PACKAGE LEAFLET:
Information for the patient

PRODEXA 4

Solution for injection – 4 mg / 1 ml
(Dexamethasone 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 only. 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 worse or if you notice any side effect not listed in this leaflet, please inform your doctor or pharmacist.

What is in this leaflet

1. WHAT PRODEXA 4 IS AND WHAT IT IS USED FOR

Prodexa 4 is a pharmaceutical product which contains dexamethasone sodium phosphate as active ingredient. Dexamethasone sodium phosphate is a synthetic glucocorticoid. Glucocorticoids affect body's metabolism. They also modify body's immune response. Dexamethasone sodium phosphate is mainly used for its antinflammatory effect in certain organs.
Dexamethasone sodium phosphate is one of the longest – acting glucocorticoids and has almost no mineralocorticoid activity.
It is the glucocorticoid of choice in the treatment of cerebral edema, because it penetrates to central nervous system better than other glucocorticoids.
Dexamethasone sodium phosphate is about 20 – 30 times more potent than hydrocortisone and 5 – 7 times more potent than prednisone.

Prodexa 4 is indicated in:
Allergic conditions
Control of allergic conditions that are severe or resistant to other medications. It is also used in the treatment of asthma, atopic dermatitis, contact dermatitis, drug hypersensitivity reactions and seasonal allergic rhinitis.

Skin diseases
Treatment of pemphigus, bullous dermatitis herpetiformis, exfoliative dermatitis, severe erythema multiforme (Stevens - Johnson syndrome).

Endocrine disorders
Primary or secondary adrenocortical insufficiency (except for acute adrenal gland insufficiency where hydrocortisone or cortisone is more appropriate due to more potent mineralocorticoid effect), congenital hyperplasia of adrenal gland, hypercalcemia in cancer patients, subacute thyroiditis and severe thyroiditis caused by radiation.

Gastrointestinal diseases
Worsening of colon's condition (ulcerative colitis, Crohn's disease), chronic autoimmune hepatitis.

Hematologic disorders
Congenital or acquired aplastic anemia, autoimmune hemolytic anemia caused by antibodies, induction therapy in acute lymphoblastic anemia, myelodysplastic syndrome, angioimmunoblastic lymphoma of malignant cells and plasmocytoma, severe anemia after myelofibrosis with myeloid metaplasia, systemic complication of systemic histiocytosis and acute leukemia in children.

Neoplastic diseases
Palliative treatment of leukemia and lymphomas in adults.

Nervous system
Cerebral edema caused by primary or metastatic brain tumors, craniotomy or primary head traumas, acute relapses of multiple sclerosis.

Renal diseases
Primary and secondary glomerulonephritis, renal function impairment in systemic diseases of connective tissue, to induce diuresis or remission of proteinuria caused by idiopathic nephrotic syndrome or lupus erythematosus.

Respiratory diseases
Berylliosis, fulminating or disseminated pulmonary tuberculosis when used concurrently with antituberculous agents, pulmonary infiltrative eosinophilia, symptomatic sarcoidosis.

Rheumatic disorders
As adjunctive therapy for short – term administration (in an acute episode or exacerbation), in acute gouty arthritis, psoriatic arthritis, acute rheumatic carditis, ankylosing spondylitis, rheumatoid arthritis including juvenile rheumatoid arthritis (in certain cases low-dose maintenance therapy may be required).

Other uses
Diagnostic testing of adrenocortical hyperfunction, trichinosis with neurologic or cardiac symptoms, severe shock.

2. WHAT YOU NEED TO KNOW BEFORE YOU TAKE PRODEXA 4

Do not take Prodexa 4 if:
- you are sensitive (allergic) to dexamethasone sodium phosphate or to any of the other ingredients of this medicine;
- you have systemic bacterial, fungal or viral infections;
- you have Cushing's syndrome;
- you have peptic ulcer;
- you have had an immunization with live virus vaccines;
- you are breastfeeding.

Take special care with Prodexa 4
Talk to your doctor or pharmacist before taking Prodexa 4.
- Before taking Prodexa 4, you should be aware that discontinuation of treatment with this medicine should not be immediate or without medical supervision.
- Prolonged use may cause adrenal insufficiency and makes patients dependent on corticosteroids.
- Prolonged use of corticosteroids increases susceptibility to infections and severity of infections.
- You should immediately inform your doctor when an acute disease appears, including fever or signs of infection.
- Withdrawal of corticosteroids after prolonged therapy may result in symptoms of the corticosteroid withdrawal syndrome including: fever, myalgia, arthralgia and other disturbances.
- Individuals treated with corticosteroids should take particular care to avoid exposure to chicken pox, measles and other viral diseases.
- Average or high doses of Prodexa 4 cause an increase in blood pressure, water and salt retention in the body and increase potassium excretion. A low – salt diet and supplementary potassium should be used in order to correct salt retention and potassium excretion.
- All corticosteroids increase calcium excretion.
- Secondary insufficiency of adrenal glands caused by immediate interruption of corticosteroids may be minimized by gradual reduction of the dose. This type of insufficiency may continue for months after discontinuation of therapy and corticosteroid therapy should be reinitiated or the dose may be increased in every stressful situation experienced by the patient.
- Prodexa 4 should be carefully used in the elderly, ulcerative colitis, abscesses or other pyogenic infections, fresh intestinal anastomoses, active or latent peptic ulcer, renal insufficiency, hypertension, osteoporosis, diabetes mellitus including family history of diabetes mellitus, congestive heart failure, recent myocardial infarction, epilepsy, glaucoma, hypothyroidism and myasthenia gravis.
- Signs of peritoneal irritation following gastrointestinal perforation in patients receiving corticosteroids may be minimal or absent. The breakdown of lipids may occur as a possible complication of hypercorticism.
- In patients with hyperthyroidism and cirrhosis, the effect of corticosteroids is exaggerated.
- Psychotic disorders may occur during corticosteroid therapy such as euphoria, insomnia, mood swings, and changes in personality. Also, emotional instability and psychotic tendencies may appear.
- Growth and development should be monitored in children receiving long-term treatment with corticosteroids.
- Corticosteroids may increase or decrease the motility and number of spermatozoids in some patients.

Other medicines and Prodexa 4
Use of other medicines with Prodexa 4 could influence its effect or the other medicine's effect.
Tell your doctor or pharmacist if you are taking or have recently taken other medicines, including medicines without prescription. Inform your doctor that you are taking Prodexa 4, if any other medicine is prescribed to you during treatment.
It is particularly important that you inform your doctor that you are taking the following medicines:
aldesleukin: avoidance of corticosteroids is advised;
beta - 2 agonists: increased risk of hypokalemia;
aminoglutethimide: may diminish adrenal suppression of corticosteroids;
amphotericin B injection and potassium-depleting agents;
antibiotics: macrolide antibiotics cause a significant decrease in corticosteroid clearance;
antihypertensives: corticosteroids antagonize the hypotensive effect;
anticholinesterases: concomitant use with corticosteroids may produce severe weakness in patients with myasthenia gravis;
oral anticoagulants: concomitant administration with warfarin usually results in inhibition of response to warfarin;
antidiabetics: corticosteroids may increase blood glucose concentrations and dosage adjustments of antidiabetic agents may be required;
antitubercular drugs: serum concentrations of isoniazid may be decreased;
antivirals: avoidance of concomitant administration of dexamethasone and rilpivirine is advised (except when given as a single dose); plasma concentration of corticosteroids possibly increased by ritonavir — increased risk of adrenal suppression;
cholestyramine: cholestyramine may increase the clearance of corticosteroids;
cyclosporine: increased activity of both cyclosporine and corticosteroids may occur;
digitalis glycosides: patients on digitalis glycosides may be at increased risk of arrhythmias due to hypokalemia;
estrogens, including oral contraceptives: estrogens may decrease the hepatic metabolism of certain corticosteroids, thereby increasing their effect;
hepatic enzyme inducers, inhibitors and substrates: drugs which induce cytochrome P450 3A4 (CYP 3A4) enzyme activity (e.g., barbiturates, phenytoin, carbamazepine, rifampicin) may enhance the metabolism of corticosteroids and an increase in the dose of the corticosteroid may be required. Drugs which inhibit CYP 3A4 such as ketoconazole or macrolide antibiotics such as erythromycin, increase plasma concentrations of corticosteroids;
ketoconazole: ketoconazole has been reported to decrease the metabolism of certain corticosteroids by up to 60%, leading to increased risk of side effects;
nonsteroidal anti-inflammatory agents: concomitant use of aspirin (or other nonsteroidal anti-inflammatory agents) and corticosteroids increases the risk of gastrointestinal side effects;
phenytoin: it has been reported that co-administration of phenytoin with dexamethasone may increase or decrease phenytoin levels making seizure control impossible;
thalidomide: co-administration with thalidomide should be employed cautiously, as toxic epidermal necrolysis has been reported;
theophylline: increased risk of hypokalemia;
vaccines: high doses of corticosteroids impair immune response to vaccines.
Dexamethasone suppression test: false-negative results may be obtained in patients being treated with indomethacin.
Hypokalemia caused by glucocorticoids may potentiate the effect of **non-depolarizing muscle relaxants.**
Concomitant use of dexamethasone with **isoprenolol** in asthmatic patients may increase the cardiac toxicity in these patients.

Taking Prodexa 4 with food and drinks
No available data.

Pregnancy
Ask for your doctor or pharmacist's advice before taking this medicine.
Category C.
Avoid use during pregnancy. Your doctor will decide whether therapeutic benefits for the mother and child are greater than the risks imposed by taking this medicine.
Infants born from mothers who have received considerable amounts of corticosteroids during pregnancy should be carefully monitored for signs of hypoadrenalism.

Breastfeeding
Corticosteroids appear in human milk and could suppress growth, interfere with endogenous corticosteroid production, or cause other untoward effects. Mothers who take pharmacologic corticosteroid doses should be warned to discontinue nursing.

Driving and using machines
No available data. You should not drive or use machines if you feel disturbing effects caused by the administration of Prodexa 4.

Important information about some of the ingredients of Prodexa 4
Prodexa 4 contains methylhydroxybenzoate and propylhydroxybenzoate, which may cause allergic reactions (possibly delayed), and exceptionally bronchospasm.
Prodexa 4, also contains sodium metabisulphite, which may rarely cause severe hypersensitivity reactions and bronchospasm.

3. HOW TO TAKE PRODEXA 4

Always take this medicine exactly as your doctor has told you.
Check with your doctor or pharmacist if you are not sure. If you feel that the effect of Prodexa 4 is too strong or too weak, talk to your doctor or pharmacist.
Route of administration: direct intravenous administration with slow injection during one or several minutes or continuous injection or by mixing with intravenous infusion. Also, it may be administered by intramuscular, intra – articular, intrasynovial, intralesional injection or by injection to soft tissues.

By intravenous or intramuscular injection:
General considerations:
(Doses in milligrams are expressed in terms of dexamethasone phosphate)
In general, initial and maintenance doses should be adjusted to each individual case according to the severity of the disease being treated and patient's response. Initial dose ranges from 0.5 – 20 mg (0.125 – 5 ml solution for injection) daily. In mild cases, lower doses may be sufficient. In urgent cases, the usual dose injected intravenously or intramuscularly is 4 – 20 mg, depending on the severity of the condition. After initial improvement, single doses of 2 – 4 mg may be sufficient, and may be repeated if needed. The total dose should not exceed 80 mg, even in severe cases.
In shock (of hemorrhagic, traumatic, surgical or septic origin): usually 2 to 6 mg / kg are intravenously injected as a single dose. This dose may be repeated after 2 to 6 hours if the shock persists. Alternatively, it may be continued with the same dose administered by intravenous perfusion. Use of high doses should continue until the patient's condition is stabilized and usually no longer than 48 – 72 hours.
In cerebral edema associated with primary or metastatic brain tumor, in preoperative preparation of the patients with increased intracranial pressure, 10 mg is administered initially intravenously followed by 4 mg injected intramuscularly every 6 hours until the symptoms of cerebral edema subside. Response is usually noted within 12 - 24 hours; the dose may be reduced after 2 - 4 days and gradually discontinued over a period of 5 - 7 days.
For treatment of recurrent or inoperable brain tumors: maintenance therapy should be determined for every individual patient; 2 mg, 2 – 3 times daily may be sufficient. In order to control cerebral edema, it is necessary to use the lowest possible dose.

If you take more Prodexa 4 than you should
If you take more Prodexa 4 than you should or if the children have taken this medicine by mistake, contact your doctor or the nearest hospital or call the emergency service.
There is no known antidote, but treatment of symptoms should be performed.

If you forget to take Prodexa 4
If you forget to take one or more doses, take the next dose at the next prescribed time. Do not take a double or higher dose to make up for a forgotten dose.
If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

Like all medicines, this medicine can cause side effects, although not everybody gets them.
Most side effects are dose – related and disappear when dose is reduced or when treatment is discontinued. Several side effects may occur at the beginning of treatment and disappear spontaneously with continuation of treatment.
Use of physiologic doses in hormone replacement therapy is not associated with side effects.
Side effects occur with the use of pharmacologic doses and depend on the used dose and treatment duration.
Use of large doses for a short period (a few days) usually is not associated with side effects.
Corticosteroids, particularly when used systemically, suppress the hypothalamic – pituitary - adrenal axis. This suppression depends on the duration of treatment, but may be reduced by taking dexamethasone every 2 days. Suppression of axis may continue up to 12 months after discontinuation of treatment.
During Prodexa 4 use, the following side effects may occur: myopathy, muscle atrophy, muscle weakness, impaired wound healing, atrophy of bone matrix (osteoporosis, fracture of long bones and vertebral bones, avascular necrosis of femur and humerus), increased susceptibility to infections and increased severity of infection. Osteoporosis is mainly related to inhibition of osteoblasts' synthesis, interference in calcium metabolism and is more common in menopausal women and advanced age individuals.
Corticosteroids inhibit bone growth and growth in general.
Corticosteroids may cause: exophthalmia, posterior subcapsular cataracts, retinopathy, increase of intraocular pressure, glaucoma, optic neuritis and other damages of ocular nerve.
Prodexa 4 may cause edema and arterial hypertension. In susceptible patients it may precipitate congestive heart failure. Long – term treatment may cause Cushing's syndrome, menstruation disorders, hyperglycemia and exacerbation of diabetes.
Gastrointestinal side effects include: nausea, vomiting, anorexia, weight loss (more rarely increased appetite, weight gain), diarrhea, constipation, abdominal pain, esophageal ulceration, gastritis, acute pancreatitis.
Corticosteroids do not cause peptic ulcer, but may activate it.
Neuro – psychotic side effects include: headache, insomnia, vertigo, nervousness, peripheral neuropathy, convulsions, changes in EEG, mood swings, depression, anxiety, euphoria, personality changes.
Other effects: skin thinning, thromboembolism.
If any of the side effects gets worse or if you notice any side effect not listed in this leaflet, please inform your doctor or pharmacist.

5. HOW TO STORE PRODEXA 4

Keep this medicine out of the sight and reach of children.
Do not use Prodexa 4 after the expiry date which is stated on the packaging.
Store below 25°C!
Keep in the original packaging protected from light.

6. OTHER INFORMATION

What Prodexa 4 contains
The active substance is Dexamethasone sodium phosphate.
Each ampoule of 1 ml contains 4.4 mg dexamethasone sodium phosphate which is equivalent to 4 mg dexamethasone phosphate.
The excipients are: creatinine, methyl hydroxybenzoate (nipagin), propyl hydroxybenzoate (nipazol), sodium metabisulphite, sodium citrate, sodium hydroxide, water for injection.

Contents of the pack
Carton box with 10 ampoules.

Explanatory of the illustration icons on the packaging:

Ask your doctor or pharmacist.

Content. Warning.

Ampoules.

Marketing Authorisation Holder and Manufacturer:

PROFARMA Sh.a.
Rruga "Myslym Keta"
Tel.: 00355 4 23 89 602
Tirana - ALBANIA

This leaflet was last revised in June 2016.

SPECIFICATION

CROPING AREA 15 x 30 cm

PAY ATENTION, all the layers are visible.
If you have to print this document please check or uncheck the specific layers.