



Provincial Health Services Authority

For the Patient: SMAVEB

Other Names: Treatment of BRAF V600 Mutation-Positive Unresectable or Metastatic Melanoma using Encorafenib and Binimetinib

SM = **S**kin and **M**elanoma

AV = **A**dvanced

EB = **E**ncorafenib and **B**inimetinib

ABOUT THESE MEDICATIONS

What are these drugs used for?

- Encorafenib (en" koe raf' e nib) and binimetinib (bin i me' ti nib) is a drug combination that is used to treat a type of skin cancer called melanoma,
 - that has spread to other parts of the body or cannot be removed by surgery, and
 - that has a certain type of abnormal "BRAF" gene.

How do these drugs work?

- Encorafenib and binimetinib target proteins made from the abnormal BRAF and MEK genes, respectively, and slows down or stops the growth of cancer cells.

INTENDED BENEFITS

- Encorafenib and binimetinib are being given to destroy and/or limit the growth of melanoma cells. This treatment may improve your current symptoms, and delay or prevent the onset of new ones.

TREATMENT SUMMARY

How are these drugs given?

- Encorafenib is a capsule and binimetinib is a tablet that you take by mouth. Binimetinib tablets contain lactose.
- Encorafenib is taken once daily, binimetinib is taken twice daily, continuously, as long as you are benefiting from treatment and not having too many side effects.

What will happen when I get my drugs?

- "BRAF" gene test of your cancer is done before starting treatment. You will only be offered this treatment if your cancer has a specific mutation (change) in the BRAF gene.
- A blood test (lab work) and other tests are done before starting treatment and each time you see your cancer care provider.
- The dose of either drug may be changed or interrupted based on your test results and/or side effects.

INSTRUCTIONS FOR THE PATIENT

How should I store this drug?

- Store encorafenib capsules in the original bottle. Do not remove desiccant. Keep out of the reach of children. Store at room temperature, away from heat, light, and moisture.
- Store binimetinib tablets out of the reach of children, at room temperature, away from heat, light, and moisture.

How should I take this drug?

- Encorafenib is taken once daily, at around the same time every day with either the morning or evening dose of binimetinib. The dose will consist of multiple capsules or tablets to make the right dose.
- Binimetinib is taken twice daily in the morning and in the evening, approximately 12 hours apart.
- You can take encorafenib and binimetinib with food or on an empty stomach. Do not take with grapefruit or grapefruit juice.
- Do not chew, open or crush encorafenib capsules or binimetinib tablets. Swallow whole with a full glass of water one at a time.
- If you miss a dose of encorafenib, take it as soon as you can if it is within 12 hours of the missed dose. If it is more than 12 hours since your missed dose, skip the missed dose and go back to your usual dosing times. Do NOT take a double dose to make up for the missed dose.
- If you miss a dose of binimetinib, take it as soon as you can if it is within 6 hours of the missed dose. If it is more than 6 hours since your missed dose, skip the missed dose and go back to your usual dosing times. Do not take any doses to make up for the missed dose.
- If you vomit the dose of encorafenib and/or binimetinib, skip the dose and go back to your usual dosing times. Do NOT repeat the dose. Let your doctor know as a medication to prevent nausea may be required for future doses.

What other drugs or foods can interact with encorafenib and binimetinib?

- Other drugs such as hormonal birth control, diltiazem, ciprofloxacin, clarithromycin, erythromycin, fluconazole and posaconazole may interact with encorafenib and/or binimetinib. Tell your doctor or pharmacist if you are taking this or any other drugs as you may need extra blood tests or your dose may need to be changed. Check with your doctor or pharmacist before you start or stop taking any other drugs.
- Avoid grapefruit and grapefruit juice for the duration of your treatment, as these may interact with encorafenib.
- The drinking of alcohol (in small amounts) does not appear to affect the safety or usefulness of encorafenib and binimetinib.

Other important things to know:

- Before you start taking encorafenib and binimetinib, talk to your doctor or pharmacist if you have any of the following:
 - Heart problems** such as heart failure, valve problems or problems in the way your heart beats, including a condition called long QT syndrome.
 - Eye problems** including iritis, uveitis or blockage of the vein draining the eye or swelling in the eye which may be caused by fluid blockage.
 - Skin problems** including rash or acne-like rash.
 - Lung or breathing problems** including difficulty in breathing often accompanied by a dry cough, shortness of breath and fatigue.
 - High blood pressure** (hypertension)
 - Liver problems.**
 - Diabetes or high blood sugar.**
 - Have or have had **blood clots** or **bleeding problems.**

Note:

- Encorafenib may damage sperm and encorafenib and binimetinib may harm the baby if used during pregnancy. It is best to use birth control while being treated and for 4 months after treatment. You must use reliable non-hormonal birth control as hormonal pills, patches or injections are not effective in pregnancy prevention as they do not work as well during treatment. Tell your doctor right away if you or your partner becomes pregnant. Do not breastfeed during treatment and for two weeks after your treatment ends.
- Tell doctors or dentists that you are being treated with encorafenib and binimetinib before you receive any treatment from them.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Are there any risks?

Unexpected and unlikely side effects can occur with any drug treatment. The ones listed below are particularly important for you to be aware of as they are directly related to the common actions of the drugs in your treatment plan.

SIDE EFFECTS	MANAGEMENT
<p>Nausea and vomiting may occur. If you are vomiting and it is not controlled, you can quickly become dehydrated.</p>	<p>You may be given a prescription for anti-nausea drug(s) to take at home. It is easier to prevent nausea than treat it once it has occurred, so follow directions closely.</p> <ul style="list-style-type: none"> • Drink plenty of fluids. • Eat and drink often in small amounts. • Try the ideas in <i>Practical Tips to Manage Nausea</i>.* <p>Tell your healthcare team if nausea or vomiting continues or is not controlled with your anti-nausea drug(s)</p>
<p>Skin rash, acne, itchiness, dryness, or redness may sometimes occur.</p>	<p>If very irritating, call your healthcare team. Otherwise, be sure to mention it at your next visit.</p>
<p>Fever may sometimes occur.</p>	<ul style="list-style-type: none"> • Take acetaminophen (e.g., TYLENOL®) every 4-6 hours, to a maximum of 4 g (4000 mg) per day. • If your fever is 38C or higher stop taking both encorafenib and binimetinib immediately and do not resume until you are fever free for at least 24 hours without taking any medications to bring down your fever (i.e. acetaminophen or non steroidal anti-inflammatories like ibuprofen). Stay well hydrated. If you also have symptoms of weakness, dizziness or dehydration with your fever call your healthcare team right
<p>Diarrhea may sometimes occur. If you have diarrhea and it is not controlled, you can quickly become dehydrated.</p>	<p>If diarrhea is a problem:</p> <ul style="list-style-type: none"> • Drink plenty of fluids. • Eat and drink often in small amounts. • Avoid high fibre foods as outlined in <i>Food Choices to Help Manage Diarrhea</i>.* <p>Tell your healthcare team if you have diarrhea for more than 24 hours.</p> <p>Note: If lactose in milk usually gives you diarrhea, the lactose in the tablet may be causing your diarrhea. Take LACTAID® tablets just before your binimetinib dose.</p>

SIDE EFFECTS	MANAGEMENT
Constipation may sometimes occur.	<ul style="list-style-type: none"> • Exercise if you can. • Drink plenty of fluids. • Try ideas in <i>Food Choices to Manage Constipation</i>. *
Sugar control may sometimes be affected.	<p>Tell your healthcare team if you are experiencing:</p> <ul style="list-style-type: none"> • Increased thirst. • Changes in how often you pass urine (go pee). <p>Check your blood sugar regularly if you have diabetes</p>
Hand-foot skin reaction may sometimes occur. The palms of your hands and soles of your feet may tingle, become red, numb, painful, or swollen. Skin may also become dry or itchy. You may not be able to do your normal daily activities if blisters, severe pain, or ulcers occur.	<ul style="list-style-type: none"> • Avoid tight-fitting shoes or rubbing pressure to hands and feet, such as that caused by heavy activity. • Avoid tight-fitting jewellery. • Clean hands and feet with lukewarm water and gently pat to dry; avoid hot water. • Apply a sunscreen with an SPF (sun protection factor) of at least 30. • Apply lanolin-containing creams (e.g., BAG BALM®, UDDERLY SMOOTH®) to hands and feet, liberally and often. • Tell your healthcare team at your next visit if you have any signs of hand-foot skin reaction as your dose may need to be changed.
Minor bleeding, such as nosebleeds , may occur.	<ul style="list-style-type: none"> • Sit up straight and tip your head slightly forward. Tilting your head back may cause blood to run down your throat. • Pinch your nostrils shut between your thumb and forefinger or apply firm pressure against the bleeding nostril for 10 full minutes. • After 10 minutes, check to see if your nose is still bleeding. If it is, hold it for 10 more minutes. • Stay quiet for a few hours and do not blow your nose for at least 12 hours after the bleeding has stopped. • Get emergency help if a nosebleed lasts longer than 20 minutes.

SIDE EFFECTS	MANAGEMENT
<p>Abnormal heart rhythm (QT prolongation) may rarely occur. Signs include feeling like heart is pounding, racing or beating irregularly, dizziness, tiredness, feeling lightheaded, shortness of breath, swelling in legs.</p>	<p>Minimize your risk of abnormal heart rhythm by:</p> <ul style="list-style-type: none"> • always checking with your pharmacist and doctor about drug interactions when starting a new medication, herbal product, or supplement • avoiding grapefruit and grapefruit juice. <p>Contact your doctor immediately or get emergency help if your heart is beating irregularly or fast, OR if you feel faint, lightheaded, or dizzy.</p>
<p>Muscle or joint pain may sometimes occur</p>	<p>You may take acetaminophen (e.g., TYLENOL®) every 4-6 hours to a maximum of 4 g (4000 mg) per day or ibuprofen (e.g., ADVIL®) for mild to moderate pain.</p> <ul style="list-style-type: none"> • Tell your healthcare team if the pain interferes with your activity
<p>Swelling of hands, feet, or lower legs may sometimes occur if your body retains extra fluid.</p>	<p>If swelling is a problem:</p> <ul style="list-style-type: none"> • Elevate your feet when sitting. • Avoid tight clothing.
<p>Headache may sometimes occur.</p>	<p>Take acetaminophen (e.g., TYLENOL®) every 4-6 hours if needed, to a maximum of 4 g (4000 mg) per day.</p>
<p>Taste alteration may sometimes occur.</p>	<p>Try the ideas in <i>Food Ideas to Cope with Taste and Smell Changes</i>.*</p>
<p>You may sometimes have trouble sleeping.</p>	<ul style="list-style-type: none"> • Tell your healthcare team if you continue to have trouble sleeping. • This will return to normal when you stop taking encorafenib and binimetinib.
<p>Loss of appetite may sometimes occur.</p>	<p>Try the ideas in <i>Food Ideas to Help with Decreased Appetite</i>.*</p>
<p>Tiredness and lack of energy may sometimes occur.</p>	<ul style="list-style-type: none"> • Do not drive a car or operate machinery if you are feeling tired. • Try the ideas in <i>Fatigue/Tiredness – Patient Handout</i>.*
<p>Hair loss sometimes occurs with encorafenib and binimetinib. Hair will grow back once you stop treatment. Colour and texture may change</p>	<p>If hair loss is a problem, refer to <i>Resources for Hair Loss and Appearance Changes – Patient Handout</i>.*</p>

SIDE EFFECTS	MANAGEMENT
<p>Numbness or tingling of the fingers or toes may sometimes occur. This will slowly return to normal once your treatments are over. This may take several months.</p>	<ul style="list-style-type: none"> • Be careful when handling items that are sharp, hot, or cold. • Be careful when walking on uneven surfaces or doing activities that need you to balance or be steady. • Tell your healthcare team at your next visit, especially if you have trouble with buttons, writing, picking up small objects, walking, or have fallen.
<p>Your skin may sunburn more easily than usual.</p>	<ul style="list-style-type: none"> • Tell your healthcare team if you have a severe sunburn or skin reaction such as itching, rash, or swelling after sun exposure. • Refer to <i>Your Medication Sun Sensitivity and Sunscreens*</i> or the <i>BC Health Guide</i> for more information.
<p>A type of skin cancer called cutaneous squamous cell carcinoma may rarely occur.</p>	<p>Check your skin and tell your healthcare team right away if you notice any skin changes including:</p> <ul style="list-style-type: none"> • a new wart, • a sore or reddish bump that bleeds or does not heal, or • a change in size or color of a mole. <p>Cutaneous squamous cell carcinoma is usually managed with simple removal (excision). Refer to the <i>BC Health Guide</i> for information about protecting your skin from sun exposure.</p>
<p>High blood pressure may sometimes occur.</p>	<p>Your blood pressure may be checked by your healthcare team during your visit.</p> <ul style="list-style-type: none"> • You may be asked to check your blood pressure frequently between visits. • Your doctor may give you a prescription for blood pressure medication if your blood pressure is high. <p>Tell your doctor if you are already on blood pressure medication. Your doctor may have to adjust your dose</p>

***Please ask your cancer care team for a copy.**

THE FOLLOWING INFORMATION IS VERY IMPORTANT

STOP TAKING ENCORAFENIB AND BINIMETINIB AND CHECK WITH YOUR HEALTHCARE TEAM OR GET EMERGENCY HELP IMMEDIATELY IF YOU HAVE:

- Signs of an **allergic reaction** (rare) including dizziness, fast heartbeat, face swelling, or breathing problems.
- **Changes in eyesight** such as blurred vision, loss of vision, seeing halos or coloured dots or you have eye pain.
- Signs of **bleeding problems** such as black and/or tarry stools, blood in urine, pinpoint red spots on skin, or extensive bruising.
- Signs of a **blood clot** such as tenderness or hardness over a vein, calf swelling and tenderness, sudden onset of cough, chest pain, or shortness of breath.
- Severe unexplained **muscle** pain, muscle swelling, or weakness.
- Signs of **heart or lung problems** such as fast or uneven heartbeat, chest pain, chest pressure, shortness of breath or difficulty in breathing, swelling of feet or lower legs, or fainting.
- **Face muscles** that are weak, don't move, or appear to droop.
- Severe **abdominal pain** or tenderness.

CHECK WITH YOUR HEALTHCARE TEAM AS SOON AS POSSIBLE (DURING OFFICE HOURS) IF YOU HAVE:

- Signs of **anemia** such as unusual tiredness or weakness.
- Signs of **liver problems** such as yellow eyes or skin, white or clay-coloured stools.
- Signs of **kidney problems** such as lower back or side pain, swelling of feet or lower legs.
- Signs of **skin changes** such as a new wart, a sore or reddish bump that bleeds or does not heal, or a change in size, shape, or colour of a mole.
- Severe **abdominal pain** or tenderness.

CHECK WITH YOUR HEALTHCARE TEAM IF ANY OF THE FOLLOWING CONTINUE OR BOTHER YOU:

- Thickening of the outer layers of the skin.
- Uncontrolled nausea, vomiting, or diarrhea.
- Muscle weakness.
- For patients with diabetes: uncontrolled blood sugars.

If you experience symptoms or changes in your body that have not been described above but worry you, or in any symptoms are severe, contact:

_____ at telephone number: _____