

Treosulfan (Grafapex™)

Pronounce: Tree-oh-SUL-fan

Classification: Alkylating Agent

About Treosulfan (Grafapex[™])

Treosulfan kills cancer cells through a process called alkylation. Alkylation damages the DNA of cells, which stops them from dividing and causes them to die. Since cancer cells divide faster than healthy cells, cancer cells are more sensitive to this damage.

Treosulfan is usually given in combination with another medication called fludarabine before an allogeneic stem cell transplant. Both medications are used in the days before your transplant to prepare your body to receive the donor's cells.

How to Take Treosulfan

Treosulfan is given by intravenous (IV, into a vein) infusion, most commonly over 2 hours. Your dosage depends on your body size. You will be given antiemetic medication (to treat and prevent nausea and vomiting) before receiving treosulfan.

Possible Side Effects of Treosulfan

There are a number of things you can do to manage the side effects of treosulfan. 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:

Infection and Low White Blood Cell Count (Leukopenia or Neutropenia)

This medication can cause life threatening infections, with or without a decrease in white blood cell counts. White blood cells (WBC) are important for fighting infection. While receiving treatment, your WBC count can drop, putting you at a higher risk of getting an infection. You should let your care team know right away if you have a fever (temperature greater than 100.4°F or 38°C), sore throat or cold, shortness of breath, cough, burning with urination, or a sore that doesn't heal.

Tips to preventing infection:

- Washing hands, both yours and your visitors, is the best way to prevent the spread of infection.
- Avoid large crowds and people who are sick (i.e.: those who have a cold, fever or cough or live with someone with these symptoms).
- When working in your yard, wear protective clothing including long pants and gloves.
- Do not handle pet waste.
- · Keep all cuts or scratches clean.
- Shower or bathe daily and perform frequent mouth care.
- Do not cut cuticles or ingrown nails. You may wear nail polish, but not fake nails.
- Ask your oncology care team before scheduling dental appointments or procedures.

• Ask your oncology care team before you, or someone you live with, has any vaccinations.

Low Red Blood Cell Count (Anemia)

Your red blood cells are responsible for carrying oxygen to the tissues in your body. When the red cell count is low, you may feel tired or weak. You should let your oncology care team know if you experience any shortness of breath, difficulty breathing or pain in your chest. If the count gets too low, you may receive a blood transfusion.

Low Platelet Count (Thrombocytopenia)

Platelets help your blood clot, so when the count is low you are at a higher risk of bleeding. Let your oncology care team know if you have any excess bruising or bleeding, including nose bleeds, bleeding gums or blood in your urine or stool. If the platelet count becomes too low, you may receive a transfusion of platelets.

- Do not use a razor (an electric razor is fine).
- Avoid contact sports and activities that can result in injury or bleeding.
- Do not take aspirin (salicylic acid), non-steroidal, anti-inflammatory medications (NSAIDs) such as Motrin/Advil (ibuprofen), Aleve (naproxen), Celebrex (celecoxib) etc. as these can all increase the risk of bleeding. Please consult with your healthcare team regarding use of these agents and all over the counter medications/supplements while on therapy.
- Do not floss or use toothpicks and use a soft-bristle toothbrush to brush your teeth.

Muscle or Joint Pain/Aches and Headache

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

Mouth Ulcers (Mucositis)

Certain treatments can cause sores or soreness in your mouth and/or throat. Notify your oncology care team if your mouth, tongue, inside of your cheek, or throat becomes white, ulcerated, or painful. Performing regular mouth care can help prevent or manage mouth sores. If mouth sores become painful, your doctor or nurse can recommend a pain reliever.

- Brush with a soft-bristle toothbrush or cotton swab twice a day.
- Avoid mouthwashes that contain alcohol. A baking soda and/or salt with warm water mouth rinse (2 level teaspoons of baking soda or 1 level teaspoon of salt in an eight-ounce glass of warm water) is recommended 4 times daily.
- If your mouth becomes dry, eat moist foods, drink plenty of fluids (6-8 glasses), and suck on sugarless hard candy.
- Avoid smoking and chewing tobacco, drinking alcoholic beverages, and citrus juices.

Fever

Fever can be a side effect of this medication. However, fever (temperature > 100.4°F or 38°C) can be a sign of infection. You should always call your care provider if you develop a fever.

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 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.

Peripheral Edema

Peripheral edema is swelling of the extremities (arms and legs) caused by retention (holding on) of fluid. It can cause swelling of the hands, arms, legs, ankles and feet. The swelling can become uncomfortable. Notify your oncology care team if you are experiencing any new or worsening swelling.

Important but Less Common Side Effects

- **Seizures:** A seizure is caused by abnormal electrical activity in the brain and can lead to uncontrollable shaking of the body and loss of consciousness. The length and severity of the seizure may vary. If you are having a seizure, have someone call 911. You may be given a medication to prevent seizures if you are at high risk. Tell your care team if you have a history of seizures.
- **Skin Problems:** This medication may cause a rash or dermatitis of your skin. If you have any occlusive dressings, these dressings should be changed after each infusion of treosulfan. On days you receive treosulfan, keep your skin clean and dry with a disposable washcloth and clear water, especially "sweaty" areas of your skin. Do not use any cream on your skin and wear loose clothing on the days you receive this medication.
 - Even when carefully and correctly administered by trained personnel, this drug may cause a feeling of burning and pain. There is a risk that this medication may leak out of the vein at the injection site, causing tissue and skin damage that can be severe. If the area of infusion becomes red, swollen, or painful at any time <u>during or after the</u> infusion, tell your care team right away. Do not apply anything to the site unless told to do so by your care team.
- **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. This can occur years after treatment. Your provider will monitor your labs closely. Consider having a complete blood count with differential checked each year by your healthcare provider. Tell your provider if you have Fanconi anemia or other DNA breakage disorders, as your risk for secondary cancer may be higher.

Sexual & 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.

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 for women during treatment and for up to 6 months after treatment, even if your menstrual cycle stops. Advise male patients with female partners of reproductive potential to use effective contraception during treatment and for 3 months after the last dose. 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. You should not breastfeed while taking this medication and for 1 week after the last dose.

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