LEMTRADA® alemtuzumab 12mg IV

Patient Guide

Important safety information for patients starting therapy with alemtuzumab

The aim of this guide is to help you understand some of the risks associated with alemtuzumab treatment and the monitoring needed to help minimise these risks.

▼ LEMTRADA Please report suspected side effects to the MHRA through the Yellow Card scheme. You can report via:

- The Yellow Card website www.mhra.gov.uk/yellowcard
- The free Yellow Card app available from the Apple App Store or Google Play Store
- Some clinical IT systems (EMIS/SystmOne/Vision/MiDatabank) for healthcare professionals.
- Alternatively you can report a suspected side effect to the Yellow Card scheme by calling 0800 731 6789 for free, Monday to Friday between 9am and 5pm. You can leave a message outside of these hours.

When reporting please provide as much information as possible. By reporting side effects, you can help provide more information on the safety of this medicine.
Suspected side effects should also be reported to Sanofi: Tel: 0800 0902314.
Email: UK-drugsafety@sanofi.com

SANOFI GENZYME

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IMPORTANT!

Since side effects can occur long after you received an alemtuzumab infusion, it's very important that you continue to attend regular blood and urine monitoring tests for at least 48 months after your last infusion.

You must also continue to watch out for signs and symptoms for at least 48 months after your last infusion of alemtuzumab:

- Carry your Patient Alert Card with you and show it to any healthcare providers (this includes doctors, nurses, dentists or pharmacists) who are providing you treatment (including for non-Multiple Sclerosis (MS) conditions) and in the event of a medical emergency

Electronic format versions

Additionally, electronic versions of these materials are available to download on the following website:

www.medicines.org.uk/emc/

If you have any enquiries or wish to request paper copies of the patient information leaflet, patient guide or patient alert card, please contact Sanofi Medical Information:

UK Telephone: 0800 035 2525

Email: UK-medicalinformation@sanofi.com

1. Introduction to alemtuzumab

This Patient Guide is to make you aware of the serious risks associated with alemtuzumab infusions, including cardiovascular events occurring soon after dosing, and to outline the necessary monitoring tests to reduce the frequency or severity of these risks.

This guide also includes a section where you should record the contact details for your prescribing neurologist, Multiple Sclerosis (MS) specialist nurse and general practitioner. This guide is not intended to replace any discussions you have with your doctor or the Patient Information Leaflet for alemtuzumab which you should still read in full.

You must urgently contact your neurologist or MS specialist nurse/ go to hospital if you notice any of the signs or symptoms of the serious risks described in this guide or seek urgent medical attention if specialist advice is not available.

In addition to this guide, you can log-in to the Sanofi MS One to One website: www.msonetoone.co.uk/ or scan the QR code below. The website contains information about MS and managing life while on treatment for MS.

Alemtuzumab is a prescription only medicine used to treat adults with relapsing remitting MS. Alemtuzumab can only be used if your MS is highly active despite being treated with at least one other disease modifying treatment or if your MS is rapidly progressing.

After treatment with alemtuzumab, you may be at risk of developing side effects. It's important that you understand what these risks are and how to monitor for them.

How is alemtuzumab given?

Alemtuzumab is given to you by intravenous infusion via a needle in one of your veins. Alemtuzumab is recommended for 2 initial treatment courses, with up to 2 additional treatment courses, if needed. Courses are given at least 12 months apart. The first course includes daily infusions given over approximately 4 hours for 5 days in a row. The second and any additional courses includes daily infusions for 3 days in a row.

Treatment with alemtuzumab may increase the risk of autoimmune conditions (conditions in which your immune system mistakenly attacks your body). These are delayed side effects which can occur many years after your treatment. You will therefore need to commit to monthly monitoring, undertaking blood and urine tests for at least 48 months after your last alemtuzumab infusion. Your doctor will check the results of these tests to see if you have developed any side effect(s).

You and your doctor will work together to make sure that these tests are done and plan them around your day-to-day life. If you're a woman, it's also important to avoid urine testing during your menstrual periods as this may give a false result.

Before starting your alemtuzumab infusion

Your doctor will also carry out checks and offer treatment and advice before starting your infusion course that may help to reduce your risk of infusion associated reactions (IARs) and infections after your alemtuzumab treatment.

Initial patient checks can include:

- Screening for Tuberculosis infection
- A scan using magnetic resonance imaging (MRI) to rule out the possibility of a rare brain infection called Progressive Multifocal Leukoencephalopathy (PML)
- Hepatitis B and/or Hepatitis C (affecting the liver) screening in high risk patients
- Human Papillomavirus (HPV) screening in female patients prior to treatment
- A screening for cytomegalovirus (related to herpes virus) Cytomegalovirus (related to the herpes virus) screening
- Prescribing a medicine to prevent a viral herpes infection
- A review of the use of effective contraception for women who could become pregnant
- Vaccination check (at least 6 weeks before starting treatment)
  - If you've not yet done so, you may be advised to complete your local vaccination programme
  - You may also be advised to receive additional vaccinations before you start treatment
- Dietary
  - To reduce your risk of Listeria infection (a bacterial infection caused by eating contaminated foods) after treatment, you should not eat uncooked or undercooked meats, soft cheeses and unpasteurised dairy products for 2 weeks prior to, during treatment and for at least 1 month after alemtuzumab infusion
  - Information about dietary recommendations can be found at: www.nhs.uk/conditions/listeriosis
- Vital signs will be checked including blood pressure and heart rate, before you start your treatment
- Blood and urine tests

Monitoring immediately before the alemtuzumab infusion

- Vital signs will be checked including blood pressure and heart rate
- To reduce your risk of infusion-associated reactions, your doctor will give you a corticosteroid treatment before the first 3 infusions of each of your alemtuzumab treatment courses as well as other treatments such as antihistamines and/ or paracetamol

Monitoring during the alemtuzumab infusion

- Vital signs including blood pressure, heart rate and overall clinical status will be checked at least once every hour for the total duration of the infusion

Monitoring immediately after alemtuzumab infusion

- You will be observed for at least 2 hours after infusion to look for any signs and/or symptoms of serious side effects. You will be monitored until they are resolved
- Blood test – immediately after infusion on day 3 and 5 of the first course and on day 3 of any subsequent courses to check platelets in the blood

Monitoring after treatment course(s)

- Blood and urine tests – monthly for at least 48 months after your last alemtuzumab infusion
- Annual HPV screening in female patients

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2. Side effects

Key Information

You should contact your doctor immediately or seek urgent medical attention if you experience any of the following signs or symptoms. It is also important to inform your relatives or caregivers about your treatment, since they may notice symptoms that you are not aware of.

Serious side effects which can occur soon after alemtuzumab infusion (occurring within 1–3 days of infusion)

When given alemtuzumab, you can be at risk of developing serious side effects that occur during or shortly after infusion.

In the majority of cases, onset of these reactions is within 1–3 days of alemtuzumab infusion, but some may occur weeks later. Tell your doctor right away if you develop any of the signs and symptoms in the table on the next below.

Side effect	Signs and symptoms to watch for
Heart attack (Frequency unknown*)	• Shortness of breath • Chest pain or discomfort • Facial or eyelid drooping • Sudden severe headache • Weakness on one side of the body • Difficulty with speech • Pain or discomfort in arms, jaw, neck, back or stomach • Coughing up blood • Exaggerated or spontaneous bleeding
Bleeding in the lung (Frequency unknown*)	
Stroke (Frequency unknown*)	
Tears in the blood vessels supplying the brain (Frequency unknown*)	
Thrombocytopenia (low platelets in blood) (Can affect 1 in every 100 patients taking alemtuzumab)	

***Only a small number of cases have been reported therefore the frequency of the risk is unknown.**

Serious infections – which can occur any time after infusion

Receiving treatment with alemtuzumab can put you at risk of getting a serious infection. Serious infections occurred in 3 in 100 people during clinical trials.

If you experience any symptoms of infection, please contact a doctor or healthcare professional immediately, showing them your Patient Alert Card.

Brain Infection – Progressive Multifocal Leukoencephalopathy (PML)

Rare cases of PML (including fatal) have been reported in people with MS after treatment with alemtuzumab. PML has been reported in patients with other risk factors, specifically prior treatment with MS products associated with PML.

PML symptoms may be similar to a relapse of MS. You should contact your doctor immediately if you develop any symptoms in the table on the next page.

It is important to inform your relatives or caregivers about your treatment and potential signs and symptoms, since they may notice symptoms that you are not aware of.

Side effect	Signs and symptoms to watch for
Serious infections	• Persistent fever • Chills • Shortness of breath • Cough • Wheezing • Chest pain or tightness • Coughing up blood • Unexplained weight loss • Headache • Neck stiffness • Rash and sensitivity to light (meningitis); widespread itchy rash with blisters (chickenpox) • Painful rash with blisters (shingles) • Sore throat with enlarged lymph glands (glandular fever)
PML	• Progressive weakness or clumsiness of limbs • Disturbance of vision • Speech difficulties • Changes in thinking, memory, and orientation leading to confusion and personality changes

Delayed autoimmune side effects (which can occur months to many years after infusion)

Treatment with alemtuzumab may increase the risk of autoimmune conditions. These are conditions in which your immune system mistakenly attacks your body, and these can occur months or many years after treatment. Therefore, regular blood and urine tests are needed until at least 48 months after your last infusion. Testing is needed even if you're feeling well and your MS symptoms are under control. In addition, these conditions may occur beyond 48 months, therefore, you must continue to look for signs and symptoms, even after you no longer need to have monthly blood and urine tests.

a. Thyroid disorders (may affect more than 1 in 10 people)

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

Alemtuzumab can cause thyroid disorders, including:

- Overactive thyroid gland (also called hyperthyroidism): when the thyroid produces too much hormone
- Underactive thyroid gland (also called hypothyroidism): when the thyroid does not produce enough hormone

Your thyroid function will be checked before you start your treatment with alemtuzumab, and every 3 months after your initial treatment course for at least 48 months after your last infusion. This blood test will help your doctor to detect any thyroid disorders early.

Side effect	Signs and symptoms to watch for
Overactive thyroid	• Excessive sweating • Unexplained weight loss • Eye swelling • Nervousness • Fast heartbeat
Underactive thyroid	• Unexplained weight gain • Feeling cold • Worsening tiredness • Newly occurring constipation

What should I do if I develop a thyroid disorder?

Tell your doctor if you experience any of the symptoms above.

Depending on the type of thyroid disorder you are experiencing, your doctor will explain which treatment is best for you. It's very important that you follow your doctor's recommendations to be sure that you benefit most from your treatment.

If you develop a thyroid disorder after receiving alemtuzumab, it's very important that you're properly treated for it, especially if you're female and become pregnant. Having an untreated thyroid disorder could harm your baby before it's born or after birth. Thyroid function tests must always be monitored during pregnancy.

b. Immune Thrombocytopenic Purpura (ITP)

Serious ITP occurs in approximately 1 in every 100 patients taking alemtuzumab. ITP is a condition which results in a low number of platelets in the blood. Platelets are necessary for normal blood clotting. As a result, ITP can cause severe bleeding. It's treatable if detected promptly, but if left untreated it can lead to serious health problems and may be fatal.

A blood test will help your doctor monitor for changes in your platelet count and catch ITP early should it arise. Therefore, your doctor will run a blood test before starting your alemtuzumab treatment, and on a monthly basis which continues for at least 48 months following your last treatment course.

Side effect	Signs and symptoms to watch for
ITP	• Small scattered spots on your skin that are red, pink or purple • Easy bruising • Bleeding from a cut that is harder to stop than usual • Heavier, longer or more frequent menstrual periods than normal • Bleeding between your menstrual periods • Bleeding from your gums or nose that is new or takes longer than usual to stop • Coughing up blood

What if I develop ITP?

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

ITP can start quickly and may occur in between the blood tests. It's therefore essential that you remain vigilant for signs and symptoms. If you notice any of the signs or symptoms described above, contact your doctor right away to report the symptoms. If you cannot reach your doctor, seek immediate medical attention and show them your alemtuzumab Patient Alert Card.

c. Kidney problems, including nephropathies such as anti-Glomerular Basement Membrane disease (anti-GBM disease)

Alemtuzumab can sometimes cause kidney problems, including a condition known as anti-GBM disease. During clinical trials this occurred in less than 1 in every 100 patients. Anti-GBM disease is an autoimmune condition that can result in severe damage to the kidneys. If left untreated, anti-GBM disease can cause kidney failure that requires chronic dialysis or transplantation and may eventually lead to death.

Blood and urine tests will help your doctor to monitor for signs of kidney disease and catch any problems early should they arise. Your doctor will run blood and urine tests before starting alemtuzumab, and on a monthly basis that will continue for at least 48 months after your last initial treatment. If you're a woman, it is also important to avoid urine testing during your menstrual period as this may give a false result.

You should be aware of the signs and symptoms of anti-GBM disease and report them to your doctor if you spot any of them.

Side effect	Signs and symptoms to watch for
Kidney problems, including nephropathies such as anti-GBM disease	• Blood in the urine: your urine may be red or tea-coloured • Swelling in your legs or feet • In some cases, anti-GBM disease can also cause damage to your lungs, which may result in coughing up blood

What if I develop kidney problems?

Kidney problems are usually treatable. However, it's best to begin treatment as early as possible. It's important that you are familiar with the signs and symptoms of kidney problems and anti-GBM disease and attend your regular blood and urine tests. Kidney problems will almost always need treatment.

If you notice any of the signs or symptoms described above, contact your doctor immediately to report them. If you cannot reach your doctor, make sure that you seek immediate medical attention.

d. Liver inflammation (also known as autoimmune hepatitis)

Some people have developed liver inflammation, also known as autoimmune hepatitis, after receiving alemtuzumab, however the frequency is unknown. Autoimmune hepatitis can be fatal or require liver transplantation. If you experience any of the symptoms listed below, you must inform your doctor.

Side effect	Signs and symptoms to watch for
Autoimmune hepatitis	• Unexplained nausea and/or vomiting • Abdominal pain and/or swelling • Unexplained itching • Loss of appetite • Yellowing of skin and/or eyes • Dark urine • Bleeding or bruising more easily than normal

e. Haemophagocytic Lymphohistiocytosis (HLH)

HLH is a rare, life-threatening condition that may affect up to 1 in 1000 people treated with alemtuzumab. HLH occurs when specific immune cells become overactive, causing too much inflammation. Ordinarily, these immune cells should destroy infected or damaged cells of the body. But in HLH, they start to damage your own tissues and organs, including the liver and bone marrow where blood is made. HLH can be challenging to diagnose because the initial symptoms may mimic other problems such as common infections. Symptoms have been reported to occur within a few months to four years following the initiation of treatment. If you experience any of the symptoms listed below you must call your doctor right away.

Side effect	Signs and symptoms to watch for
HLH	• Unexplained high fever • Severe headache • Swollen glands • Stiff neck • Lymph node enlargement • Yellow skin and eyes • Skin rash

f. Acquired haemophilia A

When treated with alemtuzumab it's possible that you may develop a disorder called acquired haemophilia A. A condition that may affect up to 1 in 100 people. This condition must be diagnosed and treated immediately. This is a bleeding disorder caused by antibodies that work against a protein needed for normal clotting of the blood, and can cause you to develop complications associated with abnormal, uncontrolled bleeding into the muscles, skin and soft tissue and during surgery or following trauma. If you experience any of the symptoms below you must call your doctor right away.

Side effect	Signs and symptoms to watch for
Acquired haemophilia A	• Spontaneous bruising • Nose bleeds • Painful or swollen joints • Other types of bleeding • Bleeding from a cut that may take longer than usual to stop

g. Thrombotic Thrombocytopenic Purpura (TTP)

TTP is a rare disease that may affect up to 1 in 1000 people. TTP causes blood clots to form inside blood vessels and can occur with alemtuzumab. TTP can occur all over the body and it needs to be treated in a hospital right away, because it can cause death. Get medical help right away if you have any of these symptoms.

Side effect	Signs and symptoms to watch for
TTP	• Anaemia and low platelet counts (may cause fatigue, pale skin, dizziness, shortness of breath, rapid heart rate) • Gastrointestinal symptoms (including abdominal pain, nausea and vomiting) • Bleeding or bruising/purpura • Neurological features (including confusion, headache, coma, stroke, transient weakness or numbness, seizure) • Kidney failure • Fever

h. Adult Onset Still's Disease (AOSD)

AOSD is a rare condition that has the potential to cause inflammation of the joints (arthritis), skin and internal organs such as the liver, lungs and heart. If you experience a combination of the symptoms listed below, contact your doctor immediately.

Side effect	Signs and symptoms to watch for
AOSD	• Fever >39°C or 102.2°F lasting more than 1 week • Pain • Stiffness with or without swelling in multiple joints • Skin rash

i. Autoimmune encephalitis (AIE)

Immune-mediated inflammation of the brain (encephalitis) can occur months to years after alemtuzumab treatment. The symptoms may resemble an MS relapse and can include memory loss, seizures, speech problems, twitching or stiffness of the face and limbs, drowsiness and behavioural or psychiatric problems such as personality changes, anxiety and abnormal thoughts. Contact your doctor immediately if you experience any of these symptoms and they are not caused by a known neurological or psychiatric problem.

Side effect	Signs and symptoms to watch for
AIE	• Behavioural and/or psychiatric changes • Abnormal movements including purposeless twitching of the body or muscle stiffness • Memory loss or seizures • Other symptoms which may resemble an MS relapse.

3. Other helpful information

Fertility

You may have alemtuzumab in your body during your treatment course and for 4 months after, and it's not known if alemtuzumab will have an effect on fertility during this period. Talk to your doctor if you are pregnant or are thinking about trying to become pregnant.

Pregnancy and contraception

It's not known if alemtuzumab could harm an unborn child. You have to use effective contraception during treatment with alemtuzumab and for 4 months after each course of treatment to ensure there's no alemtuzumab left in your body before you conceive a child. Make sure you tell your doctor if you are planning to become pregnant.

If you're already pregnant or plan to become pregnant soon, you should ask your doctor for advice before starting treatment with alemtuzumab.

Tell your doctor right away if you become pregnant after receiving alemtuzumab. Additional thyroid monitoring will be required.

Breastfeeding

It's unknown if alemtuzumab can be transferred to a baby through breast milk, but it is a possibility. It's therefore recommended that you do not breastfeed during any course of treatment and for 4 months after each alemtuzumab treatment course. However, there may be benefits of breast milk (which can help to protect a baby from infections), so you should talk to your doctor if you are planning to breastfeed. They will advise you on what is right for you and your baby.

Other medication

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's important for your doctor to know this to manage your treatment.

4. Reporting side effects

The safety of alemtuzumab is being closely monitored so it is important that any side effects are reported, even those not listed in the patient information leaflet that comes with the pack and which is available on-line.

Additionally, all pregnancies should be reported to Sanofi or MHRA via a method listed below.

▼ LEMTRADA Please report suspected side effects to the MHRA through the Yellow Card scheme. You can report via:

- The Yellow Card website www.mhra.gov.uk/yellowcard
- The free Yellow Card app available from the Apple App Store or Google Play Store
- Some clinical IT systems (EMIS/SystmOne/Vision/MiDatabank) for healthcare professionals.
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Email: UK-drugsafety@sanofi.com

5. How to reach your doctors

To make it easier to contact your healthcare team, write their contact details in the chart below.

Name of neurologist: .....
Phone number: .....
Email address: .....

Name of MS nurse: .....
Phone number: .....
Email address: .....

Name of general practitioner: .....
Phone number: .....
Email address: .....