

Package leaflet: Information for the patient

Bitifrin 0.3 mg/ml + 5 mg/ml, eye drops, solution bimatoprost/timolol

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

- 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. See section 4.

What is in this leaflet

1. What Bitifrin is and what it is used for
2. What you need to know before you use Bitifrin
3. How to use Bitifrin
4. Possible side effects
5. How to store Bitifrin
6. Contents of the pack and other information

1. What Bitifrin is and what it is used for

Bitifrin contains two different active substances (bimatoprost and timolol) that both reduce pressure in the eye. Bimatoprost belongs to a group of medicines called prostamides, a prostaglandin analogue. Timolol belongs to a group of medicines called beta-blockers.

Your eye contains a clear, watery liquid that feeds the inside of the eye. Liquid is constantly being drained out of the eye and new liquid is made to replace this. If the liquid cannot drain out quickly enough, the pressure inside the eye builds up and could eventually damage your sight (an illness called glaucoma). Bitifrin works by reducing the production of liquid and also increasing the amount of liquid that is drained. This reduces the pressure inside the eye.

Bitifrin eye drops are used to treat high pressure in the eye in adults, including the elderly. This high pressure can lead to glaucoma. Your doctor will prescribe you Bitifrin when other eye drops containing beta-blockers or prostaglandin analogues have not worked sufficiently on their own.

This medicine does not contain a preservative.

2. What you need to know before you use Bitifrin

Do not use Bitifrin

- if you are allergic to bimatoprost, timolol, beta-blockers or any of the other ingredients of this medicine (listed in section 6)
- if you have now or have had in past respiratory problems such as asthma and/or severe chronic obstructive pulmonary disease (lung disease which may cause wheeziness, difficulty in breathing and/ or long-standing cough) or other types of breathing problems
- if you have heart problems such as low heart rate, heart block, or heart failure

Warnings and precautions

Talk to your doctor or pharmacist before using Bitifrin if you have now or have had in the past:

- coronary heart disease (symptoms can include chest pain or tightness, breathlessness or choking), heart failure, low blood pressure
- disturbances of heart rate such as slow heart beat
- breathing problems, asthma or chronic obstructive pulmonary disease
- poor blood circulation disease (such as Raynaud's disease or Raynaud's syndrome)
- overactivity of the thyroid gland as timolol may mask signs and symptoms of thyroid disease
- diabetes as timolol may mask signs and symptoms of low blood sugar
- severe allergic reactions
- liver or kidney problems
- eye surface problems
- separation of one of the layers within the eyeball after surgery to reduce the pressure in the eye
- known risk factors for macular oedema (swelling of the retina within the eye leading to worsening vision), for example, cataract surgery

Tell your doctor before surgical anaesthesia that you are using Bitifrin as timolol may change effects of some medicines used during anaesthesia.

If you have a history of contact hypersensitivity to silver, you should not use this medicine.

During treatment, Bitifrin may cause a loss of fat around the eye, which may cause your eyelid crease to deepen, your eye to appear sunken (enophthalmos), your upper eyelid to droop (ptosis), the skin around your eye to tighten (involution of dermatochalasis) and the lower white part of your eye to become more visible (inferior scleral show). The changes are typically mild, but if pronounced, they can affect your field of vision. The changes may disappear if you stop taking Bitifrin.

Bitifrin may also cause your eyelashes to darken and grow, and cause the skin around the eye to darken too. The colour of your iris may also go darker. These changes may be permanent. The change may be more noticeable if you are only treating one eye. Bitifrin may cause hair growth when in contact with the skin surface.

Children and adolescents

Bitifrin should not be used in children and teenagers less than 18 years.

Other medicines and Bitifrin

Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines.

Bitifrin can affect or be affected by other medicines you are using, including other eye drops for the treatment of glaucoma.

Tell your doctor if you are using or intend to use medicines to lower blood pressure, heart medicine, medicines to treat diabetes, quinidine (used to treat heart conditions and some types of malaria) or medicines to treat depression known as fluoxetine and paroxetine.

Pregnancy and breastfeeding

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

Do not use Bitifrin if you are pregnant unless your doctor still recommends it.

Do not use Bitifrin if you are breast-feeding. Timolol may get into your breast milk. Ask your doctor for advice before taking any medicine during breast-feeding.

Driving and using machines

Bitifrin may cause blurred vision in some patients. Do not drive or use machines until the symptoms have cleared.

Bitifrin contains phosphates

This medicine contains about 0.95 mg phosphates in each millilitre. If you suffer from severe damage to the clear layer at the front of the eye (the cornea), phosphates may cause in very rare cases cloudy patches on the cornea due to calcium build-up during treatment.

3. How to use Bitifrin

Always use Bitifrin exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

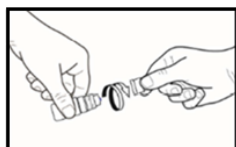
The usual dose is one drop once a day, either in the morning or in the evening in each eye that needs treatment. Use at the same time each day.

Bitifrin is a sterile solution that does not contain a preservative.

Before administering the eye drops:

- When using for the first time, practise using the dropper bottle by squeezing it slowly to deliver one drop into the air, away from the eye.
- When you are confident that you can deliver one drop at a time, choose the position that you find most comfortable for the administering the drops (sitting down, lying on your back, or standing in front of a mirror).

Instructions for use:



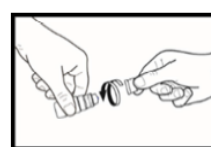
Picture 1.



Picture 2.



Picture 3.



Picture 4.

1. Wash your hands carefully before using this medicine.
2. If the packaging or bottle is damaged do not use the medicine.
3. When using the medicine for the first time, unscrew the cap after making sure that the sealed ring on the cap has not been broken. You should feel a slight resistance until this tamper-proof ring breaks off (*see picture 1*).
4. If the tamper-proof ring is loose throw it away because it may fall into your eye.
5. Tilt your head back and gently pull down your lower eyelid to form a pocket between your eye and eyelid (*see picture 2*).
6. Do not let the tip of the bottle touch your eye, eyelids or fingers. Squeeze the bottle gently in the middle to release one drop into your eye (*see picture 3*). There may be a few seconds delay between squeezing and the drop being released. Do not squeeze too hard.
7. Whilst keeping your eye closed, press your finger against the corner of the closed eye (the site where the eye meets the nose) and hold for 2 minutes. This ensures that the drop is absorbed by the eye and helps stop the medicine getting into the rest of the body.
8. Repeat steps 5, 6 and 7 in your other eye if your doctor has told you to do this.
9. After use, shake the bottle once in a downwards direction, without touching the dropper tip in order to remove any residual liquid on the tip. This will ensure delivery of subsequent drops. Screw the cap back on the bottle (*see picture 4*).

If a drop misses your eye, try again. Wipe off any excess that runs down the cheek.

If you wear contact lenses, take your lenses out before using this medicine. Wait 15 minutes after using the drops, and before you put your lenses back in.

If you use Bitifrin with another eye medicine, leave at least 5 minutes between putting in Bitifrin and the other medicine. Use any eye ointment or eye gel last.

If you use more Bitifrin than you should

If you use more Bitifrin than you should, it is unlikely to cause you any serious harm. Put your next dose in at the usual time. If you are worried, talk to your doctor or pharmacist.

If you forget to use Bitifrin

If you forget to use Bitifrin, use a single drop as soon as you remember, and then go back to your regular routine. Do not use a double dose to make up for a forgotten dose.

If you stop using Bitifrin

Bitifrin should be used every day to work properly.

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

4. Possible side effects

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

You can usually carry on taking the drops, unless the effects are serious. If you're worried, talk to a doctor or pharmacist. Do not stop using Bitifrin without speaking to your doctor.

The following side effects may be seen with Bitifrin:

Very common side effects

These may affect more than 1 in 10 patients

Affecting the eye

redness.

Affecting the eye region:

Loss of fat in the eye region which can lead to deepening of your eyelid crease, sunken eye (enophthalmos), drooping eyelid (ptosis), tightening of the skin around your eye (involution of dermatochalasis), and the lower white part of your eye to become more visible (inferior scleral show).

Common side effects

These may affect up to 1 in 10 patients

Affecting the eye

burning, itching, stinging, irritation of the conjunctiva (see-through layer of the eye), sensitivity to light, eye pain, sticky eyes, dry eyes, a feeling of something in the eye, small breaks in the surface of the eye with or without inflammation, difficulty in seeing clearly, redness and itching of the eyelids, hair growing around the eye, darkening of the eyelids, darker skin colour around the eyes, longer eyelashes, eye irritation, watery eyes, swollen eyelids, reduced vision.

Affecting other parts of the body

runny nose, headache.

Uncommon side effects

These may affect up to 1 in 100 patients

Affecting the eye

abnormal sensation in the eye, iris inflammation, swollen conjunctiva (see-through layer of the eye), painful eyelids, tired eyes, in-growing eyelashes, darkening of iris colour, eyelid has moved away from the surface of the eye, darkening of eyelashes.

Affecting other parts of the body
shortness of breath.

Side effects where the frequency is not known

Frequency cannot be estimated from the available data.

Affecting the eye

cystoid macular oedema (swelling of the retina within the eye leading to worsening vision), eye swelling, blurred vision, ocular discomfort.

Affecting other parts of the body

difficulty breathing / wheezing, symptoms of allergic reaction (swelling, redness of the eye and rash of the skin), changes in your taste sensation, slowing of heart rate, high blood pressure, difficulty sleeping, nightmare, asthma, hair loss, tiredness, skin discolouration (periocular), dizziness.

Additional side effects have been seen in patients using eye drops containing timolol or bimatoprost and so may possibly be seen with Bitifrin. Like other medicines applied into eyes, timolol is absorbed into the blood. This may cause similar side effects as seen with "intravenous" and/or "oral" beta-blocking agents. The chance of having side effects after using eye drops is lower than when medicines are for example, taken by mouth or injected. Listed side effects include reactions seen within bimatoprost and timolol when used for treating eye conditions:

- Severe allergic reactions with swelling and difficulty breathing which could be life-threatening
- Low blood sugar
- Depression; memory loss; hallucination
- Fainting; stroke; decreased blood flow to the brain; worsening of myasthenia gravis (increased muscle weakness); tingling sensation
- Decreased sensation of your eye surface; double vision; drooping eyelid; separation of one of the layers within the eyeball after surgery to reduce the pressure in the eye; inflammation of the surface of the eye, bleeding in the back of the eye (retinal bleeding), inflammation within the eye, increased blinking
- Heart failure; irregularity or stopping of the heartbeat; slow or fast heartbeat; too much fluid, mainly water, accumulating in the body; chest pain
- Low blood pressure, swelling or coldness of your hands, feet and extremities, caused by constriction of your blood vessels
- Cough, worsening of asthma, worsening of the lung disease called chronic obstructive pulmonary disease (COPD)
- Diarrhoea; stomach pain; feeling and being sick; indigestion; dry mouth
- Red scaly patches on skin; skin rash
- Muscle pain
- Reduced sexual urge; sexual dysfunction
- Weakness
- An increase in blood test results that show how your liver is working.

Other side effects reported with eye drops containing phosphates.

In very rare cases, some patients with severe damage to the clear layer at the front of the eye (the cornea) have developed cloudy patches on the cornea due to calcium build-up during treatment.

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via

HPRAs Pharmacovigilance

Website: www.hpra.ie

By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Bitifrin

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

Do not use this medicine after the expiry date which is stated on the carton and bottle. The expiry date refers to the last day of that month.

This medicine does not require any special storage condition.

After first opening of the bottle, store below 25°C and discard after 90 days.

Bitifrin should be used within 90 days after the bottle is first opened. Therefore, you must throw away the bottle 90 days after you first opened it, even if some solution is left. To help you remember, write down the date that you opened it in the space on the carton.

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. Contents of the pack and other information

What Bitifrin contains

- The active substances are bimatoprost and timolol.
Each ml of solution contains 0.3 mg of bimatoprost and 5 mg of timolol (as 6.83 mg of timolol maleate).
- The other ingredients are disodium phosphate dodecahydrate, citric acid monohydrate, sodium chloride, sodium hydroxide or hydrochloric acid, diluted (for pH-adjustment), water for injections.

What Bitifrin looks like and contents of the pack

Bitifrin is a transparent, colourless, solution.

This medicine is available in white LDPE bottles each containing 3 ml or 9 ml of solution, with multidose HDPE dropper applicator and tamper-proof HDPE screw-cap and the carton box.

Pack sizes: cartons containing 1 bottle of 3 ml solution or 1 bottle of 9 ml solution.

Not all pack sizes may be marketed.

Marketing Authorisation Holder

Farmaprojects S.A.
Calle Provença 392 6 Planta
Barcelona
08025
Spain

Manufacturer

Rafarm S.A.
Thesi Pousi Xatzi Agiou Louka
Paiania, 190 02
Greece

This medicinal product is authorised in the Member States of the European Economic Area under the following names:

Latvia: Bitifrin 0,3 mg/5 mg/ml, acu pilieni šķīdums

France: Bitifrin 0,3 mg/5 mg par mL, collyre en solution

Italy: Bitifrin

Denmark: Bitifrin

Finland: Bitifrin

Norway: Bitifrin

This leaflet was last revised in .