

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

Pr **MEKINIST**[®]

Trametinib Tablets

Read this carefully before you start taking **MEKINIST** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **MEKINIST**.

Your cancer may be treated with MEKINIST in combination with another medication called dabrafenib. When you take MEKINIST with dabrafenib, read the Patient Medication Information leaflet for dabrafenib as well as this one.

Serious Warnings and Precautions

MEKINIST should be prescribed and managed by a physician experienced in the administration of anti-cancer drugs. Serious side effects include:

- Heart problems
- Eye problems
- Lung complications
- Skin problems, including serious cases of rash, with or without infections
- Blood clots in the veins (deep vein thrombosis) and in the lung (pulmonary embolism)
- Serious bleeding into organs (brain, lung, stomach and bowels)

Other serious side effects when taking MEKINIST with dabrafenib include:

- Severe fever

What is MEKINIST used for?

Taking MEKINIST **by itself** is used to:

- treat a type of skin cancer called melanoma. This type of melanoma cannot be removed by surgery or has spread to other parts of the body.

Taking MEKINIST **with dabrafenib** is used to:

- treat a type of skin cancer called melanoma. This type of melanoma cannot be removed by surgery or has spread to other parts of the body.
- help prevent melanoma from coming back. This is after the skin cancer was completely removed by surgery.
- treat a type of lung cancer. This type of cancer is called non-small cell lung cancer. These drugs are used together when this cancer has spread to other parts of the body.

MEKINIST should only be used for people who have a cancer that has a certain change in a

gene called “BRAF”. Before taking MEKINIST, you should have your cancer tested for this gene. Your doctor will take a tumour tissue sample to test whether MEKINIST is suitable for you.

MEKINIST is not recommended for children and adolescents (less than 18 years of age).

How does MEKINIST work?

MEKINIST targets proteins made from the changed (mutated) BRAF gene. This slows down or stops the growth of cancer cells.

What are the ingredients in MEKINIST?

Medicinal ingredient: Trametinib

Non-medicinal ingredients: Croscarmellose sodium, hypromellose, iron oxide yellow (0.5 mg tablets), iron oxide red (2 mg tablets), magnesium stearate, mannitol, microcrystalline cellulose, polyethylene glycol, polysorbate 80 (2 mg tablets), silicon dioxide (colloidal), sodium lauryl sulphate, titanium dioxide.

MEKINIST comes in the following dosage forms:

Tablets: 0.5 mg and 2 mg

Do not use MEKINIST if:

- you are allergic to trametinib, or any of the other ingredients in MEKINIST.
- you do not have a particular change (mutation) in a gene called BRAF or if the mutation in BRAF is not known.

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

- are pregnant, may be pregnant or are planning to become pregnant. You must use effective non-hormonal birth control while you are taking MEKINIST and for at least 16 weeks after you stop taking it. Pills, patches and injections are not effective in preventing pregnancies when you are taking MEKINIST with dabrafenib, because they will not work as well. Use other birth control methods when taking the two drugs together. You must make sure that you do not get pregnant while using MEKINIST. If you do get pregnant, inform your doctor immediately. MEKINIST can harm an unborn baby.
- are breastfeeding. Do not breastfeed if you are taking MEKINIST.
- are a male (who has had a vasectomy or not) with a female partner who is pregnant or may become pregnant. You should use condoms with spermicide during sexual intercourse while taking MEKINIST and for at least 16 weeks after stopping MEKINIST. Men who take MEKINIST with dabrafenib may have a reduced count of sperm due to dabrafenib; this may not return to normal levels after you stop taking dabrafenib.
- have or had any **heart problems**. This can include heart failure or problems with the way your heart beats (such as irregular heartbeat or changes with the electrical activity of your heart, known as QT prolongation). This can also include any risk factors for Torsade de Pointes (dangerous rapid fluttering of the heart). Risk factors include diabetes, low potassium, magnesium or calcium levels, or a history of low heart rate, fainting, or loss of

consciousness. Your doctor should check your heart function before you start taking MEKINIST and during treatment.

- have any **eye problems**. This includes **retinal vein occlusion** (blockage of the vein draining the eye) or **chorioretinopathy** (swelling in the eye which may be caused by fluid blockage). Your doctor may arrange for you to have an eye exam before you take MEKINIST and while you are taking it.
- have any **skin problems** including rash or acne-like rash.
- have developed another type of cancer while taking MEKINIST with dabrafenib.
- have any **lung or breathing problems**, including difficulty in breathing often accompanied by a dry cough, shortness of breath and fatigue. Your doctor may arrange to check your lung function before you start taking MEKINIST.
- have **high blood pressure**.
- have **liver or kidney problems**.
- have had **blood clots**.
- have or have had **bleeding problems**.
- have a low number of white blood cells.
- have heart valve problems.
- have elevated blood sugar levels.
- plan to have surgery, dental or other medical procedures.

Other warnings you should know about:

Heart problems: MEKINIST can affect how well your heart pumps with each beat. People may be more likely to develop this side effect if they have an existing heart problem. You will be checked for any heart problems while you are taking MEKINIST. Signs and symptoms of heart problems include:

- Feeling like your heart is pounding, racing, or beating irregularly
- Dizziness
- Tiredness
- Feeling lightheaded
- Shortness of breath
- Swelling in the legs

Eye (Vision) problems: MEKINIST can cause eye problems, including blindness. MEKINIST is not recommended if you have ever had, or are at risk of certain eye conditions. These conditions include **retinal detachment** (sensation of flashing light, loss of vision) or **retinal vein occlusion**. Your doctor may tell you to get an eye exam before you take MEKINIST. Your doctor may also tell you to get an eye exam while you are taking MEKINIST. Your doctor will ask you to stop taking MEKINIST and refer you to a specialist, if you develop signs and symptoms in your vision that include:

- Colour dots
- Halo (seeing a blurred outline around objects)
- Blurred vision

MEKINIST, when taken with dabrafenib, can cause eye inflammation called **uveitis**.

Inflammatory disease: MEKINIST, when taken with dabrafenib, can cause an

inflammatory disease mainly affecting the skin, lung, eyes and lymph nodes called sarcoidosis. Common symptoms may include coughing, shortness of breath, swollen lymph nodes, visual disturbances, fever, fatigue, pain and swelling in the joints, and tender bumps on your skin. **Tell your doctor if you get any of these symptoms.**

Lung problems: MEKINIST can cause problems with your lungs such as **interstitial lung disease or pneumonitis** (inflammation of your tissues in your lung). In some cases, these lung problems can be fatal.

Skin problems: MEKINIST can cause rash, acne-like rash, serious skin reactions and infections. Tell your doctor if you if you experience any of the following symptoms:

- Rash, red skin, blistering of the lips, eyes, or mouth, skin peeling, with or without fever (**Stevens-Johnson syndrome**)
- Widespread rash, fever and enlarged lymph nodes (**drug reaction with eosinophilia and systemic symptoms (DRESS)**)

Blood clots: MEKINIST, when taken alone or with dabrafenib, can cause blood clots in your arms and legs, which can travel to your lungs or other parts of the body and can lead to death. Get medical help right away if you have any of the following symptoms:

- Chest pain
- Sudden shortness of breath or trouble breathing
- Pain in your legs with or without swelling
- Swelling in your arms or legs, especially one larger than the other
- A cool or pale arm or leg

Bleeding problems: MEKINIST, when taken alone or with dabrafenib, can cause serious bleeding problems, including in your brain, stomach, or bowel, and can lead to death. In some cases, people may develop brain tumours. Call your doctor and get medical help right away if you have any unusual signs of bleeding including:

- Headaches, dizziness, or feeling weak
- Coughing up blood or blood clots
- Vomiting blood or your vomit looks like “coffee grounds”
- Red or black stools that look like tar

Gastrointestinal problems: MEKINIST can cause diarrhoea, pain in your stomach and fever. These are possible signs of an inflamed colon. Taking MEKINIST can also increase the risk of getting holes in the wall of your intestines or stomach. This is an uncommon event. Tell your doctor if you have problems in your stomach or intestines. Also, tell your doctor if you get severe stomach pain while taking MEKINIST.

Muscle problems: MEKINIST can result in the breakdown of muscle (**rhabdomyolysis**). Tell your doctor as soon as possible if you get any of these symptoms:

- Muscle pain that you cannot explain, muscle tenderness or weakness
- Generalized weakness (especially if you don't feel well)
- Brownish or discoloured urine

Fever (temperature 38°C or higher): Taking MEKINIST with dabrafenib may cause fever. Fever may happen more often or may be more severe when MEKINIST is taken with dabrafenib. If you get a fever, or if you feel a fever coming on, stop taking MEKINIST, or MEKINIST and dabrafenib if you are taking both and tell your healthcare professional right away. In some cases, people with fever may develop severe chills, dehydration, low blood pressure, dizziness and kidney problems. Your healthcare professional may recommend that you stop taking MEKINIST while they treat your fever with other medicines. They will tell you if and when you can re-start MEKINIST. You may receive a lower dose or your treatment may be stopped altogether.

Decrease in white blood cells (neutropenia): Taking MEKINIST with dabrafenib can cause a decrease in a certain kind of white blood cells. This may lead to infection, which can be life-threatening. Decrease in white blood cells may also lead to unexpected bruising or bleeding. Your doctor will monitor you for signs of low white blood cells. Signs that certain white cell counts are low may include:

- Symptoms of infection (fever, chills, sore throat)
- Bruise or bleed easily
- Cold

Liver problems: Taking MEKINIST with dabrafenib can cause problems with your liver. This may develop into serious conditions such as hepatitis and liver failure. These conditions may be fatal. Your doctor will monitor you periodically. Signs that your liver may not be working properly may include:

- Loss of appetite
- Nausea
- Vomiting
- Pain in your stomach (abdomen)
- Yellowing of your skin or the whites of your eyes (jaundice)
- Dark-coloured urine
- Itching of your skin

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 MEKINIST:

The following list includes some, but not all, of the drugs that may interact with MEKINIST to affect the electrical activity of your heart:

- Antiarrhythmics (drugs that stabilize the heart rhythm function, such as quinidine, procainamide, amiodarone, sotalol, etc.)
- Beta-blockers used to lower blood pressure
- HIV protease inhibitors

How to take MEKINIST:

Take MEKINIST:

- exactly as your healthcare professional has told you. Check with your doctor or pharmacist if you are not sure;

- once per day on an empty stomach, at least one hour before or two hours after a meal. It is important to take MEKINIST **without food**. This is because food may affect the way MEKINIST is absorbed into your body;
- at about the same time each day;
- Swallow tablet whole with a full glass of water;
- Do not take more than one dose of MEKINIST a day.
- Take MEKINIST for as long as your doctor recommends.
- **If you take MEKINIST with dabrafenib:**
 - take MEKINIST with either the morning or the evening dose of dabrafenib. Your healthcare professional will tell you how to take dabrafenib.

Usual dose:

Taking MEKINIST by itself: the usual dose of MEKINIST is one 2 mg tablet once a day.

Taking MEKINIST with dabrafenib: the usual dose is 2 mg of MEKINIST once a day with two 75 mg capsules of dabrafenib (150 mg) twice a day.

Your doctor may decide that you should take a lower dose if you get side effects. They may also temporarily interrupt your treatment.

Overdose:

If you think you, or a person you are caring for, have taken too much MEKINIST, contact a healthcare professional, hospital emergency department or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:

If you miss a dose, take it as soon as you remember. If there are less than 12 hours until your next scheduled dose, skip the missed dose. Take the next dose at your usual time. **Do not take more than one dose of MEKINIST at a time.**

What are possible side effects from using MEKINIST?

These are not all the possible side effects you may feel when taking MEKINIST. If you experience any side effects not listed here, contact your healthcare professional.

- Diarrhea
- Nausea, vomiting
- Constipation
- Decreased appetite
- Stomach ache (abdominal pain)
- Weight increased or decreased
- Dry mouth
- Sore mouth or mouth ulcers
- Chills
- Lack of energy or feeling weak, sick or tired

- Tiredness, chills, sore throat, joint or muscles aching (flu-like illness)
- Inflammation of mucous membranes
- Swelling of the face, hands or feet localized tissue swelling
- Swelling around the eyes
- Dehydration (low levels of water or fluid)
- Headache
- Dizziness
- Thickening of the outer layers of the skin
- Redness, chapping or cracking of the skin
- Peeling on the palms, fingers and soles of the feet which may be accompanied by tingling sensation and burning pain
- Skin tags
- Wart-like growths
- Skin lesions
- Skin effect such as rash, wart-like growths, or redness and/or swelling
- Brown or yellowish thickening of skin
- Rough scaly patches of skin
- Increased sensitivity of the skin to sun
- Unusual hair loss or thinning
- Excessive sweating
- Night sweats
- Pain in the hands or feet
- Joint pain
- Muscle pain
- Muscle spasms
- Cough
- Shortness of breath, laboured breathing
- High blood pressure - MEKINIST can cause high blood pressure or make your high blood pressure worse. Your doctor should check your blood pressure during treatment with MEKINIST. Tell your doctor if you develop high blood pressure, if it gets worse, or if you have severe headache, light-headedness, or dizziness.
- Low blood pressure
- Slow heart rate
- Nose bleeds
- Nasal inflammation
- Urinary tract infections
- Inflammation of the follicles in the skin
- Skin rash with pus-filled blisters
- Nail disorders such as nail bed changes, nail pain, infection and swelling of the cuticles

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

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
VERY COMMON			
Dermatitis acneiform: Skin rash, acne-like rash, redness of the face, dry or itching skin	✓		
Fever (temperature of 38°C or higher) or any fever that may be accompanied by rigors, chills, low blood pressure or kidney problems			✓
Hyponatremia (low blood levels of sodium): tiredness, confusion, muscle twitching, convulsions			✓
Oedema: generalised swelling			✓
Serious bleeding problems involving: <ul style="list-style-type: none"> • the brain (headaches, dizziness, feeling weak), • the lungs (coughing up blood or blood clots) • the intestine (vomiting blood or vomit looking like “coffee grounds”, red or black stools that look like tar) • Other (bleeding gums, unusual bleeding from the vagina, blood in urine) 			✓ ✓ ✓
COMMON			
Allergic reaction: Rash, hives, swelling of the face, lips, tongue or throat, difficulty swallowing or breathing			✓
Cellulitis (infection of the deeper layers of the skin): red, swollen pain area of skin that can be warm or tender, fever, chills		✓	
Cutaneous squamous cell cancer including keratoacanthomas: skin sore, wart, or reddish bump that bleeds or does not heal		✓	
Eye (vision) problems: Seeing flashes of light, colour or black dots (floaters), blurred outline			

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
<p>around objects (halo), partial loss of vision. These eye problems may also include:</p> <ul style="list-style-type: none"> • Retinal Vein Occlusion (RVO): Blurred or reduced vision. This usually happens in one eye and could occur abruptly. • Uveitis (inflammation of the inner layer of the eye): red, swollen eye, eye pain, burning or sensitivity to light, blurred vision, headache • Chorioretinopathy (swelling in the eyes caused by leaking fluid): distorted, dimmed or blurred vision, dark area in the middle of your vision • Papilloedema (swelling of the optic disc in the eye): blurred or double vision, flickering, loss of vision • Retinal Pigment Epithelial Detachment (splitting of the light-sensitive membrane in the back of the eye from its supporting layers): blurred or distorted vision (uncommon) 		<p>✓</p> <p>✓</p> <p>✓</p> <p>✓</p>	<p>✓</p>

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
Heart problems (decreased ejection fraction, left ventricular dysfunction and cardiac failure): feeling like your heart is pounding, racing, or beating irregularly, dizziness, tiredness, feeling lightheaded, fatigue, weakness, shortness of breath, and swelling in the legs		✓	
Hyperglycemia (high blood sugar): increased thirst, frequent urination, dry skin, headache, blurred vision and fatigue		✓	
Pancreatitis (inflammation of the pancreas): severe upper stomach pain, fever, rapid heart beat, nausea, vomiting, tenderness when touching the abdomen			✓
Panniculitis (inflammation of the fatty layer under the skin): large tender red bumps under the skin		✓	
Papilloma of the skin: small non-cancerous lumps on the skin	✓		
Tubulointerstitial nephritis (inflammation of the kidney): high or low urine output, drowsiness, confusion, nausea as a sign of an inflamed kidney			✓
Venous thromboembolism (blood clots): chest pain, sudden shortness of breath or trouble breathing, pain in your legs with or without swelling, swelling in your arms and legs, or a cool, pale arm or leg			✓
UNCOMMON			
Gastrointestinal complications: severe stomach pain, chills, fever, nausea, vomiting of blood, black or bloody stools, holes in the intestinal wall			✓

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
Kidney failure (severe kidney problems): confusion; itchiness or rashes; puffiness in your face and hands; swelling in your feet or ankles; urinating less or not at all; weight gain			✓
Lung complications including pneumonitis / and interstitial lung disease (inflammation of the lung): shortness of breath and cough			✓
New melanoma (mole which has irregular shape, border, or colour, is growing, or changing shape or colour, new skin lesion)		✓	
Rhabdomyolysis (breakdown of damaged muscle): muscle pain that you cannot explain, muscle tenderness or weakness, generalized weakness (especially if you don't feel well), brownish or discoloured urine		✓	
Sarcoidosis (inflammatory disease mainly affecting the skin, lungs and eyes): coughing, shortness of breath, swollen lymph nodes, visual disturbances, fever, fatigue, pain and swelling in the joints, tender bumps on your skin		✓	

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to 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 (<https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html>) for information on how to report online, by mail or by fax; or

- Calling toll-free at 1-866-234-2345.

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

Storage:

Store in a refrigerator between 2°C to 8°C in the original package. Protect from light and moisture. Do not remove desiccant.

The bottle should not be removed from refrigerated conditions for more than 30 days.

Keep out of reach and sight of children.

If you want more information about MEKINIST:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html>); the manufacturer's website www.novartis.ca by calling 1-800-363-8883.

This leaflet was prepared by Novartis Pharmaceuticals Canada Inc.

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