

PART III: CONSUMER INFORMATION**PrMEKINIST®
Trametinib Tablets**

This leaflet is part III of a three-part "Product Monograph" published when MEKINIST was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about MEKINIST. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION**What the medication is used for:**

MEKINIST is a medicine 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.

MEKINIST should only be used for people whose cancer has a particular change (mutation) in a gene called "BRAF". You should have your cancer tested for this change in the BRAF gene before starting treatment with MEKINIST.

Your doctor may decide that your melanoma will be treated with MEKINIST in combination with TAFINLAR®. If you are taking these two medicines together, read the TAFINLAR Consumer Information leaflet carefully as well as this leaflet.

What it does:

MEKINIST targets proteins activated by modified BRAF. This slows down or stops the growth of cancer cells.

When it should not be used:

Do not use MEKINIST if you are allergic to trametinib, or any of the other ingredients in MEKINIST (see What the important nonmedicinal ingredients are).

What the medicinal ingredient is:

Trametinib

What the important nonmedicinal ingredients are:

Croscarmellose sodium, hypromellose, magnesium stearate, mannitol, microcrystalline cellulose, silicon dioxide (colloidal), and 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), and titanium dioxide.

What dosage forms it comes in:

MEKINIST is available as film-coated tablets in strengths of 0.5 mg, 1.0 mg or 2.0 mg.

WARNINGS AND PRECAUTIONS**Serious Warnings and Precautions**

MEKINIST should be prescribed and managed by a physician experienced in the administration of anti-cancer agents. 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)

MEKINIST in combination with TAFINLAR
In addition to the above events,

- Severe fever

BEFORE you use MEKINIST talk to your doctor or pharmacist if you:

- Are pregnant, maybe pregnant or are planning to become pregnant. You must use effective birth control while you are taking MEKINIST and for 4 months after you stop taking it. Pills, patches and injections are not effective in preventing pregnancies when you are taking MEKINIST with TAFINLAR, 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, but if you do, inform your doctor immediately. MEKINIST can harm an unborn baby.
- Are breastfeeding. Do not breastfeed if you are taking MEKINIST.
 - Have any **heart problems** such as heart failure or problems with the way your heart beats. Your doctor should check your heart function before you start taking MEKINIST and during treatment.
- Have any **eye problems** including blockage of the vein draining the eye (retinal vein occlusion) or 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 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**.

BEFORE you use MEKINIST with TAFINLAR refer also to the TAFINLAR Consumer Information Leaflet. Also talk to your doctor if you:

- Are a male. Men who take TAFINLAR may have a reduced count of sperm that may not return to normal levels after you stop taking TAFINLAR.
- Have a low number of white blood cells (*neutropenia*).
- Have or have had a heart rhythm disorder such as irregular heartbeat, prolongation of the QT interval or any risk factors for Torsade de Pointes (dangerous rapid fluttering of the heart) such as diabetes, low potassium, magnesium or calcium levels, or a history of low heart rate, fainting, or loss of consciousness.
- Have heart valve problems.
- Have elevated blood sugar levels (diabetes).
- Plan to have surgery, dental or other medical procedures.

MEKINIST should only be used to treat melanomas with a change (mutation) in the BRAF gene. Your doctor will take a tumour tissue sample, to test whether MEKINIST is suitable for you.

MEKINIST is not recommended in children and adolescents (< 18 years of age).

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 including blockage of the vein draining the eye (retinal vein occlusion). Your doctor may advise an eye exam before you take MEKINIST and while you are taking it. 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

Lung problems: MEKINIST can cause lung complications such as interstitial lung disease or pneumonitis and in some cases these have been fatal.

Skin Problems: MEKINIST can cause rash, acne-like rash and infections. Tell your doctor if you develop a rash.

Blood Clots: MEKINIST can cause blood clots in your arms and legs, which can travel to your lungs 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 can cause serious bleeding problems, including in your brain, stomach, or bowel, and can lead to death. 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, abdominal pain and fever, which are possible symptoms of an inflammation of the colon. Taking MEKINIST may also increase the risk of developing holes in the intestinal wall, although this is an uncommon event. Tell your doctor if you develop gastrointestinal problems or severe abdominal pain.

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 TAFINLAR may cause severe fever. Stop taking TAFINLAR and tell your doctor immediately if you get a fever.

In some cases, people with fever may develop chills, 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 TAFINLAR while they treat the fever with other medicines. Once controlled, your doctor may recommend that you start taking MEKINIST and TAFINLAR again.

Decrease in white blood cells (neutropenia): Taking MEKINIST with TAFINLAR can cause a decrease in a certain kind of white blood cells that may lead to infection which can be life-threatening, or to unexpected bruising or bleeding. Your doctor will monitor you periodically. 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 TAFINLAR can cause problems with your liver which may develop into serious conditions such as hepatitis and liver failure, which 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

INTERACTIONS WITH THIS MEDICATION

Tell your doctor and pharmacist about all the medicines you take including prescription and non-prescription medicines, vitamins, and herbal supplements.

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

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

PROPER USE OF THIS MEDICATION

Usual dose:

Taking MEKINIST by itself: the usual dose of MEKINIST is one 2.0 mg tablet once a day.

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

How to take MEKINIST either by itself or with TAFINLAR:

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

Swallow the tablet with a full glass of water.

Take MEKINIST at about the same time each day.

If you take MEKINIST with TAFINLAR, take MEKINIST with either the morning or the evening dose of TAFINLAR. Take TAFINLAR 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.

Do not take the morning and evening doses of TAFINLAR at the same time, and do not take more than one dose of MEKINIST a day.

Do not take more MEKINIST than your doctor has recommended.

Overdose:

In case of drug overdose, contact a health care practitioner, 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 1 dose of MEKINIST at a time.**

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

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
- Dry mouth
- Lack of energy or feeling weak or tired
- Swelling of hands or feet
- Unusual hair loss or thinning
- Cough
- Shortness of breath
- 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.

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
- Redness, chapping or cracking of the skin
- Infection of the skin (*cellulitis*)
- Nail disorders such as nail bed changes, nail pain, infection and swelling of the cuticles
- Redness, swelling and pain on the palms, fingers and soles of the feet
- Nose bleeds
- Sore mouth or mouth ulcers
- Inflammation of mucous membranes
- Swelling of the face, localized tissue swelling
- Blurred vision
- Swelling around the eyes
- Eyesight problems
- Heart pumping less efficiently
- Changes in how the heart pumps blood (*left ventricular dysfunction*)
- Slow heart rate
- Dehydration (low levels of water or fluid)

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

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

- Abnormal blood test results related to the liver

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

- Swelling in the eyes caused by fluid leakage (*chorioretinopathy*)
- Swelling of nerves at the back of the eye (*papilloedema*)
- Separation of the light-sensitive membrane in the back of the eye from its supporting layers (*retinal detachment*)

Refer to the TAFINLAR Consumer Information leaflet for possible side effects when MEKINIST is taken with TAFINLAR.

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

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

- Decreased appetite
- Chills
- Headache
- Urinary tract infections
- Nasal inflammation
- Pain in the hands or feet
- Joint pain
- Muscle pain

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

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

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

- Night sweats
- Muscle spasms
- Low blood pressure (*hypotension*)
- Dizziness
- Brown or yellowish thickening of skin
- Skin tags
- Flu-like illness
- Thickening of the outer layers of the skin
- Excessive sweating (*hyperhidrosis*)
- Rough scaly patches of skin
- Wart-like growths
- Inflammation of the fatty layer underneath the skin
- Papilloma (a type of skin cancer)
- Skin lesions

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 levels of phosphate in the blood
- Low levels of sodium in the blood
- Increase in blood sugar level (glucose)

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

- Inflammation of the eye (*uveitis*)
- 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*)

Tell your doctor or pharmacist if any of the side effects listed are or becomes severe or troublesome, or if you notice any side effects not listed in this leaflet.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM			
Symptom / effect		Talk with your doctor or pharmacist	Stop taking drug and call your doctor or pharmacist
Very Common	Skin rash, acne-like rash, redness of the face, dry or itching skin	✓	
Very Common	Serious bleeding problems: 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		✓
Very Common (when MEKINIST is taken with TAFINLAR)	Fever (high temperature > 38.5°C – 40°C)	✓	
	Fever (high temperature > 40°C) or any fever accompanied by rigors, chills, low blood pressure or kidney problems		✓

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM			
Symptom / effect		Talk with your doctor or pharmacist	Stop taking drug and call your doctor or pharmacist
Common (when MEKINIST is taken with TAFINLAR)	Cutaneous squamous cell cancer including keratoacanthomas (skin sore, wart, or reddish bump that bleeds or does not heal)	✓	
Common	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, a cool or pale arm or leg		✓
Uncommon	Heart problems: feeling like your heart is pounding, racing, or beating irregularly, dizziness, tiredness, feeling lightheaded, shortness of breath, and swelling in the legs	✓	
Uncommon	Eye (vision) problems: 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"> ▪ Retinal Vein Occlusion (RVO): Blurred or reduced vision. This usually happens in one eye and could occur abruptly ▪ Retinal Pigment Epithelial Detachment (RPEP): Blurred or distorted vision 	✓	

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect		Talk with your doctor or pharmacist	Stop taking drug and call your doctor or pharmacist
Uncommon	Lung complications (pneumonitis/ILD - inflammation of the lung): shortness of breath and cough		✓
Uncommon	Allergic reaction: Rash, hives, swelling of the face, lips, tongue or throat, difficulty swallowing or breathing.		✓
Uncommon	Gastrointestinal complications: crushing stomach pain, nausea, vomiting of blood, black or bloody stools, holes in the intestinal wall		✓
Uncommon (when MEKINIST is taken with TAFINLAR)	New melanoma (mole which has irregular shape, border, or colour, is growing, or changing shape or colour)	✓	
Uncommon (when MEKINIST is taken with TAFINLAR)	Pancreatitis (inflammation of the pancreas causing strong abdominal pain)	✓	
Uncommon	Rhabdomyolysis: muscle pain that you cannot explain, muscle tenderness or weakness, generalized weakness (especially if you don't feel well), brownish or discoloured urine	✓	

This is not a complete list of side effects. For any unexpected effects while taking MEKINIST, contact your doctor or pharmacist.

HOW TO STORE IT

Keep out of the reach and sight of children.

Store in a refrigerator between 2-8 °C in the original package. This medicine is to be protected from light and moisture. Do not remove desiccant.

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

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- Report online at www.healthcanada.gc.ca/medeffect
 Call toll-free at 1-866-234-2345
 Complete a Canada Vigilance Reporting Form and:
 - Fax toll-free to 1-866-678-6789, or
 - Mail to: Canada Vigilance Program
 Health Canada
 Postal Locator 0701E
 Ottawa, Ontario
 K1A 0K9

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at www.healthcanada.gc.ca/medeffect.

NOTE: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

This document plus the full product monograph, prepared for health professionals can be found at:

<http://www.novartis.ca> or by contacting the sponsor,

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This leaflet was prepared by:
 Novartis Pharmaceuticals Canada Inc.

Last revised: December 14, 2016

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