Betnesol
Tablets

Active ingredient - each tablet contains 0.5 mg Betamethasone (as disodium phosphate)
Inactive ingredients and allergens: See section 6 "Additional information".

Read the entire leaflet carefully before you start using this medicine. This leaflet contains essential information about this medicine. If you have any further questions, refer to the physician or the 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.

The medicine must not be used in children under the age of six except for a short-term emergency therapy.

1. What Betnesol is and what it is used for?

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

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

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

2. Before using Betnesol

Do not take Betnesol,
- If you are allergic to Betamethasone disodium phosphate or any of the other ingredients of this medicine (listed in section 6).
- If you are sensitive to glucocorticosteroids

Special warnings regarding the use of this medicine

Except for the short-term emergency therapy Benesol must not be used for
- Internal mycotic diseases that affect the whole body.
- Gastric or intestinal ulcers.
- Higher degree bone atrophy (osteoarthritis).
- Severe muscle disorder (except myasthenia gravis).
- Viral diseases such as chicken pox, ocular herpes, herpes zoster.
- Polio (poliomyelitis).
- Enlargement of lymph nodes (lymphoma) after tuberculosis vaccination (BCG).
- Approximately 8 weeks before and 2 weeks after immunization 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 using this medicine, tell your physician
- If you suffer from any of the following diseases or have received specific vaccinations:
  - Impaired liver function
  - Infectious inflammation of the liver (HBsAg-positive chronic active hepatitis).
  - Hardening of the lymph nodes after a tuberculosis vaccination.
  - Acute and chronic bacterial infections.
  - Tuberculosis in medical history, application only while taking drugs against tuberculosis.
  - Severe adjustable high blood pressure (hypertension).
  - Severe diabetes mellitus.
- Injuries and ulcers of the cornea.
- Epilepsy.
- Risk of vascular occlusion.
- Heart insufficiency.
- Renal insufficiency.
- Impaired urinary tract
- Impaired function of the immune system (e.g. AIDS).
- Severe muscle weakness.

In the cases mentioned above your physician will apply Betnesol only after careful benefit-risk analysis. If necessary he will also arrange a treatment of these diseases.

- If you suffer from intestinal diseases or had an intestinal operations.
  To avoid the risk of damage of the intestinal wall or an intestinal perforation, you must inform your physician about:
  - Severe colitis (Colitis ulcerosa) 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 missing in patients who receive high doses of glucocorticoids.
- Betnesol can affect carbohydrate metabolism and induce temporary diabetes or worsen existing diabetes. Your physician will therefore adapt or initiate diabetes treatment when needed.
- At the beginning worsening of the symptom may occur in existing muscle disorder (myasthenia gravis) therefore Betnesol adjustment should occur in hospital. If irritation in the face and throat are particularly severe and respiration is impaired treatment with Betnesol should be started slowly.
- Administration of Betnesol for severe infections may be used only in combination with an anti-infective therapy.
- Betnesol may mask the signs of an infection and so complicate the diagnosis of an existing or developing infection.
- Prolonged application of even small amounts of Betnesol leads to an increased risk of infection even with such pathogens that otherwise rarely cause infections.
- Immunization with vaccines containing inactivate pathogens are basically possible. However it should be noted that the success of vaccination could be impaired at higher dosages of Betnesol.
- Viral diseases (chickenpox, measles, Herpes zoster) 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 persons during treatment with Betnesol have contact to persons suffering from measles or chickenpox they should immediately contact their physician who will initiate a preventative treatment if necessary.
- Due to the risk of growth restriction, Betnesol should only be applied to children in presence of mandatory medical reasons and length growth should be monitored regularly.
- If physical stress occurs during treatment with Betnesol such as feverish condition, accidents, birth or operations, the physician has to be informed immediately or an emergency physician hast be advised about the ongoing treatment. Temporary increase in the daily dose of Betnesol may be required.
- In long-term treatment with Betnesol your physician should issue therefore a steroid card that you should always carry with you.
- Depending on duration and dosage of treatment a negative effect on calcium metabolism must be expected so that osteoporosis prevention is recommended. Prevention 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 for patients with thyroid hypofunction or liver cirrhosis and a general dose reduction may be necessary.
- Betnesol is basically intended for short-term use. When applied for longer time warnings that are described for glucocorticoid-containing drugs for long-term use have additionally be considered.
- At the end of a long-term treatment with Betnesol your physician will slowly reduce the dosage. In this way withdrawal symptoms, recurrence of the treated disease and a 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 physician (e.g. operations, travel, vaccinations) you need to inform him about your treatment with Betnesol.
- Administration of Betnesol tablets can lead to a positive doping test result.

### If you are taking or have recently taken other medicines, including nonprescription medications and food supplements, inform your physician or pharmacist.

<table>
<thead>
<tr>
<th>Medicine/group of medicines</th>
<th>Possible side effect as a result of the use of Betnesol</th>
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2
<table>
<thead>
<tr>
<th>Medication Class</th>
<th>Interaction / Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart glycosides (medicinal products for cardiac insufficiency, e.g. Digitalis)</td>
<td>Increased glycoside action due to potassium deficiency.</td>
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<tr>
<td>Medicinal products leading to QT prolongation (changes in the ECG)</td>
<td>Blood potassium level has to be corrected if appropriate and clinical condition has to be monitored.</td>
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<tr>
<td>Antidiabetics (medicines against Diabetes mellitus, e.g. Insulin)</td>
<td>The blood glucose-lowering effect of insulin and oral medicines can be reduced.</td>
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<tr>
<td>Cumarin-Derivates (medicines for blood thinning)</td>
<td>Blood thinning effect is decreased.</td>
</tr>
<tr>
<td>Anticoagulants (Medicines for blood thinning)</td>
<td>Increased or decreased effect of blood coagulation possible.</td>
</tr>
<tr>
<td>Barbiturates (e.g. phenobarbitone, primidone), Hydantoin (phentytoin), carbamazepine (Medicines for treatment of epilepsy), Rifampicin (Medicine against tuberculosis)</td>
<td>Action of Betnesol is decreased.</td>
</tr>
<tr>
<td>NSAIDs (Non-steroidal, anti-inflammatory medicinal) products, e.g. many analgesic and anti-rheumatics</td>
<td>Incidence of stomach ulcers and risk of bleeding in the gastrointestinal tract due to concomitant intake of non-steroidal anti-inflammatory drugs and anti-rheumatics drugs is increased.</td>
</tr>
<tr>
<td>Estrogens (sexual hormone, e.g. component of the “pill”)</td>
<td>Action of Betnesol is increased.</td>
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<tr>
<td>Vaccines</td>
<td>Life vaccines may be more toxic because of the immune-suppressant effect of Betnesol. Disseminated viral infections can occur. The effect of all vaccines can be reduced due to concomitant use of Betnesol (8 weeks before up to 2 weeks after active immunization) The formation of protective antibodies can fail completely.</td>
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<tr>
<td>Aluminium salts-complex-forming acids (e.g. Aspirin)</td>
<td>The aluminium concentration in the plasma can increase for several weeks while taking in combination with complex-forming acids such as citric acid in drinks or medicines for the treatment of acidosis or urinary alkalisation or ascorbic acid.</td>
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<tr>
<td>Bupropion (drugs for smoking cessation and antidepressant)</td>
<td>Increased risk of seizures.</td>
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<tr>
<td>Quinidine (Medicinal product for the treatment of cardiac arrhythmias)</td>
<td>The action of quinidine may be increased.</td>
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<tr>
<td>Non-depolarizing muscle relaxants (certain medicinal products for muscle relaxation, ritodrine)</td>
<td>Muscle relaxation can last longer.</td>
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<tr>
<td>Atropine, other anticholinergics (Medicines that affect certain parts of the nervous system)</td>
<td>Possible additional increase of intraocular pressure.</td>
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<tr>
<td>Praziquantel (anthelmintic)</td>
<td>Possible decrease of praziquantel blood concentration.</td>
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<tr>
<td>Chloroquine, Hydrochloroquine, Mefloquine (antimalarial drug)</td>
<td>Increased risk of muscle disorder and cardiac disease</td>
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<tr>
<td>Somatropin (growth hormone)</td>
<td>Effect of somatropin can be reduced.</td>
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<tr>
<td>Protirelin (Medicinal product for the diagnosis of thyroid)</td>
<td>It can cause wrong results in the diagnosis of thyroid disorders.</td>
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<tr>
<td>Cyclosporin (medicinal product to suppress the immune system)</td>
<td>Possible increase of cyclosporine blood levels. Increased risk of cerebral seizures.</td>
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<tr>
<td>ACE-inhibitors (certain antihypertensive drugs)</td>
<td>Increased risk of occurrence of blood count changes.</td>
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<tr>
<td>Ephedrine (medicines against cough and cold)</td>
<td>Action of Betnesol can be decreased.</td>
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<tr>
<td>Diuretics (drug to increase urine output (e.g. tiazides))</td>
<td>Increased loss of potassium - increased risk of hypokalaemia.</td>
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<tr>
<td>Azole-Antimycotics (such as ketoconazole or itraconazole (drugs against mycotic infection)</td>
<td>Increased action of Betnesol.</td>
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<tr>
<td>Copper (intrauterine devices) „copper loop“</td>
<td>Decreased action of the &quot;copper loop&quot;.</td>
</tr>
<tr>
<td>Lithium salts</td>
<td>Possible decreased action of lithium.</td>
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</tbody>
</table>

Additional medicines you should inform the physician if you are taking are: aminogluthethimide, medicines containing potassium or sodium, amphotericin B, carbonic anhydrase inhibitors. Betnesol might suppressed skin reactions to allergy tests (Prick - test)
Using the medicine with food
Swallow the medicine with water, with or without a meal.

Pregnancy and breast feeding
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your physician or pharmacist for advice before taking medicines in general and this medicine in particular

Pregnancy:
During pregnancy, especially in the first trimester, your physician will conduct the treatment only after careful benefit/risk consideration of. Therefore, women must inform their physician about an existing pregnancy or possibility of pregnancy.

Breast feeding:
Glucocorticoids enter breast milk. If treatment is required breast feeding should be stopped.

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

Important information about some of the medicine’s ingredients
Betnesol contains less than 1 mmol sodium (23 mg) per tablets Betnesol, i.e. it is almost "sodium-free".

Betnesol tablets contain saccharin.

3. How should you use Betnesol?
Always use according to the physician's instructions. You should check with the physician or the pharmacist if you are unsure. The dosage and treatment will be determined only by the physician. The recommended dose is usually:

Use in children and adolescents
The daily dose is administered usually in the morning and at once.

Short-term treatment
Acute asthma attacks, hayfever or other allergic diseases of the respiratory tract, generalised eczema, hives (urticarial), dermatitis medicamentosa, 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
½ tablet in the morning for 2 days.

Arthritis rheumatica:
1 - 4 tablets (0.5 mg to 2 mg) daily in the morning for 1 – 2 weeks, then a gradual withdrawal of the treatment, starting with one tablet less a day, later half a tablet less a day, by keeping each dosage for one week. Thus it is possible to evaluate the minimum effective dose.

Other diseases:
Betnesol tablets are indicated particularly for patients with nephrosis since it shows nearly no sodium chloride and water retention effect. In this disease the usual dose is 1–8 tablets (0.5 mg to 4 mg) daily in the morning for 1 to 3 weeks, maybe also longer.

Use in children less than 6 years
In children in general lower doses than indicated above are sufficient but the dosage should be adjusted more to the severity of the disease than to age, body weight, or body size. After sufficient response Betnesol should be withdrawn step by step as quickly as possible. Long-term treatment is not recommended. Exact dosages have not been established in clinical trials. From clinical experience following guidelines for short-time treatment were shown:

Recommended initial dose:
7 to 12 years: up to 8 tablets/day (= 4 mg).

Elderly
Caution is advised due to higher frequency of adverse events in older patients during administration of betamethasone, particularly in long-term therapy including osteoporosis, worsening of diabetes, hypertension, susceptibility to infections and thinning of the skin.

Patients with impaired liver function and thyroid disease
Betamethasone is basically metabolized in the liver. In patients with hepatic insufficiency or hypothyroidism relatively low doses may be sufficient or dose reduction may be required.

**Do not exceed the recommended dose.**

**Method of administration**

Betnesol tablets should be solved in water and then the solution should be drunk, or the tablets could be swallowed whole with some water. The total daily dose should be taken in the morning before 8 o’clock. Only for short-term treatment.

**Tests and follow-up**

- Before starting a Betnesol therapy a close medical check has to be carried out; particularly gastrointestinal ulcers must be excluded. For the prevention of ulcers in the intestinal tract administration of acid blocking drugs as well as a careful monitoring (including X-ray check/gastroscopy) is indicated in susceptible patients.
- If you suffer from high blood pressure your physician will monitor you carefully because risk of worsening exists.
- During long-term treatment with relatively high doses of Betnesol an adequate potassium intake (e.g. vegetables, bananas) has to be considered. Get a check-up of blood potassium level by your physician. This is particularly important if you are taking medicines which are known that they can lead to a so-called QT extension (a certain changes in the ECG).
- During continuous use it is recommended to limit the intake of calories, and/or sodium
- If you receive Betnesol for a long time your physician can arrange regular ophthalmologic checks (every 3 months) and X-ray checks of the backbone.
- In prolonged therapy with Betnesol independent of disease-related checks and the individual situation of the patient monitoring measures in reasonable intervals regarding possible side effects have to be carried out.

**If you take more Betnesol than you should**

In acute overdose with glucocorticoids including betamethasone a life-threatening situation is not to be expected. Your physician will give you an appropriate treatment.

If a child has accidentally swallowed the medicine, go immediately to a hospital emergency room and bring the medicine package with you.

**If you forget to take Betnesol**

Do not take a double dose to make up for a forgotten intake. Take the next dose at the usual time and consult your physician.

**If you stop taking Betnesol**

A long-term treatment should not suddenly be stopped. Your physician will gradually reduce the dose.

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

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

4. **Side effects**

As with any medicine, Betnesol may cause side effects in some users. Do not be alarmed by reading the list of side effects. You may not experience any of them.

**Stop treatment and refer immediately to the physician if sensitivity reactions appear,** such as: skin irritation, swelling, anaphylactic shock, mental instability.

**refer to the physician if the following appears:** Blurring of vision, thirst, frequent urination.

**Endocrine disorders**

*Not known frequency:* Cushing-Syndrom (moon-shaped face, bull neck, weight increase, high blood pressure, purple stripes on the skin and point-shaped skin bleeding).

Reduction of the function or atrophy of the adrenal cortex.

**Metabolism and nutritional disorders**

*Not known frequency:* decreased carbohydrate tolerance, Diabetes mellitus, osteoporosis, water retention in the tissue (oedema), increased potassium excretion, increased protein degradation, increased appetite, thirst, frequent urination.

**Nervous system disorders**
Psychiatric disorders
Not known frequency: Mental disorders, psychosis, personality changes, confusion.

Eye disorders
Not known frequency: Cataract, glaucoma, protruding eyeballs (exophthalmos), blurring of vision.

Gastrointestinal disorders
Not known frequency: Abdominal discomfort, peptic ulcer (risk of perforation), oesophagitis including ulcers, bleeding, pancreatitis; risk of perforation with pre-existing colon ulcer, nausea, vomiting.

Reproductive system and breast disorders
Not known frequency: Disturbance of sexual hormone secretion (menstrual disorder, impotence).

Skin and subcutaneous tissue disorders
Not known frequency: strip-type reddened skin (Striae rubrae), tissue atrophy, telangiectasia (enlarged skin vessels), punctual (petechiae) and planar (ecchymosis) bleeding in the skin and the mucous membranes, increased hair growth, acne-like symptoms (steroidacne), impaired wound healing, rosacea-like dermatitis, change in pigmentation of the skin, hypersensitivities (e.g. drug eruptions), skin irritation.

Vascular disorders
Not known frequency: high blood pressure (hypertension), vascular obstruction due to blood clot (thrombosis), blood vessel inflammation (vasculitis).

Infections and infestations
Not known frequency: Increased risk of susceptibility to infections; masking of infections; Exacerbation of latent infections (mycosis, virus infections, bacterial infections, Protozoa infection, candidiasis, tuberculosis, etc.);

Immune system disorders
Not known frequency: Decreased immune response; allergic reaction, anaphylactic reactions including shock.

Blood and lymphatic system disorders
Not known frequency: Change the number of white blood cells (Leucocytosis).

Cardiac disorders
Not known frequency: Myocardial rupture after recent infarct, irregular pulse.

Musculoskeletal and connective tissue disorders
Not known frequency: muscle wasting (amyotrophy) and muscle weakness (amoysthenia), muscle disorder (myopathy), growth retardation in children, osteoporosis, necrosis of bone tissue in the area of the long bones (upper arm, thighs), tendon rupture, muscle pain, back and joint pain.

If you get any side effect, if any side effect gets worse, or if you suffer from a side effect not mentioned in the leaflet, you should consult the physician.

5. How to store Betnesol?
- Avoid poisoning! This medicine and any other medicine should be kept in a closed place out of the reach of children and/or infants in order to avoid poisoning. Do not induce vomiting without an explicit instruction from the physician.
- Do not use this medicine after the expiry date which is stated on the carton, bottle or blister after “EXP”. The expiry date refers to the last day of that month.
- Store below 25° C. Store in the original package in order to protect the content from light.
- Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Additional information
In addition to the active ingredient the medicine also contains:
- Saccharin-Sodium
- Sodium carbonate
- Sodium Citrate
- Povidone 30
- Erythrosine (E 127)
- Sodium benzoate
What Betnesol looks like and what are contents of the package:

Betnesol tablets are available in blister packages with 10 and 30 packs and in bottles containing 100 tabs.

Not all packs may be marketed.

Registration Holder: Devries & Co. Ltd., 32 Ha`Barzel st. P.O. Box 53463, Tel Aviv 6153401.
Manufacturer: Sigma-tau Industrie Farmaceutiche Riunite S.p.A. Via Pontina, km 30,400, 00040 Pomezia (Roma), Italy

This leaflet was checked and approved by the Ministry of Health in: July 2015

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