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

The dispensing of this medicine requires a physician's prescription

Giotrif® 20 mg
Giotrif® 30 mg
Giotrif® 40 mg
Giotrif® 50 mg

Film-coated tables

Each film-coated tablet of Giotrif 20 mg contains 20 mg afatinib (as dimaleate).
Each film-coated tablet of Giotrif 30 mg contains 30 mg afatinib (as dimaleate).
Each film-coated tablet of Giotrif 40 mg contains 40 mg afatinib (as dimaleate).
Each film-coated tablet of Giotrif 50 mg contains 50 mg afatinib (as dimaleate).

Inactive ingredients and allergens in this medicine: See in Section 2 'Important information about some of the ingredients in this medicine' 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, refer to your physician or pharmacist. 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?

This medicine is used as a monotherapy to treat:

- Adult patients who have non-small cell lung cancer (NSCLC), identified by a mutation in the EGFR (Epidermal Growth Factor Receptor) gene, whose illness is in an advanced localized or metastatic stage and who have not yet been treated with tyrosine kinase inhibitors for EGF receptor.
- Adult patients who have the squamous type of non-small cell lung cancer (NSCLC), whose illness in an advanced localized or metastatic stage and had progressed during or after chemotherapy.

Therapeutic group: Antineoplastic, tyrosine kinase inhibitors.

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 that this medicine contains (see Section 6 in the leaflet).
- You are pregnant or breast-feeding.

Special warnings about using this medicine:
Before starting treatment with Giotrif, tell your physician if:

- Your body weight is less than 50 kg, or you are a woman, or you have kidney problems. If any of these criteria apply to you, your physician may 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 physician may do some liver tests. Treatment with this

medicine is not recommended if you have a severe liver disease.
- You use contact lenses and/or have a history of eye problems such as severe dry eyes, inflammation of the outer part of the eye (cornea) or ulcers involving the outer part of the eye.
- You have a history of heart problems. Your physician may want to monitor you more closely.

During treatment with this medicine consult your physician immediately:
- If you develop diarrhoea. It is very important to treat diarrhoea as soon as it appears.
- If you develop skin rash. It is important to treat the rash early as soon as it occurs.
- If you develop new or sudden worsening of shortness of breath, possibly with a fever or cough. These could be symptoms of an inflammation of the lungs called 'interstitial lung disease' which could be life-threatening.
- If you have severe pain in your stomach or intestines, with fever, chills, nausea, vomiting, or abdominal rigidity or bloating, as these could be symptoms of a tear in the wall of your stomach or intestines ('gastrointestinal perforation'). Also, tell your physician if you had gastrointestinal ulcers or diverticular disease in the past, or are taking anti-inflammatory drugs (NSAIDs) (used to relieve pain or swelling) or steroids (used for inflammation and allergies), as these medicines may increase this risk.
- If you develop acute or worsening redness or pain in the eye, increased eye watering, blurred vision and/or sensitivity to light. You may need urgent treatment.

See possible side effects in Section 4, 'Side Effects'.

Children and adolescents
Giotrif has not been studied in patients under the age of 18 years. This medicine should not be used for children or adolescents under the age of 18 years.
This medicine is not recommended if you have a severe liver or kidney disease.

Other medicines and Giotrif

If you are taking or have recently taken other medicines including nonprescription medicines and nutritional supplements, tell your physician or pharmacist.
If taken before Giotrif, the following medicines may increase the blood levels of Giotrif and therefore aggravates Giotrif side effects. Therefore these medicines should be taken as far as possible from the time of taking Giotrif. This means preferably 6 hours (for medicines taken twice a day) or 12 hours (for medicines taken once a day) from the time you took Giotrif:
- Ritonavir, ketoconazole (except in shampoo), itraconazole, erythromycin, nelfinavir, saquinavir - used to treat various kinds of infections.
- Verapamil, quinidine, amiodarone - used to treat heart problems.
- Cyclosporine A, tacrolimus - medicines that affect your immune system.

Taking the following medicines may reduce the effectiveness of Giotrif:
- Carbamazepine, phenytoin, phenobarbital - used to treat epilepsy.
- St. John's Wort (Hypericum perforatum) - a herbal medicine to treat depression.
- Rifampicin - an antibiotic used to treat tuberculosis.

Ask your physician if you are not sure when to take these medicines.

Giotrif may raise the amount of other medicines in your blood. Those medicines may include but are not limited to:
- Sulfasalazine - used to treat inflammation or infection.
- Rosuvastatin - used for lowering cholesterol level.

Tell your physician if you are taking any of these medicines together with Giotrif.

Pregnancy, breastfeeding and fertility

If you are pregnant or breastfeeding, think you may be pregnant or are planning to become pregnant, consult a physician or pharmacist before taking this medicine.
Avoid becoming pregnant while taking Giotrif. If there is a possibility of you getting pregnant, you should use reliable birth control during treatment and for at least a month after taking the last dose of Giotrif, because there may be a risk of harm to the fetus.
If you become pregnant while taking this medicine, you should immediately inform your physician. Your physician will decide whether treatment should be continued or not.
If you are planning to become pregnant after taking the last dose of this medicine, consult your physician because the medicine may not be entirely eliminated from your body.
Do not breastfeed while taking this medicine as any risk to your child cannot be excluded.

Driving and using machines
If you experience treatment-related symptoms affecting your eyesight (e.g. eye irritation, dry eye, tearing, light-sensitivity) or your ability to concentrate and react, it is recommended that you do not drive or operate machines until these symptoms disappear (see also Section 4 – 'Side Effects').

Important information about some of the ingredients in this medicine
The medicine contains a sugar called lactose. If you have intolerance to certain sugars, consult a physician before beginning treatment.

3. How to use this medicine?

Always use according to the physician's instructions. Check with your physician or the pharmacist if you are not sure about your dose or about how to take this medicine. Only your physician will determine your dose and how you should take the medicine. **Do not exceed the recommended dose.**

How to take the medicine
- It is important to take this tablet on an empty stomach.
- Take this tablet at least one hour before meals, or if you have already eaten, wait at least 3 hours before taking this tablet.
- Take this tablet once a day at the same time each day. This makes it easier to remember to take this medicine.
- Do not break, chew, or crush the tablet.
- Swallow the tablet whole with a glass of water.

Giotrif tablets are to be taken by mouth. If you have difficulty swallowing the tablet whole, dissolve it in a glass of water. No other liquids should be used. Drop the tablet into a glass of water whole, without crushing or breaking it, and stir occasionally for up to 15 minutes until the tablet has broken into small particles. Drink the tablet straight away. Then refill the glass with water and drink it to make sure all the medicine is taken. If you are not able to swallow and you have a gastric tube, your physician might recommend that you take the medicine via this tube.

If you have accidentally taken a higher dose, contact your physician immediately. You may experience increased side effects and your physician may decide to stop your treatment and recommend supportive care.
If you have taken an overdose, or if a child has accidentally swallowed some medicine, go immediately to a hospital emergency room and bring the medicine package with you.

If you forget to take the medicine,
- If the time for taking the next dose is more than 8 hours away, take the dose as soon as you remember.

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

Do not take a double dose to make up for a missed dose.

If you stop taking this medicine,
Do not stop taking this medicine without first consulting your physician. It is important to persist with the treatment as recommended by the physician. If you do not take this medicine as prescribed by your physician your cancer may grow again.
Do not take medicines in the dark! Check the label and dose <u>each time</u> you take the medicine. Wear glasses if you need them.
If you have any further questions about using this medicine, consult your physician or the pharmacist.

4. <u>Side effects</u>

Like all medicines, taking Giotrif may cause side effects in some people. Do not be alarmed by this list of side effects. You may not experience any of them.

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

- **Diarrhoea (very common, may affect more than 1 in 10 people)**
  Diarrhoea lasting more than 2 days or more severe diarrhoea may lead to fluid loss (common), decreased blood potassium levels (common) and deterioration of kidney function (common). Diarrhoea can be treated. At the first signs of diarrhoea drink plenty of fluids. Contact your physician immediately and start appropriate anti-diarrhoeal treatment as soon as possible. You should have anti-diarrhoeal medicine available prior to taking Giotrif.
- **Skin rash (very common, may affect more than 1 in 10 people)**
  It is important to treat the rash as soon as it occurs. Tell your physician if you develop a rash. If treatment for the rash is not effective and the rash becomes more severe (for example, you have peeling or blistering of the skin) you should notify your physician immediately, as your physician may decide to stop the treatment with Giotrif. A rash may occur or become more severe in areas exposed to sun. Sun protection with protective clothing and sunscreen is recommended.
- **Inflammation of the lungs (uncommon, may affect up to 1 in 100 people)**
  Called - 'interstitial lung disease'. Tell your physician immediately if you develop new or sudden worsening of shortness of breath, possibly with a fever or cough.
- **Eye irritation or inflammation**
  Eye irritation or inflammation (conjunctivitis is common and keratitis is uncommon). Tell your physician if you develop new or sudden worsening of eye symptoms such as pain, redness or dry eye.

Additional side effects
Very common side effects (may affect more than 1 in 10 people):
- Mouth sores and inflammation
- Nail infection
- Decreased appetite
- Bleeding from the nose
- Nausea
- Vomiting
- Dry and itchy skin

Common side effects (may affect 1-10 in 100 people):

- Pain, redness, swelling or peeling of the skin of your palms and feets
- Increased levels of liver enzymes in a blood test
- Inflammation of the bladder with burning sensation during urination and frequent, urgent need to urinate
- Abnormal taste sensations
- Stomach pain, indigestion, heartburn
- Lip infection
- Decreased weight
- Runny nose
- Muscle spasms
- Fever
- Nail disorders

Uncommon side effects (may affect up to 1-10 in 1,000 people):

- Pancreatitis (inflammation of the pancreas)
- Occurrence of a tear in the wall of your stomach or intestines (gastrointestinal perforation)

Rare side effects (may occur in up to one in 1,000 people):

- Severe blistering or peeling of skin (may indicate 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 physician.

You can report side effects to the Ministry of Health by following the link 'Reporting Side Effects of Drug Treatment' on the Ministry of Health home page (www.health.gov.il) which links to an online form for reporting side effects. 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 reach and sight of children and/or infants. Do not induce vomiting unless explicitly instructed to do so by a physician.
Do not use the medicine after the expiry date (exp. date) appearing on the package and blister pack. The expiry date refers to the last day of that month.
Storage conditions
Store at room temperature (below 25˚C).
Store in the original package to protect from moisture and light.
Use the tablets in the blister tray within 14 days from first opening the blister wrap.

6. Additional information

In addition to the active ingredient this medicine also contains:
Lactose monohydrate, cellulose microcrystalline, silica colloidal anhydrous, crospovidone, magnesium stearate, hypromellose 2910, macrogol 400, titanium dioxide, talc, polysorbate 80.

Additional ingredient in Giotrif 30 mg, Giotrif 40 mg, and Giotrif 50 mg: Indigo carmine aluminium lake.

Each Giotrif 20 mg tablet contains approximately 124 mg lactose.
Each Giotrif 30 mg tablet contains approximately 186 mg lactose.

Each Giotrif 40 mg tablet contains approximately 248 mg lactose.
Each Giotrif 50 mg tablet contains approximately 310 mg lactose.

What does the medicine look like and what are the contents of the package:
- Giotrif 20 mg film-coated tablets are round, convex on both sides and white to yellowish. "T20" is stamped on one side and Boehringer Ingelheim logo on the other side.
- Giotrif 30 mg film-coated tablets are round, convex on both sides and dark blue. "T30" is stamped on one side and Boehringer Ingelheim logo on the other side.
- Giotrif 40 mg film-coated tablets are round, convex on both sides and light blue. "T40" is stamped on one side and Boehringer Ingelheim logo on the other side.
- Giotrif 50 mg film-coated tablets are oval, convex on both sides and dark blue. "T50" is stamped on one side and Boehringer Ingelheim logo on the other side.
- There are 7 tablets in each blister, packed with a desiccant inside the aluminum pack. Do not swallow the desiccant.
- Total of 7, 14 or 28 tablets per package.

Not all package sizes may be marketed.

Manufacturer: Boehringer Ingelheim Pharma, Ingelheim am Rhein, Germany
Registration holder and importer: Boehringer Ingelheim Israel Ltd, 89 Medinat Ha-Yehudim St., P.O.B. 4124, Hertzeliya Pituach 4676672, Israel

This leaflet was reviewed and approved by the Ministry of Health in December 2016, and revised in December 2019 in accordance with Ministry of Health guidelines.

Registration number of the medicine in the National Drug Registry of the Ministry of Health:

Giotrif 20 mg film-coated tablets	151-47-33984
Giotrif 30 mg film-coated tablets	151-48-33986
Giotrif 40 mg film-coated tablets	151-49-33987
Giotrif 50 mg film-coated tablets	151-50-33988