PATIENT INFORMATION LEAFLET

SCHEDULING STATUS

S4

Zelboraf® 240 mg film-coated tablets

Active substance: Vemurafenib

Sugar free

Read all of this leaflet carefully before you start taking Zelboraf

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other health care provider.
- Zelboraf has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet

1. What Zelboraf is and what it is used for

Zelboraf is an anticancer medicine that contains the active substance vemurafenib.

It is used to treat adult patients:

1. with melanoma that has spread to other parts of the body or cannot be removed by surgery.

2. whose cancer has a change (mutation) in the “BRAF” gene. This change may have led to the development of melanoma. Zelboraf targets proteins made from this modified gene and may slow down or stop the development of your cancer.

2. What you need to know before you take Zelboraf

Do not take Zelboraf

- If you are hypersensitive (allergic) to vemurefanib or any of the other ingredients of Zelboraf (listed in section 6).
- If you have symptoms of allergic reactions which may include swelling of the face, lips or tongue, difficulty breathing, rash, or fainting sensation.
- If you are pregnant.
- If you are breastfeeding your infant.
- If you have or have had severe liver disease.

Warnings and precautions

Take special care with Zelboraf

Allergic reactions:

Allergic reactions can happen while taking Zelboraf and may be severe. Stop taking Zelboraf and get medical help immediately if you have any symptoms of an allergic reaction such as swelling of the face, lips or tongue, difficulty in breathing, rash, or a fainting sensation.

Severe skin reactions:

- Severe skin reactions can happen while taking Zelboraf. Stop taking Zelboraf and talk to your doctor immediately if you get a skin rash with any of the following symptoms: blisters on your skin, blisters or sores in your mouth, peeling of your skin, fever, redness or swelling of your face, hands, or soles of your feet.

Previous history of cancer:

- **Tell your doctor if you have had a different type of cancer than melanoma**, as Zelboraf may cause progression of certain types of cancers.

Radiation therapy reactions:

- Tell your doctor if you have had, or are going to have radiotherapy (treatment that uses high doses of radiation to kill cancer cells), as Zelboraf may worsen radiation treatment side effects.

Heart disorder:

- Tell your doctor if you have a heart disorder, such as an alteration of the electrical activity of your heart called “QT prolongation”. Your doctor will check that your heart is working properly before and during your treatment with Zelboraf. If necessary, your doctor may decide to interrupt your treatment temporarily or stop it altogether.

Eye problems:

- You should have your eyes examined by your doctor while you are taking Zelboraf. Tell your doctor immediately if you get eye pain, swelling, redness, blurred vision or other vision changes during your treatment.

Musculoskeletal/Connective Tissue disorder

- **Tell your doctor if you observe any unusual thickening of the palms of your hands** accompanied by tightening of the fingers inward or any unusual thickening of the soles of your feet which may be painful.

Check your skin before, during and after treatment

- If you notice any changes in your skin while taking Zelboraf, please talk to your doctor as soon as possible.
- Your doctor needs to check your skin for a type of cancer called “cutaneous squamous cell carcinoma”, regularly during your treatment and up to 6 months after your treatment.
- Usually, this lesion appears on sun-damaged skin, remains local and can be cured by surgical removal.
- If your doctor finds this type of skin cancer, he or she will arrange appropriate treatment.
- Your doctor needs to inspect your head, neck, mouth, lymph glands and arrange CT scans regularly. This is a precautionary measure in case a squamous cell carcinoma lesion develops inside your body. Genital examinations (for women) and anal examinations are recommended before **and** at the end of your treatment.

- You may develop new melanoma lesions while taking Zelboraf. These lesions are usually removed by surgery, and patients continue their treatment. Monitoring of these lesions occurs as outlined above for cutaneous squamous cell carcinoma.

Kidney or liver problems

- Tell your doctor if you have kidney or liver problems. This may affect the activity of Zelboraf. Your doctor will also do some blood tests to monitor your liver functions.

Sun protection

- If you are taking Zelboraf, you may become more sensitive to sunlight and get severe sunburn. During treatment, avoid exposing your skin to direct sunlight
- If you go into the sun: wear clothing which protects your skin, including your head and face, arms and legs; use a lip balm and a broad spectrum sunscreen (minimum of Sun, Protection Factor (SPF) 30+ re-applied every 2 to 3 hours).
- This will help to protect you against sunburn.

Dupuytren's contracture and plantar fascial fibromatosis:

- Cases of conditions called Dupuytren's contracture and plantar fascial fibromatosis have been reported with Zelboraf, including severe, disabling cases. Events should be managed with dose reduction, treatment interruption, or with treatment discontinuation.

Children and adolescents

Zelboraf is not recommended for children and adolescents. The effects of Zelboraf in people younger than 18 years old are not known.

Other medicines and Zelboraf

Always tell your healthcare professional if you are taking any other medicines. (This includes complementary or traditional medicines). This is very important, as using more than one medicine at the same time can strengthen or weaken the effect of the medicines.

In particular, please tell your doctor if you are taking:

- Medicines that are known to affect the way your heart beats:
  - medicines for heart rhythm problems (e.g. quinidine, amiodarone)
  - medicines for depression (e.g. amitriptyline, imipramine)

- medicines for bacterial infections (e.g. azithromycin, clarithromycin)
- medicines for nausea and vomiting (e.g. ondansetron, domperidone).

- Medicines that are mainly eliminated by metabolising proteins called CYP1A2 (e.g caffeine, olanzapine, theophylline) or called CYP3A4 (e.g. some oral contraceptives).
- Medicines that influence a protein called P-gp (e.g. verapamil, clarithromycin, cyclosporine, ritonavir, quinidine, dronedarone, amiodarone, itraconazole, ranolazine, amitriptyline, cisplatin).
- Medicines that stimulate the metabolising proteins called CYP3A4 or a metabolising process called glucuronidation (e.g. rifampicin, rifabutin, carbamazepine, phenytoin or St John's Wort [hypericum peforatum])
- A medicine used to prevent blood clots called warfarin.
- Medicines that strongly inhibit the metabolising protein called CYP3A4 (e.g. ritonavir, saquinavir, telithromycin, ketoconazole, itraconazole, voriconazole, posaconazole, nefazodone, atazanavir).
- A medicine called ipilimumab, another medicine for the treatment of melanoma. The combination of this medicine with Zelboraf is not recommended due to increased toxicity to the liver.

If you are taking any of these medicines (or if you are not sure), please talk to your doctor before taking Zelboraf.

Zelboraf with food, drink and alcohol

Take Zelboraf either 1 hour before or 2 hours after a meal in the morning and in the evening. Each dose in the morning / evening should always be taken in the same manner, either with or without a meal.

Pregnancy, breastfeeding and fertility

Use an appropriate method of contraception during your treatment and for at least 6 months after the end of your treatment. Zelboraf may decrease the efficacy of some oral contraceptives. Please tell your doctor if you are taking an oral contraceptive.

- Zelboraf must not be used during pregnancy. Tell your doctor if you are pregnant or planning to become pregnant.
- You must not breastfeed your baby while on treatment with Zelboraf.

If you are pregnant or breastfeeding your baby, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other healthcare professional for advice before taking Zelboraf.

Driving and using machines

Zelboraf has side effects that can affect your ability to drive or to operate machines. Be aware of fatigue or eye problems that could be a reason for not driving or operating machines.

Zelboraf contains:

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

3. How to take Zelboraf

Do not share medicines prescribed for you with any other person.

Always take Zelboraf exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.

Taking your tablets

- Always take Zelboraf in the same manner (i.e. either with or without a meal).

How many tablets should you take:

- The usual dose is 4 tablets twice a day (a total of 8 tablets).
- Take 4 tablets in the morning. Then take 4 tablets in the evening about 12 hours later.
- If you experience side effects, your doctor may need to lower your dose to carry on your treatment.
- In case of vomiting, continue to take Zelboraf as usual and do not take an additional dose.

Taking your tablets

- Swallow the tablets whole with a glass of water. Do not chew or crush the tablets.

Your doctor or pharmacist will tell you how long your treatment with Zelboraf will last. Do not stop

treatment early. If you have the impression that the effect of Zelboraf is too strong or too weak, tell your doctor or pharmacist.

If you take more Zelboraf than you should

If you take more Zelboraf than you should, talk to your doctor or pharmacist immediately.

Taking too much Zelboraf may make side effects more likely or more severe.

In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison control centre.

If you forget to take Zelboraf

- If you forget a dose and it is more than 4 hours before your next dose, just take your dose as soon as you remember it. Take the next dose at the usual time.
- If it is less than 4 hours before your next dose, skip the missed dose. Then take the next dose at the usual time.
- **Do not take a double dose to make up for forgotten individual doses.**

If you stop taking Zelboraf

It is important to keep taking Zelboraf for as long as your doctor prescribes it for you. If you have any further questions on the use of this product, ask your doctor.

4. Possible side effects

Zelboraf can have side effects.

Not all side effects reported for Zelboraf are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking Zelboraf, please consult your health care provider for advice.

If any of the following happens, stop taking Zelboraf and tell your doctor immediately or go to the casualty department at your nearest hospital:

Serious allergic reactions

If you get any of these:

- Swelling of the face, lips or tongue
- Difficulty in breathing

- Rash
- Fainting sensation

Call a doctor or pharmacist immediately. Do not use any more Zelboraf until you have spoken to a doctor or pharmacist.

Please talk to your doctor as soon as possible if you notice any changes in your skin.

Worsening of radiation treatment side effects can occur in patients who are treated with radiation before, during, or after Zelboraf treatment. This can occur on the area that was treated with radiation, such as the skin, oesophagus, bladder, liver, rectum, and lungs.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you experience any of the following symptoms:

- Skin rash, blistering, peeling or discoloration of the skin
- Shortness of breath, which may be accompanied by a cough, fever or chills (pneumonitis)
- Difficulty or pain when swallowing, chest pain, heartburn or acid reflux (oesophagitis).

Please talk to your doctor and pharmacist as soon as possible if you notice any changes in your skin**.**

These are all serious side effects. You may need urgent medical attention.

Side effects are listed below by frequency:

Very frequent side effects (may affect more than 1 in 10 people):

- Rash, itching, dry or scaly skin
- Skin problems including warts
- A type of skin cancer (cutaneous squamous cell carcinoma)
- Sunburn, being more sensitive to sunlight
- Headache
- Loss of appetite
- Changes in the way things taste
- Diarrhoea
- Constipation
- Feeling sick (nausea), vomiting

- Hair loss
- Joint or muscle pain, musculoskeletal pain
- Pain in the extremities
- Back pain
- Feeling tired (fatigue)
- Fever
- Swelling usually in the legs (peripheral oedema)
- Change in liver tests results
- Cough

Frequent side effects (may affect up to 1 in 10 people):

- A type of skin cancer (basal cell carcinoma)
- Palmar plantar syndrome (i.e. redness, skin peeling or blisters on hands and feet)
- Inflammation of the eye (uveitis)
- Bell's palsy (a form of facial paralysis)
- Tingling or burning feelings in hands and feet
- Inflammation of joints
- Inflammation of hair's roots
- Weight loss
- Problem with the nerves that can produce pain, loss of sensation and/or muscle weakness (peripheral neuropathy)
- Inflammation of blood vessels
- Cases of Dupuytren's contracture (condition that causes tough tissue to form under the skin of the palm and fingers curl causing deformities of the hand) and plantar fascial fibromatosis (thickening of the deep tissue under the feet).
- Change in liver tests results (ALT, alkaline phosphatase and bilirubin increase)
- Changes in electrical activity of the heart (QT prolongation)

- Inflammation of the fatty tissue under the skin
- Abnormal kidney blood test results (creatinine increased)
- Change in liver tests results (GGT increase)
- Decreased white blood cells (neutropenia)

Less frequent (may affect up to 1 in 100 people):

- Allergic reactions that may include swelling of the face and difficulty breathing
- Blockage of blood flow to part of the eye (retinal vein occlusion)
- Inflammation of the pancreas
- Change in liver laboratory tests results or liver injury, including severe liver injury where liver is injured to the extent that it is not able to fully perform its function
- A type of cancer (non-cutaneous squamous cell carcinoma)
- Thickening of deep tissues underneath the sole of the feet that may be disabling if severe

Rare (may affect up to 1 in 1 000 people)

- Progression of a type of pre-existing cancers with RAS mutations (Chronic Myelomonocytic Leukaemia, Pancreatic adenocarcinoma)
- A type of severe skin reaction characterised by rash accompanied by fever and inflammation of internal organs such as liver and kidney
- Inflammatory disease mainly affecting the skin, lung and eye (sarcoidosis)
- Types of kidney injury characterised by inflammation (acute interstitial nephritis) or damage to the tubules of the kidney (acute tubular necrosis).

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects

If you get side effects, talk to your doctor, pharmacist or nurse. You can also report side effects to SAHPRA via the “6.04 Adverse Drug Reaction Reporting Form”, found online under SAHPRA’s publications: https://www.sahpra.org.za/Publications/Index/8. By reporting side effects, you can help provide more information on the safety of Zelboraf.

5. How to store Zelboraf

- Store all medicines out of the sight and reach of children.
- Store at or below 30 °C. Keep the medicine in the original carton until required for use. Protect from moisture.
- Do not use after the expiry date stated on the pack. The expiry date refers to the last day of that month.

Return all unused medicine to your pharmacist. Do not dispose of unused medicine via waste water or household waste, in drains or sewerage systems (e.g. toilets). These measures will help protect the environment.

6. Contents of the pack and other information

What Zelboraf contains

The active substance is vemurafenib. Zelboraf contains 240 mg vemurafenib as co-precipitate of vemurafenib and hypromellose acetate succinate, per tablet.

The other ingredients are: croscarmellose sodium, hydroxypropylcellulose, hypromellose acetate succinate, iron oxide red (E172), macrogol 3350, magnesium stearate, polyvinyl alcohol, silica colloidal anhydrous, talc, titanium dioxide (E171).

What Zelboraf looks like and contents of the pack

Zelboraf: Aluminium blisters, containing 56 film-coated tablets per pack.

Zelboraf is a pinkish-white to orange-white, oval, biconvex film-coated tablet, with VEM engraved on one side.

Holder of Certificate of Registration

Roche Products (Pty) Ltd.

90 Bekker Road

Hertford Office Park, Building E

Vorna Valley, Midrand

Johannesburg

South Africa

Roche Ethical Assistance Line (REAL) toll-free: 0800 21 21 25

This leaflet was last revised in:

Registration: 26 November 2015

Last Revision: 14 April 2022

Registration number

47/32.16/0247