PACKAGE LEAFLET:
Information for the user

ALOPURIN

Tablets – 100 mg

Active substance: Allopurinol

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 personally. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If you get any side effects or if you notice side effects not listed in this leaflet, talk to your doctor or pharmacist.

In this leaflet:

1. WHAT ALOPURIN IS AND WHAT IT IS USED FOR?

Alopurin is a medicine which inhibits the formation of uric acid (uricostatic).

Alopurin is indicated:

Adults
- in cases where blood uric acid values are 500 µmol (8.5 mg/100 ml) and above, provided it is dietary unmanageable, or in clinical complications with hyperuricemic conditions, especially manifested gout, renal damage caused by uric acid (urate nephropathy), treatment and prevention of uric acid stones, and to prevent the formation of calcium oxalate stones in concomitant hyperuricemia.
- in raised blood uric acid levels and increased excretion of uric acid in urine, e.g. in strong cell decay, radiation or chemotherapy (secondary hyperuricemia).

Children
- in raised blood uric acid levels and increased excretion of uric acid in urine, e.g. in strong cell decay, radiation or chemotherapy (secondary hyperuricemia)
- in renal damage caused by uric acid (urates nephropathy) during treatment of leukemia
- in congenital enzyme deficiency disease (Lesch-Nyhan syndrome [partial or total defects of the hypoxanthine-guanine phosphoribosyl transferase] and adenine phosphoribosyltransferase deficiency).

2. WHAT YOU NEED TO KNOW BEFORE YOU TAKE ALOPURIN?

Do not take Alopurin,
- if you are hypersensitive (allergic) to allopurinol or to any of the other ingredients of Alopurin.

Take special care with Alopurin

The following describes when you may use Alopurin only under certain conditions and with special caution. Consult with your doctor. You should do this even if you have had previously these conditions.

According to recent literature recommendations, drug therapy is unnecessary under a blood uric acid value of 8.5 mg/100 ml if dietary requirements are met and there are no kidney damage.
Foods high in purines (e.g., internal organs such as thymus, kidney, brain, liver, heart, tongue and meat extract) and alcohol (especially beer, as this adds guanosine, which strongly increases the level of uric acid), should be avoided.
Upon the occurrence of hypersensitivity reactions such as skin rash, Alopurin should be discontinued immediately.

A particularly careful medical monitoring is required if you have impaired renal function or liver function, or pre-hematopoietic disorders. For the treatment of gout and uric acid stones, the urine volume should be at least 2 liters per day, so you must ensure adequate hydration.

To prevent increased uric acid concentrations in serum and urine, which may occur for example during radiation or chemotherapy of neoplasms and in the congenital enzymatic deficiency, Lesch-Nyhan syndrome, in addition to the administration of allopurinol, a large fluid intake is required to ensure adequate diuresis. In addition, an alkalinization of the urine by increasing the solubility of urate / uric acid contributes to increase the excretion of these substances in the urine.

If a urate nephropathy or other pathological changes have already impaired renal function, your doctor should adjust the dose according to renal function values (see "3. How to take Alopurin?").

In the presence of acute attacks of gout, treatment with allopurinol should be started only after the symptoms are fully subsided. At the beginning of treatment with allopurinol, acute gout attacks can be triggered by mobilizing greater uric acid deposits. Therefore, during the first 4 weeks of treatment, your doctor may consider the simultaneous analgesics or colchicine take.

In case of large uric acid stones in the renal pelvis, is not ruled out that part of the dissolved stones as a result of allopurinol treatment, may set in the ureter.

Allopurinol interacts with the metabolism of many drugs (see "Taking Alopurin with other medicines").

Taking Alopurin with other medicines

Tell your doctor or pharmacist if you are taking / using or have recently taken / used other medicines, including medicines taken without a prescription.

Allopurinol slows the excretion of probenecid (a medicine that causes an increased excretion of uric acid).
The concomitant administration of allopurinol with drugs that increase the excretion of uric acid, such as probenecid or sulfinpyrazone, accelerates its elimination, thus the effectiveness of allopurinol is reduced. The clinical significance of these interactions is to be assessed in each individual case by the physician.

If Alopurin is ingested simultaneously with 6-mercaptopurine or azathioprine, their dose should be reduced to 25% of the usual dose because their effect can be extended by Alopurin.

If allopurinol is administered simultaneously with antibiotics (medicines to treat bacterial infection-related diseases) ampicillin or amoxicillin, often allergic reactions are to be expected (skin rash). Therefore, you should - if possible - get treated with other antibiotics while you take Alopurin.
During concomitant administration of allopurinol and captopril, particularly in chronic renal failure, the risk of skin reactions may increase.

Anticoagulant drugs (anticoagulants of the coumarin type) can amplify their effect when co-administered with Alopurin. Therefore, your doctor will monitor your blood clotting more frequently. Maybe he will lower the dose of the appropriate anticoagulant drug.

In particular, in impaired renal function, co-administration of Alopurin and glucose-lowering drugs that contain chlorpropamide, prolongs the effect of the latter. Therefore, your doctor will reduce the dose of chlorpropamide.

Theophylline: after taking allopurinol, an inhibition of the metabolism of theophylline-containing drugs is noticed, which may have been prescribed e.g. for the treatment of respiratory and heart disease. Therefore, at the beginning of treatment with Alopurin or when increasing the dose of Alopurin, your doctor should determine the blood concentrations of theophylline.

If Alopurin is taken together with cytostatics (medicines used to treat malignant tumor diseases, such as cyclophosphamide, doxorubicin, bleomycin, procarbazine, alkyl halides), blood disorders may occur more frequently than in respective single use of these agents. Blood controls have to be performed by the doctor at short intervals.

Vidarabine: the retention of vidarabine-containing medicines (medicine for viral diseases) in the body may be prolonged in the presence of allopurinol. Therefore, co-administration of these drugs requires special attention in order to detect in time any increased side effects.

The concentration of cyclosporin (medicine used to reduce the body's immune system) in the blood may be increased in case of simultaneous take of Alopurin. The possibility of more frequent occurrence of cyclosporine-related side effects should therefore be taken into account.

Phenytoin: the metabolism of phenytoin-containing medicines, prescribed e.g., to treat epilepsy or certain serious heart disease, can be affected by Alopurin. It is not yet known whether this finding has a clinical significance.

Pregnancy and lactation

Consult with your doctor or pharmacist before taking / using any medicine.
Allopurinol should not be used in pregnant women because of the lack of experience in humans.
Allopurinol passes into breast milk, therefore it should not be used during lactation.

Driving and using machines

The possible side effects that may occur are: drowsiness, dizziness or ataxia. These may decrease the ability to drive or to use machines.
You may not respond quickly and effectively enough to unexpected and sudden events. Do not drive a car or other vehicles! Do not use electrical tools and machines! Do not work without a secure fit! Keep in mind particularly that alcohol worsens further your ability to drive.
Before you perform the mentioned activities, you have to be sufficiently sure that allopurinol does not impair your performance.

Important information about some of the ingredients of Alopurin

This medicinal product contains lactose. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking Alopurin.

3. HOW TO TAKE ALOPURIN?

Always take Alopurin exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.
Please follow the instructions for use, otherwise Alopurin may not exert the appropriate effect!

Unless otherwise prescribed by the doctor, the usual dose is:

Adults
Adults, depending on the current serum uric acid values, take 1 to 3 tablets Alopurin daily (corresponding to 100 mg to 300 mg of allopurinol daily).
In order to reduce the risk of occurrence of adverse effects, the treatment should be started with one tablet Alopurin daily (equivalent to 100 mg allopurinol). This dose should be increased only when the levels of uric acid in serum are not sufficiently lowered.
In exceptional cases, the dose may be increased to 6-8 tablets Alopurin daily (equivalent to 600 mg to 800 mg of allopurinol). In such case, blood tests should be performed (the oxipurinol level in serum should not exceed a value of 15 µg / ml [100 µmol]). The dose should be administered divided throughout the day.
For a better compliance, the single dose should not exceed 3 tablets Alopurin (equivalent to 300 mg of allopurinol).
The maximum daily dose is 800 mg allopurinol.

Children
The daily dose is 10 mg allopurinol per kilogram of body weight (up to max. 400 mg / day) in 3 divided doses.

Elderly
Since specific data on the use of allopurinol in elderly patients are not available, these patients should be treated with the lowest dose therapeutically acceptable.
Furthermore, the presence of impaired renal function should be considered, especially in older patients.

Impaired renal function
Allopurinol and its metabolites are excreted by the kidneys. Decreased renal function can therefore prolong the time in which the substance and its metabolites stay in the body, and in this way lead to an overdose. Thus, if you have impaired renal function, Alopurin must be used under special medical supervision. To reduce any possible risk, the physician determines the required dose on the outcome of a specific blood test (serum creatinine levels, which should be checked regularly), or determines the creatinine clearance.
In the presence of severe renal impairment, it should be taken maximum 100 mg of allopurinol per day (1 tablet Alopurin) or single doses of 100 mg of allopurinol should be taken at longer intervals than 1 day. The serum oxipurinol levels should not exceed 15.2 g/ml.

A guide for dosing in renal failure is given in the following scheme:

Creatinine clearance	Daily dose
over 20 ml/min	Standard dose
10 to 20 ml/min	100 to 200 mg
under 10 ml/min	100 mg or longer intervals

If you will do hemodialysis, you may take immediately after each treatment (i.e., 2 - or 3-times per week), 300 mg to 400 mg of allopurinol.

Impaired liver function
If you have impaired liver function, an approach as in impaired renal function is recommended. At the beginning of treatment, periodic liver function tests should be performed in addition.

Method of administration

Take the tablets whole, with a sufficient quantity of liquid, preferably a glass of water (200 ml), possibly at the same time of the day, after food.
When the total daily dose of 300 mg allopurinol is exceeded and gastrointestinal intolerances occur, you should take the dose divided throughout the day.

Please ensure adequate and regular hydration.

Duration of use

Usually, treatment with Alopurin is required over a long time. Take Alopurin regularly and according the duration set by your doctor.
As with any long-term treatment, an ongoing supervision by your doctor is necessary. Your doctor should check regularly and periodically the uric acid levels. At the same time he should check for possible side effects and the need for continuation of the treatment.
Talk to your doctor or pharmacist if you have the impression that the effect of Alopurin is too strong or too weak.

If you take more Alopurin than you should

A specific antidote is not known. After administration of a single dose of 20 g allopurinol in one patient, occurred symptoms such as nausea, vomiting, diarrhea, and dizziness.
If you suspect for an overdose, you should immediately inform the doctor, particularly if you use concomitantly azathioprine or 6-mercaptopurine. He will take measures to reduce the further uptake of the drug in the bloodstream or to accelerate the excretion of the drug, such as ample fluid intake or a hemodialysis if necessary.

If you forget to take Alopurin

Do not take a double dose if you have forgotten to take the previous dose.
If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

Like all medicines, allopurinol can cause side effects, although not everybody gets them.

For the evaluation of side effects, the following frequency indicators are used:

Very common	more than 1 in 10 patients
Common	1 to 10 patients among 100
Uncommon	1 to 10 patients among 1.000
Rare	1 to 10 patients among 10.000
Very rare	less than 1 in 10.000 patients
Unknown	frequency cannot be estimated from the available data.

If you suffer from gout, at the beginning of treatment with Alopurin, a reactive attack of gout may be caused.
The occurrence of side effects is more common if you have impaired kidney or liver function, or if you are treated concomitantly with ampicillin or amoxicillin – containing medications.

Skin disorders and hypersensitivity reactions

The most frequent observed side effects are skin reactions. They can occur at any time during treatment. They can manifest themselves with itching which may be associated with maculopapules, scaling, ecchimosis or bruising.
When such reactions occur, you should discontinue immediately Alopurin and inform your doctor because severe generalized hypersensitivity reactions may occur.

The hypersensitivity reactions described below are rare (especially those which are fatal when there is general kidney and liver impairment), however they are as severe as the immediate discontinuation of allopurinol and informing of the doctor is necessary.

Hypersensitivity reactions can be expressed as follows:
skin reactions have been noticed associated with: exfoliation, fever, lymphadenopathy, increase of the number of certain white blood cells (eosinophilia) associated with arthralgia (Stevens-Johnson syndrome), and also skin changes ressembling burnings have been noticed (Lyell's syndrome). Blood vessels inflammation (vasculitis) – even though rarely occurring – can manifest itself in various ways, such as: hepatic cells damage (hepatitis), renal inflammation, and very rarely seizures.

Furthermore, the following observations have been made in individual cases:
hypersensitivity reactions, which can manifest themselves among others with fever, chills and joint pain, liver dysfunction (reversible elevation of transaminases and alkaline phosphatases), and also biliary tract inflammation and xanthine deposits in the urinary tract.
For an acute anaphylactic (allergic) shock, which may be potentially life – threatening, has been reported very rarely.

Countermeasures
If skin reactions occur, you should not take Alopurin anymore. In such case, you should inform your doctor.
If you experience acute, generalized, eventually potentially life – threatening hypersensitivity reactions (anaphylactic shock), you should contact the nearest doctor immediately. He will take the necessary urgent measures. In this case, you should not take Alopurin anymore.

Blood and lymphatic system disorders

Reversible angioimmunoblastic lymphadenopathy has been very rarely described after taking allopurinol, which has disappeared after discontinuation of the drug.
In individual cases have been reported white blood cell disorders (leukopenia, leukocytosis, granulocytosis, eosinophilia) after taking allopurinol.

Hepatic disorders

Rarely, abnormal liver function, ranging from an asymptomatic (without signs) increase in liver values up to hepatitis (hepatic inflammation, including hepatic necrosis and granulomatous hepatitis) has been reported after using allopurinol.

Gastrointestinal tract disorders

Nausea, vomiting and diarrhea may occur after taking Alopurin. If you have a sensitive stomach, you should take the drug cautiously, after food and with sufficient fluid intake.

Bone marrow disorders

Particularly in patients with renal impairment, severe damage of bone marrow (thrombocytopenia, agranulocytose and aplastic anemia) have been occasionally reported.
If you suffer from a kidney disease, you should inform your doctor in order to control carefully the blood formula.

Other

In addition, in individual cases, the following observations have been made after taking allopurinol:
- asthenia, general malaise
- skin purulent inflammations (furunculosis)
- loss of conscience
- hypertonie
- blood in urine (hematuria); pathological raising of urine components in blood (uremia); vomiting with blood
- intestinal disorders
- enlargement of one or both breasts in men and also pale swelling of the skin and mucosa, particularly in the face area (angioneurotic edema)
- blood increased lipid values (hyperlipemia); increased excretion of lipids in the stools
- taste disturbances; inflammation of the oral mucosa
- incoordination; sensorial disorders (paresthesia)
- hair loss; discolored hair
- sore throat (angina)
- impotence, infertility
- headache
- paralysis; muscle pain
- nerve inflammation (peripheral neuritis); neuropathy
- somnolence; dizziness
- depression
- ejaculation during sleep
- blurred vision; clouding of the eye lens (cataract), changes of the retina (macular degeneration)
- bradycardia
- water retention in the tissues (edema)
- diabetes mellitus.

Talk to your doctor or pharmacist if you get any side effects or if you notice side effects not listed in this leaflet.

5. HOW TO STORE ALOPURIN?

Keep this medicine out of the sight and reach of children.

Storage conditions

Keep the blister in the box to protect the content from humidity.
You should not use this medicine after the expiry date stated on the blister and on the box after „Skad.".
The expiry date refers to the last day of that month.

6. FURTHER INFORMATIONS

What Alopurin contains

The active substance is allopurinol.
1 tablet contains 100 mg allopurinol.

The other excipients are:
lactose monohydrate, maize starch, povidone K30, magnesium stearate.

What Alopurin looks like and contents of the pack

The blisters contain round tablets, white, with a score – line on one side.

Alopurin is available in packs of 50 tablets.

Explanatory of the illustration icons on the packaging:

Ask your doctor or pharmacist.

Content. Warning. Tablet shape.

Marketing Authorisation Holder and Manufacturer:

PROFARMA Sh.a.
Rruga "Myslym Keta"
Tel.Fax: 00 355 4 23 62 800
Tirana - ALBANIA

This leaflet was last revised in November 2013.

SPECIFICATION

CROPING AREA 15 x 25 cm

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