

LEMTRADA Treatment and Infusion Reactions 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 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 used to treat relapsing forms of multiple sclerosis (MS), to include relapsing-remitting disease and active secondary progressive disease, in adults. Since treatment with LEMTRADA can increase your risk of getting certain conditions and diseases, LEMTRADA is generally prescribed for people who have tried 2 or more MS medicines that have not worked well enough. LEMTRADA is not recommended for use in patients with clinically isolated syndrome (CIS) because of its safety profile.

It is not known if LEMTRADA is safe and effective for use in children under 17 years of age. 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 can cause serious side effects, including infusion reactions and autoimmune conditions, stroke, and may cause certain cancers.

- Most patients treated with LEMTRADA will experience side effects at the time of the infusion or within 24 hours after the infusion (infusion reactions).
- Some people receiving LEMTRADA develop a condition where the immune cells in the body attack other cells or organs in the body (autoimmunity), which can be serious and may cause death.
- Some people have had serious and sometimes deadly strokes and tears in the arteries that provide blood to their brain within 3 days of receiving LEMTRADA. Get help right away if you have any of the following symptoms that may be a sign of stroke or tears in your arteries:
 - Drooping of parts of your face
 - Weakness on oneside
 - Sudden severe headache
 - Difficulty with speech
 - Neck pain

It is important to continually monitor for signs of stroke even after you've received your LEMTRADA infusion. Be sure to tell your doctor if you have had a stroke.

- 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.

If you experience any discomfort or anything that feels out of the ordinary during your infusion, be sure to immediately tell the healthcare provider providing the infusion. If symptoms occur after you have left the healthcare facility, be sure to notify your doctor as soon as possible.

What are the signs and symptoms of infusion reactions after LEMTRADA treatment, and what should I do?

Infusion reactions

Infusion reactions are side effects linked to the infusion of LEMTRADA. 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.

A serious allergic reaction called anaphylaxis, which can cause death if not properly treated was rarely reported.

The most common infusion reactions for patients who receive LEMTRADA were nausea, hives, itching, difficulty sleeping, chills, flushing, fatigue, shortness of breath, congestion of the lungs, upset stomach, dizziness, and pain.

Some serious reactions are possible, such as life-threatening allergic reactions, swelling, wheezing, trouble breathing, weakness, low/high blood pressure, chest pain, a fast, slow, or irregular heartbeat, transient neurologic symptoms, headache, fever, rash, and symptoms of stroke.

Some people have had serious and sometimes deadly strokes and tears in the arteries that provide blood to their brain within 3 days of receiving LEMTRADA.

LEMTRADA can only be given at a certified healthcare facility that has the necessary equipment and personnel to manage infusion reactions.

Steps you and your healthcare provider can take to help manage infusion reactions

- Your healthcare provider will give you medication (corticosteroids), and possibly other medications—such as anti-allergy medication (antihistamines) and anti-fever medications (antipyretics)—to help avoid infusion reactions or make them milder. Corticosteroids are usually given through a vein in your arm on the first 3 days of your infusions—just before your LEMTRADA infusion
- You will be closely monitored during the infusion and for at least 2 hours following the completion of the infusion to watch for any infusion reactions. Your healthcare provider may continue to monitor you for longer if needed
- Should an infusion reaction occur, your healthcare provider will likely provide treatment as needed
 - Medication may be given for relief of your symptoms. For example, antihistamines may help relieve an itchy rash.
 - Infusions usually take about 4 hours; however, your healthcare provider may slow down the infusion or stop it temporarily.
 - If an infusion is stopped, your healthcare provider might try to administer LEMTRADA again, but more slowly and with additional medicine to try to stop an infusion reaction from happening again.
 - If your healthcare provider suspects you might be having a serious allergic reaction, the LEMTRADA infusion will be stopped, and you may receive medication or other measures to treat this reaction. In addition to medication, IV fluids may be given.

Delayed side effects

As previously mentioned, 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
- Liver disorders

All of these conditions can be treated and when identified early, treatment may decrease the risk of complications. It is very 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. Delaying treatment of ITP raises the chance of more serious problems.

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 until 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
- Coughing up blood
- 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 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. Some people with these low blood counts have increased infections. Symptoms of low blood counts 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.

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. It is best to begin treatment for kidney problems 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 until 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
- Decrease in urine
- Fatigue
- 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 36.8% of patients experienced thyroid endocrine disorders, including 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 those symptoms. Depending on the type of thyroid disorder, your doctor will decide which treatment is best for you. 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.

Liver disorders

Inflammation of the liver (autoimmune hepatitis) causing serious liver injury, including liver failure requiring a liver transplant, has been reported in patients treated with LEMTRADA. A blood test will help your doctor watch for signs of inflammation of the liver. Your doctor will have your blood tested in the month before you start treatment with LEMTRADA, and from time to time after your initial infusion. This testing will continue until 4 years after your last infusion.

What are the signs and symptoms of autoimmune hepatitis?

- Unexplained nausea
- Vomiting
- Stomach pain
- Tiredness
- Not wanting to eat (loss of appetite)
- Yellowing of skin or whites of the eyes (jaundice)
- Dark urine
- Easily bleeding or bruising (more than normal)

What if I develop autoimmune hepatitis?

It is best to identify and treat autoimmune hepatitis as early as possible. That is why before starting treatment with LEMTRADA, your doctor will test your blood for signs of inflammation of the liver and will also check those tests from time to time until 4 years after your last infusion.

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.

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 until 4 years after your last LEMTRADA infusion**

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 autoimmune conditions?

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 until 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. 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.

It is very important that you continue to have these tests until 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 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 until 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.

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	Until 4 years after your last LEMTRADA infusion
Urine tests	Before treatment starts and every month after treatment	Until 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 initially given in 2 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).

Additional treatment courses, if needed, may be given for 3 days in a row (consecutive) at least 1 year after the prior 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 lower your chances of getting 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 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	



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