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

This medicine is dispensed with a doctor's prescription only

Braftovi 75 mg

Capsules

Active ingredient: encorafenib 75 mg

Inactive ingredients and allergens: See 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.
This medicine has been prescribed to treat your illness. Do not pass it on to others. It may harm them, even if it seems to you that their illness is similar to yours.

1. What is this medicine intended for?

Braftovi (encorafenib) is a kinase inhibitor indicated for use:

- in combination with binimetinib, for the treatment of adult patients with unresectable or metastatic melanoma with a BRAF V600E or BRAF V600K mutation.
- in combination with cetuximab, for the treatment of adult patients with metastatic colorectal cancer with a BRAF V600E mutation, as detected by an approved test after prior therapy.
- in combination with binimetinib, for the treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) adenocarcinoma with a BRAF V600E mutation, as detected by an approved test.

Therapeutic group: antineoplastic agents, protein kinase inhibitors.

2. Before using this medicine

Before beginning the treatment, your doctor will perform a test to make sure that Braftovi is right for you.
For women who are of childbearing age - your doctor will do a pregnancy test before you start treatment.

Do not use this medicine if:

You are sensitive (allergic) to encorafenib or to any of the other ingredients in this medicine (see section 6).

Special warnings about using this medicine

- Braftovi is not intended for treatment of wild-type BRAF melanoma or wild-type BRAF colorectal cancer or wild-type non-small cell lung cancer (NSCLC).
- New primary malignancies
- Tumor promotion in BRAF wild-type tumors
- Increased risk of appearance of skin side effects, when Braftovi is administered as monotherapy

Before taking Braftovi, tell your doctor about all of your medical problems, including if:

- you have had bleeding problems
- you have eye problems

- you have heart problems, including a condition called long QT syndrome, severe or uncontrolled heart failure or clinically significant bradyarrhythmias
- you have been told that you have low blood levels of potassium, calcium, or magnesium
- you have liver or kidney problems
- you are pregnant or plan to become pregnant. Braftovi can harm your unborn baby (see 'Pregnancy, breastfeeding and fertility')
- you are breastfeeding or plan to breastfeed (see 'Pregnancy, breastfeeding and fertility')

Children and adolescents
There is no information about the safety and effectiveness of use of this medicine in children.
This medicine is not intended for children and adolescents under the age of 18.

Tests and follow-up
- New primary malignancies
  Your doctor will check your skin before starting treatment, every 2 months during treatment, and up to 6 months after you stop taking Braftovi. This is done to monitor suspicious skin lesions.
- Uveitis and other eye problems
  Your doctor will examine your eyes at each visit to identify development of new visual disturbances or any worsening.
- QT prolongation
  Your doctor will do electrolyte tests before starting and during treatment.
- Heart function
  Your doctor will check your heart function before starting and during treatment with Braftovi.
- Liver function
  Your doctor will perform liver function blood tests before starting and during treatment with Braftovi.

Drug interactions
If you are taking or have recently taken other medicines, including nonprescription medications and dietary supplements, tell your doctor or pharmacist. In particular, tell your doctor if you are taking any medicine in this list or any other medicine:
- some medicines to treat fungal infections such as posaconazole
- avoid coadministration with medicines that are substrates of/broken down by CYP3A4 such as hormonal contraceptives
- medicines typically used to treat high blood pressure such as diltiazem
- avoid coadministration of this medicine with strong or moderate CYP3A4 inhibitors or inducers
- avoid coadministration of this medicine with medicines that lead to QT prolongation
- medicines that affect or are affected by certain drug transport proteins (OATP1B1, OATP1B3, BCRP).

Using this medicine and food
Braftovi can be taken with or without food. Avoid grapefruit during treatment with Braftovi.
Grapefruit products may increase the concentration of Braftovi in your body.

Pregnancy, breastfeeding and fertility

Pregnancy

Women of childbearing age must use effective, non-hormonal contraception during treatment with Braftovi and for two weeks after the last dose of Braftovi.
Birth control methods that contain hormones (such as birth control pills, injections or transdermal methods such as patches) may not work properly during treatment with Braftovi.
Talk to your doctor about the birth control methods that are right for you during the treatment period.
Your doctor will do a pregnancy test before treatment begins.
Tell your doctor right away if you are pregnant or think you might be pregnant.

Breastfeeding

Do not breastfeed during treatment with Braftovi and for 2 weeks after the last dose of Braftovi. It is not known if Braftovi passes into breast milk. Talk to your doctor about the best way to feed your baby during the treatment period.

Fertility

Braftovi may cause fertility problems in men. Talk to your doctor if this is a concern for you.

Driving and using machines

Braftovi can affect your ability to drive or use machines. Avoid driving or using machines if you have problems with your vision or have any other side effects that can affect your ability to drive or use machines. Talk to your doctor if you are not sure you can drive.

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 or about how to take this medicine.
Only your doctor will determine your dose and how you should take this medicine.
The recommended dosage is usually:

For treatment of melanoma or non-small cell lung cancer (NSCLC):

6 capsules of 75 mg once daily (corresponding to a daily dose of 450 mg) in combination with binimetinib.
For more information about binimetinib, refer to the medicine’s approved patient information leaflet.

For treatment of colorectal cancer:

4 capsules of 75 mg once daily (corresponding to a daily dose of 300 mg).
You will also receive treatment with another medicine, cetuximab, administered intravenously by the medical staff.
For more information about cetuximab, refer to the medicine’s approved patient information leaflet.

Do not exceed the recommended dose.

If you suffer from vomiting

If you vomit at any point after taking Braftovi, do not take an extra dose. Take your next dose as scheduled.

If you have taken an overdose of Braftovi
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 Braftovi
If you miss a dose of Braftovi, take it as soon as you remember. However, if your next dose is in less than 12 hours, take your next dose at your regular time. Adhere to the treatment as recommended by your doctor. Do not take a double dose to make up for the forgotten dose.
Even if your health improves, do not stop taking this medicine without consulting your doctor.

If you stop taking Braftovi
If you stop treatment with binimetinib or cetuximab, contact your doctor about your Braftovi treatment. Your Braftovi dose may need to be changed or stopped.

Do not take medicines in the dark! Check the label and dose <u>every time</u> 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
Like with all medicines, using Braftovi may cause side effects in some users. Do not be alarmed by this list of side effects. You may not experience any of them.

Serious side effects
<u>Risk of new skin cancers:</u> Braftovi, when used alone, or when taken with binimetinib or cetuximab, may cause other types of skin cancer such as cutaneous squamous cell carcinoma or basal cell carcinoma.
Contact your doctor about your risk for these types of cancer.
Check your skin and **contact your doctor right away** if you notice any skin changes, including a:
- new wart
- skin sore or reddish bump that bleeds or does not heal
- change in size or color of a mole.

Your doctor will check your skin for new malignant growths before treatment, every 2 months during treatment and for up to 6 months after you stop taking Braftovi.
Your doctor will also need to check for types of cancers that may not necessarily appear on the skin.
Tell your doctor about any new symptom that develops during treatment with Braftovi.

Heart problems, including heart failure:
Braftovi, when taken with binimetinib, can cause heart problems.
Contact your doctor immediately if you experience any of the following signs and symptoms of heart problems:
- feeling like your heart is beating or pounding strongly
- shortness of breath
- swelling in your hands, ankles, legs or feet
- feeling faint or dizzy

Liver problems:
Braftovi, when taken with binimetinib, can cause liver problems.

Contact your doctor if you experience any of the following signs and symptoms of liver problems:
- yellowing of the skin or eyes
- dark or brown urine (tea-colored)
- nausea or vomiting
- loss of appetite
- fatigue
- bruising
- bleeding

Bleeding problems:
Braftovi, when taken with binimetinib or cetuximab, can cause serious bleeding problems, including in your stomach or brain, that can lead to death.
Contact your doctor and get medical help right away if you feel signs of bleeding, including:
- headaches, dizziness, or feeling weak
- coughing up blood or blood clots
- vomiting blood or your vomit looks like “coffee grounds”
- red or black stool that look like tar

Eye problems:
Braftovi, when taken with binimetinib, can cause eye problems.
Tell your doctor right away if you have any new symptoms or worsening of existing symptoms of the following eye problems:
- blurred vision, loss of vision, or other vision changes
- seeing colored dots
- seeing halos (blurred outlines around objects)
- eye pain, swelling, or redness

Changes in the electrical activity of your heart called QT prolongation:
QT prolongation can cause irregular heartbeats that can be life threatening.
Your doctor will do tests before and during treatment with Braftovi with binimetinib or cetuximab to check your body salts (electrolytes). Tell your doctor right away if you feel weak, lightheaded, dizzy or if you feel your heart beating irregularly or fast while taking Braftovi with binimetinib or cetuximab. These symptoms may be related to QT prolongation.

Very common side effects (affect more than one in ten users) **that appear when Braftovi and binimetinib are taken together for treatment of melanoma:**
- fatigue
- nausea
- vomiting
- abdominal pain
- pain or swelling of your joints (arthralgia)
- fever
- constipation
- myopathy (muscle damage)
- pain in the extremities
- hyperkeratosis
- rash
- dry skin
- alopecia
- itching
- headache
- dizziness

- peripheral neuropathy
- bleeding
- anemia
- leukopenia
- lymphopenia
- neutropenia
- increased levels of creatinine
- increased levels of GGT
- increased levels of ALT
- increased levels of AST
- hyperglycemia (high blood sugar)
- increased levels of ALKP
- hyponatremia
- increased levels of magnesium

Very common side effects (affect more than one in ten users) **that appear when Braftovi and cetuximab are taken together for treatment of colorectal cancer:**
- fatigue
- nausea
- diarrhea
- acne-like rash (dermatitis acneiform)
- abdominal pain
- decreased appetite
- pain or swelling of your joints (arthralgia)
- rash
- fever
- constipation
- vomiting
- myopathy (muscle damage)
- pain in the extremities
- itching
- melanocytic nevus
- dry skin
- headache
- peripheral neuropathy
- bleeding
- insomnia
- anemia
- lymphopenia
- increased activated partial thromboplastin time
- decreased levels of magnesium
- increased levels of ALKP
- increased levels of ALT
- increased levels of AST
- low blood potassium level
- hyponatremia

Very common side effects (affect more than one in ten users) **that appear when Braftovi and binimetinib are taken together for treatment of non-small cell lung cancer (NSCLC):**
- fatigue
- edema
- fever
- nausea
- diarrhea

- vomiting
- abdominal pain
- constipation
- vision impairment
- musculoskeletal pain
- rash
- itching
- dry skin
- alopecia
- shortness of breath
- cough
- dizziness
- headache
- decreased appetite
- bleeding
- hypertension
- left ventricular dysfunction/cardiomyopathy
- weight gain
- insomnia
- anemia
- lymphopenia
- thrombocytopenia
- leukopenia
- neutropenia
- increased levels of creatinine
- hyperglycemia (high blood sugar)
- increased levels of creatine kinase
- increased levels of lipase
- increased levels of ALT
- hypoalbuminemia
- increased levels of AST
- increased levels of ALKP
- high blood potassium level (hyperkalemia)
- hyponatremia
- increased levels of serum amylase
- hypocalcemia (low blood calcium levels)

Common side effects (affect up to one in ten users) **that appear when Braftovi and binimetinib are taken together:**
- facial paresis
- pancreatitis
- inflammation of fatty tissue (panniculitis)
- sensitivity to light (photosensitivity)
- drug hypersensitivity

Side effects of unknown frequency (side effects whose frequency has not yet been determined) **that appear when Braftovi and binimetinib are taken together:**
- hand-foot syndrome (palmar-plantar erythrodysesthesia syndrome)
- thickening of the cornified layer of the skin (hyperkeratosis)
- skin redness (erythema)
- back pain
- pneumonia
- medical device-associated infection
- taste disorder (dysgeusia)
- edema

- pleural effusion

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 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 the reach and sight of children and/or infants. Do not induce vomiting unless explicitly instructed to do so by a doctor.
- Do not use the medicine after the expiry date (exp. date) which is stated on the package/bottle.
  The expiry date refers to the last day of that month.

Storage conditions:
- Store at a temperature below 25°C.
- After first opening: use the medicine within 45 days, and store at a temperature below 25°C.
- Do not throw away medicines via wastewater or household waste. Ask the 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:
- Capsule content:
  copovidone, microcrystalline cellulose, succinic acid, poloxamer 188, crospovidone, colloidal silicon dioxide, magnesium stearate.
- Capsule shell:
  gelatin, titanium dioxide, iron oxide red, iron oxide yellow, ferrosoferric oxide.
- Monogramming ink:
  pharmaceutical glaze (shellac-45% in ethanol), isopropyl alcohol, ferrosoferric oxide, N-Butyl alcohol, propylene glycol, ammonium hydroxide 28%.

What the medicine looks like and contents of the pack:
Braftovi 75 mg hard capsules
The hard capsule has a flesh-colored opaque cap and white opaque body, with a stylized "A" printed on the cap and "LGX 75mg" printed on the body.
Braftovi 75 mg is available in bottles of 90 capsules, 2 bottles in each pack (180 capsules).

Registration holder's name and address:
Medison Pharma Ltd., 10 Hashiloach Street, Petach Tikva, POB 7090, Israel.

Manufacturer's name and address:
Array BioPharma inc., 3200 Walnut Street Boulder, Colorado 80301, USA

Revised in August 2025.

Registration number of the medicine in the Ministry of Health's National Drug Registry: 167-76-35722-00