

Patient Guide

Important Information for Patients
Starting Therapy with LEMTRADA®

LEMTRADA®
alemtuzumab^{12mg}
IV

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Welcome

Your doctor has prescribed a medicine for your multiple sclerosis (MS) called LEMTRADA® (alemtuzumab). This guide is especially for you and includes important information about LEMTRADA.

There is also a section that will help you understand some of the medical words in this booklet, and a section to keep track of all of the doctors you may be seeing for your healthcare. This includes the doctor treating your MS and any other doctor you see on a regular basis.

By carefully reading this guide, you will learn more about LEMTRADA and some of its possible side effects. This guide is not intended to take the place of discussions with your doctor or other healthcare professionals who are treating your MS. It should also be read along with the Package Leaflet for LEMTRADA. Be sure to tell your doctor or healthcare professional if you notice any of the signs or symptoms described in this guide.

In addition to this patient guide, you can log-in to www.msonetoone.xx

1> What is LEMTRADA and how does it work?

LEMTRADA is a prescription medicine used to treat relapsing remitting multiple sclerosis (MS) in adults. LEMTRADA does not cure MS but it can decrease the number of MS relapses. It can also help to slow down some of the signs and symptoms of MS.

Multiple sclerosis (MS) is an autoimmune disease that effects the central nervous system (brain and spinal cord). A substance called myelin protects the nerve fibres in the central nervous system, which helps messages travel quickly and smoothly between the brain and the rest of the body. Normally, your immune system protects your body from attack by organisms which cause disease. In MS, cells responsible for attacking invading organisms ("lymphocytes", a type of white blood cell) can mistakenly the myelin that forms a protective layer around nerve fibres.

When your lymphocytes attack your nervous system, this causes inflammation which is often associated with a relapse. The symptoms you experience are determined by which part of your central nervous system is affected. The damage done during this inflammation may be reversible, but as your disease progresses the damage may accumulate and become permanent.

LEMTRADA adjusts your immune system to limit its attacks on your nervous system. After having a course of treatment with LEMTRADA you may be at greater risk of developing other autoimmune conditions, or experiencing serious infections. It is important you understand these risks and how to monitor for them.

2> Overview of LEMTRADA Treatment

How is LEMTRADA given?

LEMTRADA is put into your veins through a needle (an infusion). LEMTRADA is given in two courses of treatment. The first course will be given for 5 days in a row. Then, one year later, the next course will be given for 3 days in a row. LEMTRADA is not like some other drugs that you have to take regularly (for example, once a day) to have an effect. Clinical trials have shown that the 2 courses work for most patients for 2 years or sometimes longer. You will need to be monitored for side effects for 4 years after your last infusion of LEMTRADA. This is described below.

Will I need to have any tests done *before* I begin treatment with LEMTRADA?

Your doctor will perform blood tests *before* you start treatment with LEMTRADA. These tests are done to see whether that you may take LEMTRADA. Your doctor will also want to make sure that you do not have certain medical conditions or disorders before you start your treatment with LEMTRADA. This guide will give you more information about these conditions. Ask your doctor or healthcare professional if you have any questions about LEMTRADA.

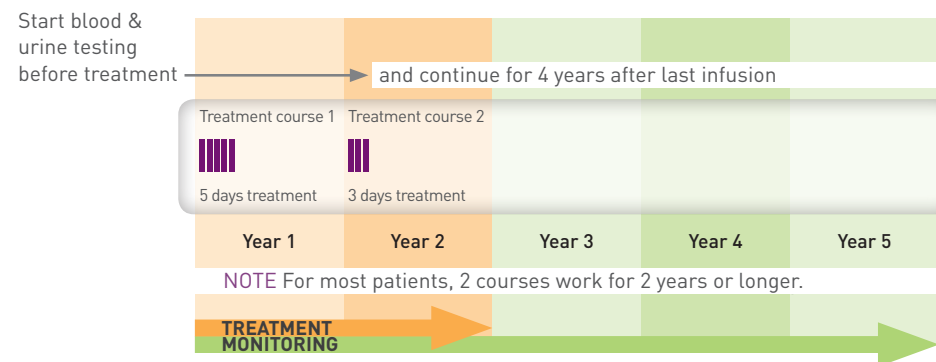
Will I need to have any tests done *after* treatment with LEMTRADA?

- 4 To check for the development of autoimmune conditions (described in Section 4 of this guide), you will have to be monitored monthly by having your blood and urine tested. Your doctor will check the results of these tests to see if you have developed a side effect.

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

This means you commit to the monthly lab tests, continuing for 4 years after your last course of treatment 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 treatment and the length of required follow-up, please refer to the diagram below.



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

Recap of Recommended Monitoring

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

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To help you remember, there are tools available to plan your tests. You can refer to Section 5 of this brochure.

How is the infusion given?

LEMTRADA is put into your veins through a needle (an infusion). The infusion takes place in hospital and will take approximately 4 hours or longer if you have side effects which may need the infusion to be stopped or slowed down. You will be observed during the infusion and for 2 hours after the infusion has been completed. In case of serious reactions, it is possible that the infusion may be stopped.

As described before, you will have your first course of treatment and then you will need to plan with your doctor to have your next course one year later. In addition to these two annual treatments, it's important to keep in mind the need for your monthly lab tests for 4 years following your last treatment. As with any medicine, side effects may occur. This guide does not cover all the side effects you could experience with LEMTRADA. These are explained in the package leaflet. Below you will learn about side effects which could occur after the infusion including autoimmune conditions and serious infections (Section 3).

3> Side effects

Delayed side effects

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

- > A condition called Immune Thrombocytopenic Purpura (ITP) (described in the next section);
- > Certain types of kidney diseases; and
- > Thyroid disorders

The cause of these side effects is not clear. However, it is known that you are at higher risk for these events if you have received LEMTRADA.

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 sections, 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.

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Immune Thrombocytopenic Purpura (ITP), (a bleeding disorder)

ITP is a condition which results in a decrease in the number of platelets in the blood. Platelets are necessary for normal blood clotting. ITP can cause severe bleeding. If detected promptly it is 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 initial treatment course. The monthly testing must continue for 4 years after your last treatment course.

Importantly, ITP can also be detected by certain signs and 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
- > Coughing up blood

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

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 (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.

These pictures show some examples of bruises and rashes caused by ITP

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



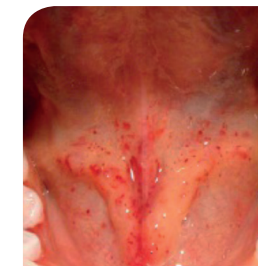
This is an example of a leg with scattered spots under the skin that are red, pink or purple. They might look like pin pricks.

It's 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's 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.

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. ▶

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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 doctor right away to report the symptoms. If you cannot reach your doctor seek immediate medical attention.

Kidney Disorders (such as anti-Glomerular Basement Membrane disease)

LEMTRADA may cause a condition known as, anti-Glomerular Basement Membrane or anti-GBM disease. Anti-GBM disease is an autoimmune condition that can result in severe damage to the kidneys. Damage to the lungs may also occur with anti-GBM disease, although this was not seen in clinical trials with LEMTRADA. If untreated it can cause kidney failure requiring chronic dialysis or transplantation, and may lead to death.

A blood test and urine test will help your doctor watch for signs of kidney disease to catch this side effect early. Your doctor will have your blood and urine tested before starting LEMTRADA, and on a monthly basis after your initial treatment course. Your doctor will test your urine monthly also. If you are a woman, it is also 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.

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

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

- > Blood in the urine: Your urine may be red or tea-colored.
- > Swelling: Swelling in your legs or feet.
- > Coughing up blood: You may cough up blood.

What if I develop kidney problems?

Most of the time doctors can treat 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 tests and urine tests). Kidney problems will almost always need treatment. Treatment can begin right away, if needed.

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 affect its ability to make and control the level of hormones.

LEMTRADA may cause development of thyroid disorders including:

- > Over-active thyroid gland – or Hyperthyroidism: This condition is when the thyroid produces too much hormone.
- > Under-active thyroid gland – or Hypothyroidism: This condition is when the thyroid does not produce enough hormone

Your blood will be checked before starting your treatment with LEMTRADA, and every 3 months after your initial treatment course until 4 years after your last infusion. This blood test will help your doctor detect thyroid disorders early.

What are the signs and symptoms of an over-active thyroid?

Symptoms may include:

- > Excessive sweating
- > Unexplained weight loss
- > Eye swelling
- > Nervousness
- > Fast heartbeat

What are the signs and symptoms of an under-active thyroid?

Symptoms may include:

- > 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. ►

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Depending on the type of thyroid disorder you are experiencing, 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 will have to take medication for the rest of your life for your thyroid disorder. In some situations, your thyroid may need to be removed.

Should 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 tests (even if you are feeling well).



You must also continue to watch for signs and symptoms.



Do this for 4 years after your last course of treatment with LEMTRADA.



Early detection and diagnosis may give you the best opportunity for improvement.

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Carry your patient alert card with you and show it to any healthcare providers who are providing you treatment (including for non-MS conditions) or in the event of a medical emergency

Serious Infections

Patients treated with LEMTRADA are at a higher risk for getting a serious infection. If you develop a serious infection you may have to go to hospital for treatment. It's important to tell the doctors in the hospital that you have received LEMTRADA.

If you are suffering from an infection before the initiation of your LEMTRADA treatment, your doctor will consider delaying the treatment until the infection is under control or resolved.

4> Other helpful information

What do I need to know about vaccination?

Before receiving each course of your treatment with LEMTRADA, your doctor will check that you are up to date with your vaccinations. If you need a vaccination, you will have to wait for 6 weeks after this to have your LEMTRADA treatment. Tell your doctor if you have already had a vaccination within the last 6 weeks.

Fertility/Pregnancy/Contraception

It is not known if LEMTRADA will have an effect on fertility during the time when it is in your system. Talk to your doctor if you are thinking about trying to become pregnant.

It is not known if LEMTRADA could harm an unborn child. You should use effective contraceptives when you receive your course of treatment with LEMTRADA and for 4 months following each course of treatment with LEMTRADA (unless your doctor tells you it is not needed since you are unable to have a child, for example if you have had a hysterectomy). This is to ensure there is no LEMTRADA left in your body before you conceive a child. You should be sure to discuss with your doctor if you are planning to become pregnant.

If you are already pregnant, you and your doctor will need to decide whether the benefit of you receiving treatment outweighs the potential risk to your unborn baby.

It is unknown if LEMTRADA can be transferred to a baby through breast milk, but there is a possibility that it could be. It is recommended that you do not breastfeed during each course of treatment with LEMTRADA or for 4 months after each treatment course. However, there may be benefits of breast milk (which can help protect a baby from infections) so talk to your doctor if you are planning to breastfeed your baby. He/she will advise you what is right for you and your baby.

What other information should I tell my doctor?

Be sure to tell your doctor or healthcare team about any new health problems you have developed and any new medicines you have taken since your last appointment. Those medicines may include prescription and non-prescription medicines, vitamins, and herbal supplements. It is important for your doctor to know this and to manage your treatments.

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5> Planning your monitoring schedule

The autoimmune conditions described in this guide could occur long after you received a course of treatment with LEMTRADA. It is very important that you continue to have your monthly tests (even if you are feeling well) for 4 years after your last treatment course. Because you only receive LEMTRADA in 2 annual courses, your testing will need to be planned separately.

Log-on to www.msonetoone.xx and use the access code in your Lemtrada handbook to access the educational materials (including this guide) electronically. The web-site contains helpful information related to your use of LEMTRADA and tools which can help you stay on track with your testing.

The following tools may be helpful to help you remember to have the monitoring tests. You can use as many, or as few, of them as you like.

<<Note: Delete as appropriate according to national approvals>>

> **Web-based reminder:** Through www.msonetoone.xx you can register to receive electronic monthly reminders about your testing. Just fill in your email address and/or mobile telephone number so that you will receive automatic monthly reminders by email or SMS.

> **Paper-based reminder:** Should you prefer to receive the monthly reminder by mail, use the Freepost card in this guide, filling in your full name and postal address. Receipt of the card will be considered consent to start receiving reminders.

Following receipt of your card, you will receive a monthly letter by post reminding you to complete your testing.

> **Calendar:** A calendar is available with stickers for you to mark your test dates. This can be sent to you. You can mark the date of your test each month, to remind you it is coming up. Should you need a replacement at any time you can order it anytime just contact <<insert contact details of selected vendor>>.

These services are offered through a third party, who will collect and process your personal data in accordance with applicable data protection legislation. Your personal data will be stored securely and will not be disseminated to others, including the manufacturer of LEMTRADA. Again, these services are optional and you can opt in or out at any time.

Don't forget, should you experience any of the events described in this guide, early detection and diagnosis will give you the best opportunity for improvement.

Always complete your testing and continue to watch out for signs and symptoms of the events described in this guide, for 4 years after your last infusion.

Recap of Recommended Monitoring

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

6> Helpful words to know

Anti-Glomerular Basement Membrane disease (anti-GBM): a disease caused by your immune system turning against the kidneys (or sometimes the lungs). The kidneys are damaged and do not work properly, or completely fail. As a result you may require dialysis, and/or kidney transplantation. If detected promptly it is treatable, but if untreated, it can lead to death.

Autoimmune Conditions/Disorders: Usually the immune system protects the body from bacteria, viruses, and other harmful agents. If the immune system turns against a person's own cells and organs, this is known as an autoimmune disorder or condition. In MS, the immune system mistakes the brain or spinal cord as foreign and damages them. Other autoimmune conditions can damage other organs or blood cells.

Autoimmune Thyroid Disorder: When the immune system mistakenly attacks the cells of the thyroid gland. Autoimmune thyroid disorders are treatable. Two examples are listed below:

- > **Hyperthyroidism:** When the thyroid produces too many hormones.
- > **Hypothyroidism:** When the thyroid does not produce enough hormones.

Dialysis: A process for removing waste and excess water from the blood when the kidneys are not working properly.

Immune System: The body's defense system against such things as infection, foreign substances, and abnormal cells.

Infusion: when a solution (a liquid containing a medicine) is slowly passed into your vein through a needle.

ITP (Immune Thrombocytopenic Purpura): ITP is a condition which results in a decrease in the number of platelets in the blood. Platelets are necessary for normal blood clotting. ITP can cause severe bleeding. If detected promptly it is treatable, but if left untreated it may lead to serious health problems and possibly death.

Lymphocytes (a type of white blood cell): cells in your blood which help your body fight infection. These cells form part of your immune system.

Platelets: Platelets are necessary for normal blood clotting. Platelets travel in the bloodstream. They help stop bleeding by sticking together to form a clot. The clot helps seal small cuts or breaks in the skin.

Thyroid: A gland found in the lower part of the neck. This gland produces hormones that are important to regulate your metabolism.

7> How to reach your doctors

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

Doctor/Healthcare Team	Telephone	Address



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Lemtrada/Patient Guide/EU Gen/Release date Nov 2013/EN

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