



Provincial Health Services Authority

For the Patient: USMAJDT

Other Names: Adjuvant Treatment of Stage III and IV, BRAF mutated, fully resected Melanoma Using daBRAFeinib and Trametinib

U = Undesignated (requires special approval)

SM = Skin and Melanoma

AJ = Adjuvant

DT = Dabrafenib and Trametinib

ABOUT THIS MEDICATION

What is this drug used for?

- Dabrafenib (da braf' e nib) and trametinib (tra me' ti nib) is a drug combination that is used to treat a type of skin cancer called melanoma,
 - that has been removed by surgery, and
 - that has a certain type of abnormal "BRAF" gene.

How does this drug work?

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

INTENDED BENEFITS

- Dabrafenib and trametinib are being given to reduce the chance of your skin cancer (melanoma) coming back.

TREATMENT SUMMARY

How are these drugs given?

- Dabrafenib is a capsule, trametinib is a tablet that you take by mouth.
- Dabrafenib is taken twice daily, trametinib is taken once 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.
- A blood test (lab work) and other tests are done before starting treatment and each time you see your oncologist.
- 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** dabrafenib capsules out of the reach of children, at room temperature, away from heat, light, and moisture.
- **Store** trametinib tablets out of the reach of children, in the **refrigerator** between **2 – 8 degrees celsius**, away from heat, light, and moisture. Keep trametinib in its original packaging. Do not remove desiccant. Once the bottle has been opened, tablets may be stored in the refrigerator or at room temperature for 30 days. Return expired tablets to your pharmacy for disposal.

How should I take this drug?

- Dabrafenib is taken twice daily, in the morning and in the evening, approximately 12 hours apart.
Trametinib is taken once daily at about the same time everyday with either the morning or evening dose of dabrafenib.
- You **take** dabrafenib and trametinib on an empty stomach at least 1 hour before or 2 hours after food.
- Do not chew, open or crush dabrafenib capsules or trametinib tablets. **Swallow whole** with a full glass of water one at a time.
- If you **miss a dose** of dabrafenib, 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.
If you **miss a dose** of trametinib, 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 **vomit** the dose of dabrafenib and/or trametinib, 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 dabrafenib and trametinib?

- Other drugs such as hormonal birth control, certain antibiotics and anti-fungal agents, the herbal product St. John's Wort, seizure medications, and medicines for heart rhythm problems (i.e., quinidine, amiodarone, beta blockers) may **interact** with dabrafenib and/or trametinib. 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.
- The **drinking of alcohol** (in small amounts) does not appear to affect the safety or usefulness of dabrafenib and trametinib.

Other important things to know:

- Before you start taking dabrafenib and trametinib, 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 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) or **elevated blood sugar** levels (diabetes).

Liver or kidney problems.

Have or have had **blood clots** or **bleeding problems.**

A low number of **white blood cells** (neutropenia).

- Dabrafenib and trametinib may damage sperm and 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.
- **Tell** doctors or dentists that you are being treated with dabrafenib and trametinib 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.

SERIOUS SIDE EFFECTS	How common is it?	MANAGEMENT
Fever may commonly occur.	Common	<ul style="list-style-type: none"> • Call your doctor as soon as possible for advice if over 38.5°C by an oral thermometer. You may need to hold the treatment during fever and/or reduce the dose. • Do not restart treatment until your fever is < 38.0°C. Suggest you speak to an oncologist before restarting your drugs, especially during the first few months of treatment. If instructed to do so: take acetaminophen (e.g., TYLENOL®) every 4-6 hours, to a maximum of 4 g (4000 mg) per day. • If you have fever (over 38.5°C by an oral thermometer) plus another sign of infection, call your doctor immediately. Other signs of infection include chills, cough, or burning when you pass urine.
Skin rashes or dry skin may sometimes occur. Acne-like rash, redness of the face, itching skin.	Sometimes	<ul style="list-style-type: none"> • If rash is accompanied by signs of an allergic reaction such as flushing, dizziness, swelling, or breathing problems, call your doctor immediately. • If rash or itching is very irritating, call your doctor. Otherwise, be sure to mention it at your next visit.

SERIOUS SIDE EFFECTS	How common is it?	MANAGEMENT
Skin cancer called cutaneous squamous cell carcinoma (cuSCC) may rarely occur.	Rare	Check your skin and tell your oncologist right away about any skin changes including a: <ul style="list-style-type: none"> • new wart • skin sore or reddish bump that bleeds or does not heal • change in size or color of a mole Cutaneous squamous cell carcinoma is typically managed with simple excision.
Eye (vision) problems may rarely occur. Signs include seeing flashes of light, colour or black dots, blurred outline around objects (halo), partial loss of vision.	Rare	Report any changes in vision to your doctor as soon as possible.
Abnormal heart rhythm (QT or PR 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.	Rare	Minimize your risk of abnormal heart rhythm by: <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 Contact your doctor immediately or get emergency help if your heart is beating irregularly or fast, or if you feel faint, lightheaded, or dizzy.
Pancreatitis: inflammation of the pancreas causing severe abdominal pain	Rare	Report any signs to your doctor as soon as possible.
Rhabdomyolysis: muscle pain that you cannot explain, muscle tenderness or weakness, generalized weakness (especially if you don't feel well), brown or discoloured urine.	Rare	Report any signs to your doctor as soon as possible.

OTHER SIDE EFFECTS	How common is it?	MANAGEMENT
Tiredness and lack of energy may sometimes occur.	Sometimes	<ul style="list-style-type: none"> • Do not drive a car or operate machinery if you are feeling tired. • Try the ideas in <i>Your Bank to Energy Savings: Helping People with Cancer Handle Fatigue</i>.*
Nausea and vomiting may sometimes occur after your treatment. Most people have little or no nausea.	Sometimes	<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. <p>Try the ideas in <i>Food Choices to Help Control Nausea</i>.*</p>
Headache may sometimes occur.	Sometimes	Take acetaminophen (e.g., TYLENOL®) every 4-6 hours if needed, to a maximum of 4 g (4000 mg) per day.
Diarrhea may sometimes occur.	Sometimes	<p>If diarrhea is a problem:</p> <ul style="list-style-type: none"> • Drink plenty of fluids. • Eat and drink often in small amounts. <p>Avoid high fibre foods as outlined in <i>Food Ideas to Help Manage Diarrhea</i>.*</p>
Muscle, limb, or joint pain may sometimes occur.	Sometimes	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. Tell your doctor if the pain interferes with your activity.

OTHER SIDE EFFECTS	How common is it?	MANAGEMENT
High blood pressure may sometimes occur. New or worsening high blood pressure during treatment.	Sometimes	Your blood pressure will be checked each time you visit with your doctor. Contact your doctor if you develop high blood pressure, your blood pressure worsens, or you have severe headache, lightheadedness or dizziness between visits.
Swelling of hands, feet, or lower legs may sometimes occur if your body retains extra fluid.	Sometimes	If swelling is a problem: <ul style="list-style-type: none"> • Elevate your feet when sitting. • Avoid tight clothing.
Constipation may sometimes occur.	Sometimes	If constipation is a problem: <ul style="list-style-type: none"> • Exercise if you can. • Drink plenty of fluids. Try ideas in <i>Suggestions for Dealing with Constipation</i> .*
Loss of appetite may sometimes occur.	Sometimes	Try the ideas in <i>Food Ideas to Help with Decreased Appetite</i> .*
Hair loss may rarely occur. Hair will grow back once you stop treatment. Colour and texture may change.	Rare	<ul style="list-style-type: none"> • Use a gentle shampoo and soft brush. • Care should be taken with use of hair spray, bleaches, dyes and perms. If hair loss is a problem, refer to <i>For the Patient: Hair Loss Due to Chemotherapy</i> *.
Sugar control may rarely be affected in diabetics. Rarely, patients can develop new onset of diabetes.	Rare	Check your blood sugar regularly if you are diabetic. Contact your oncologist if you develop new excessive thirst and frequent urination, as that could be a sign of high blood sugars.
Heart failure may rarely occur during treatment. Your heart will pump blood less efficiently.	Rare	Trametinib can have a serious effect on the heart, causing failure of the heart's pumping action, which results in shortness of breath, fatigue and leg swelling. Your heart function will be tested before you start Trametinib, 8 weeks after you start. Then every 3 months while you are getting treatment. Your treatment may be stopped or interrupted if there are concerns about your heart function.

OTHER SIDE EFFECTS	How common is it?	MANAGEMENT
<p>Hand-foot skin reaction may rarely occur during treatment. 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.</p>	Rare	<ul style="list-style-type: none"> • Avoid tight-fitting shoes, jewellery or rubbing pressure to hands and feet, such as that caused by heavy activity. • 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 (eg. BAG BALM®, UDDERLY SMOOTH®) to hands and feet liberally and often. • Tell your cancer doctor at the next visit if you have any signs of hand-foot skin reaction. • Stop taking dabrafenib and trametinib and call your cancer doctor if the skin reaction is painful, as your dose may need to be changed.
<p>Nail changes such as change in colour, nail pain, infection and swelling of the cuticles may rarely occur.</p>	Rare	<p>Take acetaminophen (e.g., TYLENOL®) every 4-6 hours, to a maximum of 4 g (4000 mg) per day.</p>
<p>Sore mouth may rarely occur during treatment. Mouth sores can occur on the tongue, the sides of the mouth or in the throat. Mouth sores or bleeding gums can lead to an infection.</p>	Rare	<ul style="list-style-type: none"> • Brush your teeth gently after eating and at bedtime with a very soft toothbrush. If your gums bleed, use gauze instead of a brush. Use baking soda instead of toothpaste. • Make a mouthwash with ½ teaspoon baking soda or salt in 1 cup warm water and rinse several times a day. • Try soft, bland foods like puddings, milkshakes and cream soups. • Avoid spicy, crunchy or acidic food, and very hot or cold foods. Try ideas in <i>Easy to Chew, Easy to Swallow Food Ideas</i>*.

***Please ask your oncologist or pharmacist for a copy.**

THE FOLLOWING INFORMATION IS VERY IMPORTANT

STOP TAKING DABRAFENIB AND TRAMETINIB AND SEE YOUR DOCTOR OR GET EMERGENCY HELP IMMEDIATELY IF YOU HAVE:

- Signs of **bleeding problems** such as headaches, dizziness or feeling weak, coughing up blood or blood clots, vomiting blood or vomit looking like “coffee grounds”, blood in urine, red or black stools that look like tar, extensive bruising, pinpoint red spots on skin.
- Signs of an **infection** such as fever (over 38.5°C by an oral thermometer), shaking chills; severe sore throat, productive cough (coughing up thick or green sputum); cloudy or foul smelling urine; painful, tender, or swollen red skin wounds or sores.
- Signs of a **blood clot** such as 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 or pale arm or leg.
- Signs of **lung complications** (pneumonitis/ILD-inflammation of the lung) such as shortness of breath and cough.
- Signs of an **allergic reaction** soon after a treatment including rash, hives, dizziness, fast heart beat, swelling of the face, lips, tongue or throat, swallowing or breathing problems.
- Signs of **heart problems** such as fast or uneven heartbeat, shortness of breath, dizziness, or fainting.
- Severe **abdominal pain**.

SEE YOUR DOCTOR 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.
- Changes in **eyesight, eye pain, or sensitivity of eyes** to light.
- 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, or thick or rough, scaly patches of the skin.
- **Numbness** or **tingling** in feet or hands.
- **Inflamed** or **infected** areas on the skin.

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

- Uncontrolled nausea, vomiting, or diarrhea.
- Headache not controlled with acetaminophen (e.g., TYLENOL®).
- Skin rash, redness, or itching.
- Trouble sleeping or night sweats.
- Dizziness.
- Muscle spasms.
- Cough or dry mouth.
- For diabetics: 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: _____