

What You Need to Know About LEMTRADA[®] (alemtuzumab) Treatment: A Patient Guide

Patients: Your doctor or nurse will go over this patient guide with you. It is important to ask any questions you might have prior to each time LEMTRADA[®] (alemtuzumab) is given to you. Keep this guide for important safety information about the serious risks and reactions of LEMTRADA.

Healthcare Providers: Review this patient guide with your patient prior to each treatment course, and provide your patient a copy to take home.


LEMTRADA[®]
alemtuzumab^{12mg} iv

What Is LEMTRADA?

LEMTRADA is a prescription medicine approved to treat adult patients with relapsing forms of multiple sclerosis. Because of serious risks with LEMTRADA, it is generally reserved for patients that have not been helped enough by 2 or more MS treatments. You and your healthcare provider have determined that LEMTRADA is an appropriate treatment for you.

LEMTRADA is only available at your doctor's office, clinic, or hospital. It is not a medicine you will give yourself at home because of the serious risks of LEMTRADA.

What Is the Most Serious Risk Information About LEMTRADA Treatment?

LEMTRADA may cause serious side effects, including infusion reactions, autoimmune conditions, and malignancy.

- > Most patients treated with LEMTRADA will experience side effects at the time of the infusion or within 24 hours after the infusion (**infusion reactions**). Common infusion reactions include nausea, hives, itching, difficulty sleeping, chills, flushing, fatigue, shortness of breath, congestion of the lungs, upset stomach, dizziness, and pain.
- > Patients receiving LEMTRADA are at risk of **autoimmune conditions**. Your body's immune system contains particular cells that help fight infections. Autoimmune side effects are illnesses that occur when these cells of the immune system fight against your own body.
- > Receiving LEMTRADA may increase your chance of getting some kinds of cancers (**malignancies**), including thyroid cancer, skin cancer (melanoma), and blood cancers called lymphoproliferative disorders and lymphoma. Call your healthcare provider if you have the following symptoms that may be a sign of thyroid cancer:
 - new lump
 - swelling in your neck
 - pain in the front of your neck
 - hoarseness or other voice changes that do not go away
 - trouble swallowing or breathing
 - cough that is not caused by a cold

You should have your skin checked before you start receiving LEMTRADA, and each year while you are receiving treatment, to monitor for symptoms of skin cancer.

What Are the Signs and Symptoms of Infusion Reactions and Autoimmune Conditions After LEMTRADA Treatment, and What Should I Do?

INFUSION REACTIONS

Most patients treated with LEMTRADA will experience side effects at the time of the infusion, some of which may be serious or life-threatening. Serious infusion reactions may happen while you receive LEMTRADA, or up to 24 hours or longer after you receive LEMTRADA.

Tell your healthcare provider right away if you have any of the following symptoms of a serious infusion reaction during the infusion or after you have left the healthcare facility:

- > swelling in your mouth or throat
- > trouble breathing
- > weakness
- > fast, slow, or irregular heart beat
- > chest pain
- > rash

In order to try to reduce these effects, your doctor will give you medication (corticosteroids) prior to the first 3 infusions of a treatment course. You may also be given other treatments before or after the infusion to try to reduce your chances of these reactions or to treat them after they happen. In addition, you will be observed during the infusion and for at least 2 hours after the infusion has been completed, or longer if your healthcare provider decides you need to stay longer. In case of serious reactions, it is possible that the infusion may be stopped.



DELAYED SIDE EFFECTS

As mentioned previously, patients receiving LEMTRADA are at risk of certain autoimmune conditions. The autoimmune conditions include:

- > Immune thrombocytopenia (ITP, or low platelets)
- > Other blood disorders (including neutropenia, hemolytic anemia, and pancytopenia)
- > Certain types of kidney diseases
- > Thyroid disorders

All of these conditions can be treated when identified early, but delaying treatment increases the risk of complications. This is why it is so important to recognize and immediately report any signs or symptoms of these conditions to your doctor.

In the following pages, you will learn more about each of these side effects, including the signs and symptoms that you may experience and what to do if they happen.

Immune Thrombocytopenia (ITP, or low platelets)

ITP is a condition which results in a decrease in the number of platelets in the blood. ITP has been observed in approximately 2% of patients treated with LEMTRADA in MS clinical trials. Platelets are necessary for normal blood clotting. ITP can cause severe bleeding. If detected early, ITP is usually treatable, but if left untreated it may lead to serious health problems and possibly death.

A blood test will help your doctor watch for changes in your platelet count in order to catch this side effect early. Therefore, your doctor will have your blood tested before starting LEMTRADA and on a monthly basis after your first infusion. The monthly testing must continue for 4 years after your last infusion, or longer if you have signs or symptoms of ITP.

Importantly, ITP may also be detected by certain signs or symptoms that you need to be aware of.

What are the signs and symptoms of ITP?

- > Small, scattered spots on your skin that are red, pink, or purple
- > Easy bruising
- > Bleeding from a cut that is harder to stop
- > Heavier, longer, or more frequent menstrual periods than normal. Bleeding between your menstrual periods could also be a sign of ITP
- > Bleeding from your gums or nose that is new or takes longer than usual to stop

Call your doctor immediately if you have any of these signs or symptoms. If you cannot reach your doctor, seek immediate medical attention.

These pictures show examples of spots and bruises caused by ITP.



This is an example of a leg with scattered spots under the skin that are red, pink, or purple. They might look like pinpricks.

It is important to note that the spots could occur anywhere on your body, not just on your leg.



This is an example of arms with easy or excessive bruising.

It is important to note bruises could occur anywhere on your body, not just on your arms.



This is an example of spots due to bleeding under the tongue.

It is important to note that this could occur anywhere in your mouth—under the tongue, on the roof of your mouth, on your inner cheeks, on your tongue, or on your gums.

Note: These pictures are only a guide in order to show examples of bruises or rashes.

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What if I develop ITP?

It is best to identify and treat ITP as early as possible. That is why it is so important that you continue to have your monthly blood test and check for symptoms, which could detect a problem before you have symptoms. It is also important that you, your family members, and/or caregivers are watching for any of the signs or symptoms described in this guide. Delaying treatment of ITP raises the chance of more serious problems.

If detected early, ITP is usually treatable. If you develop ITP, you and your doctor will decide which treatment is best for you.

If you notice any of the signs or symptoms as described above, call your healthcare provider right away to report the symptoms. If you cannot reach your healthcare provider, seek immediate medical attention.

Other blood disorders (including neutropenia, hemolytic anemia, and pancytopenia)

LEMTRADA may cause a decrease in some types of blood cells. Symptoms may include weakness, dark urine, chest pain, yellowing of the skin or whites of your eyes (jaundice), or fast heartbeat. Your healthcare provider will do blood tests to check for low blood counts.


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Kidney disorders (such as anti-glomerular basement membrane disease)

LEMTRADA may cause a condition known as anti-glomerular basement membrane disease, or anti-GBM disease. Kidney disorders, including anti-GBM disease, have been observed in 0.3% (3 per 1000) patients treated with LEMTRADA in MS clinical trials. Anti-GBM disease is an autoimmune side effect that can result in severe damage to the kidneys. Anti-GBM disease can also damage the lungs, although this was not seen in clinical trials with LEMTRADA. If untreated it can cause kidney failure requiring chronic dialysis or transplant, and may lead to death. Most of the time, doctors can treat kidney problems. It is best to begin treatment as early as possible.

A blood test and a urine test will help your doctor watch for signs of kidney disease to help catch this potential side effect early. Your doctor will have your blood and urine tested in the month before you start treatment with LEMTRADA, and on a monthly basis after your initial infusion. Your doctor will test your urine monthly, so if you are a woman, it is important to avoid urine testing during your menstrual period as this may give a false result. This testing will continue for 4 years after your last infusion, or longer if you have signs or symptoms of a kidney disorder.

Importantly, anti-GBM disease can also be detected by certain signs and symptoms that you need to be aware of.

What are the signs and symptoms of kidney problems or anti-GBM disease?

- > Blood in the urine (red or tea-colored urine)
- > Swelling in your legs or feet
- > Coughing up blood

What if I develop kidney problems?

It is best to begin treatment as early as possible. It is important that you are familiar with the signs and symptoms of kidney problems and anti-GBM disease, and complete your regular laboratory tests (blood and urine tests). Kidney problems will almost always need treatment.

If you notice any of the signs or symptoms as described above, call your doctor right away to report the symptoms. If you cannot reach your doctor, seek immediate medical attention.

Thyroid disorders

The thyroid is a gland found in the lower part of the neck. This gland produces hormones that are important throughout your body. In some people, the immune system may mistakenly attack the cells of the thyroid gland (autoimmune thyroid condition), which affects its ability to make and control the level of hormones.

LEMTRADA may cause development of thyroid disorders including:

- > Overactive thyroid gland, or hyperthyroidism, when the thyroid produces too much hormone
- > Underactive thyroid gland, or hypothyroidism, when the thyroid does not produce enough hormone

An estimated 34% of patients experienced autoimmune thyroid disorders following treatment with LEMTRADA, in MS clinical trials.

Your blood will be checked in the month before you start treatment with LEMTRADA, and every 3 months after your initial infusion, until 4 years after your last LEMTRADA infusion, or longer if you show signs or symptoms of a thyroid disorder. This blood test will help your doctor detect thyroid disorders early.

What are the signs and symptoms of a thyroid disorder?

Overactive thyroid, or hyperthyroidism	Underactive thyroid, or hypothyroidism
<ul style="list-style-type: none">> Excessive sweating> Unexplained weight loss> Eye swelling> Nervousness> Fast heartbeat	<ul style="list-style-type: none">> Unexplained weight gain> Feeling cold> Worsening tiredness> Newly occurring constipation



What if I develop a thyroid disorder?

Tell your doctor if you experience these symptoms. Most of the time, thyroid disorders are manageable with treatment. Depending on the type of thyroid disorder, your doctor will decide which treatment is best for you. It will be important to follow your doctor's recommendations to be sure to benefit the most from your treatment. In some cases, you may have to take medication for the rest of your life for your thyroid disorder. In some situations, your thyroid may need to be removed.

If you develop a thyroid disorder, it is very important that you are properly treated for it, especially if you become pregnant after using LEMTRADA. Having an untreated thyroid disorder could harm your unborn baby, or harm your baby after birth.

IMPORTANT!

Since all of these autoimmune conditions could occur long after you received a course of treatment with LEMTRADA, it is very important that you continue to have your monthly blood and urine tests (even if you are feeling well).

-  **You must continue to watch for signs and symptoms**
-  **Do this for 4 years after your last LEMTRADA infusion**
-  **Early detection and prompt treatment may give you the best opportunity for improvement**

Carry your LEMTRADA Patient Safety Information Card with you at all times and show it to any healthcare professionals who are providing you with treatment (including for non-MS conditions) or in the event of a medical emergency.

These are **NOT** all the possible side effects of LEMTRADA. Refer to the LEMTRADA Medication Guide that you were given or talk to your doctor or nurse for medical advice about other side effects.

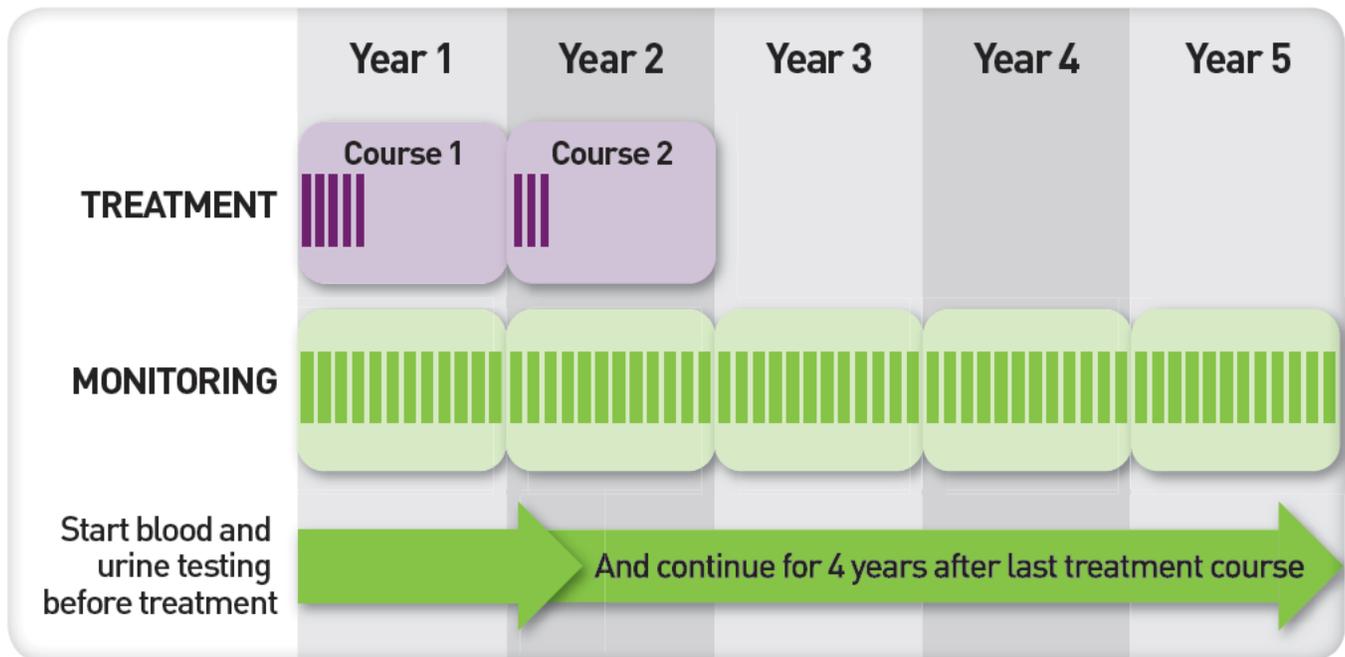
How Can I Detect the Delayed Side Effects from LEMTRADA?

To check for the development of autoimmune conditions (previously described), you will have to be monitored monthly by having your blood and urine tested. Your doctor will order blood and urine tests in the month before you start LEMTRADA treatment, and these tests will continue each month for 4 years after your last LEMTRADA infusion. Monitoring may need to continue for longer if you have signs or symptoms of autoimmune conditions. Your doctor will check the results of these tests to see if you have developed any side effects.

It is very important that you continue to have these tests for 4 years after your last LEMTRADA infusion, even if you are feeling well (no symptoms or side effects). Side effects may occur many months to years after your LEMTRADA infusion and may be (in rare cases) life-threatening, so it is very important that you continue to be checked and that you watch out for symptoms. This will help allow a problem to be detected and treatment to begin right away.

This means that you commit to the monthly blood and urine laboratory tests, continuing for 4 years after your last infusion with LEMTRADA. You and your doctor will work together as a team to make sure you get these tests done, and to plan them around your normal activities. If you are a woman, it is also important to avoid urine testing during your menstrual period, as this may give a false result.

To help you better understand the duration of the effects of LEMTRADA treatment and the length of required follow-up, please refer to the diagram below.



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The following table shows you which laboratory tests are done, when, and for how long.

Test	When?	For how long?
Blood tests	Before treatment starts and every month after treatment	For 4 years after your last LEMTRADA infusion
Urine tests	Before treatment starts and every month after treatment	For 4 years after your last LEMTRADA infusion

How Is LEMTRADA Given?

You will receive LEMTRADA through an intravenous line in your vein (infusion). LEMTRADA is given in two treatment courses. Generally, you will receive LEMTRADA for 5 days for the first treatment course and then for 3 days approximately 1 year later (second treatment course).

The infusion takes place in a healthcare facility or infusion center. It takes about 4 hours to receive a full dose each day, but can take longer if you have side effects (infusion reactions), in which case the infusion may need to be slowed down or stopped. In order to try to reduce some of these reactions, your doctor will give you medication (corticosteroids) prior to the first 3 infusions of a treatment course. You may also be given other treatments before, during, or after the infusion to try to avoid these reactions or to treat them once they happen. In addition, you will be observed during the infusion and for at least 2 hours after the infusion has been completed or longer if your healthcare provider decides you need to stay longer. In case of serious reactions, it is possible that the infusion may be stopped.

Where Can I Get More Information on LEMTRADA?

There is a LEMTRADA Medication Guide that your doctor or nurse will give you at the beginning of your treatment course. You can also find additional information at www.LemtradaREMS.com or call the LEMTRADA REMS Program at 1-855-676-6326.

How Can I Reach My Doctors?

To make it easier to contact your doctor(s) or your healthcare team, please fill in their telephone numbers and addresses in the chart below.

Doctor/Healthcare Team	Telephone Number	Address



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