

Trametinib (Mekinist®)

Pronounced: tra-ME-ti-nib

Classification: Kinase Inhibitor

About Trametinib (Mekinist®)

A kinase is an enzyme that promotes cell growth. There are many types of kinases, which control different phases of cell growth. By blocking a particular enzyme from working, this medication can slow the growth of cancer cells. MEK is a protein kinase is involved in a signaling pathway that carries messages regarding cell growth from the surface of cells to DNA. MEK is also part of the BRAF pathway which is another protein kinase involved in cell replication and survival. MEK and BRAF are often overexpressed in melanomas. Therapy with both trametinib and dabrafenib allows both signals, MEK and BRAF, to be blocked leading to inhibition of cell replication and potentially causing cell death.

How to Take Trametinib

Trametinib is given in a tablet form to be taken by mouth, typically taken once a day. Your dose may be modified throughout treatment depending on the type and degree of side effects you are experiencing. Trametinib tablets should be taken on an empty stomach (1 hour before or 2 hours after meals) and should not be crushed, broken or chewed. If you miss a dose and it has been less than 12 hours since your regular dose time, take it as soon as you remember. If it has been more than 12 hours, skip the dose. Do not take 2 doses at once to make up for a missed dose.

It is important to make sure you are taking the correct amount of medication every time. Before every dose, check that what you are taking matches what you have been prescribed.

BRAF Testing

Trametinib is often given in combination with the BRAF inhibitor, dabrafenib. Because dabrafenib only works in melanoma that has BRAF mutations, this abnormality must be tested for prior to starting the medication to identify patients appropriate for therapy. In order to test for mutated BRAF, a sample of the tumor is sent to a special laboratory that performs this test.

Storage and Handling

Store your medication in the original, labeled container in the refrigerator. It should remain in the original bottle with the desiccant packet to be protected from light and moisture. This medication should not be stored in a pillbox. Keep containers out of reach of children and pets.

If a caregiver prepares your dose for you, they should consider wearing gloves or pour the pills directly from their container into the cap, a small cup, or directly into your hand. They should avoid touching the pills. They should always wash their hands before and after giving you the medication. Pregnant or nursing women should not prepare the dose for you. Ask your oncology team where to return any unused medication for disposal. Do not flush down the toilet or throw in the trash.

Where do I get this medication?

Depending on your prescription coverage, this medication may be available at your local retail pharmacy or through a specialty pharmacy. Your oncology team will work with your prescription drug plan to identify the appropriate supplier for this medication.

Insurance Information

This medication may be covered under your prescription drug plan. Patient assistance may be available to qualifying individuals depending upon prescription drug coverage. Co-pay cards, which reduce the patient co-pay responsibility for eligible commercially (non-government sponsored) insured patients, may also be available. Your care team can help you find these resources, if they are available.

Possible Side Effects of Trametinib

There are a number of things you can do to manage the side effects of trametinib. Talk to your care team about these recommendations. They can help you decide what will work best for you. These are some of the most common or important side effects:

Rash

Some patients will develop skin rash, redness, or a rash that looks like acne. This rash can become severe and result in a skin infection and hospitalization. Your skin may become very dry. Use an alcohol free moisturizer on your skin and lips; avoid moisturizers with perfumes or scents. If your skin does crack or bleed, be sure to keep the area clean to avoid infection. Be sure to notify your healthcare provider of any rash that develops, as this can be a serious reaction. They can give you more tips on caring for your skin and prescribe topical or oral therapy to help with the itching and rash.

Notify your healthcare team right away if you notice any skin reactions so they can make recommendations or dose changes to prevent them from getting worse.

Diarrhea

Diarrhea can be a serious side effect that can lead to dehydration. Notify your healthcare provider if you develop diarrhea.

Your oncology team can recommend medications to relieve diarrhea. Also, try eating low-fiber, bland foods, such as white rice and boiled or baked chicken. Avoid raw fruits, vegetables, whole grain breads, cereals and seeds. Soluble fiber is found in some foods and absorbs fluid, which can help relieve diarrhea. Foods high in soluble fiber include: applesauce, bananas (ripe), canned fruit, orange sections, boiled potatoes, white rice, products made with white flour, oatmeal, cream of rice, cream of wheat, and farina. Drink 8-10 glasses on non-alcoholic, un-caffeinated fluid a day to prevent dehydration

This medication is often given with another medication called dabrafenib. The following side effects were seen in studies of this combination, but not when trametinib was given alone. You should be aware of these side effects regardless if you are taking both medications or not.

Liver Toxicity

This medication can cause liver toxicity, which your doctor may monitor for using blood tests called liver function tests. Notify your healthcare provider if you notice yellowing of the skin or eyes, your urine appears dark or brown or pain in your abdomen, as these can be signs of liver toxicity.

High Blood Pressure

This medication can cause high blood pressure (hypertension). Hypertension typically occurs within the first few months of therapy. Patients should have their blood pressure checked regularly during therapy. If you develop headaches, light headedness or dizziness, notify your healthcare team.

Nausea and/or Vomiting

Talk to your oncology care team so they can prescribe medications to help you manage nausea and vomiting. In addition, dietary changes may help. Avoid things that may worsen the symptoms, such as heavy or greasy/fatty, spicy or acidic foods (lemons, tomatoes, oranges). Try saltines, or ginger ale to lessen symptoms.

Call your oncology care team if you are unable to keep fluids down for more than 12 hours or if you feel lightheaded or dizzy at any time.

Fever

Fever can be a serious side effect of these medications. If you develop a fever of 100.4°F or 38°C or greater, call your

healthcare team right away and before taking the next dose of medication.

High Blood Sugar

These medications can cause elevated blood sugar levels in patients with and without diabetes. Your healthcare team will monitor your blood sugar. If you develop increased thirst, urination or hunger, blurry vision, headaches or your breath smells like fruit, notify your healthcare team. Diabetics should monitor their blood sugar closely and report elevations to the healthcare team.

Muscle or Joint Pain/Aches and Headache

Your healthcare provider can recommend medication and other strategies to relieve pain.

Less common, but important side effects can include:

- Secondary Cancers: A secondary cancer is one that develops as a result of cancer treatment for another cancer. This is quite rare, but you should be aware of the risk. There is a very low risk of developing non melanoma skin cancer or other type of cancer due to treatment with this medication, which can occur many years after treatment. Because this medication has been associated with the development of skin cancers, it is important to practice sun safety. Avoid the sun between 10-2pm, when it is strongest. Wear sunscreen (at least SPF 15) everyday; wear sunglasses, a hat and long sleeves/pants to protect your skin and seek out shade whenever possible. You should have skin examinations prior to starting treatment, and then every 2 months while on therapy, and for 6 months after the medication has been stopped. Check your own skin regularly and report any new growths, sores or bumps that bleed or do not heal, or notice any changes in moles to your oncology care team.
- *Heart Problems:* Trametinib can cause a heart problem called cardiomyopathy, which affects the heart muscle, making it weaker and less able to pump blood (called heart failure). Your healthcare provider will monitor for this problem with periodic heart scans (called MUGA scans), before and during treatment. If you develop shortness of breath, swelling in the legs, feet or ankles, irregular heartbeats, light-headedness or chest pain, notify your healthcare provider right away.
- *Eye Issues*: In rare circumstances, this medication may cause eye problems, including retinal pigment epithelial detachment and retinal vein occlusion. Symptoms of these conditions include blurry vision, loss or change in vision, seeing colored dots or halos (blurry outline around objects). If you develop any of these symptoms, notify your healthcare provider right away. You will be referred to an eye doctor for monitoring of these vision changes.
- Lung Problems: In a few cases, patients developed a rare lung problem called Interstitial Lung Disease (ILD) while receiving trametinib. Notify your healthcare team right away if you develop shortness of breath, new or worsening cough or have any difficulty breathing.
- Blood Clots: These medications can increase the risk of blood clots in your arms, legs or lungs (DVT, pulmonary
 embolism or PE). Symptoms can include: swelling, redness, or pain in a leg or arm, chest pain or pressure, or shortness
 of breath. If you experience symptoms of these problems, you should contact your healthcare provider immediately or go
 to an emergency room.
- **Bleeding:** These medications may increase the risk of bleeding. If you experience headaches, dizziness, cough up blood or blood clots, vomit blood or have red or black tar like looking stools, contact your care team immediately.
- *Gl Bleed & Tear*: This medication can cause bleeding or a tear in the intestinal wall. Signs of these problems include: unexpected bleeding, blood in the stool or black stools, coughing up blood, vomiting blood, vomit that looks like coffee grounds, fever, severe pain in the abdomen or new abdominal swelling. If you experience any of these, contact your oncology care team immediately or go to the emergency room.

Sexual and Reproductive Concerns

This medication may affect your reproductive system, resulting in the menstrual cycle or sperm production becoming irregular or stopping permanently. Women may experience menopausal effects including hot flashes and vaginal dryness. In addition, the desire for sex may decrease during treatment. You may want to consider sperm banking or egg harvesting if you may wish to have a child in the future. Discuss these options with your oncology team.

Exposure of an unborn child to this medication could cause birth defects, so you should not become pregnant or father a child while on this medication. Effective birth control is necessary during treatment and for at least 4 months after treatment. Even if

your menstrual cycle stops or you believe you are not producing sperm, you could still be fertile and conceive. You should not breastfeed while taking this medication or for 4 months after your last dose.

Birth control using hormones (such as birth control pills, injections, or patches) may not work as well while you are taking dabrafenib. You should use another effective method of birth control while taking this medication.

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