LEMTRADA®
alemtuzumab 12mg IV

A healthcare professional's guide to using LEMTRADA® (alemtuzumab) in patients with relapsing remitting multiple sclerosis (RRMS)

Important safety and risk minimisation information for healthcare professionals prescribing LEMTRADA

▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Health Care Professionals (HCPs) are advised to report any suspected adverse reactions.

In case of any drug related adverse events, please contact: The National Pharmacovigilance Centre (NPC- Saudi Food Authority
(SFDA))
Call Center: 19999
E-mail: npc.drug@sfda.gov.sa
Website: ade.sfda.gov.sa

For SANOFI Pharmacovigilance center, please contact:
Mobile +966-544-284-797 or E-mail: Ksa_pharmacovigilance@sanofi.com

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This document is approved by The Executive Directorate of Pharmacovigilance, at SFDA

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Contents

Executive summary

Using LEMTRADA® (alemtuzumab) in patients with relapsing remitting multiple sclerosis (RRMS) – a guide for healthcare professionals.

This is an abbreviated guide – refer to the full guide for more information.

Please be aware that this guide does not cover all the identified safety events associated with the use of LEMTRADA and does not take the place of the Summary of Product Characteristics (SmPC).

LEMTRADA is indicated as a monotherapy for adults with highly active relapsing-remitting multiple sclerosis (RRMS) who have an inadequate response to at least one disease-modifying therapy (DMT), or with rapidly evolving severe RRMS.

This guide is part of the LEMTRADA Educational Programme to support physicians in initiating and managing LEMTRADA treatment. It emphasizes the need for at least 48 months of post-infusion follow-up, ongoing patient monitoring regardless of symptom control, and educating patients to recognize and promptly report adverse events to ensure safe and effective treatment.

Exposure to LEMTRADA in case of Pregnancy

Women of childbearing potential should use effective contraception when receiving and for at least 4 months after each course of LEMTRADA treatment.

LEMTRADA should only be administered during pregnancy only if the potential benefit justifies the potential risk to the foetus. Breastfeeding is not recommended during and for at least 4 months following a treatment course even if it is unknown whether LEMTRADA is excreted in human milk.

Serious infections

Side effect	Monitoring procedures	Management
Serious infections	• **Post-infusion:** Patients should be informed about the symptoms associated with serious infections so they can self-monitor post-infusion	• Various risk minimisation procedures
Progressive Multifocal Leukoencephalopathy (PML)	• **Before starting** or re-administering LEMTRADA, an MRI should be performed to check for signs of PML. **After infusion**, patients and their caregivers should be informed about PML symptoms —including progressive weakness, vision changes, cognitive or behavioral changes, and speech difficulties—so they can recognize early warning signs.	• Further evaluation, including cerebrospinal fluid (CSF) testing for JC Viral DNA and repeat neurological assessments should be performed if PML is clinically suspected.

Serious side effects temporally associated with LEMTRADA infusion

Side effect	Monitoring procedures	Management
Myocardial ischaemia and/or infarction	• Perform baseline ECG and record vital signs, including heart rate and blood pressure. • **During infusion:** Monitor vital signs and overall clinical status regularly, at least once every hour • **Post-infusion:** Observe patients for at least 2 hours after infusion. Patients should be informed about symptoms suggestive of serious infusion reactions and instructed to report them immediately and seek medical attention if they occur	• Patients who develop clinically significant changes in vital signs or report sudden onset of concerning symptoms should be evaluated immediately. • If a serious infusion-associated reaction occurs, treatment should be discontinued immediately. • Patients with clinical symptoms should be closely monitored until complete resolution.
Pulmonary alveolar haemorhage		
Haemorrhagic stroke		
Cervicocephalic arterial dissection		
Thrombocytopenia	• **Pre-infusion:** Baseline platelet count • **Post-infusion:** Perform platelet counts on Day 3 and Day 5 of the first course, and on Day 3 of any subsequent course. • • Patients should be informed about symptoms of thrombocytopenia (e.g., easy bruising, petechiae, prolonged bleeding) and instructed to report them immediately rather than only self-monitor.	• Clinically significant thrombocytopenia should be monitored closely and followed until resolution. • Referral to a haematologist should be considered, and is strongly recommended in cases of severe, persistent, or symptomatic thrombocytopenia.

BP=blood pressure; ECG=electrocardiogram

Delayed autoimmune side effects

Side effect	Monitoring procedures	Management
Thyroid disorders	• Perform baseline thyroid function tests and repeat every 3 months for at least 48 months after the last infusion. Educate patients on thyroid disorder symptoms (e.g., unexplained weight changes, palpitations, fatigue, heat/cold intolerance) and instruct them to report promptly, not just self-monitor.	• Consider referral to an endocrinologist
Immune thrombocytopenic purpura (ITP)	• Perform a complete blood count with differential at baseline and monthly for at least 48 months after the last infusion. Educate patients on ITP symptoms (e.g., easy bruising, petechiae, prolonged bleeding) and instruct them to report immediately, not just self-monitor.	• Appropriate medical intervention should be initiated promptly, including immediate referral to a haematologist
Nephropathies, including anti-Glomerular Basement Membrane (anti-GBM) disease	• Perform serum creatinine and urinalysis with microscopy at baseline and monthly for at least 48 months after the last infusion. Educate patients on nephropathy symptoms (e.g., blood in urine, leg/foot swelling, foamy urine, sudden weight gain, shortness of breath) and instruct them to report immediately.	• Consider referral to a nephrologist for diagnosis and treatment
Autoimmune hepatitis	• Perform liver function tests at baseline and monthly for at least 48 months after the last infusion. Educate patients on autoimmune hepatitis symptoms (e.g., nausea, vomiting, abdominal pain, dark urine, jaundice, fatigue, easy bruising) and instruct them to report immediately.	• Consider referral to a specialist for diagnosis and treatment
Haemophagocytic lymphohistiocytosis (HLH)	• Patients should be informed about the symptoms associated with HLH so they can self-monitor post-infusion	• Consider referral to a specialist for diagnosis and treatment
Acquired haemophilia A	• Patients should be informed about the symptoms associated with acquired haemophilia A so they can self-monitor post-infusion	• Consider referral to a haematologist for diagnosis and treatment
Thrombotic thrombocytopenic purpura (TTP)	• Perform a complete blood count with differential at baseline and monthly for at least 48 months after the last infusion. Educate patients on TTP symptoms (e.g., easy bruising, petechiae, jaundice, dark urine, persistent fever, confusion, severe headache, neurological changes) and instruct them to report immediately.	• Appropriate medical intervention should be initiated promptly, including immediate referral to a haematologist
Adult onset still disease (AOSD)	• Patients should be informed about the symptoms associated with AOSD so they can self-monitor post-infusion	• Consider referral to a specialist for diagnosis and treatment
Autoimmune encephalitis (AIE)	• Patients with suspected AIE should undergo diagnostic investigations (MRI, CSF analysis, EEG, antibody testing) to confirm the diagnosis and rule out other causes. Educate patients on AIE symptoms (behavioral/psychiatric changes, cognitive decline, seizures, movement disorders) and instruct them to seek immediate medical attention and inform their healthcare provider if these occur.	• Consider referral to a specialist for diagnosis and treatment

Overview of LEMTRADA

LEMTRADA is indicated for the treatment of adult patients with relapsing remitting multiple sclerosis (RRMS) with highly active disease, defined by clinical or imaging features, in the following patient groups:

- Patients with high disease activity despite an adequate course of at least one disease-modifying therapy (DMT)
- Patients with rapidly evolving severe RRMS

- Patients with highly active disease despite a full and adequate course of treatment with at least one disease modifying therapy (DMT) or
- Patients with rapidly evolving severe RRMS defined by 2 or more disabling relapses in one year, and with 1 or more gadolinium enhancing lesions on brain magnetic resonance imaging (MRI) or a significant increase in T2 lesion load as compared to a previous recent MRI

This guide, part of the LEMTRADA Educational Programme, supports physicians in initiating and managing LEMTRADA treatment. It summarizes key safety risks, both immediate and delayed, to help improve patient management and monitoring. Take a look at the overview below for more on what you can expect from this guide:

1. A description of the most important safety events associated with the use of LEMTRADA that may occur in proximity of the infusion or delayed after the lymphocyte repopulation

Serious infections

Progressive Multifocal Leukoencephalopathy (PML) Temporally associated side effects occurring during or shortly after infusion

- Myocardial ischaemia and infarction, pulmonary alveolar haemorrhage, haemorrhagic stroke, cervicocephalic arterial dissection, ITP and thrombocytopenia

Delayed autoimmune conditions (in order of frequency, most to least) events

- Thyroid disorders
- Immune Thrombocytopenic Purpura (ITP)
- Nephropathies, including anti-Glomerular Basement Membrane (anti-GBM) disease
- Autoimmune hepatitis
- Haemophagocytic lymphohistiocytosis (HLH)
- Acquired haemophilia A
- Thrombotic thrombocytopenic purpura (TTP)
- Adult onset still disease (AOSD)
- Autoimmune encephalitis (AIE)

2. Recommendations on how to mitigate these potential safety events through appropriate patient selection, counselling, monitoring and management
3. A frequently asked questions (FAQ) section

A Prescriber Checklist is also to be used at initial LEMTRADA prescription and patient follow-up visits.

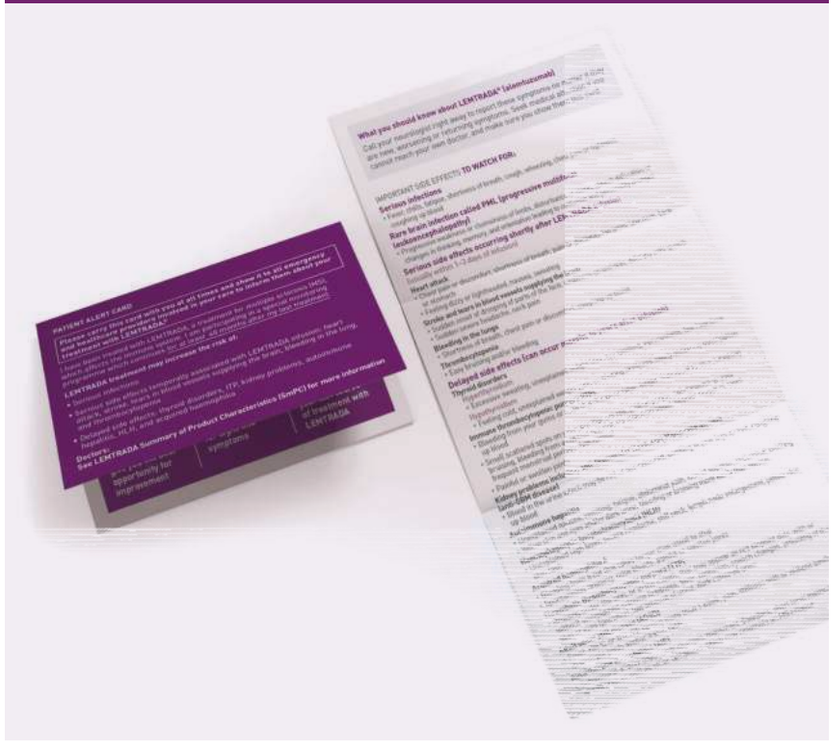
In addition, a **Patient Guide** and **Patient Alert Card** have been developed and these should be given to patients at the time of LEMTRADA treatment initiation.

Patient Guide

Review with patients at treatment initiation and follow-up visits to educate them on potential safety events, the importance of adhering to monitoring, staying vigilant for symptoms, and seeking immediate medical attention if needed.

Patient Alert Card

To be used as a tool to inform any HCPs treating patients receiving LEMTRADA. Patients (or care givers, when appropriate) should carry this card at all times and show this to any HCPs treating them.



These materials are available upon request from the Sanofi Medical Affairs Department.

Please be aware that this guide does not cover all the identified safety events associated with the use of LEMTRADA and does not take the place of the SmPC.

Introduction to LEMTRADA

LEMTRADA treatment should only be initiated and supervised by a neurologist experienced in the treatment of patients with MS in a hospital setting with ready access to intensive care.

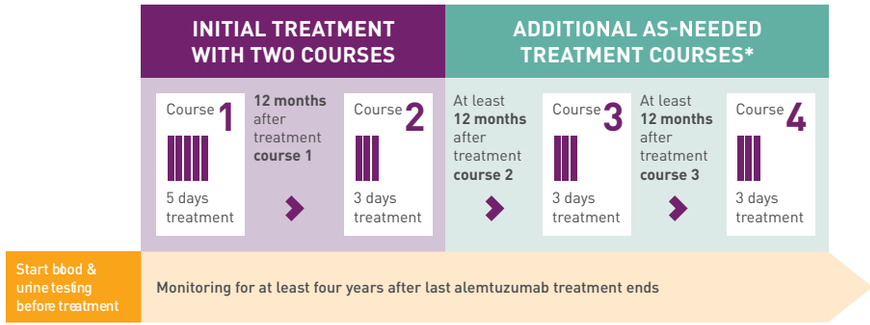
Ensure access to specialists and resources to manage serious adverse events, including cardiovascular, neurological, autoimmune, and infusion-related reactions.

In order to minimise possible risks and side effects of LEMTRADA, prescribers and patients must commit to at least 48 months of follow-up after the last infusion of LEMTRADA. It is important that patients understand that they should continue with the monitoring, even if they are feeling well and their MS disease is well controlled.

Creating a partnership between you, your patient and their MS care team, along with careful review on how to use the patient education tools, will help your patient to comply with periodic tests, identify and report symptoms in a timely manner and receive prompt and appropriate treatment if needed. **Detailed monitoring requirements are described in Section 3.**

To enhance your understanding of the treatment and the length of required follow-up, please refer to Figure 1.

Figure 1 – Overview of LEMTRADA posology



***Note:** A study following patients for 6 years after the first infusion (course 1) has shown that a majority of patients do not need further treatment after the 2 initial treatment courses.

What are the main risks associated with the use of LEMTRADA?

1. Serious infections
(affects ≥ 1 in 10 patients)

LEMTRADA use is associated with a risk of serious infections which may occur in the weeks following treatment, but can also arise years later. To minimise the risk of serious infection, it is important to:

- Delay treatment until any active infection is fully resolved
- Screen for infections (HIV, TB, HBV, HCV; HPV in females with annual follow-up)
- Complete vaccinations ≥6 weeks before treatment (consider HPV vaccination)
- Assess CMV status in high-risk patients
- Advise listeriosis-prevention diet around treatment period
- Start anti-herpes prophylaxis from Day 1 for at least 1 month post-treatment
- Avoid concomitant immunomodulatory therapies

2. Progressive Multifocal Leukoencephalopathy

Rare (including fatal) PML cases have been reported with alemtuzumab. Perform baseline MRI before initiation/re-treatment, and monitor closely—especially in patients with prior immunosuppressive therapy. If suspected, conduct CSF JC virus testing and neurological assessment, and remain alert to subtle cognitive, neurological, or psychiatric changes.

3. Serious side effects temporally associated with LEMTRADA infusion

Rare but serious (sometimes fatal) infusion-related reactions have been reported with LEMTRADA, typically occurring within 1–3 days, and may happen after any dose or treatment course.These safety events included:

- Myocardial ischaemia and/or myocardial infarction (not known incidence)
- Pulmonary alveolar haemorrhage (not known incidence)
- Haemorrhagic stroke (not known incidence)
- Cervicocephalic arterial dissection (not known incidence)
- Thrombocytopenia (affects < 1 in 10 patients)

Patients with abnormal vital signs (heart rate, blood pressure) or sudden symptoms of serious infusion reactions should seek immediate medical attention. Refer to Section 3: Summary of recommended patient monitoring for infusion guidance

4. Delayed autoimmune side effects

LEMTRADA use is associated with risk of autoimmune conditions that may occur with a delay of months to years following infusion, including:

- Thyroid disorders (affect ⩾ 1 in 10 patients)
- Immune thrombocytopenic purpura (ITP) (affects < 1 in 10 patients)
- Nephropathies, including anti-Glomerular Basement Membrane (anti-GBM) disease (affect < 1 in 100 patients)
- Autoimmune hepatitis (not known incidence)
- Haemophagocytic lymphohistiocytosis (HLH) (affects < 1 in 1,000 patients)
- Acquired haemophilia A (affects < 1 in 100 patients)
- Thrombotic thrombocytopenic purpura (TTP) (affects < 1 in 1,000 patients)
- Adult onset still disease (AOSD) (Not know incidence)
- Autoimmune encephalitis (AIE) (affects < 1 in 100 patients)

Serious events can occur, peaking 18–36 months post-treatment and sometimes after 48 months. Monitoring and early detection improve outcomes. Vigilantly track laboratory values and symptoms and refer to Section 3: Summary of recommended patient monitoring to reduce LEMTRADA risks.

Thyroid disorders (affect ⩾ 1 in 10 patients)

During clinical trials, autoimmune thyroid disorders including hyperthyroidism and hypothyroidism were reported. Thyroid disorders were very common in clinical trials and most were mild to moderate in severity. Some cases were transient and did not require treatment. The majority of thyroid-related events were managed with medical therapy, however some patients required surgical intervention.

Patients should be informed that some thyroid conditions may require lifelong treatment. Obtain TSH tests before starting LEMTRADA and every 3 months for at least 48 months after the last infusion. Educate and monitor patients for thyroid symptoms, and exercise special caution in pregnant women, as untreated thyroid disease can harm the fetus or newborn, with risks including miscarriage, neurodevelopmental impairment, and growth retardation; Graves' disease requires particular vigilance due to antibody transfer.

Immune thrombocytopenic purpura (ITP) (affects < 1 in 10 patients)

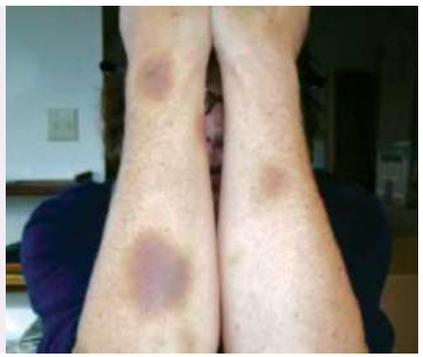
ITP is an autoimmune disorder often linked to anti-platelet antibodies. Symptoms may include easy bruising, bleeding, or heavy/irregular menstrual bleeding, which can appear even when platelet counts are normal, and may precede serious bleeding.

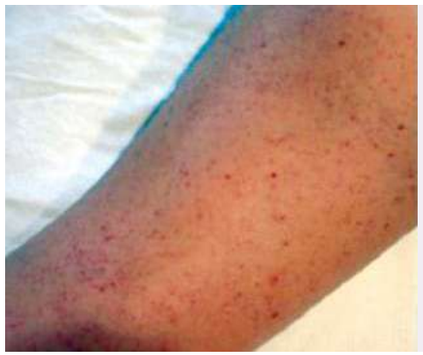
ITP can be a serious condition leading to morbidity and mortality, and can occur several years after dosing. In clinical trials, patients with ITP were diagnosed and managed in a timely manner with most cases responding to first-line medical therapy. It is important to monitor all patients for ITP as follows:

Figure 2 - Examples of ITP

Example of arms with easy or excessive bruising.

Location: This could occur anywhere on the patient's body, not just the arms.





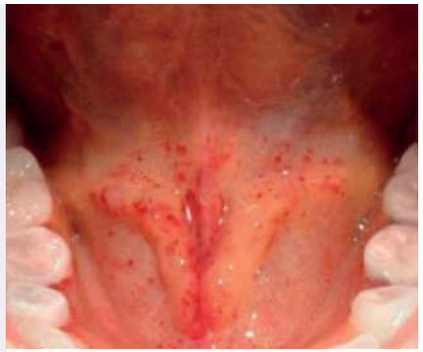
Example of a leg with petechia and purpura.

Petechiae are small, scattered, "pin prick" spots under the skin that are red, pink or purple.

Location: This could occur anywhere on the patient's body.

Example of purpura under the tongue.

Location: Petechiae and purpura could also occur on any mucous membrane, including anywhere in the mouth (under the tongue, roof of the mouth, inner cheeks, tongue, gums).



Note: These pictures are only a guide in order to show examples of bruises or petechiae. The patient may have a less severe type of bruise or petechiae than these pictures and still have ITP.

- Complete blood counts (CBC) with differential should be obtained prior to initiation of treatment and at monthly intervals thereafter until at least 48 months following the last infusion
- Assess patients for clinical signs and symptoms of ITP
- Advise patients on the importance of compliance of their blood and the need to continue for at least 48 months after their last infusion
- Educate the patient on how to recognize ITP-related symptoms, and emphasize the need to remain vigilant
- If ITP is suspected, appropriate medical intervention should be promptly initiated including immediate referral to a haematologist. Severe or widespread bleeding is life threatening and demands immediate care

The potential risk associated with retreatment with LEMTRADA following the occurrence of ITP is unknownand retreatment is generally not recommended unless the potential benefit clearly outweighs the risk.

Nephropathies, including anti-GBM disease
(affect < 1 in 100 patients)

Rare but serious autoimmune kidney disorders, including anti-GBM disease, have been reported with LEMTRADA, mostly within 39 months of the last infusion.

Clinical signs may include increased serum creatinine, hematuria, proteinuria, and, rarely, alveolar hemorrhage (hemoptysis). Because patients may be asymptomatic, monthly serum creatinine and urinalysis are required for at least 48 months after the last infusion, with timing in menstruating females considered to avoid false positives.

Any significant changes should prompt immediate nephrology evaluation, as early detection and treatment reduce the risk of severe outcomes. Anti-GBM disease is life-threatening without prompt intervention, potentially leading to renal failure, dialysis, transplantation, or death.

Autoimmune hepatitis (not known incidence)

Autoimmune hepatitis causing clinically significant liver injury, including fatal cases, has been rarely reported in patients treated with LEMTRADA in the post-marketing setting.

Patients should be informed about the related symptoms of hepatic injury. If a patient develops clinical signs or symptoms suggestive of hepatic dysfunction, e.g. enlarged liver, spider angiomas, ascites, unexplained nausea, vomiting, abdominal pain and/or swelling, aching joints, fatigue, anorexia, or jaundice and/or dark urine, autoimmune hepatitis should be considered as a differential diagnosis.

Haemophagocytic lymphohistiocytosis (HLH) (affects < 1 in 1,000 patients)

This severe systemic inflammatory syndrome has been rarely reported in patients treated with LEMTRADA in the post-marketing setting and is associated with high mortality rates if not recognised early and treated.

HLH may present with persistent high fever, rash, enlarged liver/spleen, low blood cell counts (pancytopenia), lymphadenopathy, and neurological symptoms such as seizures, irritability, or altered consciousness. Patients should be informed about these signs, and referral to a specialist is recommended if HLH is suspected.

Acquired haemophilia A (affects < 1 in 100 patients)

Cases of acquired haemophilia A have been reported in both clinical trials and the post-marketing setting.

Patients should seek immediate medical attention in case of signs or symptoms of unexplained and excessive bleeding from cuts or injuries, or after surgery or dental work, many large or deep bruises, unusual bleeding after vaccinations, pain or swelling in the joints, haematuria or bloody stool

Thrombotic thrombocytopenic purpura (TTP) (affects < 1 in 1,000 patients)

During postmarketing use, TTP, which can be fatal, has been reported in patients treated with LEMTRADA

TTP is a serious condition that requires urgent evaluation and treatment. TTP may be characterised by thrombocytopenia, microangiopathic haemolytic anaemia, neurological sequelae, fever and renal impairment. It is associated with high morbidity and mortality rates if not recognised and treated early.

Adult onset still disease (AOSD) (not known incidence)

During postmarketing use, AOSD has been reported in patients treated with LEMTRADA. AOSD is a rare inflammatory condition that requires urgent evaluation and treatment.

AOSD may present with fever, arthritis, sore throat, rash, easy bruising or bleeding, and high white blood cell counts (leukocytosis) without evidence of infection, malignancy, or other rheumatic conditions. Consider interrupting or discontinuing LEMTRADA if no alternative cause is identified.

Autoimmune Encephalitis (AIE) (affects < 1 in 100 patients)

Cases of autoimmune encephalitis have been reported in patients treated with LEMTRADA.

AIE typically presents with subacute, rapidly progressing memory loss, altered mental status, or psychiatric symptoms, often accompanied by new focal neurological deficits and seizures. Suspected cases should undergo MRI, EEG, lumbar puncture, and serologic testing for neural autoantibodies to confirm the diagnosis and rule out other causes.

Summary of recommended patient monitoring

Table 1 – Overview of pre-treatment recommendations to reduce the risk of side effects

	Pre-infusion
Pre-treatment	• Corticosteroids: Administer immediately before each of the first 3 days of a treatment course (1,000 mg methylprednisolone or equivalent). • Supportive pre-medication: Consider daily antihistamines and/or antipyretics. • Herpes prophylaxis: Start oral antiviral on Day 1 of each treatment course and continue for at least 1 month (e.g., 200 mg aciclovir twice daily or equivalent, such as valaciclovir).

Table 2 – Overview of peri-infusion prevention and monitoring recommendations

	Pre-infusion	During infusion	Post-infusion
ECG, vital signs including heart rate and BP	• Obtain baseline vital signs, including heart rate and BP • Baseline ECG	• Monitoring: Check heart rate, blood pressure, and overall clinical status at least hourly during infusion. • Action: Stop infusion immediately if signs or symptoms of a serious adverse event appear (e.g., myocardial ischemia, hemorrhagic stroke, pulmonary hemorrhage).	
Platelet Counts	• Baseline platelet count		• Obtain platelet count at the end of infusion on Day 3 and Day 5 of the first course, and on Day 3 of any subsequent courses of treatment
Observation			• Post-infusion observation: Monitor patients for at least 2 hours. Action: If serious adverse events occur (e.g., infusion reaction, cardiovascular or pulmonary event), continue monitoring until symptoms fully resolve.

AE=adverse event; BP=blood pressure; ECG=electrocardiogram

Table 3 – Overview of risk minimisation of delayed autoimmune side effects

	Pre-infusion	Post-infusion (Monthly) For at least 48 months	Post-infusion (Quarterly) For 48 months
Monitoring	• Thyroid function tests, including TSH levels • Complete blood count with differential • Serum creatinine • Urinalysis with microscopy • Serum transaminases	• Complete blood count with differential • Serum creatinine • Urinalysis with microscopy • Serum transaminases	• Thyroid function tests, including TSH levels

TSH=Thyroid Stimulating Hormone

Together with your patient, it is important to plan and manage their periodic monitoring – evaluate their test results and remain vigilant for symptoms of adverse events (AEs).

It is extremely important that you ensure your patient understands the commitment to have periodic testing for at least 48 months following their last LEMTRADA infusion, even if they are asymptomatic and their MS disease is well controlled.

- Patient education: Review the LEMTRADA Patient Guide and Package Leaflet at initial prescription and follow-ups.
- Risk awareness: Inform patients about potential benefits and serious risks, including delayed-onset autoimmune conditions beyond the 48-month monitoring period. Advise them to seek medical help if symptoms occur.
- Patient Alert Card: Encourage carrying it at all times and showing it to any healthcare provider, especially in emergencies.

Exposure to LEMTRADA in case of Pregnancy

- Pregnancy risk: Limited data exist; LEMTRADA may cross the placenta and pose fetal risk. Use only if benefits outweigh risks.
- Contraception: Women of childbearing potential should use effective contraception during treatment and for 4 months after each course.
- Breastfeeding: Avoid during treatment and for 4 months afterward. Benefits of breastfeeding should be weighed against potential drug exposure.

Frequently Asked Questions (FAQs)

Patients treated with LEMTRADA are at a higher risk of experiencing the safety events addressed in this guide than the general population. Please consider the steps required to minimise the risks associated with these side effects before prescribing LEMTRADA.

Contraindications

What if my patient has an infection when I want to begin a course of treatment with LEMTRADA?

You should delay the initiation of LEMTRADA administration in patients with severe active infection until the infection is fully resolved. LEMTRADA is contraindicated in patients with HIV infection (Human Immunodeficiency Virus (HIV) infection)

What are the contraindications of LEMTRADA treatment?

Do not use LEMTRADA if a patient:

- Is allergic to alemtuzumab or any of the other excipients listed in SmPC section 6.1
- Has Human Immunodeficiency Virus (HIV) infection
- Has severe active infections until complete resolution
- Has uncontrolled hypertension
- Has a history of arterial dissection of the cervico cephalic arteries
- Has a history of stroke
- Has a history of angina pectoris or myocardial infarction
- Has a known coagulopathy, and is on anti-platelet or anti-coagulant therapy
- Has other concomitant autoimmune diseases (besides MS)

Treatment

How is LEMTRADA administered and how long does the infusion take?

Treatment schedule:
1st course: Daily IV infusion for 5 consecutive days.
2nd course (12 months later): Daily IV infusion for 3 consecutive days.
Additional courses: Considered ≥12 months after prior course if MS activity returns; daily IV infusion for 3 consecutive days.

Infusion management:
Treat infusion-related side effects symptomatically.
Extend infusion duration if poorly tolerated; stop immediately for severe reactions. Evaluate patient before restarting therapy; consider permanent discontinuation if at high risk for serious outcomes.

Safety precautions:
Anaphylaxis is rare but possible; ensure resources are available for management. Assess cardiovascular, cerebrovascular, and pulmonary risk factors, and review concomitant medications to mitigate infusion-related reactions.

Are there any prophylactic treatments that should be taken?

Premedication: Administer corticosteroids (1,000 mg methylprednisolone or equivalent) immediately before LEMTRADA for the first 3 days of each treatment course.

Additional pre-treatment: Consider antihistamines and/or antipyretics prior to infusion.

Herpes prophylaxis: Start oral antiviral (e.g., aciclovir 200 mg twice daily) on Day 1 and continue for at least 1 month after each course.

Monitoring side effects

Before starting LEMTRADA treatment, what laboratory tests need to be performed?

The tests that need to be performed are:

- Complete blood count with differential
- Serum transaminases
- Serum creatinine
- Urinalysis with microscopy
- Thyroid function tests, such as thyroid-stimulating hormone (TSH)

Do I continue the laboratory tests during and after receiving treatment with LEMTRADA? For how long?

Yes. Testing starts before treatment (baseline tests) and should be continued for at least 48 months after receiving the last infusion. Details on which tests to conduct, when and for how long can be found in Section 3: Summary of recommended patient monitoring.

How long should patients be observed for after receiving a LEMTRADA infusion?

Patients should be observed for at least 2 hours after treatment. Those displaying clinical symptoms of a serious adverse event should be closely monitored until complete resolution of symptoms and hospitalisation extended as appropriate.

When should platelet counts be taken?

A baseline platelet count should be obtained prior to infusion. Platelet counts should also be taken immediately after infusion on Day 3 and Day 5 of the first course and on Day 3 of any subsequent courses.

Managing side effects

What are the signs and symptoms of serious side effects temporally associated with infusion?

Patients experiencing abnormal vital signs or sudden symptoms such as chest pain, facial drooping, breathing difficulties, severe headache, weakness, speech problems, or bleeding should be evaluated immediately, and LEMTRADA infusion stopped if severe. They must seek urgent medical attention.

How should I manage a patient with suspected serious side effects temporally associated with their LEMTRADA infusion?

Patients should be closely monitored for myocardial ischemia, infarction, pulmonary alveolar hemorrhage, hemorrhagic stroke, cervicocephalic arterial dissection, and thrombocytopenia. Vital signs, including blood pressure and heart rate, should be checked at baseline and regularly thereafter, with platelet counts recommended on Day 3 and Day 5 of the first treatment course and on Day 3 of any subsequent course.

What are the signs and symptoms of immune thrombocytopenic purpura (ITP)?

Symptoms of ITP may include easy bruising, petechiae, spontaneous mucocutaneous bleeding (such as nosebleeds or coughing up blood), and heavy or irregular menstrual bleeding. These signs can appear before severe bleeding occurs, and a drop in platelet count from baseline—even within the normal range—may also indicate ITP. See Figure 2 for further details.

How should I manage a patient with suspected ITP?

All patients should be closely monitored for ITP to ensure timely diagnosis and management. Complete blood counts must be performed before starting treatment and monthly for at least 48 months after the last infusion. If ITP is suspected, a platelet count should be checked immediately, and confirmed cases require prompt medical intervention, including urgent referral to a haematologist. Severe or widespread bleeding is life-threatening and requires immediate attention.

Which symptoms could be associated with nephropathy, such as anti-Glomerular Basement Membrane (anti-GBM) disease?

Nephropathy may present with elevated serum creatinine, haematuria, or proteinuria, and in rare cases, alveolar haemorrhage with haemoptysis may occur in anti-GBM disease. As patients can be asymptomatic, it is essential to perform regular laboratory monitoring, including serum creatinine and urinalysis with microscopy, monthly for at least 48 months after the last infusion.

How should I manage a patient with suspected nephropathy?

The observation of clinically significant changes from baseline in serum creatinine, unexplained haematuria and/or proteinuria, should prompt further evaluation for nephropathies including immediate referral to a specialist. Early detection and treatment of nephropathies may decrease the risk of poor outcomes.

What are the signs and symptoms of autoimmune hepatitis?

Symptoms of autoimmune hepatitis could include enzyme elevations and symptoms suggestive of hepatic dysfunction (e.g. unexplained nausea, vomiting, abdominal pain, fatigue, anorexia, or jaundice and/or dark urine).

What are the signs and symptoms of haemophagocytic lymphohistiocytosis (HLH)?

Among the signs and symptoms characteristic of HLH are high and unremitting fever, rash, hepatosplenomegaly, pancytopenias and lymphadenopathy.
neurological symptoms, cytopenias, and high ferritin.

How should I manage a patient with suspected autoimmune hepatitis?

Serum transaminases should be monitored on a regular basis. If hepatic injury is confirmed, appropriate medical intervention should be promptly initiated, including immediate referral to a specialist. Early detection and treatment of hepatic injury, including autoimmune hepatitis, may decrease the risk of poor outcomes.

How should I manage a patient with suspected HLH?

Regular urgent specialist referral (e.g. haematology/immunology) if HLH suspected, because it is life-threatening and time-sensitive should be carried out and if patients develop early manifestations of pathologic immune activation they should be evaluated immediately, and a diagnosis of

HLH should be considered.

What are the signs and symptoms of acquired haemophilia A?

Patients should seek urgent care for unexplained bleeding, large bruises, blood in urine or stool, joint swelling, or spontaneous hematomas.

How should I manage a patient with suspected acquired haemophilia A?

Patients presenting with symptoms of acquired haemophilia A should have a complete blood count and a coagulopathy panel, including aPTT; prolonged aPTT warrants urgent haematology referral.

How should I manage a patient with suspected Thrombotic Thrombocytopenic Purpura (TTP)?

All patients should be monitored for TTP with baseline and monthly complete blood counts for at least 48 months after the last infusion. If TTP is suspected, platelet counts must be checked immediately, and confirmed cases require urgent medical intervention and haematology referral, as TTP is life-threatening.

How should I manage a patient with suspected AOSD?

AOSD is a rare inflammatory condition requiring prompt evaluation and treatment. If no alternative cause is identified, consider interrupting or discontinuing LEMTRADA. Patients usually present with fever, arthritis, rash, and often leukocytosis.

How should I manage a patient with suspected AIE?

Patients with suspected autoimmune encephalitis should undergo MRI, EEG, lumbar puncture, and serologic testing for neural autoantibodies to confirm diagnosis and rule out other causes. Clinical presentation may include subacute cognitive decline, psychiatric symptoms, seizures, or movement disorders.

Pregnancy, contraception and breastfeeding counselling

Should female patients use contraception?

Alemtuzumab has an alpha half-life of approximately 4–5 days, with serum levels becoming low or undetectable around 30 days after each course. Women of childbearing potential should use effective contraception during treatment and for 4 months afterward.

Is it possible to administer LEMTRADA during pregnancy?

LEMTRADA should only be used during pregnancy if the potential benefits outweigh the risks to the foetus. As an IgG antibody, LEMTRADA may cross he placenta and could pose a risk, though its effects on foetal development or reproductive capacity are unknown. Untreated thyroid disease during pregnancy increases risks such as miscarriage, neurocognitive impairment, and growth restriction. In mothers with Graves' disease, TSH receptor antibodies may transfer to the foetus, potentially causing transient neonatal Graves' disease.

If women want to become pregnant, how long should they wait after a LEMTRADA treatment course?

Women of childbearing potential should use effective contraception during LEMTRADA treatment and for at least 4 months after each course. As full LEMTRADA therapy consists of two courses spaced 12 months apart, patients should be advised not to discontinue contraception between courses.

Will LEMTRADA affect future female or male fertility?

There are no sufficient clinical data on LEMTRADA's effects on fertility. A small sub-study in 13 male patients showed no consistent impact on sperm count, motility, or morphology. While CD52 is present in reproductive tissues and animal studies suggest potential fertility effects, the impact on human fertility during treatment remains unknown.

Should a patient who is breastfeeding receive a course of treatment with LEMTRADA?

It is unknown if LEMTRADA is excreted in human milk. To avoid potential risk to the infant, breastfeeding should be paused during each treatment course and for 4 months after the last infusion. The benefits of breastfeeding may be weighed against this potential risk.

Vaccinations

What considerations should be given to vaccinations when considering LEMTRADA treatment?

Live vaccines should be avoided during and after LEMTRADA treatment until immune recovery is confirmed, as their safety post-treatment is unknown. Patients should be up to date with national vaccination guidelines at least 6 weeks before starting LEMTRADA, and VZV vaccination should be considered for antibody-negative individuals. Contraception must be maintained between treatment courses.

Notes

LEMTRADA®
alemtuzumab 12mg IV

sanofi