

## PACKAGE LEAFLET: INFORMATION FOR THE USER

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### NIZON

5 mg tablet

PREDNISONONE

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*• This leaflet is a copy of the Summary of Product Characteristics and Patient Information Leaflet for a medicine, which outlines the conditions under which the medicine should be used and information on its known safety • The product information may be updated several times within its shelf life, and there could be differences between the version of information shown here and other information in the public domain or in the package insert • This leaflet may not contain all the information about the medicine or the information may not be the most up to date version for this product • If you have any questions or are not sure about anything, ask your doctor or pharmacist • Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.*

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*• 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 signs of illness are the same as yours • If you get any side effects, talk to your doctor or pharmacist • This includes any possible side effects not listed in this leaflet •*

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#### What is in this leaflet?

1. What Nizon is and what it is used for
2. Before you take Nizon
3. How to take Nizon
4. Possible side effects
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#### *1. WHAT NIZON IS AND WHAT IT IS USED FOR*

Nizon 5 mg tablets contain the active substance prednisone which belongs to a group of medicines called systemic corticosteroids-glucocorticoids.

NIZON 5 mg tablets are used in diseases that required systemic treatment with glucocorticoids. Depending on the type and severity of the disease this includes (Scheme of dosing (SD) of "a" to "d" is described in detail in the section "How to use NIZON 5 mg tablets"):

#### **Replacement therapy**

- Addison's disease
- Insufficiency of the anterior pituitary (medicines of first choice are hydrocortisone and cortisone)
- States of stress after long-term treatment with corticosteroids
- Adrenogenital syndrome (after a period of growth)

#### **Pharmacodynamic therapy**

- Rheumatic diseases:
  - Polymyalgia rheumatica with or without temporal arteritis (SD: c);

- Temporal arteritis (SD: a) in acute vision loss pulse therapy with glucocorticoids administered intravenously, for example prednisone);
- The active phase of collagenosis (systemic inflammatory disease of connective tissue due to the fall of the defense system of the body (SD: A to B): systemic lupus erythematosus, Wegener's granulomatosis, periarteritis nodosa or other forms of vasculitis, polymyositis / dermatomyositis, unless they are directly induced by pathogens, visceral forms of progressive systemic sclerosis, relapsing polychondritis;
- Chronic polyarthritis (SD: b to a) highly active inflammatory phase and special forms, ie forms with rapid destructive flow and / or visceral manifestations;
- Rheumatic fever when required by the course of the disease (SD: a).
  - Heart disease:
    - Pericarditis, endomyocardial fibrosis with eosinophilia (SD: b).
  - Diseases of the Lungs and bronchi:
    - Bronchial asthma (SD: c to a) concomitant use of bronchodilators is recommended;
    - Interstitial lung diseases such as acute alveolitis (SD: b), pulmonary fibrosis (SD: b) long-term treatment of chronic forms of sarcoidosis II and III (wheezing, coughing, and deterioration of lung function) (SD: b) .
    - Diseases of the upper respiratory tract:
      - Severe forms of pollinosis and allergic rhinitis in which the use of inhaled glucocorticoids proved ineffective (SD: c);
      - Acute stenosis of the pharynx and trachea (Quincke edema, obstructive subglottic laryngitis (SD: b to a);
      - Prophylaxis with respiratory distress syndrome of preterm babies (SD: b, twice a day).
    - Skin Diseases:
      - Allergic dermatoses with systemic effect if covered more than 20% of the surface of the skin (severe acute urticaria, Quincke's edema, Lyell's disease, severe rash caused by medicines) (SD: a);
      - Inflammatory dermatoses (SD: c to a): erythroderma, severe dermatitis of large surface area, erythema, lichen ruber exanthematicus, acute febrile neutrophilic dermatosis (Sweet's syndrome), granulomatous disease of the skin;
      - Other skin diseases (SD: b to a) post-herpetic neuralgia, Jarisch-Herxheimer reaction in the treatment of syphilis with penicillin, cavernous hemangioma, Behcet's disease, gangrenous pyoderma;
      - Pemphigus (SD: a), bullous pemphigoid (SD: b).
    - Diseases of the blood and blood-forming organs / therapy of tumors:
      - Autoimmune hemolytic anemia (SD: c to a);
      - Thrombocytopenic purpura (SD: a);
      - Thrombocytopenia (SD: b to a);
      - Acute lymphoblastic leukemia, Hodgkin's disease, non-Hodgkin's lymphoma, chronic lymphocytic leukemia, Waldenstrom's disease, multiple myeloma (SD: b to, application within the multi-agent chemotherapy);
      - Hypercalcaemia in malignant lymphoma, multiple myeloma, leukemia and breast cancer (SD: a to c);
      - Palliative therapy of malignant diseases (SD: c to a). Note: prednisone, to relieve symptoms such as loss of appetite, anorexia and general weakness in advanced malignant diseases, may be used only after you have tried all specific therapeutic options;
      - prophylaxis and treatment of vomiting caused by cytostatics (SD: b to a), the application in the antiemetic schema.
    - Neurological diseases (SD: s):
      - myasthenia gravis (remedy of first choice is azathioprine);
      - chronic Guillain-Barre;
      - Tolosa-Hunt's syndrome;
      - polyneuropathy and monoclonal gamopathy;
      - multiple sclerosis (acute episodes);
      - Jackknife convulsions;
      - prophylaxis of post herpetic neuralgia.

- Infectious diseases:
  - toxic condition with severe infectious diseases (in combination with an antibiotic/chemotherapy), for example, tuberculosis meningitis, and severe forms of tuberculosis of the lung (SD: b).
- Diseases of the eye (SD: b):
  - sclerotic, episcleritis, keratitis, chronic cyclitis, uveitis (only after an unsuccessful local treatment);
  - endocrine ophthalmopathy.
- Diseases of the gastrointestinal tract and the liver:
  - Burns of the esophagus (SD: a);
  - ulcerative colitis (SD: b to c);
  - Crohn's disease (SD: b);
  - chronic aggressive autoimmune hepatitis (SD: b).
- Kidney and efferent parts of the urinary system disease:
  - Glomerulonephritis of minimal change (SD: a);
  - membranous Glomerulonephritis (SD: b), if necessary in combination with cytostatics;
  - extracapillar-prolyferative Glomerulonephritis (a rapidly progressive Glomerulonephritis) (SD: for high-dose therapy, usually in combination with cytostatics, with Goodpasture syndrome and cessation of reduction of treatment, with all other forms of continuation of the long-term treatment (SD: d) ;
  - idiopathic retroperitoneal fibrosis (SD: b).

## 2. BEFORE YOU TAKE NIZON

Inform your doctor if you are taking other medicines, you have a chronic disease, a metabolic disorder, hypersensitivity to other medicine or have had an allergic reaction to some of them.

Do not use Nizon 5 mg tablets

Nizon 5 mg tablets should not be administered if you have hypersensitivity to prednisone and/or any of the other ingredients of the medicine.

In the short-term treatment of life-threatening diseases there are no other contraindications.

The medicine NIZON 5 mg tablets should not be applied for long-term treatment of:

- Acute viral infections (eg. herpes simplex, herpes zoster, poliomyelitis, chickenpox);
- HBsAg positive chronic active hepatitis;
- Approximately 8 weeks before and 2 weeks after prophylactic vaccination;
- lymph node disease after vaccination against tuberculosis.

In the following cases, the medicine NIZON 5 mg tablets can be applied only after you have consulted with your doctor to determine the type of medical monitoring and / or appropriate accompanying treatment:

- peptic ulcer: simultaneous anti-ulcers therapy;
- acute and chronic bacterial infection: specific antibiotic and/or anti-tuberculosis therapy;
- Protection of internal organs: concurrent, antifungal therapy;
- Certain forms of parasitosis (infection by amoeba): concomitant use of antiparazitcs;
- high blood pressure that is difficult to control: combined antihypertensive therapy and regular monitoring;
- severe diabetes: clinical monitoring and adjustment of therapy of diabetes mellitus;
- Osteoporosis: simultaneous intake of calcium, and when necessary vitamin d. for severe osteoporosis applied only temporarily, and for life-threatening diseases for as long as required;
- patients who have previously had a psychiatric illness: neurological monitoring;
- increased eye pressure (glaucoma, narrow and wide angle): careful follow-up and treatment.

Because of the risk of intestinal perforation NIZON 5 mg tablets should only be used for life-threatening diseases with careful monitoring of:

- severe ulcerative colitis with threatening perforations;
- diverticulitis;
- after certain procedures on the intestines (enteroanastomosis) immediately after surgery.

### ***Be careful with NIZON 5 mg tablets***

It is necessary to carefully follow the dosing scheme (dose, time, and duration of administration) that is prescribed by a doctor.

In existing severe infections the medicine can only be used in combination with specific anti-infectives. In patients with tuberculosis, it is only possible with the application of tuberculostatics. The medicine NIZON 5 mg tablets may mask the signs of infection and thus prevent the diagnosis of existing or developing infection.

With long-term treatment, you need regular medical controls (including ophthalmological).

With diabetes you must regularly control the metabolism, as doses of insulin or oral antidiabetic should be increased.

Especially with long-term therapy with comparatively high doses, it is necessary to ensure an adequate supply of potassium (eg. Vegetables, bananas) and reduced intake of sodium (kitchen salt), and monitor the level of serum potassium.

In long-term treatment one can expect a negative effect on bone metabolism whose weight depends on the duration of treatment and dose. Therefore, the protective measures for the prevention of osteoporosis are recommended.

This is especially true with present hereditary factors like hereditary predisposition, older age, and the loss of female sex hormones at menopause, insufficient intake of protein and calcium food, excessive smoking and lack of physical activity. Protective measures consist of calcium intake (i.e. 1 litre of milk per day), vitamin D intake (milk, eggs, fish), and physical activity. It is possible the need for protective measure of prevention in the form of medicines. When osteoporosis is already present, it must be started with an additional treatment.

Patients with severe hypertension or severe heart failure must be under strict supervision because of the risk for deteriorating health.

With a strong physical stress, for example due to illness accompanied by high fever, an accident or surgery, they should immediately inform your doctor or emergency room doctors about treatment with NIZON 5 mg tablets. It is possible to temporarily increase the daily dose of corticoids.

In patients treated with NIZON 5 mg tablets the viral diseases can have serious complications. . Children with decreased resistance (immunosuppression) and persons who did not have chickenpox or measles are particularly vulnerable. If such a person during treatment should come into contact with persons suffering from chicken pox or measles, preventive treatment should begin.

Because of the risk of growth retardation, children can be treated with this medicine only if there are exceptional reasons.

In older people it is necessary to carefully evaluate the ratio of benefit and risk, bearing in mind the side effects such as osteoporosis.

### ***Use of other medicines with NIZON 5 mg tablets***

Keep in mind that this information can apply to medicines that you no longer take, as well as to the medicine that you are planning to take in the future. Inform your doctor if you are taking, or have recently taken any other medicine, including the medicine being purchased without a prescription.

The following medicines may affect the effects of NIZON 5 mg tablets:

- Rifampicin, phenytoin, primidone, barbiturates: reduced effect of oral or injectable corticosteroids;
- Contraceptives containing estrogens: enhanced effect of corticoids.

NIZON 5 mg tablets can affect the effects of the following medicines:

- Non-steroidal anti-inflammatory medicines: increased risk of bleeding in the digestive system;
- Antidiabetic agents: reduced effect on lowering blood sugar;
- Oral anticoagulants (coumarin derivatives): weakened anticoagulant effect;
- Praziquantel: a possible decrease of the concentration of prazikvantela in the blood;

- AGE inhibitors: an increased risk of changes of blood pictures;
- Chloroquine, hidroxychloroquine, Mefloquine: increased risk of myopathy and cardiomyopathy;
- Cardiac glycosides: enhanced glycoside effect as a result of the loss of potassium;
- Diuretics: additional potassium loss;
- Somatropin: in long-lasting treatment effect of somatropin decreases;
- Cyclosporine: increased risk of stroke;
- Protirelin: reduced increase of TSH (a hormone that stimulates the thyroid gland);
- Laxatives: the increase in the loss of potassium;
- Atropine, other anticholinergics: possible further increase in intraocular pressure.

### ***Taking food and drinks with NIZON 5 mg tablets***

There are no data on the impact of food and beverages on efficacy of NIZON 5 mg tablets.

### ***Pregnancy and breastfeeding***

Before you begin to take some medicine, you should consult with your doctor or pharmacist.

#### ***Pregnancy***

Pregnant women can take this medicine only after doctor's advice. Therefore, patients should inform their doctor if they are pregnant or if they get pregnant during the use of the medicine.

Long-term use of corticosteroid in people so far did not show any increase in the risk of fetal malformation.

However, the risk of intrauterine growth disorders caused by long-term glucocorticoid treatment cannot be excluded. In the case of treatment at the end of pregnancy, there is a risk of atrophy of the fetal adrenal.

#### ***Breast feeding***

Prednisone is excreted into breast milk, although until today, there were no adverse effects on the infant, a medicine during breastfeeding may be applied only if there are exceptional reasons. In the treatment with high doses, it is advisable to interrupt breastfeeding and switch to an artificial diet for infants.

### ***Driving and using machines***

According to existing data, NIZON 5 mg tablets do not affect the ability to drive and use machines.

### ***Other warnings***

Nizon 5 mg tablets contain lactose (a type of sugar).

If your doctor told you that you have intolerance to some sugars, before you start using this medicine, consult your doctor.

## ***3. HOW TO TAKE NIZON***

Take the medicine according to the enclosed instructions.

If you think that the effect of the medicine is too strong or too weak, talk to your doctor or pharmacist.

### ***Method of administration***

The medicine is administered orally (by mouth).

You should take tablets with enough fluids during or after a meal; during or after breakfast.

As a rule, the daily dose should be administered once in the morning (between 6 and 8 a.m.) (circadian treatment).

The tablet has a division line which enables dosing in accordance with the individual needs of the patient.

### ***Dosing***

#### ***• Adults***

The dose depends on the type and severity of the disease, as well as on the individual response of the patient. As a rule, relatively high doses are applied initially, which are in severe acute forms significantly higher than that in chronic diseases. Depending on the clinical symptoms and the individual patient's response, the dose

may be reduced to the lowest possible dose (typically 5 to 15 mg of prednisone per day) in different time intervals. Chronic illnesses often require long-term treatment with low doses.

With careful monitoring of the disease, the following scheme can be applied as a guide for dose reduction:

Over 30 mg	reduce by	10 mg	every 2 - 5 days
from 30 to 15 mg/day	reduce by	5 mg	every week
from 15 to 10 mg/day	reduce by	2,5 mg	every 1 - 2 weeks
from 10 to 6 mg/day	reduce by	1 mg	every 2 - 4 weeks
under 6 mg	reduce by	0,5 mg	every 4 - 8 weeks

Please follow the instructions about the dosage. For some diseases, the following dosing schemes are recommended (SD: a-to-d):

### **Replacement therapy**

The dose of prednisone, the recommended treatment for Addison's disease and anterior pituitary insufficiency is 1 to 1 ½ NIZON 5 mg tablet (5 mg-7.5 mg prednisone) a day, divided into two doses (morning and noon). Additional application of Mineral corticoid (fludrocortisones) may be necessary. It is necessary to pay attention to the dose modification in the conditions of stress.

The state of stress after long-term treatment, glucocorticoid therapy: in the beginning, up to 50 mg of prednisone a day. After that, gradually reducing the dose over several days.

Adrenogenital syndrome: after a period of growth, 1 to 1½ NIZON 5 mg tablets (5 mg-7.5 mg prednisone) a day, divided into morning and evening dose.

### **Pharmacodynamic treatment**

In the pharmacodynamic treatment, in certain diseases the following dosing schedule is determined (SD) "and - d".

High doses (dosing scheme a): initial dose is 80 mg to 250 mg of prednisone a day, divided into 4 individual doses. After having reached the desired clinical effect, the dose is gradually reduced: in the beginning dose is reduced in larger increments, and when it reaches about 25 mg per day, in smaller increments.

High doses (dosing scheme b): initial dose is 40 mg to 80 mg of prednisone a day. Daily dose is divided into 2 to 3 individual doses, and after reaching effects the evening dose is reduced, and then, if possible, a midday dose. Further is the reduction of the maintenance dose of a medicine or interruption of treatment.

Low dose (dosing scheme c): starting dose 1½ to 8 NIZON 5 mg tablets (7.5 mg to 40 mg of prednisone) per day. The entire daily dose can be applied at once, in the morning, and in this case comes the reduction of the maintenance dose of a medicine or interruption of treatment.

Very low doses (dosing scheme d): ½ to 1½ NIZON 5 mg tablet or appropriate combinations of 1 mg to 5 mg (up to 7.5 mg) prednisone a day. This dose corresponds to a maintenance dose of long-term treatment.

#### • Children

High doses of treatment: 2 mg-3 mg prednisone/kg/day

High doses of treatment: 1 mg prednisone/kg/day

Maintenance dose: 0.25 mg prednisone/kg/day

In children (growth period) prednisone treatment should be intermittent or alternating.

### **How long do I have to take Nizon 5 mg tablets?**

The duration of treatment depends on the progress of the disease. As soon as you get satisfactory therapeutic results, the dose is reduced to maintenance dose or the treatment is interrupted. Method of treatment is determined by the doctor and his/her instructions should be strictly observed.

### **If you use more Nizon 5 mg tablets than you should**

If you have taken a larger amount of medicine than prescribed, immediately contact your doctor, or pharmacist.

As a rule NIZON is well tolerated without complications with long-term high doses. There is no need for any special countermeasures. If you experience intense or unexpected side effects, contact your doctor.

### ***If you forget to take Nizon 5 mg tablets***

If you forget to take the medicine, do not take a double dose of the medicinal product subsequently, but continue to use the medicinal product according to the regular schedule.

If you forget to apply a dose, use it during the day and the next day continue with usual prescribed dose. If you forget to apply a few doses, the disease can be recovered or worsened. In this case consult your doctor to check and, if necessary, adjust the dosage scheme.

### ***If you stop using Nizon 5 mg tablets***

Use this medicine for as long as your doctor has prescribed.

Without the instructions of your doctor, you may not interrupt the use of the medicinal product. If that's what you need to do, for example, due to side effects or if you feel better, you're bringing into question not only the success of treatment, but the state of your health. You must never cease to apply NIZON 5 mg tablets according to your own decision, especially after long-term treatment. Always consult your doctor.

## **4. POSSIBLE SIDE EFFECTS**

Like all medicines, Nizon 5 mg tablets may cause side effects.

Side effects can occur especially in long-term treatment (more than 2 weeks):

### **Skin**

- stretch marks on the skin, atrophy, a small dotted skin hemorrhages (petechiae), bleeding into the skin (ecchymosis), Steroid Acne, slow healing of wounds, perioral dermatitis, in rare cases, hypersensitivity reactions, ie Exanthema.

### **Musculo-skeletal system**

- muscle atrophy, osteoporosis, aseptic bone necrosis (head of the femur and humerus).

Eyes

- increase in intraocular pressure (glaucoma) and clouding of the lens (cataract).

### **The nervous system**

- depression, irritability, euphoria, increased appetite, pseudo tumor cerebri, the emergence of latent epilepsy.

Gastrointestinal system

- peptic ulcer, gastrointestinal bleeding, pancreatitis.

Electrolytes, metabolism, endocrine system

- the moon face, expressed the thickness of the hull, reduced glucose tolerance, diabetes mellitus, retention of sodium with the appearance of edema, increased excretion of potassium (attention: the possible occurrence of arrhythmia), damage to or loss of cortex atrophy of the adrenal glands, slow growth in children, abnormal secretion of sex hormones (amenorrhea, hirsutism, impotence).

### **Cardiovascular system**

- hypertension, increased risk of thrombosis and arteriosclerosis, Vasculitis (also in the form of abstinence symptoms after long-term treatment).

### **Blood, blood producing organs, immunity**

- moderate Leukocytosis, lymphopenia, eosinopaenia, Polycythemia, damaged the immune processes, masking signs of infection.

Important: fast reduction of the dose after long-term treatment can lead to symptoms typical of abstinence, such as aching muscles and joints.

If you notice any side effects, talk to your doctor or pharmacist.

## 5. HOW TO STORE NIZON

Keep out of reach and sight of children.

Keep at temperature up to 30 ° c.

Shelf life: 2 years.

Nizon 5 mg tablets should not be used after the expiry date stated on the carton.

## 6. FURTHER INFORMATION

### **What Nizon 5 mg tablets contain**

One of NIZON 5 mg tablets contains: Prednisone 5.00 mg

NIZON 5 mg tablets also contain the following auxiliary substances: lactose, sodium starch glycolate, DC, sodium laurylsulfate, silicon dioxide colloidal, and magnesium stearate.

### **How Nizon 5 mg tablets look like and contents of the Pack**

NIZON 5 mg tablets are white, round in shape, with a division line.

NIZON 5 mg tablets are packed in the box with 10 tablets.

### **Regime of dispensing**

The medicine is issued on doctor's prescription

### **Manufacturer**

Bosnalijek d.d.

Jukićeva 53, Sarajevo, Bosnia and Herzegovina

### **Manufacturer of the medicinal product**

Bosnalijek d.d.

Jukićeva 53, Sarajevo, Bosnia and Herzegovina