

BEZALIP® Actavis

Agent to reduce elevated blood lipid levels associated with disorders of lipid metabolism.

Composition:

1 film-coated tablet of Bezalip contains:

Active Ingredient: bezafibrate.

Film-coated tablets 200 mg. Bezalip film-coated tablets are round, white and imprinted G6.

Other Ingredients:

Maize starch; starch. pregelatinised; cellulose microcrystalline; sodium starch glycolate (Type A); silica, colloidal anhydrous; magnesium stearate.

The film-coat contains: polyvinyl alcohol; titanium dioxide; macrogol 3350 and talc.

Indications:

Bezalip reduces elevated blood lipid levels (triglycerides and cholesterol) and is therefore intended for the treatment of certain disorders of lipid metabolism.

Along with high blood pressure and smoking, elevated blood lipid levels are regarded as one of the major risk factors for the development and progression of atherosclerosis (hardening of the arteries) and its consequences, namely changes in the blood vessels that can lead to myocardial infarction or disturbance of the blood flow to the limbs or the brain.

Bezalip can therefore be used in:

- disorders of lipid metabolism that cannot be adequately influenced either by a change in diet or by other means such as increased physical activity and weight reduction;
- disorders of lipid metabolism that are secondary to other diseases (e.g. diabetes) and that persist despite systematic treatment of the disease concerned.

Dosage and administration

The following information applies unless your doctor has prescribed Bezalip differently for you. Please observe the instructions for use, as otherwise Bezalip cannot work properly.

How many Bezalip film-coated tablets should you take at what intervals?

Adults take one Bezalip film-coated tablet three times daily (equivalent to 600 mg of bezafibrate per day).

If you suffer from a sensitive stomach, the dose can be increased gradually, starting with one Bezalip film-coated tablet once daily (equivalent to 200 mg of bezafibrate per day); after 3 to 4 days you take one Bezalip film-coated tablet twice daily (equivalent to 400 mg of bezafibrate per day); and after a further period of 3 to 4 days you take one Bezalip film-coated tablet three times daily (equivalent to 600 mg of bezafibrate per day).

If treatment is very successful your doctor can, especially in certain types of metabolic disorder (hypertriglyceridemia), reduce the daily dose to two Bezalip film-coated tablets, i.e. one in the morning and one in the evening (equivalent to 400 mg of bezafibrate per day).

If your renal function is impaired, Bezalip must be used under particularly close medical supervision.

Your doctor calculates the dose required on the basis of the result of a certain blood test (serum creatinine level, which must be checked regularly) and/or on the basis of creatinine clearance as determined via the following table:

Serum Creatinine	Creatinine Clearance	Bezalip Dosage
Up to 1.5 mg/dl Up to 135 µmol/l	Over 60 ml/min	3 film-coated tablets daily
1.6-2.5 mg/dl 136-225 µmol/l	60-40 ml/min	2 film-coated tablets daily
2.6-6 mg/dl 226-530 µmol/l	40-15 ml/min	1 film-coated tablet daily every 1-2 days
Over 6 mg/dl Over 530 µmol/l	Less than 15 ml/min	Must not be used

Particularly in elderly patients, creatinine clearance should be determined in order to calculate the dose required.

In pronounced hypoalbuminemia (low-level of protein in the blood), e.g. in nephrotic syndrome, and in dialysis patients, your doctor can reduce the dose to one Bezalip film-coated tablet every third day. In order to calculate the precise dose required and thus avoid overdosage and consequent severe muscle damage (rhabdomyolysis), your doctor will determine the concentration of bezafibrate in your blood (plasma).

Please ensure that your fluid intake is adequate and regular.

How and when should you take Bezalip?

Please swallow the film coated tablets whole with an adequate amount of liquid (e.g. a glass of water) with or after a meal. If your prescription is for three film-coated tablets daily, take one film coated tablet in the morning, one at midday, and one in the evening. If your prescription is for two film-coated tablets daily, take one film-coated tablet in the morning and one in the evening.

For how long should you take Bezalip?

Treatment with Bezalip generally has to be continued for a longer period of time. Please take Bezalip regularly and for as long as specified by your doctor. As with any long-term treatment, regular monitoring is required: blood lipid levels should be checked repeatedly and regularly, possible side effects should be watched, and the need for continued drug treatment should be reviewed.

Contraindications

Under what circumstances must you not use Bezalip?

Bezalip must not be used in severe impairment of renal function (serum creatinine level above 6 mg/dl or creatinine clearance less than 15 ml/min; see also Dosage Instructions), in severe impairment of liver function, in gallbladder diseases with or without gallstones, during pregnancy or lactation, in patients with known hypersensitivity to any ingredient of the product, or in patients with known photosensitivity of the skin (photoallergic or phototoxic reactions) following use of fibrate-containing medicines (certain lipid-lowering medicines).

Under what circumstances may you use Bezalip only after consulting your doctor?

Under any of the circumstances described below, you may take Bezalip only under certain conditions and only with particular care.

Please refer to your doctor for further information.

These restrictions also apply if any of the circumstances described below applied to you previously.

If you suffer from mild to moderate renal impairment, you may use Bezalip only under strict medical supervision and only after calculation of the dose required (see Dosage Instructions).

What must you be aware of in relation to pregnancy and breastfeeding?

Bezalip must not be used during pregnancy or lactation, as experience on use in pregnancy and lactation in humans is inadequate.

What must be taken into account in children?

In children, the need for treatment with Bezalip must be particularly carefully considered by the doctor.

Warnings and precautions for use

What precautions must be observed?

At the start of any treatment of disorders of lipid metabolism, you should seek the advice of your doctor. In many cases, disorders of lipid metabolism can be favourably influenced by dietary change, increased physical activity, weight reduction, and adequate treatment of any other metabolic disorders present (e.g. diabetes, gout).

You should continue these measures while taking Bezalip.

Basically, treatment with Bezalip is useful only as an additional measure and only if the disorder of lipid metabolism cannot be corrected by the above measures alone.

The intensity of the effect of Bezalip varies between individuals.

Long-term regular use is required if the objective of treatment is to be achieved. Another precondition is strict observance of all measures prescribed by your doctor.

In patients being treated with coumarin-type anticoagulants or blood glucose-lowering agents

(e.g. sulfonylureas, insulin), the doctor will check the coagulation values or blood glucose level, respectively, especially at the start of treatment.

Your doctor may need to alter the dose of these medicines. Therefore, please take particular care to keep the appointments for these tests.

Please inform your doctor if you are taking a hormonal contraceptive ('the pill'), as this can unfavourably influence lipid metabolism.

If you suffer from renal impairment, you should take particular care to keep the appointments with your doctor and you should ensure that your fluid intake is adequate and regular.

Undesirable effects

What are the possible undesirable effects of Bezalip?

Gastrointestinal tract gastrointestinal symptoms such as bloating, nausea, and loss of appetite occur occasionally.

Nervous system: headache and dizziness occur occasionally.

The above side effects are generally transitory and do not require stopping of the medicinal product.

Liver: there have been isolated reports of impairment of liver function, e.g. elevated levels of liver enzymes (transaminases) or cholestasis (reduced flow of bile).

Blood: In isolated cases, a slight reduction in the concentration of hemoglobin (the red pigment of blood) and in the number of white blood cells has been observed. There have also been isolated cases of a reduction in the number of platelets, in some cases leading to bleeding (e.g. punctate skin hemorrhages). There have been isolated reports of pancytopenia (simultaneous reduction in the numbers of all three series of blood cells).

Miscellaneous: hair loss occurs rarely, and erectile dysfunction in isolated cases.

Most of the above side effects generally subside rapidly after Bezalip is stopped.

Hypersensitivity reactions: allergic skin reactions such as itch, hives, or other skin phenomena occur occasionally. In isolated cases, even after months of use without complications, hypersensitivity of

the skin to light with reddening, itch, blisters, and nodules on areas of skin that have been exposed to sunlight or artificial light (e.g. in a solarium) - can occur. Should these skin phenomena occur, Bezalip must be discontinued. After discontinuation of Bezalip, the phenomena generally subside (see What countermeasures should be taken if side effects occur?).

There have been isolated reports of acute, generalised, potentially life-threatening hypersensitivity reactions (anaphylactic shock) accompanied by a feeling of tightness in the chest, breathing difficulty, increased heart rate, skin phenomena, a fall in blood pressure, fluid accumulation in the body, circulatory collapse, chills, and brief impairment of consciousness.

Occurrence of these allergic reactions calls for appropriate emergency measures and immediate discontinuation of the medication (see What countermeasures should be taken if side effects occur?).

Kidneys: long-term treatment frequently leads to a slight rise in the serum level of creatinine (a blood constituent whose concentration rises with diminishing renal function).

Muscles: an important, though rare, side effect is muscle damage leading to muscle pain, muscle weakness, and muscle cramps. Should this occur, your doctor will order a particular blood test (determination of creatine phosphokinase [CPK]).

Rarely, severe muscle damage (rhabdomyolysis) occurs. This is generally due to overdosage of Bezalip, especially in patients with impaired renal function.

Bile: Bezalip alters the composition of bile.

Whether as has been observed with other medications with the same mechanism of action long-term treatment with Bezalip leads to increased occurrence of gallstones, or whether existing gallstones can increase in size during treatment with Bezalip, is disputed. There have been isolated reports of formation of gallstones.

Should you experience any side effects, in particular any not referred to in this package leaflet, please inform your doctor or pharmacist.

What countermeasures should be taken if side effects occur?

Should allergic reactions such as itch or other skin phenomena occur (especially in association with light exposure), or should you develop muscle pain, muscle weakness, or muscle cramps, you must stop taking Bezalip. In such cases, please contact your doctor. Should acute, generalised, potentially life-threatening hypersensitivity reactions (anaphylactic shock) occur, the nearest available doctor must be informed at once in order that the necessary emergency measures can be initiated. In such cases, Bezalip must be discontinued.

Interactions**What other medicine influence the action of Bezalip?**

Bezalip should not be combined with HMG-CoA reductase inhibitors (another class of drug that reduces elevated lipid levels), as this can lead to rhabdomyolysis (severe muscle damage with destruction of striated muscle fibres).

Bezalip must not be taken concurrently with perhexiline hydrogen maleate (a medicinal product that dilates blood vessels) or MNJ inhibitors (a class of antidepressant).

When Bezalip is used concurrently with cholestyramine, an interval of at least two hours should be maintained between taking the two medications, as the absorption of bezafibrate is impaired by cholestyramine.

What other medicines are influenced by Bezalip?

In isolated cases, organ transplant recipients receiving immunosuppressive therapy (treatment with drugs to suppress the body's immune response) concurrently with fibrate-containing medicines have developed substantial though reversible, renal impairment (with a corresponding rise in serum creatinine level).

Renal function should therefore be closely monitored in these patients, and in the event of any significant changes in the laboratory parameters concerned, Bezalip should be stopped.

Bezalip can increase the effect of certain anticoagulant and blood glucose-lowering medicines (see Warnings and precautions for use).

Please note that these warnings can apply also to recently taken medicines.

Overdosage**What should be done if too much Bezalip has been taken (intentional or accidental overdosage)?**

Overdosage can lead to severe muscle damage (rhabdomyolysis), especially in patients with impaired renal function. In the event of suspected overdosage, please inform a doctor so that any measures required to accelerate elimination of the drug from the body can be initiated.

Stability

The expiry date of this medicine is printed on the folding box and the blister strips. Do not use this medicine after the expiry date.

Packs

Film coated tablets 200 mg

Date of Last Review: March 2010

Marketing Authorization Holder: Actavis hf, 220 Hafnarfjörður, Iceland

Manufactured by: CENEXI, 94120 Fontenay-sous-bois, France.