primary factors in determining dosage.

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

Blood pressure, body weight, routine laboratory studies, including two-hour postprandial blood glucose and serum potassium, and a chest X-ray should be obtained at regular intervals during prolonged therapy. Upper GI X-rays are desirable in patients with known or suspected peptic ulcer disease.

The initial dosage of prednisolone syrup 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 syrup 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**

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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 syrup 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.

HOW SUPPLIED: Prednisolone Syrup, USP is a cherry flavored red liquid containing 15 mg of Prednisolone in each 5 mL (teaspoonful). It is supplied as follows:

NDC 51079-888-44
Bottles of 240 mL

NDC 51079-888-38
Bottles of 480 mL

Pharmacist: Dispense with a suitable calibrated measuring device to assure proper measuring of dose.

Dose/Volume Chart

15 mg prednisolone = 1 teaspoon

10 mg prednisolone = 2/3 teaspoon

7.5 mg prednisolone = 1/2 teaspoon

5 mg prednisolone = 1/3 teaspoon

Dispense in tight, light-resistant and child-resistant containers as defined in USP/NF.

Store at controlled room temperature 15°-30°C (59°-86°F). Do Not Refrigerate.

℞ only

UDL Laboratories, Inc.
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