

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

This medicine is dispensed with a doctor's prescription only

Giotrif® 20 mg
Giotrif® 30 mg
Giotrif® 40 mg
Film-coated tablets

Each Giotrif 20 mg film-coated tablet contains 20 mg afatinib (as dimaleate).

Each Giotrif 30 mg film-coated tablet contains 30 mg afatinib (as dimaleate).

Each Giotrif 40 mg film-coated tablet contains 40 mg afatinib (as dimaleate).

Inactive ingredients and allergens in this medicine - see section 2 'Before using this medicine', 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 this medicine. If you have any further questions, consult your doctor or pharmacist.

Keep this leaflet. You may need to read it again.

This medicine has been prescribed for you. 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?

Giotrif is used as a single drug (monotherapy) to treat:

- adults patients with non-small cell lung cancer (NSCLC) identified by a change (mutation) in the gene for EGFR (Epidermal Growth Factor Receptor) whose disease is locally advanced or metastatic and have not been previously treated with tyrosine kinase inhibitors for the EGFR receptor.
- adult patients with non-small cell lung cancer (NSCLC) of squamous type whose disease is locally advanced or metastatic and has progressed during or after platinum-based chemotherapy.

Therapeutic group: antineoplastic, tyrosine kinase inhibitors.

Giotrif is a medicine that contains the active ingredient afatinib. It works by blocking the activity of a group of proteins called the ErbB family. These proteins are involved in the growth and spread of cancer cells, and can be affected by changes (mutations) in the genes that produce them. By blocking the activity of these proteins, this medicine can inhibit growth and spread of cancer cells.

2. Before using this medicine

Do not use this medicine if:

- you are sensitive (allergic) to the active ingredient afatinib or to any of the other ingredients in this medicine (see section 2 'Before using this medicine' under 'Important information about some of this medicine's ingredients' and section 6 'Additional information').
- you are pregnant or breastfeeding.

Special warnings about using this medicine

Before taking Giotrif, tell your doctor if:

- you have a low body weight of less than 50 kg, are a female, or have kidney problems. If any of these apply to you, your doctor may want to monitor you more closely as the side effects may be more pronounced.
- you have a history of lung inflammation (interstitial lung disease).
- you have liver problems. Your doctor may tell you to do certain liver tests. Treatment with this medicine is not recommended if you have severe liver disease.
- you have a history of eye problems such as severe dry eyes, inflammation of the transparent layer at the front of the eye (cornea) or ulcers involving the outer part of the eye, or if you use contact lenses.
- you have a history of heart problems. Your doctor may want to monitor you more closely.

Inform your doctor immediately if while taking this medicine:

- you develop diarrhoea. Treatment at the first signs of diarrhoea is important.
- you develop skin rash. Early treatment of skin rash is important.
- you develop new or sudden worsening of shortness of breath, possibly with a cough or fever. These could be symptoms of an inflammation of the lungs (interstitial lung disease) which can be life-threatening.
- you have severe pain in your stomach or intestines, fever, chills, nausea, vomiting, or abdominal rigidity or bloating. These could be symptoms of a tear in the wall of your stomach or intestines (gastrointestinal perforation). Also, tell your doctor if you have had gastrointestinal ulcers or diverticular disease in the past, or are being concomitantly treated with anti-inflammatory drugs (NSAIDs) (used to relieve pain and treat swelling) or steroids (used to treat inflammation and allergies), as they may increase this risk.
- you develop acute or worsening redness and pain in the eye, increased eye watering, blurred vision and/or sensitivity to light. You may need urgent treatment.

See also section 4 'Side effects'.

Children and adolescents

Giotrif is not recommended for use in children or adolescents. Do not give this medicine to children or adolescents under the age of 18 years.

Interactions with other medicines

Tell your doctor or pharmacist if you are taking, have recently taken, or might take any other medicines, including non-prescription medicines and dietary supplements.

In particular, if taken before Giotrif, the following medicines may increase the blood levels of Giotrif and therefore the risk of side effects. They should therefore be taken as far apart from the time you take Giotrif as possible. This means preferably a 6-hour interval (if you take your other medicine twice daily) or a 12-hour interval (if you take your other medicine once daily) from the time you take Giotrif:

- ritonavir, ketoconazole (except in shampoo), itraconazole, erythromycin, nelfinavir, saquinavir – used to treat different kinds of infections.
- verapamil, quinidine, amiodarone – used to treat heart conditions.
- cyclosporine A, tacrolimus – medicines that affect your immune system.

The following medicines may reduce the effectiveness of Giotrif:

- carbamazepine, phenytoin, phenobarbital – used to treat seizures.
- extract of St. John's wort (*Hypericum perforatum*), a herbal medicine used to treat depression.
- rifampicin, an antibiotic used to treat tuberculosis.

Ask your doctor if you are unsure when to take these medicines.

Giotrif may increase the blood levels of other medicines, including but not limited to:

- sulfasalazine, used to treat inflammation/infection.
- rosuvastatin, used for lowering cholesterol.

Tell your doctor before taking any of these medicines together with Giotrif.

Using this medicine and food

It is important to take this medicine on an empty stomach. Take this tablet at least 1 hour before a meal, or if you have already eaten, wait at least 3 hours before taking the tablet.

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 doctor or pharmacist for advice before taking this medicine.

Pregnancy

You should avoid becoming pregnant while taking this medicine. If you could become pregnant, you should use reliable birth control methods during treatment and for at least 1 month after taking the last dose of this medicine. This is because there may be a risk of harm to the unborn baby.

If you become pregnant while receiving this medicine, you should immediately inform your doctor. Your doctor will decide with you whether treatment should be continued or not.

If you plan to become pregnant after taking the last dose of this medicine, you should ask your doctor for advice as your body may not have fully eliminated this medicine.

Breast-feeding

Do not breast-feed while taking this medicine as a risk to the breast-fed child cannot be excluded.

Driving and using machines

If you experience treatment-related symptoms affecting your eye sight (e.g. redness and/or irritation of the eye, dry eye, tearing, light-sensitivity) or your ability to concentrate and react, it is recommended that you do not drive or use machines until the side effects disappear (see section 4 'Side effects').

Important information about some of this medicine's ingredients

This medicine contains a sugar called lactose. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.

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 and about how to take this medicine.

Only your doctor will determine your dose and how you should take this medicine.

Your doctor may adjust (increase or decrease) your dose depending on how well you tolerate this medicine.

This medicine is not recommended for patients with severe liver or kidney disease.

Do not exceed the recommended dose.

How to use this medicine:

- It is important to take this medicine on an empty stomach.
- Take this tablet at least 1 hour before a meal, or if you have already eaten, wait at least 3 hours before taking the tablet.
- Take this medicine once daily. Be sure to take it at the same time every day, this makes it easier to remember to take it.
- Do not break, chew, or crush the tablet.

- Swallow the tablet whole with a glass of water.

Giotrif is to be taken by mouth. If you have difficulties swallowing the tablet, dissolve it in a glass of water. Do not dissolve the tablet in any liquid other than water. Drop the tablet into the water without crushing it and stir occasionally, for up to 15 minutes, until the tablet is broken up into very small particles. Drink the liquid straight away. Then fill the glass again with water and drink, to make sure all the medicine is taken.

If you are not able to swallow and have a gastric tube, your doctor might suggest that the medicine is given to you via the tube.

If you have accidentally taken a higher dose

Contact your doctor or pharmacist immediately. You may experience increased side effects and your doctor may interrupt your treatment and provide supportive care.

If you have taken an overdose, or 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 the medicine

- If your next scheduled dose is more than 8 hours away, take the missed dose as soon as you remember.
- If your next scheduled dose is less than 8 hours away, skip the missed dose and take your next dose at the usual time. Then carry on taking your tablets at the regular times as usual.

Do not take a double dose (two tablets at the same time instead of one) to make up for a missed dose.

Adhere to the treatment as recommended by your doctor.

Even if your health improves, do not stop taking this medicine without consulting your doctor.

If you stop taking this medicine

Do not stop taking this medicine without first consulting your doctor. It is important to take this medicine every day, as long as your doctor prescribes it for you. If you do not take this medicine as prescribed by your doctor your cancer may grow again.

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

As with any medicine, using Giotrif may cause side effects in some users. Do not be alarmed by this list of side effects. You may not experience any of them.

Contact your doctor as soon as possible if you suffer from any of the serious side effects listed below. In some cases your doctor may need to interrupt treatment and reduce your dose of Giotrif, or stop treatment:

- **Diarrhoea** (very common side effect, affects more than 1 in 10 users)
Diarrhoea lasting more than 2 days or more severe diarrhoea may lead to fluid loss (common, may affect up to 1 in 10 users), low blood potassium (common) and worsening kidney function (common). Diarrhoea can be treated. At the first signs of diarrhoea drink plenty of fluids. Contact your doctor immediately and start appropriate anti-diarrhoeal treatment as soon as possible. You should have anti-diarrhoeal medicine available before you start taking Giotrif.

- **Skin rash** (very common side effect, affects more than 1 in 10 users)
It is important to treat the rash as soon as it appears. Tell your doctor if a rash starts. If the treatment for rash is not working and the rash is getting more severe (for example, you have peeling or blistering of the skin) you should notify your doctor immediately, since your doctor may decide to stop your treatment with Giotrif. Rash may occur or worsen in areas exposed to sun. It is recommended to protect yourself from the sun with protective clothing and sunscreen.
- **Inflammation of the lungs** (uncommon side effect, affects 1–10 in 1,000 users) called 'interstitial lung disease'. Tell your doctor immediately if you develop new or sudden worsening of shortness of breath, possibly with a cough or fever.
- **Eye irritation or inflammation**
Eye irritation or inflammation may occur [conjunctivitis/dry eye (common side effects) and keratitis (uncommon side effect)]. Tell your doctor if you have sudden or worsening eye symptoms such as pain or redness or dry eye.

If you experience any of the symptoms above, contact your doctor as soon as possible.

Additional side effects:

Very common side effects (affect more than 1 in 10 users):

- mouth sores and inflammation
- nail infection
- decreased appetite
- bleeding from the nose
- nausea
- vomiting
- itching
- dry skin

Common side effects (affect 1–10 in 100 users):

- pain, redness, swelling or peeling of the skin of your hands and feet
- increased levels of the liver enzymes (AST–aspartate aminotransferase and ALT–alanine aminotransferase) in blood tests
- inflammation of the lining of the bladder with burning sensation during urination and frequent, urgent need to urinate (cystitis)
- abnormal taste sensations (dysgeusia)
- stomach pain, indigestion, heartburn
- lip inflammation
- decreased weight
- runny nose
- muscle spasms
- fever
- nail problems

Uncommon side effects (affect 1–10 in 1,000 users):

- inflammation of the pancreas (pancreatitis)
- occurrence of a tear in the wall of your stomach or intestines (gastrointestinal perforation)
- abnormal growth of your eyelashes (including misdirected growth that may lead to damage to the eye surface)

Rare side effects (affect 1–10 in 10,000 users):

- severe blistering or peeling of skin (suggestive of Stevens-Johnson syndrome and toxic epidermal necrolysis).

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.

Reporting side effects

You can report side effects to the Ministry of Health by following the 'Reporting Side Effects of Drug Treatment' link on the Ministry of Health home page (www.health.gov.il), which opens an online form for reporting side effects, or 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 your doctor.
- Do not use this medicine after the expiry date which is stated on the carton package, the blister wrapper, and the blister. The expiry date refers to the last day of that month.
- **Storage conditions:** Store below 25°C. Keep in the original package in order to protect from moisture and light. Use the tablets in the blister within 14 days of first opening the blister wrapper.
- Do not throw away 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, this medicine also contains:
Giotrif 20 mg: lactose monohydrate, cellulose microcrystalline, crospovidone, magnesium stearate, hypromellose 2910, titanium dioxide, silica colloidal anhydrous, talc, macrogol 400, polysorbate 80.
Giotrif 30 mg: lactose monohydrate, cellulose microcrystalline, crospovidone, magnesium stearate, hypromellose 2910, talc, silica colloidal anhydrous, macrogol 400, titanium dioxide, Indigo carmine aluminium lake, polysorbate 80.
Giotrif 40 mg: lactose monohydrate, cellulose microcrystalline, crospovidone, magnesium stearate, hypromellose 2910, titanium dioxide, silica colloidal anhydrous, talc, macrogol 400, polysorbate 80, Indigo carmine aluminium lake.

Each Giotrif 20 mg film-coated tablet contains 124 mg lactose monohydrate.

Each Giotrif 30 mg film-coated tablet contains 186 mg lactose monohydrate.

Each Giotrif 40 mg film-coated tablet contains 248 mg lactose monohydrate.

- **What the medicine looks like and contents of the pack:**
 - Giotrif 20 mg: white to yellowish, round, biconvex, bevel-edged film-coated tablet. One side debossed with 'T20' and the other side with the Boehringer Ingelheim logo.
 - Giotrif 30 mg: dark blue, round, biconvex, bevel-edged film-coated tablet. One side debossed with 'T30' and the other side with the Boehringer Ingelheim logo.
 - Giotrif 40 mg: light blue, round, biconvex, bevel-edged film-coated tablet. One side debossed with 'T40' and the other side with the Boehringer Ingelheim logo.
- Each blister contains 7 film-coated tablets, packaged in the blister wrapper with a desiccant. Do not swallow the desiccant.
- A total of 7, 14, or 28 film-coated tablets in a carton package.
- Not all pack sizes may be marketed.

- **Registration holder and importer's name and address:** Boehringer Ingelheim Israel Ltd., 89 Medinat HaYehudim St., POB 4124, Herzlia Pituah 4676672.
- **This leaflet was revised in June 2025.**
- **Registration number of the medicine in the Ministry of Health's National Drug Registry:**

Giotrif 20 mg	151-47-33984-00
Giotrif 30 mg	151-48-33986-00
Giotrif 40 mg	151-49-33987-00