PACKAGE LEAFLET: Information for the patient

PREDNIZOLON

Solution for injection – 25 mg / 2 ml

(Prednisolone sodium phosphate)

Read all of this leaflet carefully before you start taking this medicine.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects gets serious or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. WHAT PREDNIZOLON IS AND WHAT IT IS USED FOR

Prednisolone sodium phosphate is one of the first synthetic glucocorticoids which is used in medicine. Its pharmacologic effects are similar with those of cortisol (natural endogenous glucocorticoid). Its mineralocorticoid effects are weak, whereas its antiinflammatory and immunosuppressive effects are strong and for this reason it is used clinically.

Following intramuscular or intravenous administration, prednisolone sodium phosphate is rapidly absorbed and also peak plasma concentrations are obtained rapidly. Prednisolone sodium phosphate has a plasma half-life of 2 to 4 hours. It is extensively bound to plasma proteins,

although less than hydrocortisone (cortisol). The volume of distribution, and also the clearance increase with an increase from low to moderate doses; at very high doses, clearance appears to become saturated. Prednisolone sodium phosphate is excreted in the urine as free and conjugated metabolites, together with an appreciable proportion of unchanged prednisolone. Prednisolone is largely inactivated as it crosses the placenta; small amounts are excreted in breast milk.

A. By intravenous or intramuscular injection when oral therapy is not feasible

1. Endocrine disorders – primary, secondary or acute adrenocortical insufficiency etc.
2. Rheumatic disorder – as adjunctive therapy for short-term administration in: post-traumatic osteoarthritis; synovitis; rheumatoid arthritis, including juvenile rheumatoid arthritis; acute and subacute bursitis etc.
3. Collagen diseases – as maintenance therapy in selected cases of: acute rheumatic carditis; systemic dermatomyositis.
4. Dermatologic diseases – exfoliative dermatitis, severe seborrheic dermatitis, psoriasis, mycosis fungoides.
5. Allergic states – bronchial asthma, contact dermatitis, seasonal allergic rhinitis, drug hypersensitivity reactions, urticarial transfusion reactions.
6. Gastrointestinal diseases – ulcerative colitis (systemic therapy); regional enteritis (systemic therapy).
7. Respiratory diseases – pneumonitis; as antituberculous therapy.
8. Hematologic disorders – hemolytic anemia; idiopathic thrombocytopenia in adults (I.V. only; I.M. administration is contraindicated).
9. Neoplastic diseases – leukemias and lymphomas in adults; acute leukemia of childhood.

B. By intra-articular or soft tissue injection: as adjunctive therapy for short-term administration in: post-traumatic osteoarthritis, synovitis; rheumatoid arthritis; acute and subacute bursitis; acute nonspecific tenosynovitis;

C. By intralesional injection: localized hypertrophic, infiltrated, inflammatory lesions of: psoriatic plaques, granuloma annulare, neurodermatitis, necrobiosis lipoidica diabeticorum; in cystic tumor.

2. BEFORE YOU TAKE PREDNIZOLON

Do not take Prednizolon if you:

- are hypersensitive (allergic) to prednisolone sodium phosphate or any of the other ingredients of this product;
- have systemic, mycotic infections;
- are being administered vaccines against viruses;
- have idiopathic thrombocytopenia or cerebral malaria.

Take special care with Prednizolon

Ask your doctor before taking Prednizolon.

- Systemic corticosteroids should be used with great caution in the presence of heart failure, recent myocardial infarction, or hypertension. Also, much care is required if you suffer from diabetes mellitus, epilepsy, glaucoma, hypothyroidism, tuberculosis, hepatic failure, osteoporosis, peptic ulceration, psychoses or severe affective disorders, renal impairment, diverticulitis, recent intestinal anastomoses, history of steroid myopathy, Duchenne's muscular dystrophy, myasthenia gravis, ocular herpes simplex, thromboembolic disorders.
- Rare instances of anaphylactic reactions have occurred in patients receiving parenteral corticosteroid therapy, anyway appropriate precautionary measures should be taken prior to administration, especially when the patient has a history of allergy to any drug.
- Injection with prednisolone sodium phosphate contains sulphites that may cause allergic-type reactions with anaphylactic symptoms where asthmatic patients are more sensible than nonasthmatic patients.
- Secondary adrenocortical insufficiency may result from too rapid withdrawal of corticosteroids and may be minimized by gradual reduction of dosage.
- For patients receiving corticosteroid therapy under special "stress" is particularly necessary the dose adjustment in relation to the value of the stress condition.
- Corticosteroids mask some signs of infection, and new infections may appear during their use. They decrease resistance and make impossible the localization of infection.
- Prolonged use of corticosteroids may produce glaucoma with possible damage to the optic nerves, and may cause secondary ocular infections due to fungi or viruses.
- Contact your doctor if you experience blurred vision or other visual disturbances.

- The risks of chickenpox and probably of severe herpes zoster are increased in non-immune patients receiving therapeutic doses of systemic corticosteroids; therefore, avoid close contact with any of the infections.
- During long - term administration, you should make regular examinations. There may be a need to reduce sodium intake as well as additional intake of potassium and calcium. Back pain may signify osteoporosis.
- Rapid intravenous injection of massive doses of corticosteroids may sometimes cause cardiovascular collapse and injections should therefore be given to you slowly or by infusion.
- The elderly may be at greater risk from adverse effects.
- Talk to your doctor before taking Prednizolon if you have scleroderma (also known as systemic sclerosis, an autoimmune disorder) because daily doses of 15 mg or more may increase the risk of a serious complication called scleroderma renal crisis. Signs of scleroderma renal crisis include increased blood pressure and decreased urine production. The doctor may advise that you have your blood pressure and urine regularly checked.

Effects of misuse as doping agent

The use of Prednizolon may cause positive doping results.

The use of Prednizolon as a doping agent may constitute a health hazard.

Taking other medicines

Other concomitant drug treatment may affect or be affected by Prednizolon.

Please contact your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription. Remember to tell your doctor about the treatment with Prednizolon if you are prescribed another drug during treatment.

It is especially important for your doctor to be aware of the fact that you are being treated with:

- antibacterials: rifampicin reduces the effects of corticosteroids; macrolides are thought to increase exposure to corticosteroids;
- antiepileptics: carbamazepine, primidone increase the clearance of corticosteroids and phenytoin and phenobarbital reduce the efficacy of corticosteroids in asthmatic patients, patients with arthritis, renal transplant patients;
- antimycotics: ketoconazole, itraconazole, voriconazole reduce the total clearance of

prednisolone given intravenously; avoid concomitant use or monitor side effects;

- antivirals: possible effect of corticosteroids on the metabolism of HIV- protease inhibitors;
- some medicines may increase the effects of prednisolone and your doctor may wish to monitor you carefully if you are taking these medicines (including some medicines for HIV: ritonavir, cobicistat);
- sex hormones: effect of corticosteroids in women also receiving oestrogens or oral contraceptives increases, for this reason the dose of the corticosteroid should be reduced;
- thalidomide: should not be given with prednisolone sodium phosphate because of the reduced effect of prednisolone;
- analgesics (aspirin): corticosteroids decrease serum concentrations of salicylates and decrease the effect of anticholinesterases in myasthenia gravis;
- nonsteroidal anti-inflammatory drugs: there may be an increased incidence of gastrointestinal bleeding and ulceration when corticosteroids are given with nonsteroidal anti - inflammatory drugs;
- anticoagulants (warfarin): response to anticoagulants may be altered by corticosteroids and requirements for antidiabetic drugs and antihypertensives increases;
- xanthines (theophylline), amphotericin B, carbenoxolone, beta-2 agonists, potassium-eliminating diuretics, such as thiazides or furosemide: risk of hypokalaemia increases.
- mifepristone: is thought to decrease corticosteroid efficacy.
- somatropin: corticosteroids are thought to reduce the effect of somatropin.

This list of interactions is not exhaustive. There are other drugs that may interact with Prednizolon.

Taking Prednizolon with cigarette smoking

Plasma corticosteroids concentration increases after cigarette smoking.

Pregnancy

Ask your doctor or pharmacist for advice before taking this medicine.

There is a risk of harm to the child. Prednisolone sodium phosphate (Category C) should only be used during pregnancy if your doctor deems it necessary. Always, therefore, consult your doctor

before using this medicine during pregnancy.

Breastfeeding

Prednisolone sodium phosphate passes in human breast milk and should therefore not be used during breastfeeding. Mothers taking pharmacologic doses of corticosteroids should be advised not to breastfeed.

Driving and using machines

This medicinal product has minor influence on the ability to drive and use machines. Side effects, such as vertigo, visual disturbance and fatigue are possible after treatment with corticosteroids. If affected, patients should not drive or operate machinery.

Important information about some of the ingredients of Prednizolon

This medicinal product contains sodium metabisulphite which rarely may cause severe hypersensitivity reactions and bronchospasm.

3. HOW TO TAKE PREDNIZOLON

Always take Prednizolon as your doctor has told you. Contact your doctor or pharmacist if you are not sure. If you feel that the effects of Prednizolon are too strong or too weak, talk to your doctor or pharmacist.

The routes of administration are: intravenous (IV), intramuscular (IM), intra-articular, intralesional and soft tissue injection.

Dosage is variable and must be individualized on the basis of the disease and the response of the patient.

<u>Intravenous and intramuscular</u>

The initial dose varies from 4 to 60 mg a day depending on the disease being treated and dosage interval is every 4 to 8 hours. The initial dose should be maintained or adjusted according to the satisfactory response of the patient, afterwards the dose is reduced gradually. The injection can be given directly from the ampoule or it can be added to the solution of 0.9% sodium chloride or 5% glucose and given by intravenous drip. Solutions for infusion should not contain

preservatives, especially when used in the neonates or infants.

Intra-articular, intralesional and soft tissue injection

Dosage and frequency of injection vary depending on the condition being treated and the site of injection. The usual dose is from 2 to 30 mg. The frequency of injection usually ranges from 1 to 3 times for 5 days then 1-2 times for 3 weeks.

The dose may however need to be increased or reduced. Your doctor will advise you accordingly.

If you take more Prednizolon than you should

If you take more Prednizolon than you should, or if the children take it accidentally, please contact your doctor, the hospital or any medical care site to seek advice on the risk and the appropriate measures.

Overdosage of this corticosteroid is rare and no specific antidote is available and the treatment is symptomatic. Symptoms of overdose can include: cushingoid syndrome symptoms, moonface, obesity, acne, hypertension, osteoporosis, myopathy, sexual dysfunction, diabetes mellitus, hyperlipidemia, peptic ulcer, gastrointestinal bleeding, increased susceptibility to infection, electrolyte and fluid imbalance, psychosis etc.

If you forget to take Prednizolon

If you forget to take one dose (or more than one dose), take the next dose in its usual time.

Do not take a double dose (or more) to make up a forgotten dose (doses).

If you stop taking Prednizolon

Abrupt withdrawal after a prolonged period can lead to acute adrenal insufficiency, hypotension or death. Withdrawal can also be associated with fever, myalgia, arthralgia, rhinitis, conjunctivitis, painful, itchy skin nodules and weight loss.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Prednizolon can cause side effects, although not everybody gets them.
During corticosteroids therapy some adverse reactions may appear:
Metabolic – hypokalemic and metabolic alkalosis, sodium and fluid retention, hypokalemia, hypocalcemia, negative nitrogen balance in protein catabolism.
Musculoskeletal – weakness, myopathy, osteoporosis, muscle mass loss, spontaneous fractures.
Gastrointestinal – peptic ulcer with perforation and hemorrhage, pancreatitis, ulcerative esophagitis, nausea, vomiting, diarrhoea.
Dermatologic – impaired wound healing, thin and fragile skin, erythema, burning especially in the application area (after I.V. injection), other cutaneous reactions, such as allergic dermatitis, urticaria, angioneurotic oedema.
CNS (neurology) – convulsions, vertigo, headache, psychic disturbances, neuritis, psychosis.
Endocrine abnormalities – adrenal suppression, menstrual irregularities, cushingoid state, growth suppression in children, manifestations of latent diabetes mellitus, increased insulin or sulfonylurea requirements in diabetic patients, hyperglycemia, glycosuria.
Ophthalmic – posterior subcapsular cataracts, increased intraocular pressure, glaucoma, exopthalmos, central serous chorioretinopathy.
Cardiovascular – myocardial rupture following recent myocardial infarction, thromboembolism, hypertension, slow heart rate (frequency not known).
Renal and urinary disorders – scleroderma renal crisis in patients already suffering from scleroderma (an autoimmune disorder) (unknown frequency). Signs of scleroderma renal crisis include increased blood pressure and decreased urine production.
Other – anaphylactoid or hypersensitivity reactions, aggravation or masking of infections, fatigue, insomnia, hiccups, Kaposi's sarcoma.
With intra-articular administration – osteonecrosis, skin atrophy, hypersensitivity, facial flushing.
If any of the side effects gets serious, or if you notice side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE PREDNIZOLON

Keep out of the reach and sight of children.

Do not use Prednizolon after the expiry date which is stated on the package.

Do not store above 25°C.

Store in the original package in order to protect from light.

6. FURTHER INFORMATION

What Prednizolon contains

The active substance is prednisolone sodium phosphate.

Each ampoule 2 ml contains prednisolone sodium phosphate equivalent with 25 mg prednisolone phosphate.

The other ingredients are: niacinamide (Vitamin PP), disodium EDTA, sodium metabisulphite, sodium hydroxide, phenol, water for injection.

Contents of the pack

Box with 10 ampoules.

Marketing Authorisation Holder (MAH) and Manufacturer:

PROFARMA sh.a.,

St. “Skënder Vila”,

Tirana, Albania.

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