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

This medicine is dispensed with a doctor's prescription only

Mektovi 15 mg

Film-coated tablets

Active ingredient: Each film-coated tablet contains 15 mg binimetinib

Inactive ingredients and allergens: see section 2 '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.

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?

Mektovi (binimetinib) is a kinase inhibitor indicated for use:

- in combination with encorafenib, for the treatment of adult patients with metastatic or unresectable melanoma with a BRAF V600E or BRAF V600K mutation.
- in combination with encorafenib, for the treatment of adult patients with metastatic lung cancer known as non-small cell lung cancer (NSCLC) adenocarcinoma with a BRAF V600E mutation.

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 Mektovi is right for you. See the 'Tests and follow-up' section.

Do not use this medicine if:

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

Special warnings about using this medicine

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

- you have heart problems
- you have had blood clots
- you have bleeding problems
- you have eye problems
- you have muscle problems
- you have high blood pressure
- you have lung or breathing problems
- you have liver or kidney problems
- you are pregnant or plan to become pregnant. Mektovi can harm your unborn baby (see section 'Pregnancy, breastfeeding and fertility').
- you are breastfeeding or plan to breastfeed (see section 'Pregnancy, breastfeeding and fertility').

Children

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
Before starting use of the medicine and during treatment, your doctor will refer you for the following tests:

- Heart function using echocardiography or MUGA scan - before starting treatment, one month after starting treatment and every 2-3 months during treatment.
- Eye examinations - your doctor will examine your eyes at each visit to identify development of new visual disturbances or any worsening.
- Liver function tests - before starting treatment and every month during treatment.
- Testing creatine phosphokinase (CPK) and creatinine levels - before starting treatment and periodically during treatment.
- Testing new or advanced pulmonary symptoms or findings.
- Skin examination before starting treatment with Mektovi in combination with encorafenib, every two months during treatment and up to six months after completion of treatment to detect new skin cancer.
- Tests for types of cancer that may not appear on the skin.

Drug interactions
If you are taking or have recently taken other medicines, including nonprescription medications and dietary supplements, tell your doctor or pharmacist.

Using this medicine and food
Mektovi can be taken with or without food.

Pregnancy, breastfeeding and fertility
Pregnancy
Mektovi can harm your unborn baby. If you are a woman who is able to become pregnant, you should use reliable birth control while taking Mektovi, and you should continue to use reliable contraception for at least 30 days after taking your final dose. Talk to your doctor about birth control that is right for you during the treatment period. Your doctor will do a pregnancy test before treatment with Mektovi begins. If you become pregnant while taking Mektovi, contact your doctor right away.

Breastfeeding
Do not breastfeed during treatment with Mektovi and for 3 days after the final dose. It is not known if Mektovi passes into breast milk. Talk to your doctor about the best way to feed your baby during this time.

Driving and using machines
Mektovi 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.

Important information about some of this medicine's ingredients
Mektovi contains lactose. If you have been told by your doctor that you have an intolerance to some sugars, talk to 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 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:
45 mg (3 tablets of 15 mg) twice daily, taken about 12 hours apart in combination with the medicine, encorafenib.
Your doctor may change your dose of Mektovi, temporarily or completely stop your treatment if you suffer from certain side effects.
For more information about encorafenib, refer to the medicine's approved patient information leaflet.

Do not exceed the recommended dose.

Method of administration - Swallow the tablets whole with water.
No information is available regarding crushing, splitting or chewing of the tablets.

If you suffer from vomiting
Do not take an extra dose if you vomit after taking Mektovi. Take your next dose as scheduled.

If you have accidentally taken a higher dose of Mektovi
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 Mektovi
If you miss a dose of Mektovi, take it as soon as you remember. However, if the delay in taking the dose is more than 6 hours, skip this dose and take your next dose at the usual time and consult your doctor.
Do not take an extra dose to make up for the forgotten 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.
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 Mektovi in combination with encorafenib, may cause side effects in some users. Do not be alarmed by this list of side effects. You may not experience any of them.

Severe side effects
Mektovi may cause serious side effects. Report to your doctor immediately if you suffer from the following serious side effects:
<u>Risk of new skin cancer:</u>
The use of Mektovi in combination with encorafenib may cause types of skin cancer called squamous cell carcinoma (SCC) or basal cell carcinoma (BCC).
Talk to your doctor about your risk for these cancers.
Check your skin and inform your doctor right away of any change in your skin, including:
- New wart
- Sore or reddish bump that bleeds or does not heal
- Change in size or color of mole

Talk to your doctor about any new symptom that develops during the combination treatment with Mektovi and encorafenib.

Heart problems, including heart failure:
Use of Mektovi in combination with encorafenib may cause heart problems.
Talk to your doctor right away if you have any symptoms of heart problems, such as:
- shortness of breath
- feeling like your heart is pounding or racing
- swelling of your ankles and feet
- feeling lightheaded

Blood clots:
Mektovi in combination with encorafenib can cause blood clots in your arms or legs, and if a blood clot travels to your lungs, it can lead to death. Get medical treatment right away if you have the following symptoms:
- chest pain
- sudden shortness of breath or trouble breathing
- pain in your legs with or without swelling
- swelling in your arms and legs
- a cool pale arm or leg

Eye problems:
Mektovi in combination with encorafenib can cause serious eye problems.
Talk to your doctor right away if you have any new symptoms or worsening of eye problems, such as:
- blurred vision, loss of vision, or other vision changes
- seeing colored dots
- seeing halos (blurred outline around objects)
- eye pain, swelling, or redness

Lung or breathing problems:
Mektovi in combination with encorafenib can cause lung or breathing problems. Talk to your doctor right away if you have any worsening or symptoms of lung or breathing problems, such as:
- shortness of breath
- cough

Liver problems:
Mektovi in combination with encorafenib may cause liver problems. Talk to your doctor right away if you have any symptoms of liver problems, such as:
- yellowing of your skin or the white part of your eyes
- dark or brown (tea-colored) urine
- nausea or vomiting
- loss of appetite
- fatigue
- bruising
- bleeding

Muscle problems (rhabdomyolysis):
Mektovi in combination with encorafenib can cause muscle problems that can be severe. Use of Mektovi may increase your blood levels of the enzyme creatine phosphokinase (CPK), which can be a sign of muscle damage. Your doctor will do blood tests to check your blood levels of CPK before and during treatment. Talk to your doctor right away if you have any of the following symptoms:
- weakness

- muscle pain
- dark, reddish urine

Bleeding problems:
Mektovi, when taken with encorafenib, can cause serious bleeding problems, including in your brain and stomach, that can lead to death. Tell your doctor right away if you have any abnormal bleeding or signs of bleeding, including:
- headaches, dizziness, or weakness
- coughing up blood or blood clots
- vomiting blood, or your vomit looks like “coffee grounds”
- red or black stool that looks like tar

Other side effects:
Besides the serious side effects mentioned above, people taking Mektovi and encorafenib together may also develop the following side effects:

Very common side effects (effects that appear in more than one in ten users) **that appear when Mektovi and encorafenib are taken together for the treatment of melanoma:**
- dizziness
- bleeding
- problems with your vision (visual impairment)
- abdominal pain
- diarrhea
- vomiting
- nausea
- constipation
- rash
- fever
- swelling of the hands or feet (peripheral edema)
- fatigue
- increase in creatine phosphokinase
- severe retinal disease (retinopathy/RPED)
- high blood pressure
- reduced red blood cell count (anemia)
- leukopenia (decreased number of white blood cells - leukocytes)
- lymphopenia (decreased number of lymphocytes in the blood)
- neutropenia (decreased number of neutrophils in the blood)
- increased levels of creatinine
- increased levels of GGTA
- increased levels of ALT
- increased levels of AST
- increased levels of alkaline phosphatase (ALKP)
- hyponatremia (low sodium levels in the blood)

Very common side effects (effects that appear in more than one in ten users) **that appear when Mektovi and encorafenib are taken together for treatment of non-small cell lung cancer (NSCLC):**
- fatigue
- swelling of the hands or feet (peripheral 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
- high blood pressure
- 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 (effects that appear in up to one in ten users) **that appear when Mektovi and encorafenib are taken together:**
- colitis
- inflammation of fatty tissue (panniculitis)
- peripheral neuropathy
- taste disorder (dysgeusia)
- facial nerve palsy
- pancreatitis
- thickening of the cornified layer of the skin (hyperkeratosis)
- skin redness (erythema)
- sensitivity to light (photosensitivity)
- drug hypersensitivity

Side effects of unknown frequency (side effects whose frequency has not yet been determined) **that appear when Mektovi and encorafenib are taken together:**
- pneumonia
- medical device-associated infection
- 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 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:

- Tablet core:

lactose monohydrate, microcrystalline cellulose, croscarmellose sodium, magnesium stearate, colloidal silicon dioxide.

- Tablet coating:

polyvinyl alcohol-part hydrolyzed, macrogol/PEG 3350, titanium dioxide, talc, ferric oxide yellow and ferrosoferric oxide.

What the medicine looks like and contents of the pack:
A pack of Mektovi contains yellow/dark yellow, unscored biconvex oval film-coated tablets debossed with "A" on one side and "15" on the other side.
Mektovi is available in bottles of 180 tablets.

Registration holder's name and address:
Medison Pharma Ltd. 10 Hashiloach Street, POB 7090, Petach Tikva, 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: 167-73-35723-00