Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) - 1986

This medicine is dispensed with a doctor's prescription only

Betnesol Tablets

Active ingredient

Each tablet contains 0.5 mg betamethasone as sodium phosphate

Inactive ingredients and allergens: see section 2 under 'Important information about some of this medicine's ingredients', and section 6 'Additional information'.

Read the entire leaflet carefully before you start using this medicine. This leaflet contains concise information about the medicine. If you have any further questions, consult your doctor or pharmacist.

This medicine has been prescribed to treat your illness. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar to yours.

1. What is this medicine intended for?

Betnesol is used to treat diseases that respond to oral glucocorticosteroid therapy. If necessary, this treatment can be given in addition to the basic treatment.

Therapeutic group: a group of medicinal products called corticoids (cortisone derivatives).

Corticoids are used in many inflammatory and allergic processes due to their anti-inflammatory effect. Cortisone is an endogenous substance that is produced in the adrenal cortex and plays an important part in various processes in our body. These also include the regulation of inflammatory processes.

2. Before using this medicine

Do not use this medicine if:

you are sensitive (allergic) to the active ingredient or to any of the other ingredients in this medicine (listed in section 6).

Special warnings about using this medicine

Except for short-term emergency therapy, do not use Betnesol in the following cases:

- internal mycotic diseases that affect the whole body
- gastric or intestinal ulcers
- severe bone loss (osteoporosis)
- severe muscle disorder (except myasthenia gravis)
- viral diseases such as chicken pox, ocular herpes, shingles (herpes zoster)
- polio (poliomyelitis)
- enlargement of lymph nodes (lymphoma) after tuberculosis vaccination (BCG)
- approximately 8 weeks before and 2 weeks after immunisation or 1 year after a tuberculosis vaccination (BCG)
- narrow-angle glaucoma and open-angle glaucoma
- tuberculosis
- amoebic infections
- mental illness only in case of emergency
- Herpes keratitis (a virus-induced keratitis)
- children under 6 years of age.

Before taking this medicine, tell your doctor

if you suffer from any of the following diseases or have received specific vaccinations:

- pheochromocytoma (a tumour of the adrenal gland)
- infectious inflammation of the liver (HBsAg-positive chronic active hepatitis)
- hardening of the lymph nodes after a tuberculosis vaccination
- acute and chronic bacterial infections
- with a medical history of tuberculosis, therapy is given only with simultaneous medication for tuberculosis
- severe adjustable high blood pressure
- severe diabetes mellitus
- injuries and ulcers of the cornea
- epilepsy
- risk of vascular occlusion
- heart insufficiency
- renal insufficiency.

In the cases mentioned above, your doctor will only prescribe Betnesol after a careful benefit-risk analysis.
If necessary, they will also arrange treatment of these diseases.

- To avoid the risk of damage to the intestinal wall or of intestinal perforation, inform your doctor of any intestinal diseases or intestinal operations; namely:
  - severe colitis (ulcerative colitis) with imminent perforation, with purulent inflammation or abscess
  - inflamed protuberances of the intestinal wall (diverticulitis)
  - after certain intestinal operations (enteroanastomosis) immediately after operation.

Additional warnings

- Symptoms of peritoneal irritation after gastrointestinal perforation may be absent in patients who receive high doses of glucocorticoids.
- Betnesol can affect carbohydrate metabolism and induce temporary diabetes or worsen existing diabetes. Your doctor will therefore adapt or initiate diabetes treatment when needed.
- In existing muscle disorders (myasthenia gravis), the symptoms may worsen at the beginning of treatment, therefore Betnesol dose adjustment should be carried out in hospital. If irritation in the face and throat are particularly severe and respiration is impaired, treatment with Betnesol should be started slowly.
- Betnesol to treat severe infections may be used only in combination with an anti-infective therapy.
- Betnesol may mask the signs of an infection and so make it difficult to diagnose an existing or developing infection.
- Prolonged use of even small amounts of Betnesol can lead to an increased risk of infection even with such pathogens that rarely cause infections.
- Immunisation with vaccines containing inactivated pathogens is generally possible. However, it should be noted that success of the vaccination could be impaired at higher dosages of Betnesol.
- Viral diseases (chickenpox, measles, shingles) can have particularly severe consequences in patients who are treated with Betnesol. Immunosuppressed children, as well as persons who never had measles or chickenpox are particularly at risk. If these people come into contact with persons suffering from measles or chickenpox during treatment with Betnesol, they should immediately contact their doctor who will initiate a preventative treatment if necessary.
- Due to the risk of growth inhibition, Betnesol should be only used in children if there are compelling reasons and height growth should be monitored regularly.
- If physical stress occurs during treatment with Betnesol, such as feverish condition, accidents, childbirth or operations, the doctor has to be informed immediately or an emergency room doctor must be consulted about continued treatment. Temporary increase in the daily dose of Betnesol may be required.
- Depending on duration of treatment and dosage, a negative effect on calcium metabolism is expected, so treatment for osteoporosis prevention is recommended. Preventive treatment

consists of adequate calcium and vitamin D intake and physical activity. For existing osteoporosis, additional medical treatment should be considered.
- Relatively low doses may be sufficient to treat patients with thyroid hypofunction or liver cirrhosis and a general dose reduction may be necessary.
- Betnesol is basically intended for short-term use. If used for longer periods of time, the warnings that are described for glucocorticoid-containing medicines for long-term use, must also be checked.
- At the end of long-term treatment with Betnesol your doctor will slowly reduce the dosage. In this way, withdrawal symptoms, the resurgence of the treated disease, and possible insufficiency of the adrenal cortex (especially under stress, such as infections, accidents, increased physical stress and fever) can be avoided. In addition, too rapid reduction of the dose can cause muscle and joint pain.
- If you change your doctor (e.g. for operations, travel, vaccinations) you need to inform them about your treatment with Betnesol.
- Administration of Betnesol tablets can lead to a positive doping test result.

Children and adolescents

Do not use this medicine in children under 6 years of age, except for short-term emergency therapy.

Tests and follow-up

- Before starting treatment with Betnesol a careful medical examination must be performed; it is specifically necessary to rule out gastrointestinal ulcers. Antacids, in combination with careful monitoring (including x-ray/gastroscopy), are indicated for preventing gastrointestinal ulcers in patients who are prone to develop ulcers.
- If you have high blood pressure, your doctor will monitor you carefully because it might get worse.
- During long-term treatment with relatively high doses of Betnesol, be careful to consume sufficient potassium (for example vegetables, bananas). Your doctor must check your blood potassium level. This is particularly important if you are taking medicines that are known to prolong the QT interval (certain changes in ECG).
- If you are taking Betnesol in the long term, your doctor can arrange regular eye examinations (once every 3 months) and x-rays of your spine.
- During long-term treatment with Betnesol, depending on your dose and initial condition, you must be monitored at suitable intervals to identify possible side effects regardless of tests related to your disease.

Other medicines and Betnesol

If you are taking or have recently taken other medicines, including nonprescription medications and dietary supplements, tell your doctor or pharmacist. Particularly if you are taking:

Medicine / group of medicines	**Possible side effects of combined use with Betnesol**
Heart glycosides (medicines for cardiac insufficiency)	Increased glycoside action due to potassium deficiency.
Medicines causing QT prolongation (changes in the ECG)	Blood potassium level has to be corrected depending on the condition and clinical condition has to be monitored.
Antidiabetics	There may be a decrease in the effectiveness of insulin and oral medications in lowering the glucose level.
Cumarin derivates (medicines for blood thinning)	Blood thinning effect is decreased.
Anticoagulants (blood thinning medicines)	Possible increased or decreased effect on blood coagulation.
Barbiturates (sleeping medicines), hydantoin (medicines for treatment of epilepsy), rifampicin (medicine for tuberculosis)	Action of Betnesol is decreased.
Non-steroidal anti-inflammatory drugs (NSAIDs),	Increased frequency of stomach ulcers and

such as many painkillers and anti-rheumatics	increased risk of bleeding in the gastrointestinal tract due to combination with NSAIDs and anti-rheumatic medicines.
Oestrogens (sex hormones, e.g. component of the “Pill’)	Action of Betnesol is increased.
Vaccines	Live vaccines may be more toxic due to the immunosuppressant effect of Betnesol. Disseminated viral infections can occur. The effect of all vaccines could be reduced as a result of concomitant use of Betnesol (for 8 weeks before and up to 2 weeks after active immunisation). The formation of protective antibodies may fail completely.
Aluminium salts-complex-forming acids (e.g. aspirin)	If Betnesol is taken in combination with complex-forming acids, such as citric acid in drinks or medicines for the treatment of acidosis or urinary alkalinisation or ascorbic acid, the aluminium concentration in the plasma can increase for several weeks.
Bupropion (medicine for smoking cessation and anti-depressant)	Increased risk of seizures.
Quinidine (medicine for the treatment of cardiac arrhythmias)	The action of quinidine may be increased.
Non-depolarising muscle relaxants (certain medicines for muscle relaxation)	Muscle relaxation can last longer.
Atropine, other anticholinergics (medicines that affect certain parts of the nervous system)	Possible additional increase of intraocular pressure.
Praziquantel (anthelmintic)	Possible decrease of the concentration of praziquantel in the blood.
Chloroquine, hydrochloroquine, mefloquine (antimalarial medicine)	Increased risk of muscle disorder and cardiac disease.
Somatropin (growth hormone)	Effect of somatropin could be reduced.
Protirelin (medicinal product for the diagnosis of thyroid disorders)	This medicinal product can cause incorrect results in the diagnosis of thyroid disorders.
Ciclosporin (medicine to suppress the immune system)	Possible increase of ciclosporin blood levels. Increased risk of cerebral seizures.
ACE-inhibitors (certain medicines for hypertension)	Increased risk of changes in blood counts.
Ephedrine (medicines for cough and cold)	Action of Betnesol can be decreased.
Diuretics (medicines to increase urine output)	Increased loss of potassium - increased risk of hypokalaemia.
Azole-antimycotics, such as ketoconazole or itraconazole (medicines for mycotic infection)	Increased action of Betnesol.
Copper (intrauterine devices) “copper coil”	Decreased action of the “copper coil”.
Lithium salts	Action of lithium can be decreased.
Effect on analytical tests	Skin reactions to allergy tests (prick-test) can be suppressed.
Some medicines including some medicines for HIV: (ritonavir, cobicistat).	May increase the effects of Betnesol and your doctor may wish to monitor you carefully if you are taking these medicines.

Using this medicine and food
Swallow the medicine with water, with or without a meal.

Pregnancy and breastfeeding
If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Pregnancy*:*
During pregnancy, especially in the first trimester, your doctor will prescribe treatment only after a careful benefit/risk assessment. Therefore, women must inform their doctor about an existing or new pregnancy or possibility of pregnancy.

Breastfeeding*:*
Glucocorticoids are excreted in breast milk. If treatment is required, breastfeeding should be stopped.

Driving and using machines
Betnesol has no influence on the ability to drive or use machines.

Important information about some of this medicine's ingredients
Betnesol contains less than 1 mmol sodium (23 mg) per tablet, so it is considered essentially "sodium-free".

Betnesol contains 6 mg sodium benzoate (**E211**) in each tablet. Sodium benzoate may increase jaundice (yellowing of the skin and eyes) in newborn babies (up to 4 weeks old).

3. How to use this medicine?

Always use this medicine according to your doctor's instructions. Check with your doctor or pharmacist if you are not sure about your dose or about how to take this medicine. Only your doctor will determine your dose and how you should take this medicine. The recommended dosage is usually:

Use in adults and in adolescents aged 12 years and up:
The daily dose is usually administered in the morning and all at once.

Short-term treatment
Acute asthma attacks, hay fever or other allergic diseases of the respiratory tract, generalised eczema, hives (urticaria), dermatitis caused by a medicine, and various inflammatory skin diseases.

6 tablets in the morning for 2 days, followed by
1 tablet in the morning for 2 days, followed by
half a tablet in the morning for 2 days.

Rheumatoid arthritis:
1-4 tablets (0.5 mg to 2 mg) daily in the morning for 1–2 weeks, then a gradual withdrawal of treatment, first by reducing by one tablet per day, then by half a tablet per day, and maintaining each dose for one week. In this way, the minimum effective dose can be evaluated.

Other diseases:
Betnesol tablets are particularly suitable for patients with nephrotic syndrome (nephrosis), as Betnesol has almost no effect on sodium chloride and water retention. In this disease, the usual dose is 1–8 tablets (0.5 mg to 4 mg) daily in the morning for 1-3 weeks, possibly longer.

Use in children over 6 years old
In children, lower doses than indicated above are generally sufficient, but dosage should be adjusted more for severity of the disease than for age, body weight, or body size. After sufficient response is achieved, Betnesol should be withdrawn gradually, as quickly as possible. Long-term treatment is not recommended. Exact dosages have not been established in clinical trials. The following guidelines for short-time treatment have been established based on clinical experience:
Recommended initial dose:
7 to 12 years old: up to 8 tablets a day (= 4 mg).

Elderly

Apply caution when treating elderly patients with betamethasone, particularly during long-term therapy due to the increased frequency of side effects, including osteoporosis, worsening diabetes, hypertension, increased susceptibility to develop infections, and thinning of the skin.

Patients with impaired liver function and thyroid disease

Betamethasone is mainly metabolized in the liver. Comparatively low doses may be sufficient in patients with hepatic dysfunction or hypothyroidism, or a dose reduction may be necessary.

Do not exceed the recommended dose.

The tablets may be dissolved or split. Do not crush or chew.

Method of administration

Dissolve Betnesol tablets in water and drink the solution, or the tablets can be swallowed whole with a little water. The total daily dose should be taken in the morning before 8 a.m.
Only for short-term treatment.

If you have taken a higher dose of Betnesol than recommended
A life-threatening situation is not expected in acute overdose with glucocorticoids including betamethasone. Your doctor will give you the appropriate treatment.
If a child has accidentally swallowed some medicine, immediately see a doctor or go to a hospital emergency room and bring the medicine package with you.

If you forget to take Betnesol
If you forget to take the medicine at the scheduled time, do not take a double dose. Take the next dose at the usual time and consult your doctor. Adhere to the treatment as recommended by your doctor.

If you stop taking Betnesol
Do not stop long-term treatment abruptly. Your doctor will gradually reduce the dose.

Do not take medicines in the dark! Check the label and dose every time you take medicine. Wear glasses if you need them.

If you have any further questions about using this medicine, consult your doctor or pharmacist.

4. Side effects

Like with all medicines, using Betnesol may cause side effects in some users. Do not be alarmed by this list of side effects; you may not experience any of them.

Stop taking this medicine and consult a doctor immediately if you experience signs of allergic reactions, including anaphylaxis.
Consult your doctor if you experience blurred vision or any other vision disturbance.

Side effects of unknown frequency *(the frequency of these effects has not been established yet):*

Endocrine disorders
Cushing's syndrome (moon face, bull neck, weight increase, high blood pressure, bluish-red stripes on the skin and punctiform bleeding of the skin).
Reduced function or atrophy of the adrenal cortex.

Metabolic and nutritional disorders
Decreased carbohydrate tolerance, diabetes mellitus, osteoporosis, water retention in tissue (oedema), increased potassium excretion, increased protein breakdown.

Nervous system disorders
Sleep disorders, dizziness, headache, pseudotumor cerebri (signs of brain tumour such as an increase in intracranial pressure without the presence of a tumour, especially in children), the appearance of a yet unseen epilepsy and increased susceptibility to seizures if epilepsy is already present, increased excitability and restlessness.

Psychiatric disorders
Mental disorders, psychosis, personality changes, confusion.

Eye disorders
Cataract, glaucoma, protruding eyeballs (exophthalmos), blurred vision.

Digestive system disorders
Abdominal discomfort, stomach and duodenal ulcers (risk of perforation), oesophagitis with ulcers, bleeding, pancreatitis, with pre-existing ulcer of the colon (ulcerative colitis); risk of perforation.

Disorders of the reproductive system and mammary glands
Disturbance of sex hormone secretion (menstrual disorder, impotence).

Skin and subcutaneous tissue disorders
Red stripes appear on skin (striae rubrae), tissue atrophy, telangiectasia (enlarged skin blood vessels), punctiform (petechiae) and planar (ecchymosis) bleeding in the skin and mucous membranes, increased hair growth, acne-like symptoms (steroid acne), impaired wound healing, rosacea-like dermatitis, change in pigmentation of the skin, hypersensitivities (e.g. drug induced skin rash).

Vascular disorders
High blood pressure (hypertension), vascular obstruction due to blood clot (thrombosis), blood vessel inflammation (vasculitis).

Infections and infestations (parasite infections)
Increased risk of susceptibility to infections; masking of infections; exacerbation of latent infections (mycosis, viral infections, bacterial infections, protozoa infections, candidiasis, tuberculosis, etc.).

Immune system disorders
Decreased immune response; allergic reaction, anaphylactic reactions including shock.

Blood and lymphatic system disorders
Change in the number of white blood cells.

Cardiac disorders
Myocardial rupture after recent infarction.

Musculoskeletal and connective tissue disorders
Muscle wasting and muscle weakness, muscle disorders, growth retardation in children, osteoporosis, necrosis of bone tissue in the area of the long bones (upper arm, thighs), tendon rupture.

Respiratory, thoracic and mediastinal disorders
Hiccups.

If you experience any side effect, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet, consult your doctor.
You can report side effects to the Ministry of Health by following the link 'Reporting Side Effects of Drug Treatment' on the Ministry of Health home page (www.health.gov.il) which links to an online form for reporting side effects. You can also use this link: https://sideeffects.health.gov.il.

5. How to store the medicine?

- Prevent poisoning! To prevent poisoning, keep this, and all other medicines, in a closed place, out of the reach and sight of children and/or infants. Do not induce vomiting unless explicitly instructed to do so by a doctor.
- Do not use the medicine after the expiry date (exp. date) which is stated on the carton, bottle or blister tray after EXP. The expiry date refers to the last day of that month.
- **Storage conditions:** Store below 25°C. Store in the original package in order to protect the contents from light.
- Do not throw away this medicine via wastewater or household waste. Ask your pharmacist how to throw medicines you no longer use. This will help protect the environment.

6. Additional information

In addition to the active ingredient the medicine also contains:

sodium acid citrate, sodium bicarbonate, sodium benzoate, povidone 30, saccharin-sodium, erythrosine (E127).

What the medicine looks like and contents of the pack:
Betnesol tablets are round pink tablets with bevelled edges, a score line on one side and "BETNESOL" embossed on the other side. Tablets can be divided into equal doses.

Betnesol tablets are available in blister packs of 10 and 30 tablets.

Not all pack sizes may be marketed.

Registration holder: Devries & Co. Ltd., 32 Habarzel St., Tel Aviv.

Manufacturer's name and address:

Alfasigma S.p.A., Via Ragazzi del '99, n.5, Bologna, Italy.

This leaflet was revised in January 2022 according to MOH guidelines.

Registration number of the medicine in the Ministry of Health's National Drug Registry: 135 65 22066 00