Package leaflet: Information for the patient

Mektovi 15 mg film-coated tablets
Mektovi 45 mg film-coated tablets

binimetinib

Read all of this leaflet carefully before you start taking 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, pharmacist or nurse.
- 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, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Mektovi is and what it is used for

Mektovi is an anti-cancer medicine that contains the active substance binimetinib. It is used in adults in combination with another medicine containing encorafenib to treat a type of skin cancer called melanoma when it has
- a particular change (mutation) in a gene responsible for producing a protein called BRAF, and
- spread to other parts of the body or cannot be removed by surgery.

Mutations in the BRAF gene can produce proteins that cause the melanoma to grow. Mektovi targets another protein called "MEK" that stimulates cancer cell growth. When Mektovi is used in combination with encorafenib (which targets the changed "BRAF" protein), the combination slows down or stops the growth of your cancer.

2. What you need to know before you take Mektovi

Before starting treatment your doctor will check for BRAF mutation.

As Mektovi is to be used in combination with encorafenib, read the encorafenib leaflet carefully as well as this leaflet.

Do not take Mektovi
- if you are allergic to binimetinib or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions
Talk to your doctor, pharmacist or nurse before taking Mektovi about all of your medical conditions, particularly if you have any of the following:
- heart problems

- bleeding problems or if you are taking medicines that may cause bleeding
- eye problems including glaucoma or increased pressure in your eyes
- muscle problems
- high blood pressure
- blood clots
- lung or breathing problems
- liver problems

Tell your doctor if you have ever had blockage in the vein carrying blood away from the eye (retinal vein occlusion), as Mektovi is not recommended in such cases.

Tell your doctor if you have had a different type of cancer than melanoma, as binimetinib when taken with encorafenib may worsen certain other types of cancers.

Tell your doctor, pharmacist or nurse immediately if you get the following while you are taking this medicine:

- Heart problems: Mektovi can make your heart work less well, or make existing heart problems worse. Your doctor will check that your heart is working properly before and during your treatment with this medicine. Talk to your doctor immediately if you have any symptoms of heart problems such as feeling dizzy, tired, lightheaded, if you have shortness of breath, if you feel like your heart is pounding, racing, beating irregularly or if you have swelling in the legs.

- Bleeding problems: Mektovi may cause serious bleeding problems. Talk to your doctor immediately if you have any symptoms of bleeding problems such as coughing up of blood, blood clots, vomit containing blood or that looks like "coffee grounds", red or black stools that look like tar, passing blood in the urine, stomach (abdominal) pain, unusual vaginal bleeding. Also tell your doctor if you have headache, dizziness or weakness.

- Eye problems: Mektovi can cause serious eye problems. Talk to your doctor immediately if you get blurred vision, loss of vision or other vision changes (such as coloured dots in your vision), halo (seeing blurred outline around objects). Your doctor will examine your eyes for any problems with your sight while you are taking Mektovi.

- Muscle problems: Mektovi can cause breakdown of muscle (rhabdomyolysis). Your doctor will run blood tests to check for muscle problems before and during treatment. As a precaution, drink plenty of fluids during treatment. Talk to your doctor immediately if you get muscle pain, cramps, stiffness, spasm, dark urine.

- High blood pressure: Mektovi can raise blood pressure. Your doctor or nurse will check your blood pressure before and during treatment with Mektovi. Talk to your doctor immediately if you get severe headache, feel dizzy, lightheaded or if your blood pressure measured on a home blood pressure device is much higher than usual.

- Blood clots: Mektovi can cause blood clots in your arms or legs, and if a clot travels to your lungs it could lead to death. Talk to your doctor immediately if you get chest pain, sudden shortness of breath, trouble breathing, pain in your legs with or without swelling, swelling in your arms and legs, or a cool, pale arm or leg. If necessary, your doctor may interrupt your treatment or stop it altogether.

- Lung or breathing problems: This medicine may cause lung or breathing problems including inflammation of the lungs (pneumonitis or interstitial lung disease); signs and symptoms can include: cough, shortness of breath or fatigue. If necessary, your doctor may interrupt your treatment or stop it altogether.

- Skin changes: Mektovi, when taken with encorafenib, may cause other types of skin cancer

such as cutaneous squamous cell carcinoma. Your doctor will check your skin before initiation of treatment, every 2 months during treatment, and for up to 6 months after you stop taking these medicines to look for any new skin cancer. Tell your doctor immediately if you detect any skin changes during and after the treatment including: new wart, skin sore or reddish bump that bleeds or does not heal, or a change in size or colour of a mole. Additionally, your doctor needs to check for squamous cell carcinoma on your head, neck, mouth and lymph glands, and you will have CT scans regularly. This is a precaution in case a squamous cell carcinoma develops inside your body. Genital examinations (for women) and anal examinations are also recommended before the initiation and at the end of your treatment.

- Liver problems: Mektovi can cause abnormal blood tests related to your liver (raised levels of liver enzymes). Your doctor will run blood tests to check your liver before and during treatment.

If you experience the following symptoms, contact your doctor immediately as this can be a life-threatening condition: nausea, shortness of breath, irregular heartbeat, muscular cramps, seizures, clouding of urine, decrease in urine output and tiredness. These may be caused by a group of metabolic complications that can occur during treatment of cancer that are caused by the breakdown products of dying cancer cells (Tumour lysis syndrome (TLS)) and can lead to changes in kidney function (see also section 4: Possible side effects).

Children and adolescents
Mektovi is not recommended for children and adolescents under 18 years of age. This medicine has not been studied in this age group.

Other medicines and Mektovi
Tell your doctor, pharmacist or nurse if you are taking, have recently taken or might take any other medicines.
Some medicines may affect how Mektovi works or make it more likely that you will have side effects. In particular, tell your doctor if you are taking anything in this list or any other medicines:

- some medicines to treat bacterial infections such as rifampicin, ciprofloxacin
- some medicines typically used to treat epilepsy such as phenobarbital, phenytoin, carbamazepine
- some medicines to treat HIV such as indinavir, atazanavir
- a medicine for carcinoma treatment called sorafenib
- an herbal treatment for depression: St. John’s wort
- medicine used to treat depression such as duloxetine
- medicine typically used to treat high cholesterol such as pravastatin
- a medicine used to treat breathing problems, theophylline.

Pregnancy
Mektovi is not recommended during pregnancy. It may cause permanent harm or birth defects to an unborn baby.
If you are pregnant, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine.
If you are a woman who could become pregnant, you must use reliable contraception while you are taking Mektovi, and you must continue to use reliable contraception at least 1 month after taking your last dose. Contact your doctor straightaway if you become pregnant while taking Mektovi.

Breast-feeding
Mektovi is not recommended while breast-feeding. It is not known if Mektovi passes into breast milk. If you are breast-feeding, or planning to breast-feed, ask your doctor for advice before taking this medicine.

Driving and using machines
Mektovi can affect your ability to drive or use machines. Avoid driving or using machines if you have any problems with your vision or have any other side effects that can affect your ability to drive or use machines (see section 4), while taking Mektovi. Talk to your doctor if you are not sure you can drive.

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.

This medicine contains less than 1 mmol sodium (23 mg) per dosage unit, that is to say essentially 'sodium-free'.

3. How to take Mektovi

How much to take
Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

The recommended dose of Mektovi is 45 mg (three 15 mg tablets or one 45 mg tablet) twice daily, approximately 12 hours apart**,** corresponding to a total daily dose of 90 mg. You will also receive treatment with another medicine, encorafenib.

If you get serious side effects (such as heart, eye or skin problems) your doctor may lower the dose or stop treatment temporarily or permanently.

How to take Mektovi
Swallow the tablets whole with water. Mektovi can be taken with food or between meals.

If you are sick
If you vomit at any time after taking Mektovi, do not take an additional dose. Take the next dose as scheduled.

If you take more Mektovi than you should
If you take more tablets than you should, contact your doctor, pharmacist or nurse straightaway. If possible, show them this leaflet and the medicine package.

If you forget to take Mektovi
If you miss a dose of Mektovi, take it as soon as you remember. However, if the missed dose is more than 6 hours late, skip that dose and take your next dose at the usual time. Then continue taking your tablets at regular times as usual.
Do not take a double dose to make up for a forgotten dose.

If you stop taking Mektovi
It is important to take Mektovi for as long as your doctor prescribes it. Do not stop taking this medicine unless your doctor tells you to.

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

4. Possible side effects

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

Serious side effects

Mektovi may cause serious side effects. Tell your doctor immediately if you have any of the following serious side effects, either for the first time or if they get worse (see also section 2).

Heart problems: Mektovi can affect how well your heart works (left ventricular ejection fraction decrease); signs and symptoms can include:
- feeling dizzy, tired or lightheaded
- shortness of breath
- feeling like your heart is pounding, racing or beating irregularly
- swelling in the legs

High blood pressure: Mektovi can increase blood pressure. Tell your doctor immediately if you get severe headache, feel dizzy or lightheaded or if your blood pressure measured on a home blood pressure device is much higher than usual.

Blood clots: Mektovi may cause blood clots (venous thromboembolism including pulmonary embolism); signs and symptoms can include:
- 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 can cause fluid to leak under the retina in the eye, leading to detachment of different layers in the eye (retinal pigment epithelial detachment) which could lead to:
- blurred vision, loss of vision, or other vision changes (such as coloured dots in your vision)
- halo (seeing blurred outline around objects)
- eye pain, swelling or redness

Muscle problems: Mektovi can cause breakdown of muscles (rhabdomyolysis) which can lead to kidney damage and can be fatal; signs and symptoms can include:
- muscle pain, cramps, stiffness or spasm
- dark urine

Bleeding problems: Mektovi can cause serious bleeding problems. Tell your doctor right away if you have any unusual bleeding or signs of bleeding, including:
- headaches, dizziness or weakness
- coughing up of blood or blood clots
- vomit containing blood or that looks like “coffee grounds”
- red or black stools that look like tar
- passing blood in the urine
- stomach (abdominal) pain
- unusual vaginal bleeding

Other skin cancers: When Mektovi is taken with encorafenib, the patient may develop different types of skin cancer such as cutaneous squamous cell carcinoma. Usually, these skin cancers (see also section 2) are confined to a small area and can be removed with surgery and treatment with Mektovi (and encorafenib) can continue without interruption.

Tumour lysis syndrome: Mektovi can cause a rapid breakdown of cancer cells which in some people may be fatal. Symptoms may include nausea, shortness of breath, irregular heartbeat, muscular cramps, seizures, clouding of urine, decrease in urine output and tiredness.

Other side effects when Mektovi and encorafenib are taken together
Besides the serious side effects mentioned above, people taking Mektovi and encorafenib together

may also get the following side effects.

Very common (may affect more than 1 in 10 people)
- reduced red blood cell count (anaemia)
- problem with the nerves resulting in pain, loss of sensation or tingling in hands and feet
- headache
- dizziness
- bleeding at various sites in the body
- problems with your vision (visual impairment)
- stomach pain
- diarrhoea
- being sick (vomiting)
- feeling sick (nausea)
- constipation
- itching
- dry skin
- hair loss or thinning (alopecia)
- skin rash of various types
- thickening of the outer layers of the skin
- joint pain (arthralgia)
- muscle pain, weakness or spasm
- back pain
- pain in the extremities
- fever
- swelling of the hands or feet (peripheral oedema), localised swelling
- fatigue
- abnormal blood test results for liver function
- abnormal blood test result related to blood creatine kinase, indicating damage to heart and muscle

Common (may affect up to 1 in 10 people)
- some types of skin tumours such as skin papilloma and basal cell carcinoma
- allergic reaction that may include swelling of the face and difficulty breathing
- changes in the way things taste
- inflammation of the eye (uveitis)
- inflammation of the colon (colitis)
- redness, chapping or cracking of the skin
- inflammation of the fatty layer under the skin, symptoms include tender skin nodules
- skin rash with a flat discoloured area or raised bumps like acne (dermatitis acneiform)
- redness, skin peeling or blisters on hand and feet (palmar plantar erythrodysesthesia or hand and foot syndrome)
- kidney failure
- abnormal kidney test results (creatinine elevations)
- abnormal blood test results for liver function (blood alkaline phosphatase)
- abnormal blood test results for pancreas function (amylase, lipase)
- increased skin sensitivity to sunlight

Uncommon (may affect up to 1 in 100 people)
- weakness and paralysis of face muscles
- inflammation of the pancreas (pancreatitis) causing severe abdominal pain

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via: Yellow Card Scheme Website: https://yellowcard.mhra.gov.uk or search for MHRA Yellow Card in the Google Play or Apple App Store.

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

5. How to store Mektovi

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 blister and the carton after EXP. The expiry date refers to the last day of that month.

This medicine does not require any special storage conditions.

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 Mektovi contains

- The active substance is binimetinib.
  Mektovi 15 mg film-coated tablet: each film-coated tablet contains 15 mg of binimetinib.
  Mektovi 45 mg film-coated tablet: each film-coated tablet contains 45 mg of binimetinib.
- The other ingredients are:
  - Tablet core: lactose monohydrate, cellulose microcrystalline (E460i), silica colloidal anhydrous (E551), croscarmellose sodium (E468) and magnesium stearate (E470b). See section 2 "Mektovi contains lactose".
  - Tablet film-coat:

  Mektovi 15 mg film-coated tablet: poly(vinyl alcohol) (E1203), macrogol 3350 (E1521), titanium dioxide (E171), talc (E533b), iron oxide yellow (E172) and iron oxide black (E172).
  Mektovi 45 mg film-coated tablet: poly(vinyl alcohol) (E1203), macrogol 4000 (E1521), calcium carbonate (E170), talc (E533b).

What Mektovi looks like and contents of the pack

Mektovi 15 mg film-coated tablets
The film-coated tablets are yellow/dark yellow, unscored biconvex, oval film-coated tablets debossed with "A" on one side and "15" on the other side.

Mektovi 15 mg film-coated tablets are available in packs of 84 tablets (7 blisters of 12 tablets each) or 168 tablets (14 blisters of 12 tablets each).
Not all pack sizes may be marketed.

Mektovi 45 mg film-coated tablets
The film-coated tablets are white to off-white, unscored biconvex, ovaloid film-coated tablets debossed with "45" on one side.

Mektovi 45 mg film-coated tablets are available in packs of 28 tablets (2 blisters of 14 tablets each) or 56 tablets (4 blisters of 14 tablets each).
Not all pack sizes may be marketed.

Marketing Authorisation Holder

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