Patient Medication Information

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

[Pr]BRAFTOVI®

Encorafenib capsules

This Patient Medication Information is written for the person who will be taking **BRAFTOVI**. This may be you or a person you are caring for. Read this information carefully. Keep it as you may need to read it again.

This Patient Medication Information is a summary. It will not tell you everything about this medication. If you have questions about this medication or want more information about **BRAFTOVI**, talk to a healthcare professional.

Your cancer will be treated with BRAFTOVI in combination with other medications called binimetinib, cetuximab or mFOLFOX6 (leucovorin, fluorouracil, oxaliplatin). Read the Patient Medication Information leaflet for the other medications that you will receive as well as this one.

Serious warnings and precautions box

BRAFTOVI can cause serious side effects including:

- **New skin cancers** such as squamous cell carcinoma of the skin, keratoacanthoma, basal cell carcinoma and other melanomas.
- **Hemorrhage (bleeding problems):** These are serious bleeding problems. Bleeding problems can happen in the stomach, intestinal tract or brain, that could lead to death.
- **Uveitis**: This **eye problem** happens when part of the eye wall becomes inflamed. It can include **iritis** (inflammation of the coloured part of your eye) and **iridocyclitis** (inflammation of the coloured part of your eye and the muscles and tissue that help the eye to focus).
- **QTc Interval Prolongation:** This condition happens when there are changes in electrical activity of your heart. Braftovi can also worsen any other heart problems you have. Your healthcare professional will check that your heart is working properly before and during your treatment.
- **Blood clots: Venous thromboembolism** (blood clots in a vein of your arms or legs) or **pulmonary embolism** (blood clot in the lung) have happened in patients taking BRAFTOVI.

What BRAFTOVI is used for:

For the following indication BRAFTOVI has been approved with conditions (NOC/c). This means it has passed Health Canada's review and can be bought and sold in Canada, but the manufacturer has agreed to complete more studies to make sure the drug works the way it should. For more information, talk to your healthcare professional.

- BRAFTOVI is used in combination with drugs called cetuximab and mFOLFOX6 (chemotherapy), to treat adults with a type of large intestine cancer called metastatic colorectal cancer (mCRC). This type of intestine cancer must have:
    - a change (mutation) in the BRAF gene, and

- spread to other parts of the body.

Before taking BRAFTOVI, a test will be performed. This test is to confirm that BRAFTOVI is right for you.

BRAFTOVI is not approved for use in children and adolescents under 18 years of age.

For the following indications BRAFTOVI has been approved without conditions. This means it has passed Health Canada's review and can be bought and sold in Canada.

- BRAFTOVI is used with a drug called binimetinib to treat adults with a type of skin cancer called melanoma. This type of skin cancer must have:
  - a change (mutation) in the BRAF gene, and
  - spread to other parts of the body, or cannot be removed by surgery.
- BRAFTOVI is also used with a drug called cetuximab to treat adults with a type of large intestine cancer called metastatic colorectal cancer (mCRC). This type of intestine cancer must have:
  - a change (mutation) in the BRAF gene, and
  - spread to other parts of the body and has already been treated with other cancer drugs.

Before taking BRAFTOVI, a test will be performed. This test is to confirm that BRAFTOVI is right for you.

BRAFTOVI is not approved for use in children and adolescents under 18 years of age.

What is a Notice of Compliance with Conditions (NOC/c)?

A Notice of Compliance with Conditions (NOC/c) is a type of approval to sell a drug in Canada.

Health Canada only gives an NOC/c to a drug that treats, prevents, or helps identify a serious or life-threatening illness. The drug must show promising proof that it works well, is of high quality, and is reasonably safe. Also, the drug must either respond to a serious medical need in Canada, or be much safer than existing treatments.

Drug makers must agree in writing to clearly state on the label that the drug was given an NOC/c, to complete more testing to make sure the drug works the way it should, to actively monitor the drug's performance after it has been sold, and to report their findings to Health Canada.

How BRAFTOVI works:

Mutations in the BRAF gene can produce proteins that cause cancer cells to grow. BRAFTOVI targets these proteins.

Binimetinib acts on a different protein that causes melanoma cells to grow. When BRAFTOVI and binimetinib are used together, they may help to slow down or stop the growth of melanoma.

Mutations in the BRAF gene for metastatic colorectal cancer work in a similar way. When BRAFTOVI and cetuximab or BRAFTOVI, cetuximab and mFOLFOX6 are used together, they may help to slow down or stop the growth of metastatic colorectal cancer.

The ingredients in BRAFTOVI are:

Medicinal ingredients: encorafenib
Non-medicinal ingredients: colloidal silicon dioxide, copovidone, crospovidone, ferrosoferric oxide, gelatin, iron oxide red, iron oxide yellow, magnesium stearate of vegetable origin, microcrystalline cellulose, pharmaceutical glaze, poloxamer 188, propylene glycol, succinic acid and titanium dioxide.

BRAFTOVI comes in the following dosage form:

Capsules: 75 mg

Do not use BRAFTOVI if:

- you are allergic to encorafenib or any of the other ingredients in this medicine.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take BRAFTOVI. Talk about any health conditions or problems you may have, including if you:

- have or have had heart problems including:
    - long QT syndrome. This is a condition that affects the rhythm of the heart where heartbeats can be fast or irregular.
    - bradyarrhythmia, which is a slow heart rate.
    - heart failure
- have or have had **eye problems**, including **uveitis, iritis**, **iridocyclitis**
- are taking certain medications that might affect your heart rate.
- have or have had **liver problems**.
- have diabetes or high blood sugar (**hyperglycaemia**)

Other warnings you should know about:

Skin changes (rash, skin cancer, serious skin reactions): Treatment with BRAFTOVI can cause skin changes including rash and skin cancer. Severe skin reactions that can be life-threatening are also possible. Throughout your treatment, your healthcare professional will check your skin. They will look for any new skin cancers before treatment, every 2 months during your treatment, and for up to 6 months after you stop taking BRAFTOVI. They will also monitor you for skin reactions. Tell your healthcare professional immediately if you notice any changes in your skin both during and after treatment.

Other non-skin cancers: Treatment with BRAFTOVI can cause cancer in other parts of your body. Your healthcare professional will monitor you for signs and symptoms of cancer.

Liver problems: Treatment with BRAFTOVI can cause liver problems. You will have regular blood tests done before starting your treatment and then every month while you are taking BRAFTOVI. These blood tests will tell your healthcare professional how your liver is working.

High blood sugar (hyperglycaemia): Treatment with BRAFTOVI can cause high blood sugar. Your healthcare professional will monitor your blood sugar levels.

See the "**Serious side effects and what to do about them**" table, below, for more information on these and other serious side effects.

Check-ups and testing: You will have regular visits with your healthcare professional, before, during and at the end of your treatment. In addition to checking your skin, they will also:

- Check your eyes for new or worsening eye problems. You may be sent to see an eye specialist.
- Check that your heart is working properly.
- Do a physical exam and blood tests.

Pregnancy and breastfeeding:

Female patients

- If you are pregnant, able to get pregnant or think you are pregnant, there are specific risks you should discuss with your healthcare professional.
- You should not take BRAFTOVI if you are pregnant. It may harm your unborn baby.
- If you are able to become pregnant:
    - Your healthcare professional will do a pregnancy test before you start taking BRAFTOVI. This test must show that you are not pregnant.
    - Avoid becoming pregnant while you are taking BRAFTOVI. Use effective birth control during your treatment and for at least 2 weeks after your last dose. The birth control methods you use must not contain hormones. This is because BRAFTOVI may cause these types of birth control to not work as well as they should. Ask your healthcare professional about methods of birth control available to you.
    - Tell your healthcare professional right away if you become pregnant or think you may be pregnant during your treatment with BRAFTOVI.
- Do not breastfeed while you are taking BRAFTOVI and for at least 2 weeks after your last dose.

Male patients

- Avoid fathering a child while you are taking BRAFTOVI.
- During your treatment with BRAFTOVI, use a condom each time you have sex with a woman who is pregnant, may be pregnant or could get pregnant. Continue using condoms until 1 week after your last dose.
- If, during your treatment with BRAFTOVI, your sexual partner becomes pregnant or thinks she may be pregnant, tell your healthcare professional right away.

Male patients – fertility:

- Treatment with BRAFTOVI may affect your ability to father a child. If you have questions about this, talk to your healthcare professional.

Driving and using machines: BRAFTOVI can cause fatigue and vision problems. Before you drive or do tasks that require special attention, wait until you know how you respond to BRAFTOVI.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with BRAFTOVI:

- medicines to treat fungal infections such as itraconazole, posaconazole, fluconazole;
- medicines to treat bacterial infections such as rifampicin, clarithromycin, telithromycin,

erythromycin, ciprofloxacin, rifabutin, nafcillin;
- medicines typically used to treat epilepsy (seizures) such as phenytoin, carbamazepine, phenobarbital;
- medicines typically used to treat high cholesterol such as rosuvastatin, atorvastatin;
- a medicine used to treat angina called verapamil;
- an herbal treatment for depression called St. John's wort;
- medicines for HIV treatment such as ritonavir, amprenavir, cobicistat, indinavir, saquinavir, nelfinavir, boceprevir, telaprevir, efavirenz, etravirine;
- medicines used to treat hepatitis C such as boceprevir and telaprevir;
- birth control medicines containing hormones;
- medicines typically used to treat high blood pressure including diltiazem, bosentan, furosemide, losartan;
- a medicine used to treat sleep disorders called modafinil;
- a medicine used to treat an uneven heartbeat called amiodarone;
- a medicine used to produce sleepiness or drowsiness called midazolam;
- medicines, supplements or any other products containing caffeine;
- a medicine used to treat excess stomach acid called omeprazole;
- a medicine used to treat depression called bupropion.

Do NOT eat grapefruit or drink grapefruit juice during your treatment with BRAFTOVI. This is because it could affect the way the medicine works and may lead to side effects.

How to take BRAFTOVI:

- Take exactly as your healthcare professional has told you. Check with your healthcare professional if you are not sure.
- Swallow capsules whole, with water.
- Take with or without food.
- Take BRAFTOVI for as long as your healthcare professional prescribes it. Do not stop taking this medicine unless your healthcare professional tells you to.

Usual dose:

Melanoma:

Recommended total daily adult dose: 450 mg per day. To make this dose, take six 75 mg capsules once per day.

You will also receive treatment with another medicine, binimetinib. Your healthcare professional will tell you how much of this medicine you will take and how to take it.

Metastatic Colorectal Cancer (mCRC):

Recommended total daily adult dose: 300 mg per day. To make this dose, take four 75 mg capsules once per day.

You will also receive treatment with another medicine, cetuximab or cetuximab in combination with mFOLFOX6. Cetuximab and mFOLFOX6 are given through your veins (intravenously). Your healthcare professional will determine your dose and schedule.

Your healthcare professional may lower your dose, stop your treatment for a period of time or recommend that you stop treatment completely. This may happen if you:

- experience serious side effects, or
- your disease gets worse, or
- your binimetinib or cetuximab dose is stopped.

If you have liver problems or are taking certain medications that may interact with BRAFTOVI, your healthcare professional may start you on a lower dose.

Overdose:

If you think you, or a person you are caring for, have taken too much BRAFTOVI, contact a healthcare professional, hospital emergency department, regional poison control centre or Health Canada's toll-free number, 1-844 POISON-X (1-844-764-7669) immediately, even if there are no signs or symptoms.

Missed dose:

If you miss a dose of BRAFTOVI and,

- there are less than 12 hours until your next scheduled dose, skip the missed dose. Take your next dose at the usual time.
- there are more than 12 hours until your next scheduled dose, take your dose as soon as you remember.
- Continue taking your capsules according to your usual schedule.

Do not take two doses at the same time to make up for a forgotten dose.

If you vomit at any time after taking BRAFTOVI, do not take another dose. Take the next dose at your usual time.

Possible side effects from using BRAFTOVI:

These are not all the possible side effects you may have when taking BRAFTOVI. If you experience any side effects not listed here, tell your healthcare professional.

BRAFTOVI is taken with binimetinib, cetuximab or cetuximab and mFOLFOX6 . Please also read the leaflets for binimetinib or cetuximab or the drugs in mFOLFOX6 (leucovorin, fluorouracil and oxaliplatin) to learn about possible specific side effects they may cause.

- pain, loss of sensation or tingling in hands and feet
- difficulty sleeping
- headache
- dizziness
- fever
- fatigue

- changes in the way things taste
- decreased appetite
- stomach pain
- diarrhea
- vomiting
- nausea
- constipation
- itching
- redness, chapping or cracking of the skin
- dry skin
- hair loss or thinning
- skin rash
- thickening of the outer layers of the skin
- increased skin sensitivity to sunlight
- dark spots on the skin
- joint pain
- muscle pain, weakness or spasm
- back pain
- pain in the extremities
- swelling including in the hands or feet
- weight loss

BRAFTOVI can cause abnormal blood test results. Your healthcare professional will do blood tests during your treatment. These will tell your healthcare professional how BRAFTOVI is affecting your blood, heart, liver, pancreas, kidneys and muscles.

Serious side effects and what to do about them:

Frequency / Side Effect / Symptom	Talk to your healthcare professional		Stop taking this drug and get immediate medical help
	Only if severe	In all cases	
VERY COMMON			
Anemia (decreased number of red blood cells): fatigue, loss of energy, irregular heartbeats, pale complexion, shortness of breath, weakness	**X**		
Bleeding problems: 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, nosebleeds, unusual vaginal bleeding.			**X**

Frequency / Side Effect / Symptom	Talk to your healthcare professional		Stop taking this drug and get immediate medical help
	Only if severe	In all cases	
Dermatitis acneiform (Skin / Acne condition): small, raised acne-like red bumps on the face, scalp, chest, upper back; bumps may be filled with pus	**X**		
Eye problems, including: • **uveitis** (inflammation of part of the eye wall), • **Iritis** (inflammation of the coloured part of the eye), • **Iridocyclitis** (inflammation of the coloured part of the eye and the muscles and tissues that help the eye to focus) • **retinal pigment epithelial detachment** (separation of the retinal pigment epithelium (an inner layer of the eye from the inner part of the eye) Symptoms include: blurred vision, loss of vision, inflammation or other vision changes (such as coloured dots in your vision), halo (seeing blurred outline around objects), eye pain, swelling or redness. Symptoms can appear suddenly and worsen quickly.			**X**
Heart problems including QTc prolongation (changes in the electrical activity of the heart): feeling dizzy, tired or lightheaded, shortness of breath, feeling like your heart is pounding, racing or beating irregularly, swelling in the legs.			**X**
Kidney problems: confusion, itchiness or rash, puffiness in face and hands, swelling in feet or ankles, urinating less or not at all; weight gain		**X**	
Liver problems: yellowing of your skin and eyes (jaundice), right upper stomach area pain or swelling, nausea or vomiting,		**X**	

Frequency / Side Effect / Symptom	Talk to your healthcare professional		Stop taking this drug and get immediate medical help
	Only if severe	In all cases	
unusual dark urine, unusual tiredness			
Skin Changes: new wart, skin sore or reddish bump that bleeds or does not heal, a new mole or change in size or colour of a mole.		**X**	
COMMON			
Allergic reaction: difficulty swallowing or breathing, wheezing; drop in blood pressure; feeling sick to your stomach and throwing up; hives or rash; swelling of the face, lips, tongue or throat			**X**
Bowel problems [including colitis (inflammation of the bowel)]: severe or persistent diarrhea, abdominal pain or cramping, pain in the rectum, bleeding from the rectum	**X**		
Cerebral hemorrhage (bleeding in the brain): sudden, severe headache; confusion; nausea and vomiting; seizures; loss of consciousness.			**X**
Facial paresis (weakness and paralysis of face muscles): loss of movement of the face; face muscles may appear to droop			**X**
Hyperglycaemia (high blood sugar): increased thirst, frequent urination, dry skin, headache, blurred vision and fatigue		**X**	
Hypertension (high blood pressure): shortness of breath, fatigue, severe headache, dizziness or fainting, lightheaded, chest pain or pressure, swelling in your ankles and legs, bluish colour to your lips and skin, racing pulse or palpitations		**X**	
Palmar-plantar erythrodysesthesia (Hand and foot syndrome): redness, tingling and	**X**		

Frequency / Side Effect / Symptom	Talk to your healthcare professional		Stop taking this drug and get immediate medical help
	Only if severe	In all cases	
loss of feeling, skin peeling or blisters on hand and feet			
Pancreatitis (inflammation of the pancreas): upper abdominal pain, fever, rapid heart rate, nausea, vomiting, tenderness when touching the abdomen		**X**	
Panniculitis (inflammation of the fatty layer under the skin): tender, red bumps on the arms and legs, abdomen, breasts face or buttocks	**X**		
Pulmonary embolism (blood clot in the lung): chest pain that may increase with deep breathing, sudden shortness of breath, trouble breathing, cough, coughing up bloody sputum			**X**
Skin cancer including cutaneous squamous cell cancer, keratoacanthomas, basal cell carcinoma and melanoma: skin sore, wart, or reddish bump that bleeds or does not heal		**X**	
Venous thromboembolism (blood clot in a deep vein of the arm or leg): pain in your legs with or without swelling, swelling in your arms and legs, or a cool, pale arm or leg, arm or leg may also be warm to the touch and may appear red			**X**
UNKNOWN			
Severe skin reactions including Stevens-Johnson syndrome (SJS), Toxic Epidermal Necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS) and acute generalized exanthematous pustulosis (AGEP): redness, blistering and/or peeling of the skin and/or inside of the lips, eyes, mouth, nasal passages or genitals, itching, pain, skin dryness, accompanied by fever, chills,			**X**

Frequency / Side Effect / Symptom	Talk to your healthcare professional		Stop taking this drug and get immediate medical help
	Only if severe	In all cases	
headache, cough, body aches or swollen glands, small pus-filled bumps			

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting side effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (canada.ca/drug-device-reporting) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your healthcare professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

Store at 15 to 30°C.

Keep BRAFTOVI in the original bottle. Keep bottle tightly closed to protect from moisture. Do not remove the desiccant from the bottle. Keep out of reach and sight of children.

If you want more information about BRAFTOVI:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes the Patient Medication Information by visiting the Health Canada Drug Product Database website: (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html; the manufacturer's website www.Pfizer.ca, or by calling 1-800-463-6001.

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