

## PATIENT MEDICATION INFORMATION

### READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

Pr **MEKINIST**<sup>®</sup>

#### 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**.

#### 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

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

#### What is MEKINIST used for?

MEKINIST can be taken by itself or with dabrafenib. When you take MEKINIST with dabrafenib, read both leaflets.

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.

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.

### **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, magnesium stearate, mannitol, microcrystalline cellulose, silicon dioxide (colloidal), sodium lauryl sulphate. *Tablet coating*: hypromellose, iron oxide yellow (0.5 mg tablets), iron oxide red (2 mg tablets), polyethylene glycol, polysorbate 80 (2 mg tablets), titanium dioxide.

### **MEKINIST comes in the following dosage forms:**

Film-coated 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.
- 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:**

***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 sensation of flashing light, loss of vision (*retinal detachment*) or blockage of the vein draining the eye (*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 (*uveitis*).

**Inflammatory disease (sarcoidosis):** MEKINIST, when taken with dabrafenib, can cause an inflammatory disease mainly affecting the skin, lung, eyes and lymph nodes. 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 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 (high temperature > 38.5°C):** Taking MEKINIST with dabrafenib may cause severe fever. Fever may happen more often or may be more severe when taking MEKINIST with dabrafenib. If you get a fever while you are taking MEKINIST, refer to the **Serious side effects and what do to about them** table below for more information.

In some cases, people with fever may develop severe chills, dehydration, low blood pressure, dizziness and kidney problems. For these complications or if the fever is severe, your doctor may recommend that you stop taking both MEKINIST and dabrafenib while they treat the fever with other medicines. Once controlled, your doctor may recommend that you start taking MEKINIST and dabrafenib again.

**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
- Feeling sick (*nausea*)
- Being sick (*vomiting*)
- Pain in your stomach (abdomen)
- Yellowing of your skin or the whites of your eyes (*jaundice*)
- Dark-coloured urine
- Itching of your skin

**Other warnings you should know about:**

**BEFORE you use MEKINIST either by itself or with dabrafenib talk to your doctor 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 blockage of the vein draining the eye (*retinal vein occlusion*) or swelling in the eye which may be caused by fluid blockage (*chorioretinopathy*). 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** (*hypertension*).
- Have **liver or kidney problems**.
- Have had **blood clots**.
- Have or have had **bleeding problems**.
- Have a low number of white blood cells (*neutropenia*).
- Have heart valve problems.
- Have elevated blood sugar levels (*diabetes*).
- Plan to have surgery, dental or other medical procedures.

**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:**

It is important to take MEKINIST without food, because food may affect the way MEKINIST is absorbed into your body.

#### ***How to take MEKINIST either by itself or with dabrafenib:***

Take MEKINIST on an empty stomach at least one hour before or two hours after a meal.

Swallow the tablet whole, with a full glass of water.

Take MEKINIST at about the same time each day. Do not take more than one dose of MEKINIST a day.

If you take MEKINIST with dabrafenib, take MEKINIST with either the morning or the evening dose of dabrafenib. Take dabrafenib at about the same time two times each day.

Always take MEKINIST exactly as your doctor has told you to. Your doctor may decide that you should take a lower dose if you get side effects or to temporarily interrupt the treatment.

Take MEKINIST for as long as your doctor recommends.

#### **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.

#### **Overdose:**

If you think you have taken too much MEKINIST, contact your 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. Do not take it if it is close (within 12 hours) to your next dose. Just take the next dose at your regular 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.

#### **Side effects that can occur when you take MEKINIST are:**

##### **Very common side effects – these may affect more than 1 in 10 people:**

- Diarrhoea
- Feeling sick (*nausea*), being sick (*vomiting*)
- Constipation
- Stomach ache (*abdominal pain*)
- Dry mouth
- Lack of energy or feeling weak, sick or tired (*asthenia including malaise and fatigue*)
- Swelling of hands or feet (*oedema peripheral*)
- Unusual hair loss or thinning (*alopecia*)
- Cough
- Shortness of breath, laboured breathing (*dyspnoea*)
- Bleeding (from the gums, eyes, lungs, vagina, rectum and blood in urine) (*haemorrhage*)
- High blood pressure - MEKINIST can cause new or worsening high blood pressure

(*hypertension*). Your doctor should check your blood pressure during treatment with MEKINIST. Tell your doctor if you develop high blood pressure, your blood pressure worsens, or you have severe headache, light-headedness, or dizziness.

**Very common side effects that may show up in your blood tests:**

- Abnormal blood test results related to the liver

**Common side effects – these may affect up to 1 in 10 people:**

- Inflammation of the follicles in the skin
- Skin rash with pus-filled blisters (*rash pustular*)
- Redness, chapping or cracking of the skin (*skin fissure*)
- Infection of the skin (*cellulitis*)
- Nail disorders such as nail bed changes, nail pain, infection and swelling of the cuticles
- Skin effect such as rash, wart-like growths, or redness and/or swelling
- Possibly peeling on the palms, fingers and soles of the feet which may be accompanied by tingling sensation and burning pain (*palmar plantar erythrodysesthesia syndrome*)
- Nose bleeds (*epistaxis*)
- Sore mouth or mouth ulcers (*stomatitis*)
- Inflammation of mucous membranes
- Swelling of the face, localized tissue swelling (*face oedema*)
- Eyesight problems (blurred vision)
- Swelling around the eyes (*periorbital oedema*)
- Tiredness, chest discomfort, light headedness pain, palpitations (*ejection fraction decreased*)
- Changes in how the heart pumps blood (*left ventricular dysfunction*)
- Slow heart rate (*bradychardia*)
- Dehydration (low levels of water or fluid)
- Splitting of the light-sensitive membrane in the back of the eye from its supporting layers (*retinal detachment*)
- Swelling in the eyes caused by leaking fluid. This can cause blurred vision. (*chorioretinopathy*)

**Common side effects that may show up in your blood tests:**

- Decreased red blood cells (*anaemia*)
- Abnormal test related to creatine phosphokinase, an enzyme found mainly in heart, brain, and skeletal muscle

**Uncommon side effects – these may affect up to 1 in 100 people:**

- Swelling of nerves at the back of the eye (*papilloedema*)

Refer to the dabrafenib Patient Medication Information for possible side effects when MEKINIST is taken with dabrafenib.

**In addition to the above, other side effects that can occur when you take MEKINIST with dabrafenib are:**

**Very common side effects - these may affect more than 1 in 10 people:**

- Decreased appetite
- Chills
- Headache

- Dizziness
- Urinary tract infections
- Nasal inflammation (*nasopharyngitis*)
- Pain in the hands or feet (*pain in extremity*)
- Joint pain (*arthralgia*)
- Muscle pain (*myalgia*)
- Weight decreased
- Thickening of the outer layers of the skin (*hyperkeratosis*)
- Muscle spasms
- Low blood pressure (*hypotension*)
- Tiredness, chills, sore throat, joint or muscles aching (flu-like illness)

**Very common side effects that may show up in your blood tests:**

- Low levels of a type white blood cells (*neutropenia*)
- Low sodium (*hyponatraemia*)

**Common side effects – affects less than 1 in 10 but more than 1 in 100 people:**

- Night sweats
- Brown or yellowish thickening of skin (*seborrhoeic keratosis*)
- Skin tags (*acrochordon*)
- Excessive sweating (*hyperhidrosis*)
- Rough scaly patches of skin (*actinic keratosis*)
- Wart-like growths
- Inflammation of the fatty layer underneath the skin (*panniculitis*)
- Papilloma (a type of harmless (benign) skin cancer)
- Skin lesions
- Weight increased
- Increased sensitivity of the skin to sun (*photosensitivity*)

**Common side effects that may show up in your blood tests:**

- Decrease in the number of blood platelets (cells that help blood clot)
- Decrease in a type of white blood cells (*leukopenia*)
- Increase in some substances (enzymes) produced by the liver
- Low phosphorous (*hypophosphatemia*)
- Increase in blood sugar (glucose)

**Uncommon side effects – affects less than 1 in 100 but more than 1 in 1000 people:**

- Inflammation of the kidneys (*nephritis*)
- Kidney disorders that may result in decreased urine output (*kidney failure*)
- Inflammation of the pancreas causing strong abdominal pain (*pancreatitis*)
- Inflammatory disease mainly affecting the skin, lungs and eyes (*sarcoidosis*)



<b>Serious side effects and what to do about them</b>		
Symptom / effect	Talk to your healthcare professional	Stop taking drug and get immediate medical help
<b>VERY COMMON</b>		
<b>Dermatitis acneiform:</b> Skin rash, acne-like rash, redness of the face, dry or itching skin	✓	
<b>Serious bleeding problems:</b> headaches, dizziness or feeling weak, coughing up blood or blood clots, vomiting blood or vomit looking like “coffee grounds”, red or black stools that look like tar		✓
<b>VERY COMMON (when MEKINIST is taken with dabrafenib)</b>		
<b>Fever</b> (high temperature > 38.5°C – 40°C)	✓	
<b>Fever</b> (high temperature > 40°C) or any fever accompanied by rigors, chills, low blood pressure or kidney problems		✓
<b>Oedema:</b> generalised swelling		✓
<b>Hyponatremia (low blood levels of sodium):</b> tiredness, confusion, muscle twitching, convulsions		✓
<b>COMMON</b>		
<b>Venous thromboembolism (blood clots):</b> 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		✓
<b>Allergic reaction:</b> Rash, hives, swelling of the face, lips, tongue or throat, difficulty swallowing or breathing		✓
<b>COMMON (when MEKINIST is taken with dabrafenib)</b>		
<b>Cutaneous squamous cell cancer including keratoacanthomas</b> (skin sore, wart, or reddish bump that bleeds or does not heal)	✓	
<b>Acute pancreatitis:</b> acute, severe upper stomach pain		✓
<b>Tubulointerstitial nephritis:</b> high or low urine output, drowsiness, confusion, nausea as a sign of an inflamed kidney		✓

<b>Serious side effects and what to do about them</b>		
Symptom / effect	Talk to your healthcare professional	Stop taking drug and get immediate medical help
<b>Uveitis</b> (red, swollen eye): eye pain, burning or sensitive to light. Blurred vision Headache		✓
<b>UNCOMMON</b>		
<b>Heart problems:</b> feeling like your heart is pounding, racing, or beating irregularly, dizziness, tiredness, feeling lightheaded, shortness of breath, and swelling in the legs	✓	
<b>Eye (vision) problems:</b> Seeing flashes of light, colour or black dots (floaters), blurred outline around objects (halo), partial loss of vision. These problems can arise from: <ul style="list-style-type: none"> <li>• Retinal Vein Occlusion (RVO): Blurred or reduced vision. This usually happens in one eye and could occur abruptly.</li> <li>• Retinal Pigment Epithelial Detachment (RPEP): Blurred or distorted vision</li> </ul>	✓	
<b>Lung complications</b> (pneumonitis/ILD - inflammation of the lung): shortness of breath and cough		✓
<b>Gastrointestinal complications:</b> severe stomach pain, chills, fever, nausea, vomiting of blood, black or bloody stools, holes in the intestinal wall		✓
<b>Rhabdomyolysis:</b> muscle pain that you cannot explain, muscle tenderness or weakness, generalized weakness (especially if you don't feel well), brownish or discoloured urine	✓	
<b>UNCOMMON (when MEKINIST is taken with dabrafenib)</b>		
<b>New melanoma</b> (mole which has irregular shape, border, or colour, is growing, or changing shape or colour, new skin lesion)	✓	
<b>Pancreatitis</b> (inflammation of the pancreas causing strong abdominal pain)	✓	

<b>Serious side effects and what to do about them</b>		
Symptom / effect	Talk to your healthcare professional	Stop taking drug and get immediate medical help
<b>Sarcoidosis</b> (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](http://www.novartis.ca), or by calling 1-800-363-8883.

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