

PART III: CONSUMER INFORMATION

PrTAFINLAR®

Dabrafenib (as dabrafenib mesylate) Capsules

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

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

TAFINLAR is a medicine to treat a type of skin cancer called melanoma that has spread to other parts of the body or cannot be removed by surgery.

TAFINLAR 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 mutation in the BRAF gene before starting treatment with TAFINLAR.

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

What it does:

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

When it should not be used:

Do not use TAFINLAR if you are allergic to dabrafenib mesylate, or any of the other ingredients in TAFINLAR (see 'What the important non-medicinal ingredients are').

You should not use TAFINLAR if you do not have a particular change (mutation) in a gene called BRAF or if the mutation in BRAF is not known.

What the medicinal ingredient is:

Dabrafenib mesylate

What the important nonmedicinal ingredients are:

Colloidal silicon dioxide, magnesium stearate, microcrystalline cellulose.

Capsule shell: hypromellose, red iron oxide, titanium dioxide.

Printing ink: black iron oxide, shellac, propylene glycol.

What dosage forms it comes in:

TAFINLAR is available as 50 mg and 75 mg hard capsules.

WARNINGS AND PRECAUTIONS**Serious Warnings and Precautions**

TAFINLAR should only be prescribed by a doctor who is experienced in the use of anti-cancer drugs.

- Taking TAFINLAR may cause severe fever
- TAFINLAR can harm an unborn baby
- Birth control using hormones (pills, injections, or patches) may not work as well while you are taking TAFINLAR
- TAFINLAR has not been studied in patients with moderate or severe liver problems
- Patients taking TAFINLAR have reported second cancers

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

- Serious bleeding
- Blood clots

TAFINLAR 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 TAFINLAR is suitable for you.

TAFINLAR is not recommended for children and adolescents (< 18 years of age).

Fever (high temperature > 38.5°C): Taking TAFINLAR may cause fever. Fever may happen more often or may be more severe when TAFINLAR is taken with MEKINIST. 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. If the fever is severe, your doctor may recommend that you stop taking TAFINLAR while they treat the fever with other medicines. Once the fever is controlled, your doctor may recommend that you start taking TAFINLAR again.

Bleeding problems: TAFINLAR, when taken with 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

Blood Clots: TAFINLAR, when taken with 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

Changes in your skin: If you notice any skin lesions while taking this medicine, talk to your doctor as soon as possible.

Up to 1 in 10 people taking TAFINLAR may develop a different type of skin cancer called *cutaneous squamous cell carcinoma*. Usually, this remains local and can be removed with surgery and people can continue treatment.

Some people taking TAFINLAR also may notice that new melanomas have appeared. These are usually removed by surgery and people can continue treatment.

Your doctor will check your skin for any new cancers before you start taking TAFINLAR, and every 2 months while you take TAFINLAR. Your doctor will check your skin again every 2 or 3 months for 6 months after you stop taking TAFINLAR.

Check your skin regularly while taking TAFINLAR for any of the following:

- new wart
- skin sore or reddish bump that bleeds or does not heal
- change in size or colour of a mole

Tell your doctor as soon as possible if you get any of these symptoms - either for the first time or if they get worse.

Eye Problems: TAFINLAR can cause an eye problem called uveitis which could damage your vision if it is not treated. Uveitis may develop rapidly; symptoms include:

- eye redness and irritation
- blurred vision
- eye pain
- increased sensitivity to light
- floating spots in front of your eyes

Contact your doctor immediately if you get these symptoms. **It is very important to tell your doctor immediately if you develop these symptoms**, especially if you have a painful, red eye that does not clear up quickly. They may arrange for you to see a specialist eye doctor for a complete eye examination.

Liver problems: TAFINLAR, when taken with MEKINIST, 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

Decrease in white blood cells (neutropenia): TAFINLAR, when taken with MEKINIST, 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

Non-Skin Cancers: Have been reported in patients receiving TAFINLAR. Your doctor will monitor you periodically.

Heart Problems: TAFINLAR has an effect on the electrical activity of the heart known as QT prolongation.

Diabetes: TAFINLAR may cause an elevation in blood sugars or worsening of diabetes. If you are diabetic your blood sugar may be monitored more frequently while on TAFINLAR.

Driving and using machines: TAFINLAR can have side effects that may affect your ability to drive or use machines.

Avoid driving or using machines if you have problems with your vision or if you feel tired or weak, or if your energy levels are low.

Discuss with your doctor, pharmacist or nurse if you are unsure about anything. Even your disease, symptoms and treatment situation may affect your ability to drive or use machines.

BEFORE you use TAFINLAR either by itself or with MEKINIST talk to your doctor if you:

- are pregnant, think you may be pregnant or are planning to become pregnant. You must use reliable non-hormonal birth control while receiving TAFINLAR and for 4 weeks after you stop the treatment. Pills, patches and injections are not effective in preventing pregnancies because they may not work as well while you are taking TAFINLAR; therefore you should use an alternative method. You must make sure that you do not get pregnant while receiving TAFINLAR, but if you do, inform your doctor immediately. TAFINLAR can harm an unborn baby.

- are breastfeeding. Do not breastfeed if you are taking TAFINLAR. If you wish to restart breastfeeding after TAFINLAR treatment, you must discuss this with your doctor, who will tell you when it is safe to do so.
- 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 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).
- have any liver problems. Your doctor may take blood samples to monitor your liver function while you are taking TAFINLAR.
- have or have ever had any kidney problems.
- plan to have surgery, dental or other medical procedures.
- have any other medical conditions.

BEFORE you use TAFINLAR with MEKINIST also talk to your doctor if you have:

- had bleeding problems or blood clots.
- heart problems such as heart failure or problems with the way your heart beats.
- eye problems including blockage of the vein draining the eye (retinal vein occlusion) or swelling in the eye which may be caused by fluid leakage.
- any skin problems including rash or acne-like rash.
- high blood pressure (hypertension).
- a low number of white blood cells (neutropenia).
- any lung or breathing problems, including difficulty in breathing often accompanied by a dry cough, shortness of breath and fatigue (pneumonitis).

INTERACTIONS WITH THIS MEDICATION

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

Do not start, stop or change any medicine without talking to your doctor, nurse or pharmacist first.

Some medicines may affect how TAFINLAR works, or make it more likely that you will have side effects. TAFINLAR can also affect how some other medicines work. These include:

- birth control using hormones such as pills, injections, or patches

- warfarin, to thin the blood
- medicines to treat fungal infections, such as ketoconazole
- some antibiotic medicines, such as clarithromycin or rifampin
- dexamethasone
- some medicines to treat HIV, such as ritonavir
- medicines to treat seizures, such as phenytoin, phenobarbital, or carbamazepine
- the anti-depressant medicine nefazodone
- the lipid lowering medicine gemfibrozil
- medicines that reduce stomach acid (e.g. esomeprazole, ranitidine, magnesium hydroxide)
- the herbal product, St John's wort
- medicines known to cause heart rhythm changes

Tell your doctor if you are taking any of these. Your doctor may decide to adjust your dose. Keep a list of the medicines you take, so you can show it to your doctor when you get a new medicine.

It is important to take TAFINLAR on an empty stomach, because food may affect the way TAFINLAR is absorbed into your body and how effective it works.

PROPER USE OF THIS MEDICATION

Always take TAFINLAR exactly as your doctor has told you to. Check with your doctor or pharmacist if you are not sure.

Usual Dose:

Taking TAFINLAR by itself: the usual dose of TAFINLAR is two 75 mg capsules (150 mg), twice a day (a total of four capsules equalling 300 mg).

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

How to take TAFINLAR either by itself or with MEKINIST:

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

Swallow the TAFINLAR capsules whole with a full glass of water, one after the other.

Take TAFINLAR at about the same time two times each day.

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

Your doctor may decide that you should take a lower dose if you get side effects.

Take TAFINLAR for as long as your doctor recommends.

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.

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.

If you take too much TAFINLAR or MEKINIST, call your doctor or poison control centre, or go to the nearest hospital emergency room right away. Take TAFINLAR capsules and MEKINIST tablets with you when possible.

Missed Dose:

If the missed dose is less than 6 hours late, take it as soon as you remember. If the missed dose is more than 6 hours late, skip that dose and take your next dose at the usual time. Then continue to take your capsules at regular times as usual. **Do not take a double dose to make up for a missed dose.**

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Side effects that can occur when you take TAFINLAR are:

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

- Thickening of the outer layers of the skin
- Skin effects such as rash, dryness, wart-like growths, or redness and swelling of the palms, fingers and soles of the feet
- Headache
- Nausea, vomiting, or diarrhoea
- Decreased appetite
- Chills
- Feeling weak
- Lack of energy
- Fever
- Joint pain, muscle pain, or pain in the hands or feet
- Cough
- Unusual hair loss or thinning
- Itching
- Constipation
- Nasal inflammation

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

- Flu-like illness

- Skin effects including rough scaly patches of skin, brown or yellowish thickening of the skin, skin tags, or redness of the skin
- Inflammation of the fatty layer underneath the skin (*panniculitis*)

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

- Low phosphorus
- Increase in sugar (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 kidney (nephritis)
- Kidney disorder that may result in decreased urine output (kidney failure)

Refer to the MEKINIST Consumer Information leaflet for possible side effects when TAFINLAR is taken with MEKINIST including heart problems, eye problems and rash.

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

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

- Swelling of the hands or feet
- Stomach ache
- High blood pressure
- Urinary tract infections
- Acne-like problem
- Dizziness
- Bleeding (haemorrhage)

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

- Abnormal blood test results related to the liver
- Low levels of a type of white blood cells (*neutropenia*)

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

- Night sweats
- Shortness of breath
- Muscle spasms
- Heart pumping less efficiently
- Low blood pressure (*hypotension*)
- Slow heart rate
- Eyesight problems
- Dry mouth
- Sore mouth or mouth ulcers
- Inflammation of the mucous membranes
- Swelling of the face, localized tissue swelling
- Low levels of water or fluid (*dehydration*)
- Infection of the skin (*cellulitis*)

- Papilloma (a type of skin cancer)
- Inflammation of the follicles in the skin
- Nail disorders such as nail bed changes, nail pain, infection and swelling of the cuticles
- Skin rash with pus-filled blisters
- Excessive sweating (*hyperhidrosis*)
- Skin cracking

Common side effects that may show up in your blood tests

- Low levels of red blood cells (anaemia) and a type of white blood cells (leukopenia)
- Increase in creatine phosphokinase, an enzyme found mainly in heart, brain, and skeletal muscle
- Increase in some substances (enzymes) produced by the liver
- Decrease in the number of blood platelets (cells that help blood clot)
- Low sodium

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

- Lung inflammation (*pneumonitis*)
- Swelling around the eyes
- Swelling in the eye cause by fluid leakage (*chorioretinopathy*)
- Separation or tear of the lining of the back part of the eye (*retinal detachment or tear*)

If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. Tell your doctor if you have any side effect that bothers you or that does not go away.

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
	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		✓
Common (when TAFINLAR is taken alone)	New primary melanoma (mole which has irregular shape, border, or colour, is growing, or changing shape or colour)	✓	
Common	Cutaneous squamous cell cancer including keratoacanthomas (skin sore, wart, or reddish bump that bleeds or does not heal)	✓	
	Eye problems (redness, pain, blurred vision, floating spots, light sensitivity)	✓	
Common (when TAFINLAR is taken with MEKINIST)	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	Allergic Reactions (rash, hives, swelling of the face, lips, tongue, or throat, difficulty swallowing or breathing)		✓
	Pancreatitis (inflammation of the pancreas causing strong abdominal pain)	✓	

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	Fever (high temperature > 38.5°C) that may be 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
Uncommon (when TAFINLAR is taken with MEKINIST)	New primary melanoma (mole which has irregular shape, border, or colour, is growing, or changing shape or colour)	✓	

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

HOW TO STORE IT

Keep this medicine out of the sight and reach of children.

Store TAFINLAR between 15°C to 30°C.

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:

www.novartis.ca or by contacting the sponsor,

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