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دانشگاه علوم پزشکی و خدمات
بهداشتی درمانی البرز
معاونت غذا و دارو

جهش تولید با مشارکت مردم (مقام معظم رهبری)

دبیرخانه سازمان نظام پزشکی کرج
شماره: ۱۴۰۳/۱۲۱۹
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معاونت محترم درمان دانشگاه علوم پزشکی البرز

ریاست محترم مرکز آموزشی درمانی/بیمارستان.....

ریاست محترم نظام پزشکی استان البرز

ریاست محترم انجمن داروسازان استان البرز

موضوع: انتشار مطالب آموزشی فرآورده Lemtrada جهت اطلاع رسانی به پزشکان

با سلام و احترام:

با عنایت به نامه شماره ۶۵۸/۴۸۷۹۵ مورخ ۱۴۰۳/۰۵/۲۰ دفتر نظارت و پایش مصرف فرآورده های سلامت سازمان غذا و دارو، به پیوست فایل های آموزشی مرتبط با فرآورده **Lemtrada**، به منظور اطلاع رسانی مقتضی به پزشکان و بیماران حصورتان ارسال می گردد.

دکتر مریم دانی
سرپرست معاونت غذا و دارو دانشگاه

PDF فایل های آموزشی

نامه فوق بدون مهر فاقد اعتبارمی باشد

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شماره ۲۵۸۱۲۸۷۹۵
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پیوست داره ---
چهش تولید با مشارکت مردم

جمهوری اسلامی ایران
وزارت بهداشت، درمان و آموزش پزشکی

IFDA سازمان غذا و دارو

از طریق سیستم جارگون دریافت شد

معاون محترم غذا و دارو دانشگاه/دانشکده های علوم پزشکی، خدمات بهداشتی و درمانی سراسر کشور

موضوع: ارسال مطالب آموزشی فراورده Lemtrada جهت اطلاع رسانی به پزشکان و بیماران - معاونت های غذا و داروی سراسر کشور

با سلام و احترام؛

محلق به نامه شماره ۱۶/۲۰۴۳۰ مورخ ۱۴۰۲/۴/۱۰ شرکت روژین دارو، به پیوست فایل های آموزشی مرتبط با فراورده Lemtrada به زبان فارسی و انگلیسی، جهت اطلاع رسانی به پزشکان و بیماران، جهت استحضار و انجام اقدام لازم، خدمتتان ارسال می گردد

دکتر زهرا جهانگرد
سرپرست دفتر نظارت و پایش مصرف فراورده های سلامت

رونوشت:
سرکار خانم دکتر مرجان کریمی قوانلو رئیس محترم گروه ثبت و گزارش ایمنی و عوارض ناخواسته فراورده های سلامت

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به نام خدا

ROUGINE
DAROU
شرکت روژین دارو

تاریخ ۱۴۰۳/۰۲/۰۹
شماره: ۰۵۳۰-ص-۰۲
پیوست دارد

جناب آقای دکتر غلامحسین صادقیان
سرپرست محترم اداره کل امور دارو و مواد تحت کنترل

موضوع: ارسال مطالب آموزشی فرآورده Lemtrada

با سلام و احترام،

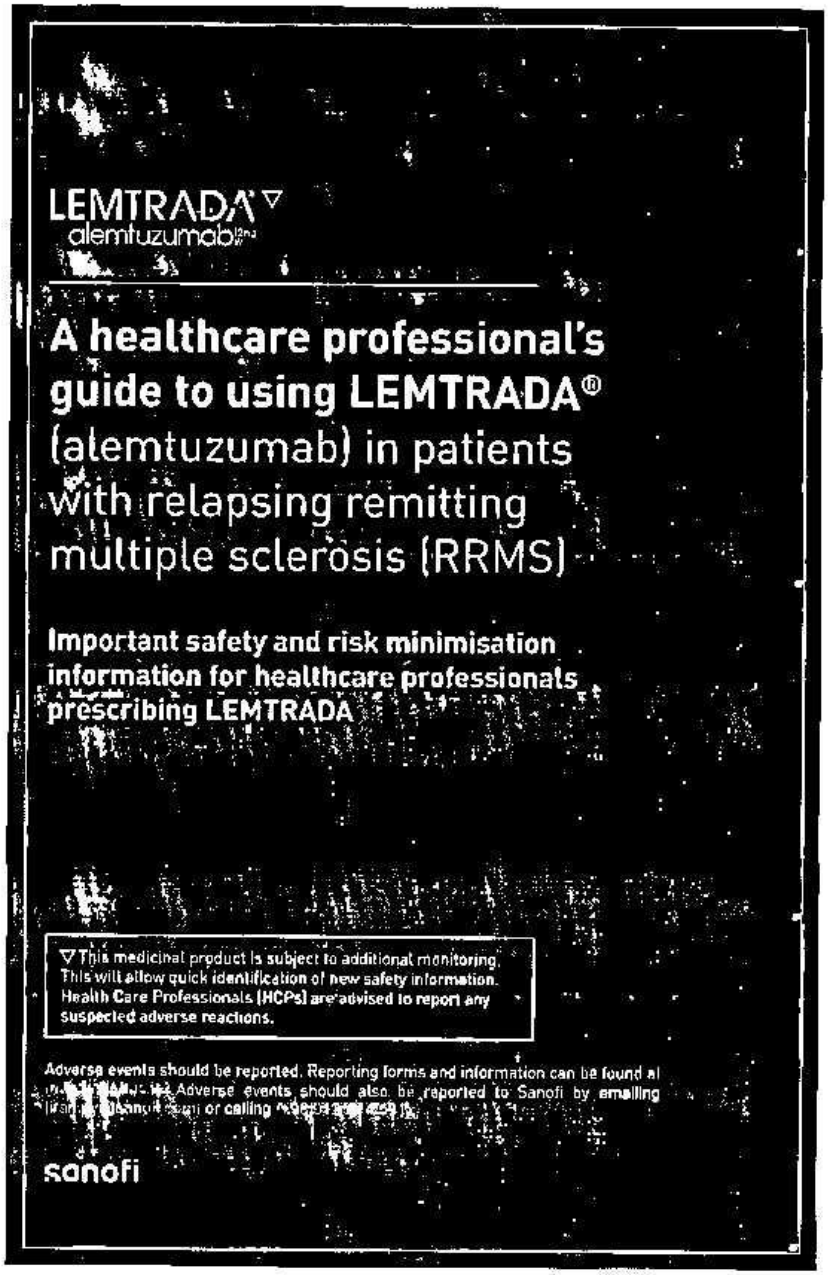
به پیوست مطالب آموزشی مرتبط با فرآورده Lemtrada جهت اطلاع رسانی به بیماران و پزشکان به زبان فارسی و انگلیسی، جهت اقتضاء به حضورتان ارسال می گردد.

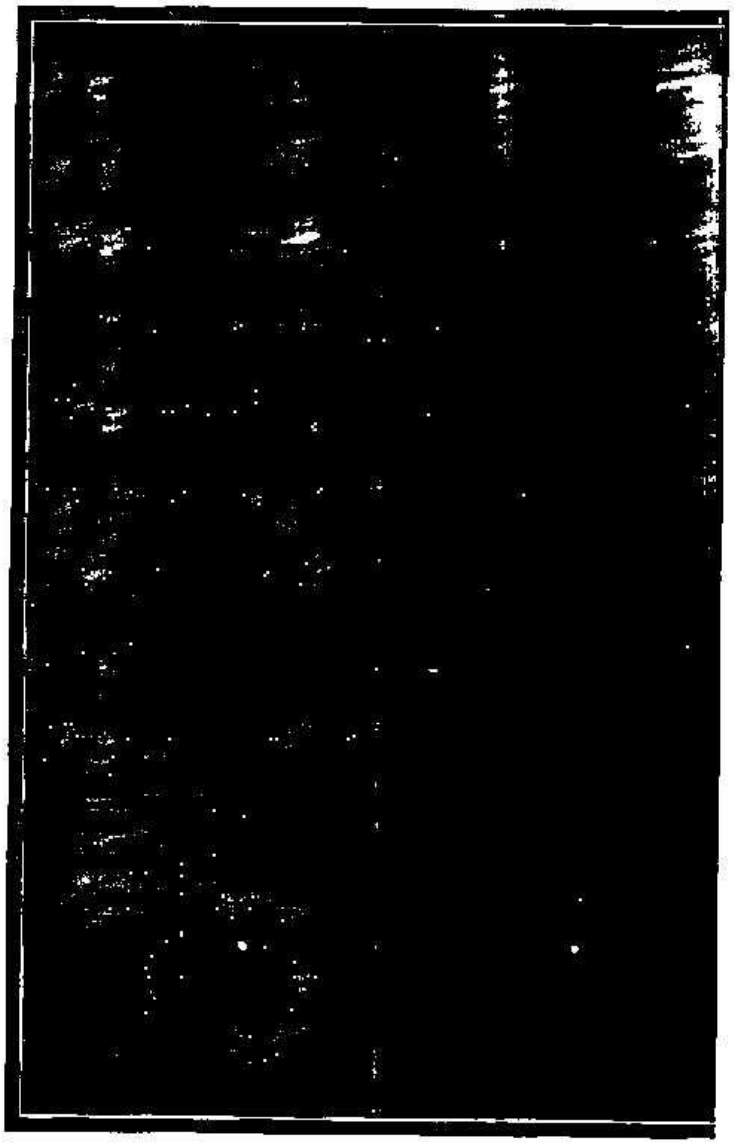
با احترام

دکتر فراز فرجام
رئیس هیات مدیره و مدیرعامل

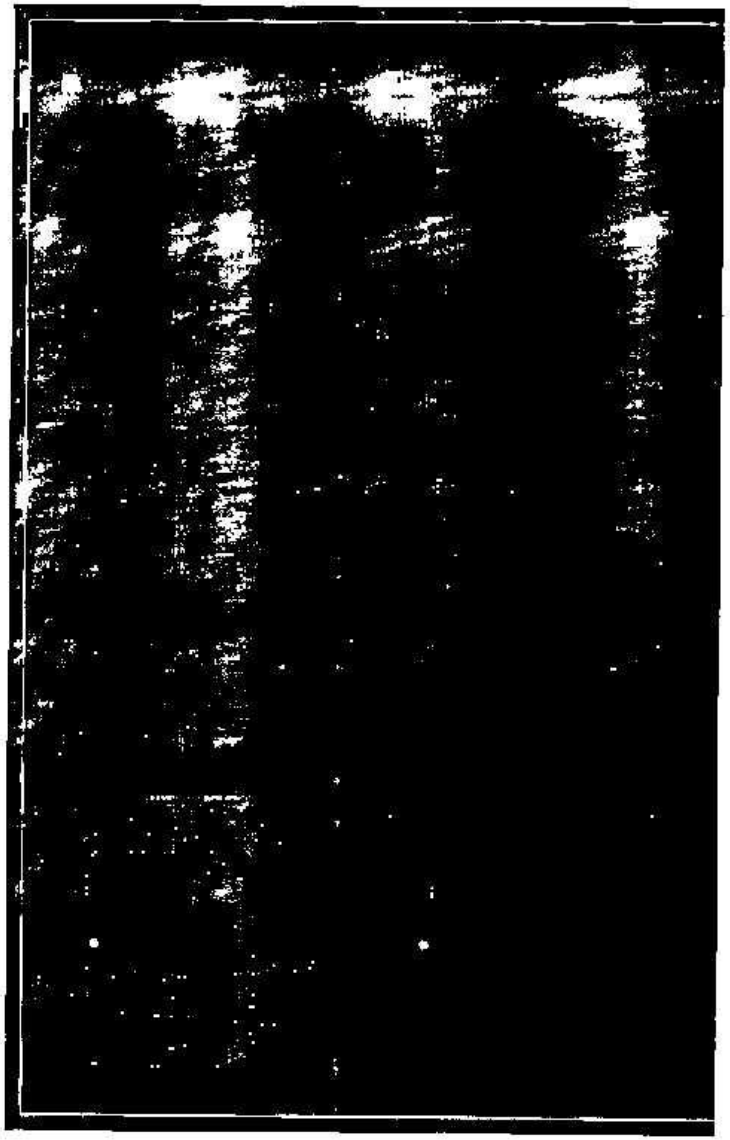
دکتر مریم نادر محمدی
مدیر فارماکوویژیلانس

دکتر مریم صادق شهابی
نظام پزشکی ۵۴۲۱۶


LEMTRADA▽
alemtuzumab
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.
Adverse events should be reported. Reporting forms and information can be found at
Adverse events should also be reported to Sanofi by emailling
or calling
sanofi



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 single disease modifying therapy for special populations of adults with highly active relapsing remitting multiple sclerosis (RRMS).

This guide has been developed as part of the LEMTRADA Educational Programme to support you in initiating and supervising LEMTRADA treatment, and to provide further information about the potential serious risks associated with its use to improve the monitoring and management of patients who are being treated.

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

Patients should be informed about the signs of side effects and advised to seek urgent medical attention should any occur.

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 if you consider the potential patient benefit to justify 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. However, the benefits of conferred immunity through breast milk may outweigh the risks of potential exposure to LEMTRADA for the suckling newborn.

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
	• **Prior to initiation and readministration of treatment:** MRI scan should be made and evaluated for signs that are consistent with PML	
Progressive Multifocal Leukoencephalopathy (PML)	• **Post-infusion:** Patients should be informed about the symptoms associated with PML and should inform their relatives or caregivers about their treatment	• Further evaluation, including cerebrospinal fluid (CSF) testing for JC Viral DNA and repeat neurological assessments should be performed as appropriate

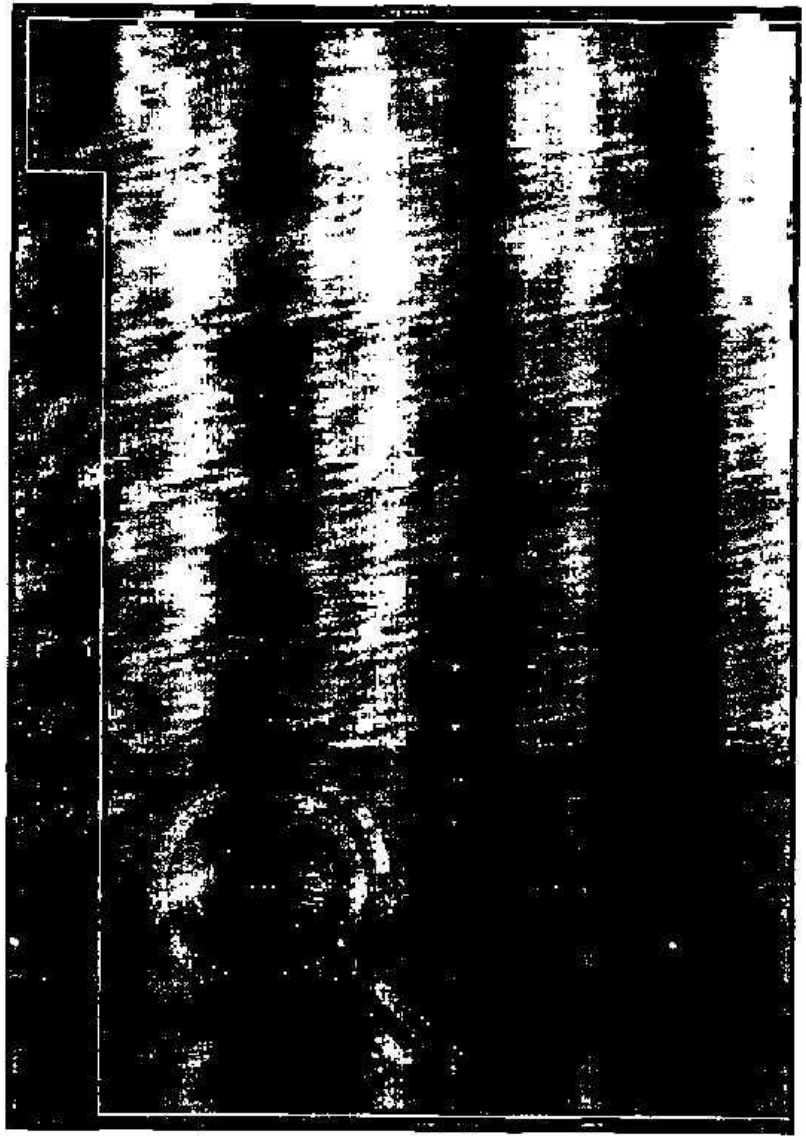
Serious side effects temporally associated with LEMTRADA infusion

Side effect	Monitoring procedures	Management
Myocardial ischaemia and/or infarction	• **Pre-infusion:** Baseline ECG and vital signs, including heart rate and BP **During infusion:** Regular monitoring of vital signs and overall clinical status at least once every hour • **Post-infusion: Observation for at least 2 hours post-infusion. Patients should be informed about the symptoms associated with serious reactions so they can self-monitor post-infusion**	• **Patients who develop abnormal vital signs or report sudden onset of symptoms should be evaluated immediately** • Immediate discontinuation of treatment if reaction occurs during infusion • **Patients with clinical symptoms should be closely monitored until complete resolution of symptoms**
Pulmonary alveolar haemorrhage		
Haemorrhagic stroke		
Cervicocephalic arterial dissection		
Thrombocytopenia	• **Pre-infusion: Baseline platelet count** • **Post-infusion:** Platelet count immediately after infusion on **Day 3** and **Day 5** of first course, and on **Day 3** of any subsequent course. Observation for at least 2 hours after infusion. **Patients should be informed about the symptoms associated with thrombocytopenia so they can self-monitor post-infusion**	• Clinically significant thrombocytopenia should be followed until resolved • Consider referral to a haematologist

BP=blood pressure; ECG=electrocardiogram

Delayed autoimmune side effects

Side effect	Monitoring procedures	Management
Thyroid disorders	• Thyroid function tests pre- and post-infusion. Patients should be informed about the symptoms associated with thyroid disorders so they can self-monitor post-infusion	• Consider referral to an endocrinologist
Immune thrombocytopenic purpura (ITP)	• Complete blood count with differential pre- and post-infusion. Patients should be informed about the symptoms associated with ITP so they can self-monitor post-infusion	• Appropriate medical intervention should be initiated promptly, including immediate referral to a haematologist
Nephropathies, including anti-Glomerular Basement Membrane (anti-GBM) disease	• Serum creatine levels test and urinalysis with microscopy pre- and post-infusion. Patients should be informed about the symptoms associated with nephropathies so they can self-monitor post-infusion	• Consider referral to a nephrologist for diagnosis and treatment
Autoimmune hepatitis	• Liver function tests pre- and post-infusion. Patients should be informed about the symptoms associated with autoimmune hepatitis so they can self-monitor post-infusion	• 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)	• Complete blood count with differential pre- and post-infusion. Patients should be informed about the symptoms associated with TTP so they can self-monitor post-infusion	• 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 autoimmune encephalitis should have appropriate complementary exams to confirm diagnosis and exclude alternative aetiologies. Patients should be informed about the symptoms associated with AIE so they can self-monitor post-infusion	• Consider referral to a specialist for diagnosis and treatment



Overview of LEMTRADA

LEMTRADA is indicated as a single disease modifying therapy in adults with highly active relapsing remitting multiple sclerosis (RRMS) for the following patient groups:

- 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 has been developed as part of the LEMTRADA Educational Programme to support you in initiating and supervising LEMTRADA treatment. It provides further information about the serious risks associated with LEMTRADA use, helping to improve the management of patients who are receiving treatment by providing a summary of its usage 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 and thrombocytopenia

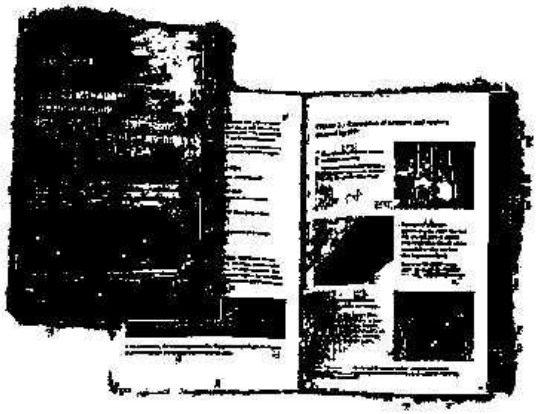
Delayed autoimmune conditions (in order of frequency, most to least) events

- 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

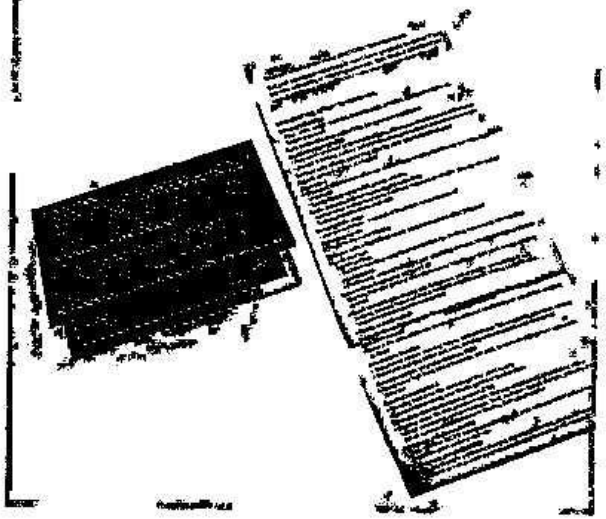


Patient Guide

To be carefully reviewed with your patient at initial prescription, and on a regular basis at follow-up visits. It aims to educate patients regarding the signs and symptoms of potential safety events and to make them aware of the need to be compliant with testing, keep an eye out for symptoms and to seek immediate medical attention should they occur.

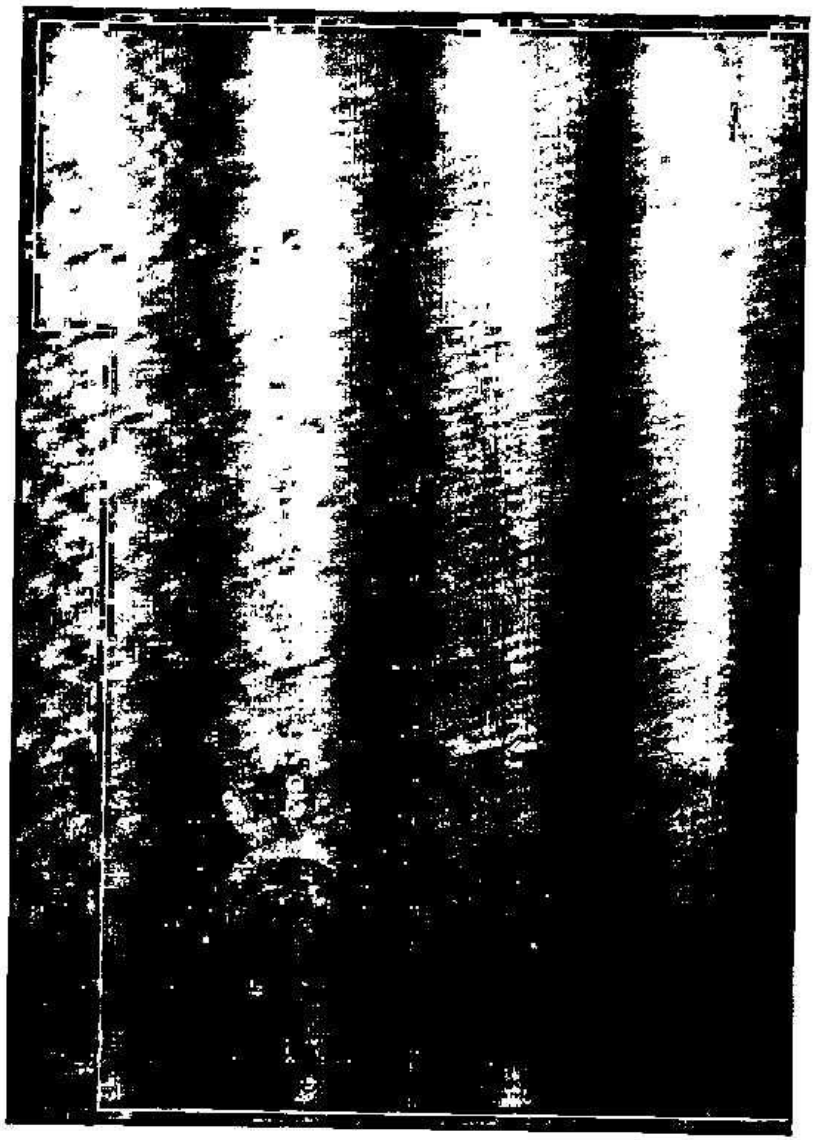
Patient Alert Card

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.

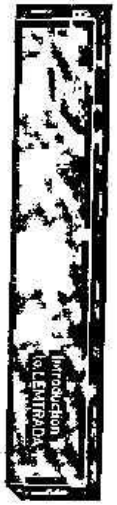


These materials are available upon request from the Sanofi Medical Affairs Department (local contact to be added).

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.

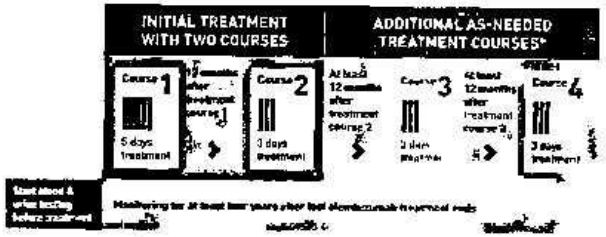
Specialists and equipment required for the timely diagnosis and management of adverse reactions, especially myocardial ischaemia and myocardial infarction, cervicocephalic arterial dissection, haemorrhagic stroke, autoimmune conditions and infections, should be available. Resources for the management of cytokine release syndrome, hypersensitivity and/or anaphylactic reactions should be available.

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 this 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 • ıı 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 start of treatment when active infection is present until completely resolved
- Screen for HIV, evaluate both active or inactive ("latent") tuberculosis risk according to local guidelines, screen for hepatitis B virus (HBV) and hepatitis C virus (HCV)
- Screen for human papillomavirus (HPV) in female patients and repeat screening annually. Consider vaccination prior to treatment
- Consider completing local immunisation requirements at least 6 weeks prior to starting treatment. The ability to generate an immune response to any vaccine following LEMTRADA has not been studied
- Before initiation of therapy, evaluation of cytomegalovirus (CMV) immune serostatus could be considered according to local guidelines
- Recommend listeriosis-prevention diet two weeks prior to, during and for at least 1 month after infusion. To reduce the risk of infection, patients receiving LEMTRADA should avoid ingestion of uncooked or undercooked meats, soft cheeses and unpasteurised dairy products two weeks prior to, during, and for at least one month after infusion
- Start anti-herpes prophylaxis on Day 1 of treatment and continue for at least 1 month following each course of treatment
- Avoid concomitant therapy with other immunomodulating agents

2. Progressive Multifocal Leukoencephalopathy

Rare cases of PML (including fatal), have been reported in MS patients after treatment with alemtuzumab. Patients treated with alemtuzumab must be monitored for any signs that may be suggestive of PML. Risk factors of special importance include previous immunosuppressive treatment, in particular other MS treatments with known risk of causing PML.

Prior to initiation and readministration of alemtuzumab treatment, an MRI scan should be made and evaluated for signs that are consistent with PML. Further evaluation, including cerebrospinal fluid (CSF) testing for JC Viral DNA and repeat neurological assessments should be performed as appropriate.

The physician should be particularly alert to symptoms suggestive of PML that the patient may not notice (e.g. cognitive, neurological or psychiatric symptoms).

3. Serious side effects temporally associated with LEMTRADA infusion

During post-marketing use, rare, serious and sometimes fatal temporally associated adverse events have been reported. In the majority of cases, time to onset was within 1–3 days of the LEMTRADA infusion. Reactions have occurred following any of the doses and after the second 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 who develop abnormal vital signs, including heart rate and blood pressure, or report sudden onset of symptoms characteristic of the above, should be advised to seek immediate medical attention. See "Section 3. Summary of recommended patient monitoring", for important information on infusion instructions.

4. Delayed auto mmune 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)

These events can be serious, leading to morbidity and/or mortality with peak incidence at 18–36 months post-treatment and in some cases, can occur after the 48-month monitoring period. Monitoring and early detection can improve the outcomes of patients experiencing these events.

It is important to carefully monitor laboratory values and be vigilant for signs and symptoms. Please review the following sections carefully to gain a better understanding of these risks. See Section 3: Summary of recommended patient monitoring, for important information about reducing the risk of LEMTRADA use.

Thyroid d sorders (affect ≥ ' 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.

It is important to let your patient know that depending on the type of thyroid condition, they may require lifelong treatment

- Thyroid function tests such as thyroid-stimulating hormone (TSH) levels should be obtained prior to initiation of treatment, and then every 3 months thereafter continuing for at least 48 months following the last infusion
- Additionally, watch out for signs and symptoms of thyroid disorders
- Thyroid disease poses special risks in women who become pregnant. Untreated thyroid disease can cause harm to the unborn and newborn baby. Untreated hypothyroidism during pregnancy increases risk of miscarriage and damage to the fetus, such as mental retardation and dwarfism. Special caution should be taken for pregnant women with Basedow's disease (also known as Graves' disease), as maternal TSH receptor antibodies can be transferred to a developing foetus and can cause transient neonatal Basedow's disease

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

ITP is an autoimmune disorder usually associated with anti-platelet antibodies. Please refer to Figure 2 for examples of ITP. Symptoms of ITP could include (but are not limited to) easy bruising, easy bleeding, and heavier than normal or irregular menstrual bleeding.

These clinical signs of ITP may or may not be apparent before serious bleeding develops. It is also not uncommon to observe the signs and symptoms of ITP soon after a normal thrombocyte count

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 with differential should be obtained prior to initiation of treatment and at monthly intervals thereafter until at least 48 months following the last infusion
- Check the patient for clinical symptoms of ITP
- Counsel the patient on the importance of complying with monthly monitoring of their blood and the need to continue for at least 48 months after their last infusion
- Educate the patient on how to recognise ITP-related symptoms, and emphasise 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 unknown.

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

Nephropathies, including anti-GBM disease, have rarely been reported after treatment with LEMTRADA in MS patients in clinical trials, but generally occurred within 39 months following the last administration.

Clinical manifestation of nephropathies may include elevation in serum creatinine, haematuria and/or proteinuria. While not observed in clinical trials, alveolar haemorrhage which manifests as haemoptysis, may occur with anti-GBM disease (Goodpasture Syndrome).

Since patients may be asymptomatic, it is important that periodic laboratory tests are conducted until at least 48 months after the last infusion of LEMTRADA

- Serum creatinine levels should be obtained prior to initiation of treatment and at monthly intervals thereafter
- Urinalysis with microscopy should be obtained prior to initiation of treatment and at monthly intervals thereafter. In menstruating females, consider the timing of urinalysis to avoid false positives. After the 48-month period, testing should be performed based on clinical findings suggestive of nephropathies

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

Anti-GBM disease is life threatening if not treated and therefore demands immediate care. Without prompt treatment, patients can rapidly develop renal failure requiring dialysis and/or transplantation, and may lead to 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 [illegible] 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.

Signs and symptoms characteristic of HLH include a high and unremitting fever, rash, hepatosplenomegaly, pancytopenias and lymphadenopathy. Patients should be informed about these potential symptoms of HLH. Consider referring your patients to a specialist for evaluation if you suspect they have developed HLH.

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)

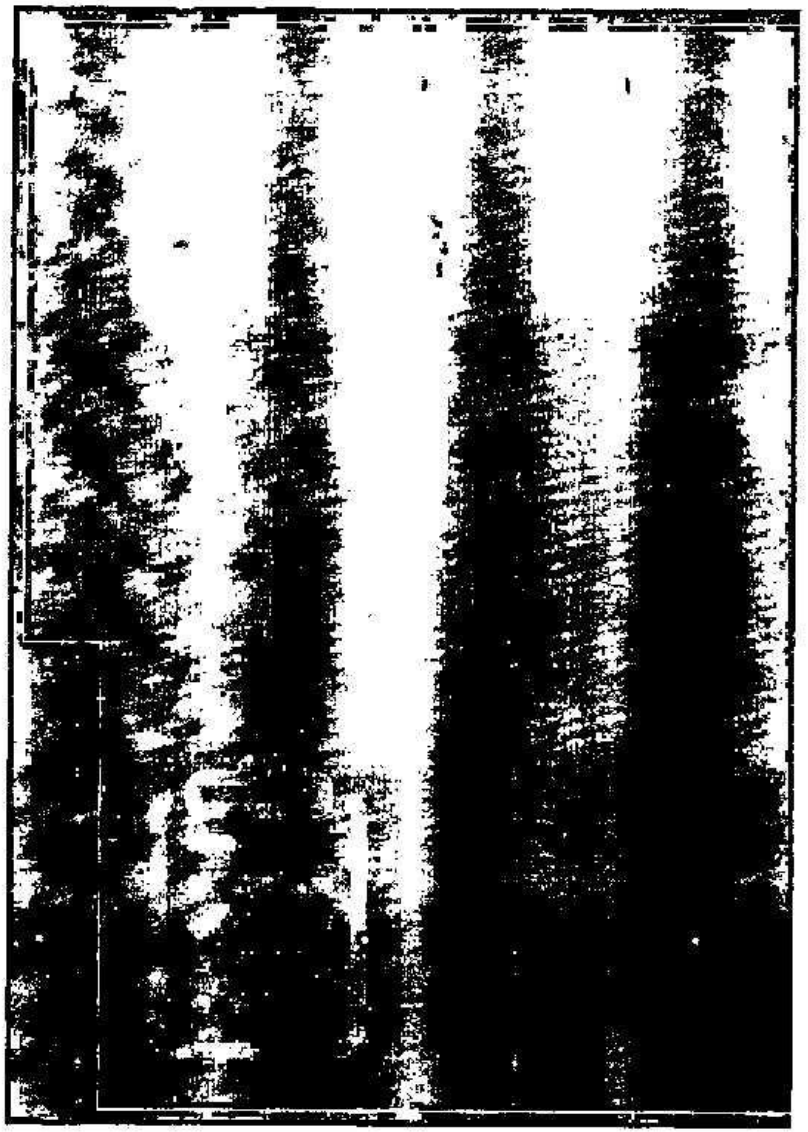
During postmarketing use, AOSD has been reported in patients treated with LEMTRADA. AOSD is a rare inflammatory condition that requires urgent evaluation and treatment.

Patients with AOSD may have a combination of the following signs and symptoms: fever, arthritis, rash and leukocytosis in the absence of infections, malignancies, and other rheumatic conditions. Consider interruption or discontinuation of treatment with LEMTRADA if an alternate etiology for the signs or symptoms cannot be established.

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

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

Autoimmune encephalitis is characterized by subacute onset (with rapid progression over months) of memory impairment, altered mental status or psychiatric symptoms, generally in combination with new onset focal neurological findings and seizures. Patients with suspected autoimmune encephalitis should have neuroimaging (MRI), EEG, lumbar puncture and serologic testing for appropriate biomarkers (e.g. neural autoantibodies) to confirm diagnosis and exclude alternative etiologies.



Summary of recommended patient monitoring

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

	Pre-infusion
Pre-treatment	Corticosteroids must be administered immediately prior to treatment on each of the first 3 days of any treatment course (1,000 mg methylprednisolone or equivalent) • Consider pre-treatment with antihistamines and/or antipyretics • Oral prophylaxis for herpes infection should be administered to all patients starting on the first day of each treatment course and continuing for a minimum of 1 month after treatment with LEMTRADA (200 mg acyclovir twice a day or equivalent)

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	• Perform frequent monitoring of heart rate, BP and overall clinical status at least once every hour • Discontinue infusion if patient shows clinical signs and/or symptoms suggestive development of a serious AE	
Platelet Counts	• Baseline platelet count		• Obtain platelet count immediately after infusion on Day 3 and Day 5 of the first course, and on Day 3 of any subsequent courses
Observation			• Observation for at least 2 hours – patients developing clinical symptoms of a serious AE should be closely monitored until complete resolution of symptoms

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 period[ic] testing for at least 48 months following their final LEMTRADA infusion, even if they are asymptomatic and their MS disease is well controlled.

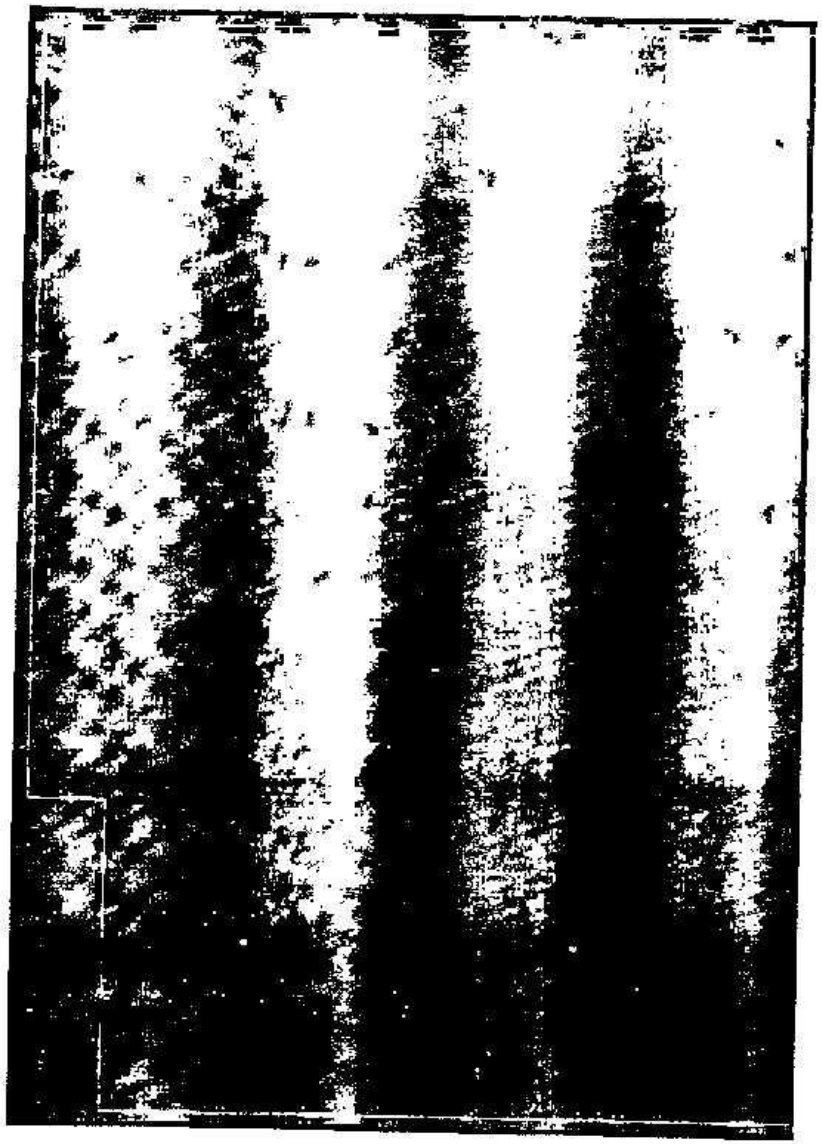
- **Review the LEMTRADA Patient Guide and Package Leaflet with your patient at initial prescription and on a regular basis at follow-up visits. Before treatment, patients must be informed about the risks and benefits of the treatment. Remind the patient to remain vigilant for symptoms related to autoimmune conditions even after the 48-month monitoring period, and to seek medical help if they have any concerns.**
- **Encourage the patient to carry the Patient Alert Card with them at all times. Patients should show the Patient Alert Card to any HCP who is treating them for any reason, and especially in case of a medical emergency.**

Exposure to LEMTRADA in case of Pregnancy

Although there are limited available data evaluating the use of LEMTRADA in pregnant women, there is the potential for LEMTRADA to cross the placental barrier and pose a risk to the foetus. Therefore, LEMTRADA should only be administered during pregnancy if you consider the potential benefit to justify the potential risk to the foetus.

Women of childbearing potential should use effective contraception when receiving and up to 4 months after each course of LEMTRADA treatment.

As it is also possible for LEMTRADA to be transferred through breast milk, breastfeeding is not recommended during or in 4 months following a treatment course. However, the benefits of conferred immunity through breast milk may outweigh the risks of potential exposure to LEMTRADA for the suckling newborn.



Managing patients treated with LEMTRADA

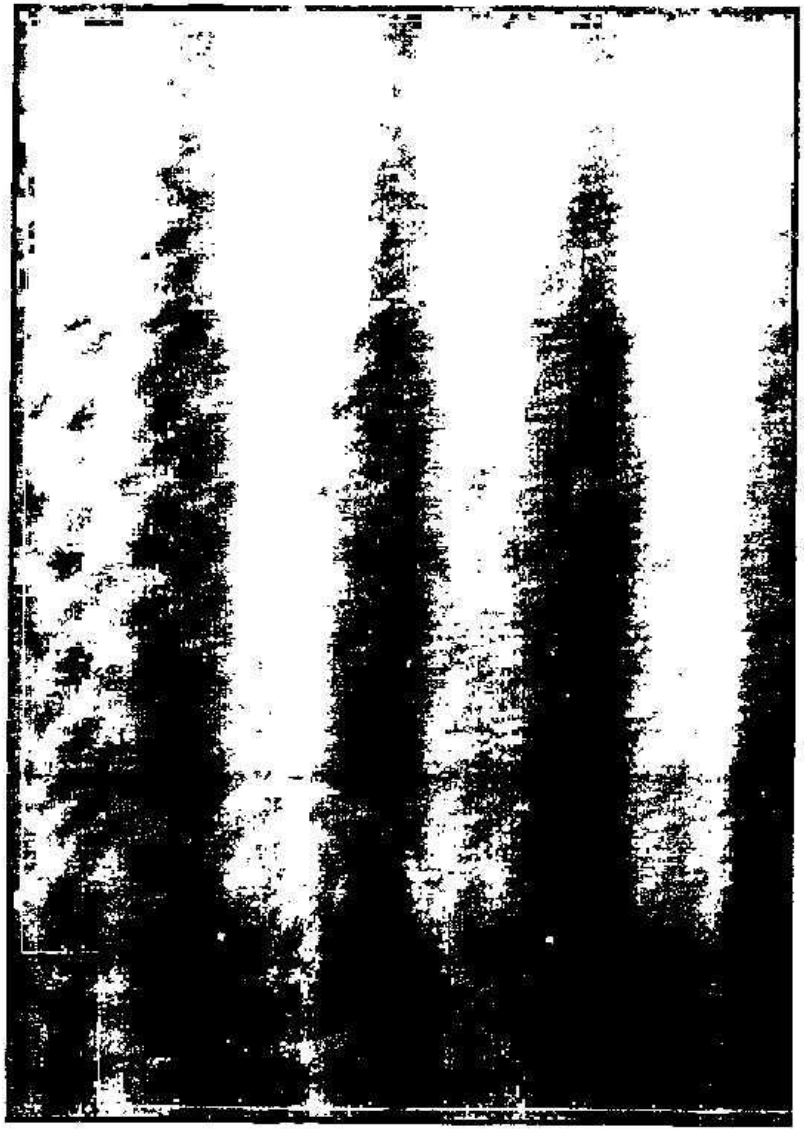
Tools to aid patient compliance

There are many tools available to patients receiving LEMTRADA that can help to support them and ensure they are compliant with laboratory testing.

- **We[illegible]as[illegible]reminder**
  Patient[illegible]ugh online to provide their email address or telephone number to generate automatic reminders by email or SMS relating to monthly laboratory tests. A web address will be provided in the patient guide
- **Paper-[illegible]ed reminder**
  Patients provide their mailing address (via a freepost card) so that they can be sent a reminder relating to monthly laboratory tests by postal mail.
- **Calendar**
  Patients will be given the option of ordering calendars with customised reminder stickers to ensure the relevant date is marked for the periodic laboratory tests. They will have printed instructions to refer to within the calendar

These services will be offered through a third party, who will collect and process patients' personal data in accordance with appropriate data protection legislation. Patients' personal data will be stored securely and will not be shared with others, including the manufacturer of LEMTRADA.

- **Lemcheck (not available in all European countries)**
  An MS One to One application for patients prescribed with LEMTRADA that helps to support patient adherence to their monitoring programme.
- **Oto - MS One to One voice assistant**
  A Google assistant designed to help patients prescribed with LEMTRADA to plan and prepare for appointments with their neurologist or MS nurse



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 complete resolution. Human Immunodeficiency Virus (HIV) infection is a contraindication for the use of LEMTRADA.

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?

A full treatment with LEMTRADA is administered by intravenous infusion over two courses. The first course of treatment consists of a daily infusionover 5 consecutive days. The second course of treatment is administered 12 months later and consists of a daily infusion over 3 consecutive days. Upon evidence of MS disease activity by clinical and/or imaging criteria, additional third and fourth as-needed treatment course(s) can be considered, which consist of a daily infusion over 3 consecutive days administered at least 12 months after the prior treatment course.

If a side effect temporally associated with infusion occurs, provide the appropriate symptomatic treatment, as needed. If the infusion is not well tolerated, the infusion duration may be extended. If severe reactions occur, treatment should be discontinued immediately.

Medically evaluate the patient guided by the adverse event profile of LEMTRADA prior to restarting therapy. Consider permanently discontinuing the LEMTRADA infusion if the patient is deemed to be at a future risk of a serious clinical outcome (please refer to Section 3 for more details).

Reactions attributed to anaphylaxis have been reported rarely in contrast to infusion-associated reactions. However, resources for the management of anaphylaxis or serious reactions should be available.

You should be aware of patient's potential cardiovascular and cerebrovascular risk factors, lung disease, and concomitant medications for timely mitigation of infusion-associated reactions.

Are there any prophylactic treatments that should be taken?

Patients should be premedicated with corticosteroids (1,000 mg methylprednisolone or equivalent) immediately prior to LEMTRADA administration for the first 3 days of any treatment course. Additionally, pre-treatment with antihistamines and/or antipyretics prior to LEMTRADA administration may also be considered.

Oral prophylaxis for herpes infection should be administered to all patients during and for a minimum of 1 month following treatment. In clinical trials, patients were administered 200 mg aciclovir (or equivalent) twice a day.

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 who develop abnormal vital signs including blood pressure or report sudden onset of chest pain, neck pain, facial drooping, difficulty breathing, severe dyspnoea, severe headache, weakness on one side, difficulty with speech, coughing up blood or bruising should be evaluated immediately. Patients should be advised to seek immediate medical attention if any of the symptoms occur.

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

It is important to monitor patients for myocardial ischaemia and infarction, pulmonary alveolar haemorrhage, haemorrhagic stroke, cervicocephalic arterial dissection and thrompocytopenia. Vital sign monitoring including blood pressure and heart rate is advised at baseline and regularly thereafter. It is recommended that a platelet count is taken on Day 3 and Day 5 of the first treatment course and on Day 3 of any subsequent course. See more details in Section 3: Summary of recommended patient monitoring.

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

Symptoms of ITP could include (but are not limited to) easy bruising, petechiae, spontaneous mucocutaneous bleeding (e.g. epistaxis, haemoptysis), heavy or irregular menstrual bleeding. These clinical signs of ITP may be apparent before severe bleeding develops. Low platelet counts, or clinically significant changes from baseline, may also be a sign of ITP. See more details in Figure 2.

How should I manage a patient with suspected ITP?

It is important to monitor all patients for ITP so patients are diagnosed and managed in a timely manner. Therefore, complete blood counts should be obtained prior to initiation of treatment and at monthly intervals for at least 48 months following the last infusion.

If ITP is suspected, a platelet count should be obtained immediately. If onset is confirmed, appropriate medical intervention should be promptly initiated, including immediate referral to a haematologist. Severe or widespread bleeding is life threatening and demands immediate care.

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

Manifestations of nephropathy may include elevation in serum creatinine, haematuria and/or proteinuria. While not observed in clinical trials, alveolar haemorrhage manifested as haemoptysis may occur with anti-GBM disease. Since patients may be asymptomatic, it is important that the periodic laboratory tests (serum creatinine and urinalysis with microscopy) are conducted.

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 lymphohitiocytosis (HLH)?

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

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 laboratory monitoring 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 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.

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

Complete blood count should be monitored on a regular basis and a coagulopathy panel including activated partial thromboplastin time (aPTT) must be obtained in all patients that present with such symptoms of acquired haemophilia A. In case of a prolonged aPTT the patient should be referred to a haematologist.

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

It is important to monitor all patients for TTP so patients are diagnosed and managed in a timely manner. Therefore, complete blood counts should be obtained prior to initiation of treatment and at monthly intervals for at least 48 months following the last infusion.

If TTP is suspected, a platelet count should be obtained immediately. If onset is confirmed, appropriate medical intervention should be promptly initiated, including immediate referral to a haematologist. TTP is life threatening and demands immediate care.

How should I manage a patient with suspected AOSD?

AOSD is a rare inflammatory condition that requires urgent evaluation and treatment. Consider interruption or discontinuation of treatment with LEMTRADA if an alternate etiology for the signs or symptoms of AOSD cannot be established.

How should I manage a patient with suspected AIE?

Patients with suspected autoimmune encephalitis should have neuroimaging (MRI), EEG, lumbar puncture and serologic testing for appropriate biomarkers (e.g. neural autoantibodies) to confirm diagnosis and exclude alternative etiologies.

Pregnancy, contraception and breastfeeding counselling

Should female patients use contraception?

The alpha half-life of alemtuzumab approximated 4–5 days and was comparable between courses leading to low or undetectable serum concentrations within approximately 30 days following each treatment course. Therefore, women of childbearing potential should use effective contraceptive measures during treatment and for 4 months following each course of LEMTRADA treatment.

Is it possible to administer LEMTRADA during pregnancy?

LEMTRADA should be administered during pregnancy only if the potential benefit justifies the potential risk to the foetus. Human immunoglobulin G (IgG) is known to cross the placental barrier; LEMTRADA may cross the placental barrier as well and thus potentially pose a risk to the foetus. It is not known whether LEMTRADA can cause foetal harm when administered to pregnant women or whether it can affect reproductive capacity.

Thyroid disease poses special risks in women who are pregnant. Without treatment of hypothyroidism during pregnancy, there is an increased risk for miscarriage and foetal effects such as mental retardation and dwarfism. In mothers with Graves' disease (also known as Basedow's disease), maternal TSH receptor antibodies can be transferred to a developing foetus and can cause transient neonatal Graves' disease.

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

Women should use effective contraceptive measures and wait at least 4 months following each course of LEMTRADA treatment before trying to become pregnant. It needs to be taken into account that full treatment of LEMTRADA consists of 2 courses, 12 months apart. Women of childbearing potential need to be alerted to this and discouraged to stop contraception between treatment courses.

Will LEMTRADA affect future female or male fertility?

There are no adequate clinical safety data on the effect of LEMTRADA on fertility. In a sub-study in 13 male alemtuzumab-treated patients (treated with either 12 mg or 24 mg), there was no evidence of aspermia, azoospermia, consistently depressed sperm count, motility disorders or an increase in sperm morphological abnormalities. CD52 is known to be present in human and rodent reproductive tissues. Animal data have shown effects on fertility in humanised mice (see section 5.3 of the Summary of Product Characteristics (SmPC)), however a potential impact on human fertility during the period of exposure is unknown based on the available data.

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

It is unknown whether LEMTRADA is excreted in human milk. As risk to the breastfed child cannot be excluded, breastfeeding should be discontinued during each course of treatment and for 4 months following the last infusion of each course. However, benefits of conferred immunity through breast milk may outweigh the risks of potential exposure to LEMTRADA for the baby.

Vaccinations

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

Since the safety of immunisation with live vaccines following LEMTRADA therapy has not been studied, live vaccines should not be administered to patients who have recently been treated with LEMTRADA.

It is recommended that patients are up to date with their vaccinations (according to national guidelines) at least 6 weeks prior to commencing treatment with LEMTRADA. Consider varicella zoster virus (VZV) vaccination of antibody negative patients, prior to treatment with LEMTRADA.

Notes

LEMTRADA
alemtuzumab

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sanofi

What you should know about LEMTRADA® (alemtuzumab)

Call your neurologist right away to report these symptoms no matter if they are new, worsening or returning symptoms. Seek medical attention if you cannot reach your own doctor, and make sure you show them this card.

IMPORTANT SIDE EFFECTS TO WATCH FOR:

Serious infections

- Fever, chills, fatigue, shortness of breath, cough, wheezing, chest pain or other pain, coughing up blood

Rare brain infection called PML (progressive multifocal leukoencephalopathy)

- Progressive weakness or numbness of limbs, disturbance of vision, speech, mind, thinking or changes in walking, memory and orientation leading to confusion and personality changes

Serious side effects occurring shortly after LEMTRADA infusion (usually within 1–3 days of infusion)

Heart attack

- Chest pain or discomfort, shortness of breath, pain or discomfort in arms, jaw, neck, back or stomach
- Feeling dizzy or lightheaded, nausea, sweating

Stroke and injury to blood vessels supplying the brain

- Sudden onset of drooping of parts of the face, weakness on one side, difficulty with speech
- Sudden severe headache or neck pain

Bleeding in the lungs

- Dizziness, shortness of breath, chest pain or discomfort, coughing up blood

Thrombocytosis

- Easy bruising or bleeding

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

Thyroid disorders

Hyperthyroidism

- Excessive sweating, unexplained weight loss, eye swelling, nervousness, fast heartbeat

Hypothyroidism

- Feeling cold, unexplained weight gain, worsening tiredness, newly occurring constipation

Immune thrombocytopenic purpura (ITP)

- Bleeding from your gums or nose that is new or takes longer than usual to stop, coughing up blood
- Small red-to-purple spots on your skin that are not from injury, pinpoint areas or easy bruising, or red or brown urine, which may be signs that your blood platelets are not working properly or there are fewer than normal
- Painful or swollen joints

Kidney problems including anti-Glomerular Basement Membrane disease (anti-GBM disease)

- Blood in the urine which may be red or tea-colored, coughing up blood, shortness of breath, coughing up blood

Autoimmune hepatitis

- Unexplained nausea, vomiting, fatigue, abdominal pain, loss of appetite, abdominal swelling
- Yellow skin and eyes and/or dark urine, bleeding or bruising more easily than normal

Hemophagocytic lymphohistiocytosis (HLH)

- Unexplained high fever, severe headache, stiff neck, lymph nodes enlargement, severe skin rash

Acquired hemophilia A

- Bleeding from a cut that takes longer than usual to stop
- Spontaneous bruising, nose bleeds, painful swollen joints

Thrombotic thrombocytopenic purpura (TTP)

- Bruising under the skin or in the mouth that may appear as red or purple spots, with or without unexplained extreme tiredness, fever, confusion, skin changes, yellowing of the skin or eyes (jaundice), low amount of urine, dark colored urine

Adult onset still disease (AOSD)

- Fever ≥39°C or 102.2°F lasting more than a week, pain, stiffness with or without swelling in multiple joints and/or a sunburn

Autoimmune encephalitis (AIE)

- Behavioral and/or psychiatric changes, movement disorders, short term memory loss or seizures, as well as other symptoms which may resemble an MS relapse

It's very important that you continue to attend your monthly tests for at least 48 months [4 years] after your last infusion [even if you are feeling well].

[illegible]

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

You must also continue to watch for signs and symptoms

Do this for at least 48 months after your last course of treatment with LEMTRADA

[illegible]

PATIENT ALERT CARD

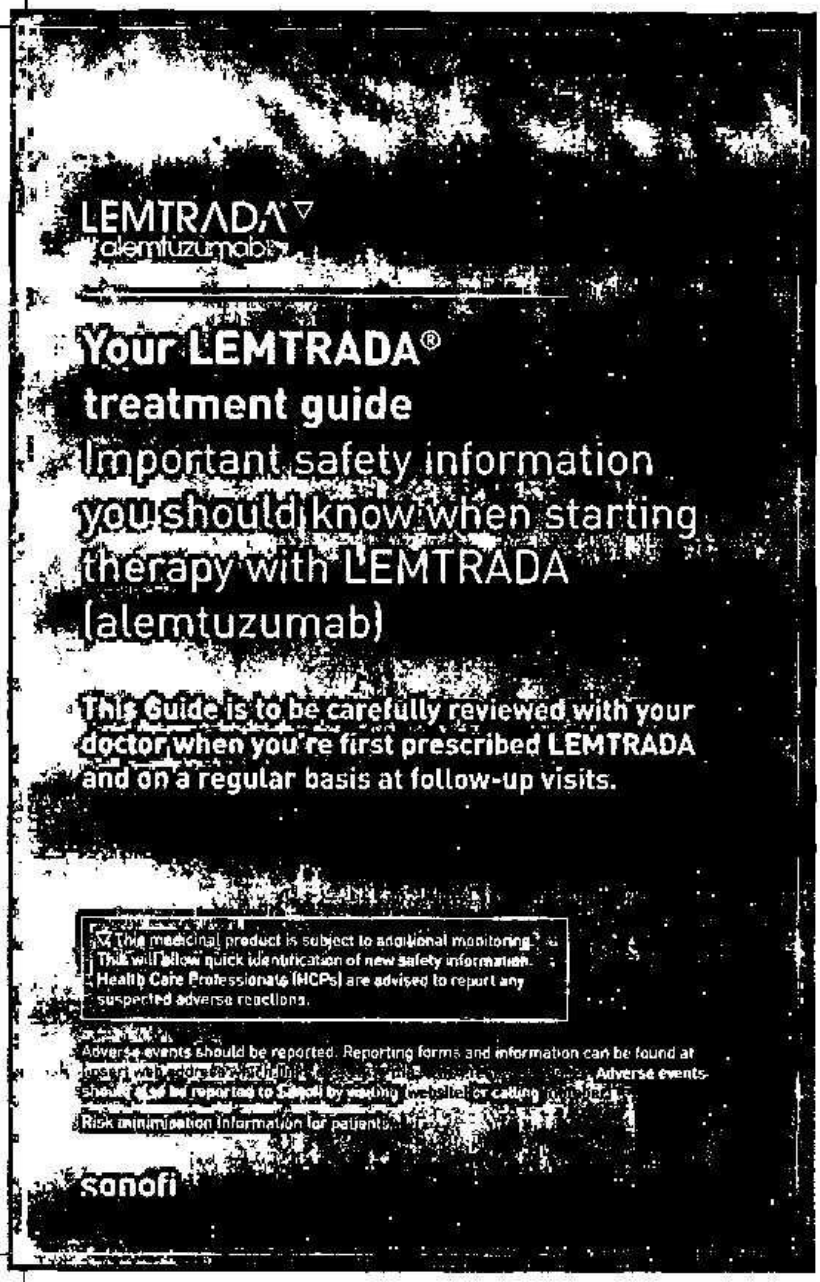
Please carry this card with you at all times and show it to all emergency and healthcare providers involved in your care to inform them about your treatment with LEMTRADA.

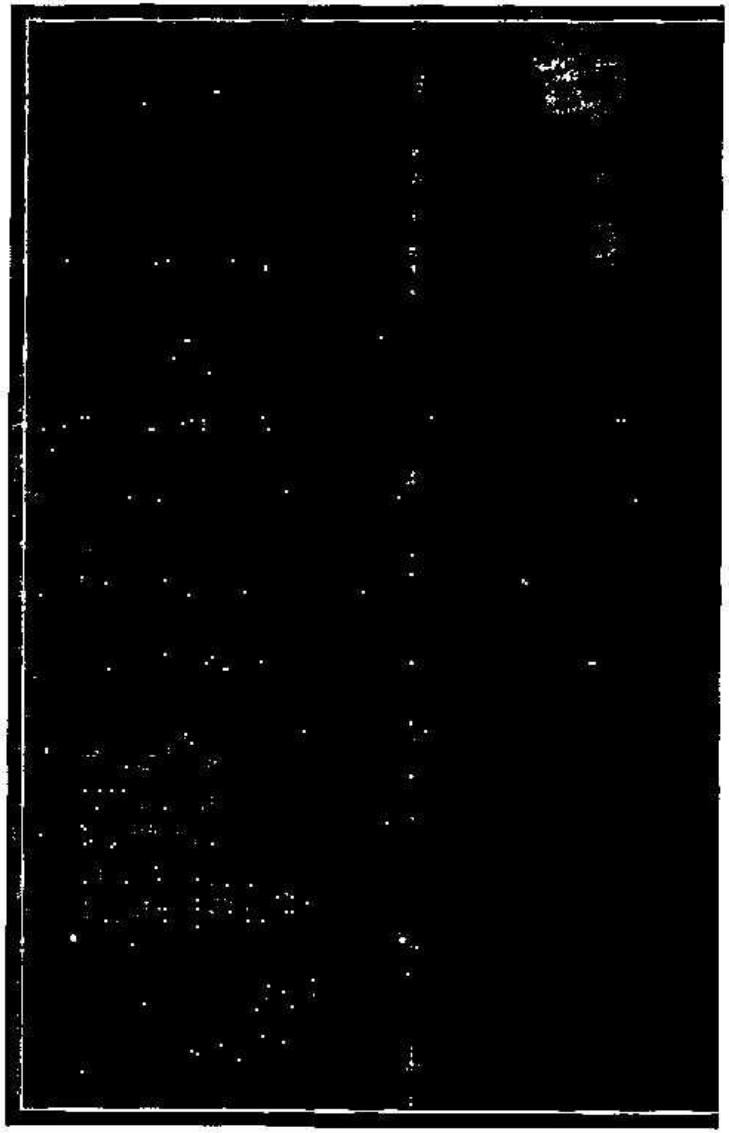
[illegible]

LEMTRADA treatment may increase the risk of:

- [illegible]
- [illegible]
- [illegible]

Doctors:
See LEMTRADA Summary of Product Characteristics (SmPC) for more information.


LEMTRADA▽
alemtuzumab
Your LEMTRADA®
treatment guide
Important safety information you should know when starting therapy with LEMTRADA (alemtuzumab)
This Guide is to be carefully reviewed with your doctor when you're first prescribed LEMTRADA and on a regular basis at follow-up visits.
▽ 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.
Adverse events should be reported. Reporting forms and information can be found at
Adverse events
Risk minimisation information for patients
sanofi



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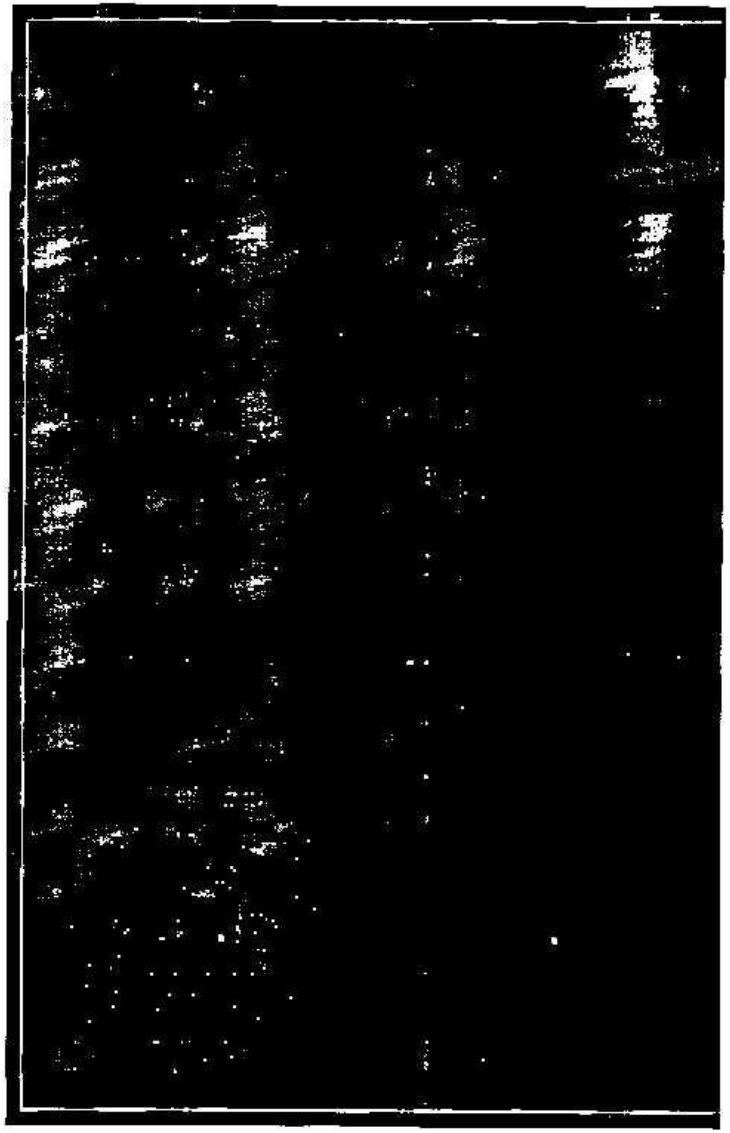


Executive summary

A guide to your LEMTRADA (alemtuzumab) infusions for treating relapsing remitting multiple sclerosis (MS).

This is an abbreviated guide – please refer to the full guide for more information. This guide is not intended to replace the Package Leaflet or discussions you have with your doctor or other healthcare professionals who are treating you with LEMTRADA.

LEMTRADA is a prescription medicine used to treat adults with relapsing remitting multiple sclerosis (MS). LEMTRADA can only be used in patients with highly active disease, despite treatment with at least one disease modifying therapy, or in patients with rapidly evolving severe MS.

Receiving LEMTRADA can put you at risk of experiencing serious side effects that may occur within 1-3 days of infusion, or delayed autoimmune side effects which can occur months to years after infusion.

Early identification of these side effects is vital, because a delay in diagnosis and treatment can increase the risk of complications. This is why it's so important to remain vigilant and immediately report any signs or symptoms of these conditions to your doctor.

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

See the following tables for a summary of signs and symptoms to look out for.

Serious infections

Side effect	Signs and symptoms to watch for
Serious infections	Fever, chills, fatigue, shortness of breath, cough, wheezing, chest pain or tightness, coughing up blood
Brain infection (Progressive Multifocal Leukoencephalopathy, PML))	Progressive weakness or clumsiness of limbs, disturbance of vision, speech difficulties or changes in thinking, memory, and orientation leading to confusion and personality changes

Serious side effects occurring shortly after LEMTRADA infusion

Side effect	Signs and symptoms to watch for
Heart attack	Shortness of breath, chest pain or discomfort, coughing blood
Bleeding in the lung	Chest pain or discomfort, shortness of breath, pain or discomfort in arms, jaw, neck, back or stomach
Stroke	Feeling dizzy or lightheaded, nausea, sweating
Tears in blood vessels supplying the brain	Sudden onset of drooping of parts of the face, weakness on one side, difficulty with speech
	Sudden severe headache, neck pain
Thrombocytopenia	Easy bruising and/or bleeding

Delayed autoimmune side effects

Side effect	Signs and symptoms to watch for
Thyroid disorders	Hyperthyroidism: Excessive sweating, unexplained weight l... eye swelling, nervousness, fast heartbeat Hypothyroidism: Feeling cold, unexplained weight gain, worsening tiredness, newly occurring constipation
Immune thrombocytopenic purpura (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, purplish or swollen joints
Kidney problems, including nephropathies such as anti-Glomerular Basement Membrane (anti-GBM) disease	Blood in urine, swelling in legs and/or feet, coughing up blood
Autoimmune hepatitis	Unexplained nausea, vomiting, abdominal pain and/or swelling, fatigue, loss of appetite, yellowing of skin or eyes and/or dark coloured urine, bleeding or bruising more easily than normal
Haemophagocytic lymphohistiocytosis (HLH)	Unexplained high fever, severe headache, stiff neck, lymph node enlargement, yellow skin, skin rash
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
Thrombotic thrombocytopenic purpura (TTP)	Bruising under the skin or inside the mouth, yellowing of skin and eyes and/or dark coloured urine, low amount of urine, red pinpoint dots with or without unexplained extreme tiredness, very pale skin, fever, fast heartbeat or short of breath, headache, speech changes, confusion, coma, stroke, seizure, stomach area pain, nausea, vomiting, or diarrhoea, vision changes, persistent low sugar symptoms
Adult onset still disease (AOSD)	Fever >39°C or 102.2°F lasting more than 1 week, pain, stiffness with or without swelling in multiple joints and/or a skin rash
Autoimmune encephalitis (AE)	Behavioural and/or psychiatric changes, movement disorders, short term memory loss or seizures, other symptoms which may resemble an MS relapse

Monitoring requirements

Monitoring test	When?	For how long?
Observation	Immediately after each infusion	For at least 2 hours. If you start to display signs and/or symptoms of serious side effects, you will be monitored until they are resolved
Electrocardiogram (ECG) and vital signs, including heart rate and blood pressure (BP)	Baseline tests right before infusion Frequent monitoring of heart rate, BP and overall clinical status at least once every hour during your infusion	Once before each infusion and at least once every hour for the total duration of infusions
Blood and urine tests	Before treatment starts and once every month after finishing each treatment course	For at least 48 months after your last LEMTRADA infusion
Platelet count	Immediately after infusion on Day 3 and Day 5 of the first course, and on Day 3 of any subsequent courses	

To minimise the risk of side effects associated with LEMTRADA, it is advised that you make changes to your diet and complete the recommended vaccination programme in the weeks prior to starting your LEMTRADA treatment. Your doctor will also give you corticosteroids right before the first 3 infusions of each course to reduce your risk of infusion-associated reactions.

You will need to be monitored for side effects for at least 4 years (48 months) after your last LEMTRADA infusion. See the table below for a summary of monitoring tests that are required when you're prescribed with LEMTRADA.

Welcome

Your doctor has given you this Patient Guide and a Patient Alert Card to inform you about your current **treatment with LEMTRADA.**

This guide **has been created to support you in identifying the symptoms of the side effects that have been reported with the use of** LEMTRADA, **as well as outlining the importance of being compliant** with testing, vigilant for symptoms and **to seek immediate medical attention should they occur.**

Side effects that may occur shortly after LEMTRADA infusion (within 1–3 days of infusion), or later, and include **infections and other serious reactions. Delayed side effects include autoimmune disorders that can develop with a delay of months to years after treatment with** LEMTRADA; these are conditions in which your immune system mistakenly attacks your body.

There s also a section in this guide that will help you to understand some of the medical terms used in this document, and a section to **keep a note of the contact details of all the doctors you may be seeing for your healthcare. This includes the doctor treating your multiple sclerosis (MS) as well as any other doctor you see on a regular basis.**

This Patient Guide is to be carefully reviewed with your doctor **when you're first prescribed LEMTRADA and on a regular basis at follow-up visits.**

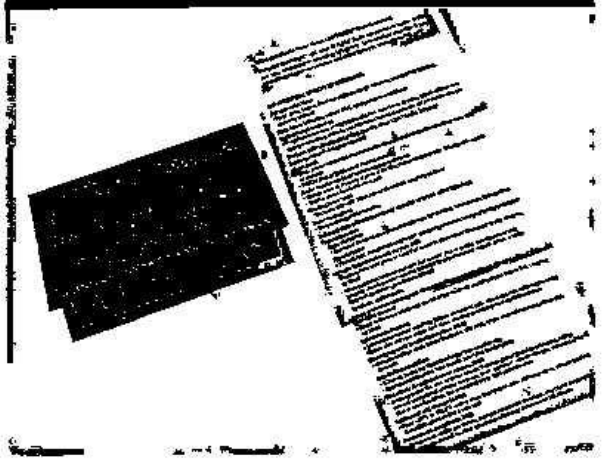
This guide is not intended to replace any discussions you have with your doctor or the Package Leaflet for LEMTRADA which you should still read in full. Make sure you tell your doctor if you notice any of the signs or symptoms of side effects described in this guide.

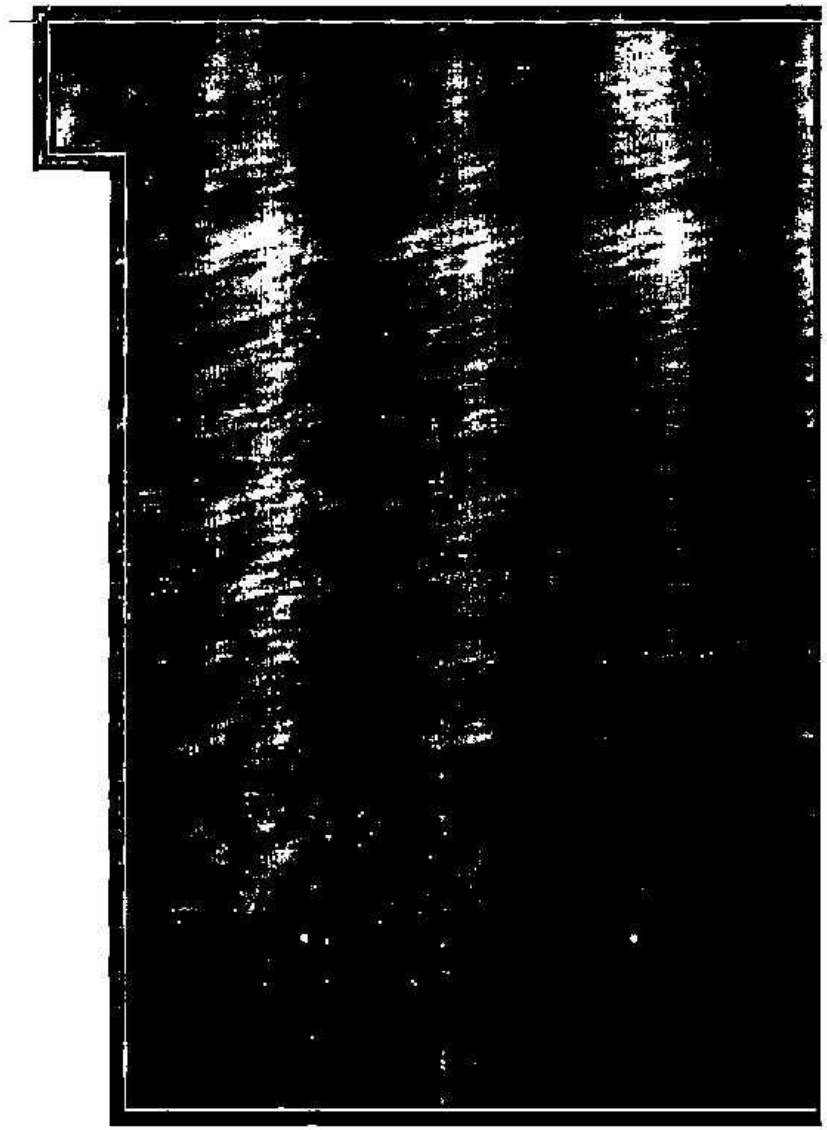
[Note: Delete/add as appropriate according to national practices/circumstance.]

In addition to this guide, you can log in to www.sanetpone.xx to access helpful information related to the use of LEMTRADA and tools which can help you to stay on track with your monitoring programme. Use the access code given in your LEMTRADA handbook to access all available educational materials, including this guide, electronically.

Patient Alert Card

The purpose of your Patient Alert Card is to inform healthcare professionals about your LEMTRADA treatment. **You must carry your Patient Alert Card with you at all times and show it to any member of the medical team involved in your care (including for non-MS conditions) and in the event of a medical emergency.**



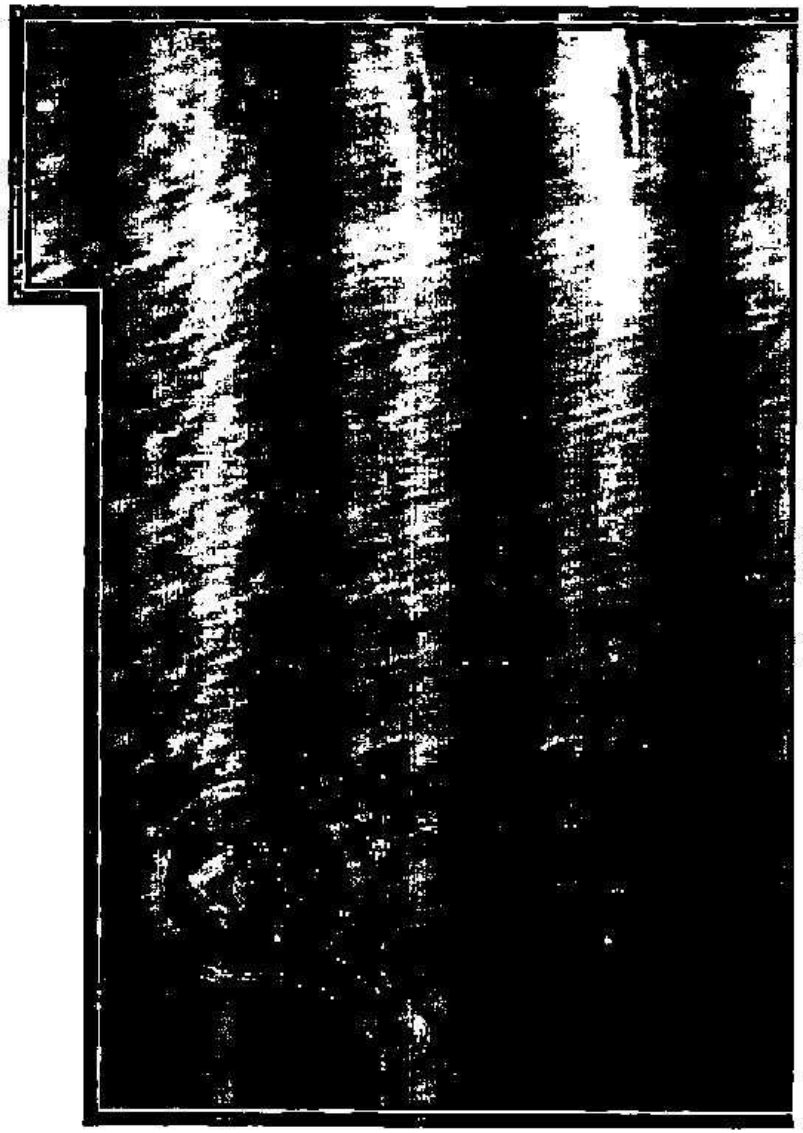


Introduction to LEMTRADA

What is LEMTRADA and how does it work?

LEMTRADA is a prescription medicine used to treat adults with relapsing remitting multiple sclerosis (MS). LEMTRADA can only be used if your MS is highly active despite being treated with at least one other medicine for MS or if your MS is rapidly evolving. In clinical studies, patients treated with LEMTRADA had fewer relapses and were less likely to experience disability progression and more likely to experience disability improvement compared to patients treated with a beta-interferon injected multiple times per week.

LEMTRADA adjusts your immune system to limit its attacks on your nervous system. After treatment with LEMTRADA, 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.



Overview of LEMTRADA treatment

How is LEMTRADA given?

LEMTRADA is given to you by infusion using a needle through which it will be delivered into your blood stream. LEMTRADA is given in at least 2 courses of treatment. You will receive the first course for a few hours per day for 5 days in a row. Then, one year later, you will receive the next course for 3 days in a row. Studies have shown that the 2 courses work for most patients for at least 6 years. However, you may need an additional treatment in the years after your initial 2 courses.

You will need to be regularly monitored for side effects for at least 48 months after your last infusion of LEMTRADA (see SAFETY) even if you have only been treated with LEMTRADA.

Do I need to do anything before I can be treated with LEMTRADA?

To make sure LEMTRADA is the right therapy for you, your doctor needs some information. Therefore, you need to inform your doctor about:

- All medicines that you are taking
- If you're suffering from any infection
- If you've been diagnosed with cancer
- If you've been diagnosed with abnormalities of the cervix (the neck of the womb)
- If you are pregnant or plan to become pregnant very soon
- If you're suffering from hypertension or other concomitant disorders
- If you've suffered in the past from heart attack or chest pain, tears in blood vessels, cerebral haemorrhage, bleeding disorder, or other autoimmune conditions (besides MS)

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 and infections after your LEMTRADA treatment. These include:

- Vaccination check
  - If you've not yet done so, you may be advised to complete your local vaccination programme at least 6 weeks before starting treatment
  - You may also be advised to receive additional vaccinations before you start treatment
- Tuberculosis screening
  - If you live in an area where tuberculosis is often seen, your doctor will arrange a screening
- Dietary recommendation
  - To reduce your risk of infections after treatment, your doctor will recommend that you avoid uncooked or undercooked meats, soft cheeses and unpasteurised dairy products two weeks prior to, during and for at least 1 month after your LEMTRADA infusion
- Pre-treatment
  - To reduce your risk of infusion-associated reactions, your doctor will give you corticosteroid treatment before the first 3 infusions of each of your LEMTRADA treatment courses
  - Other treatments to limit these reactions can also be given before infusions
- Vital signs check
  - Your doctor will check your vital signs, including blood pressure and heart rate, before you start your treatment
- Blood and urine tests
  - Will be performed before you start your LEMTRADA treatment

Add reference to local information with regard to guidelines regarding listeriosis prevention diet, if applicable (such as CDC guidelines) and CMV serostatus have to be considered (as per local guidelines)

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

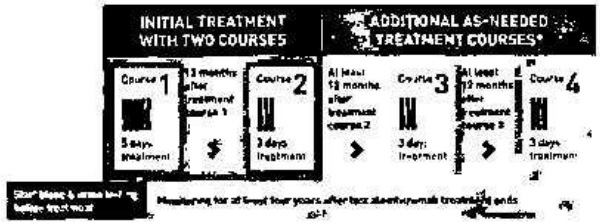
Treatment with LEMTRADA may increase the risk of autoimmune conditions (conditions in which your immune system mistakenly attacks your body). These are delayed side effects which can occur many years after your treatment (described in Section 3 of this guide). You will therefore need to commit to monthly monitoring, undertaking blood and urine tests for at least 48 months after your last LEMTRADA infusion. Your doctor will check the results of these tests to see if you have developed any side effect(s).

It's very important that you continue to have these checks for at least 48 months after your last course of treatment with LEMTRADA, even if you are feeling well (this means that you have no symptoms of side effects) and your MS symptoms are under control. Side effects can even occur years after your last course of treatment with LEMTRADA, when your monthly checks are no longer required. In some cases, side effects can be life-threatening, so it's very important that you continue to be checked and keep an eye out for symptoms. By doing so, any problems will most likely be detected early and treatment can start right away.

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.

To help you better understand the timescale of possible treatment side effects and the length of required follow-up, see Figure 1 opposite.

Figure 1 – Duration of the effects of treatment and the length of required follow-up



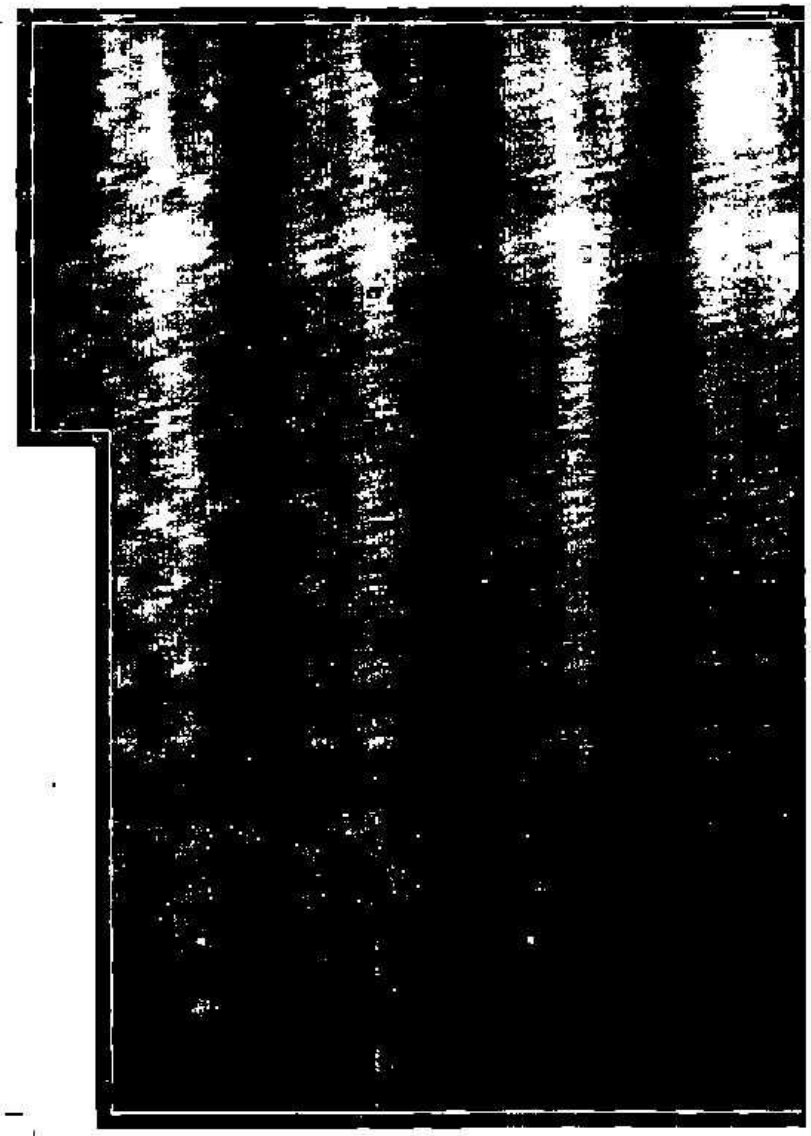
*Note: A study following patients for 6 years after the first infusion (course 1) has shown that a majority of patients do not need further treatment after the 2 initial treatment courses.

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

Table 1 – Summary of monitoring tests

Monitoring test	When?	For how long?
Observation	Immediately after each infusion	For at least 2 hours, if you start to display signs and/or symptoms of serious side effects, you will be monitored until they are resolved
Electrocardiogram (ECG) and vital signs, including heart rate and blood pressure (BP)	Baseline tests right before infusion Frequent monitoring of heart rate, BP and overall clinical status at least once every hour during your infusion	Once before each infusion and at least once every hour for the total duration of infusions
Blood and urine tests	Before treatment starts and once every month after finishing each treatment course	Monthly, for at least 48 months after your last LEMTRADA infusion
Platelet count	Immediately after infusion on Day 3 and Day 5 of the first course, and on Day 3 of any subsequent courses	

There are tools available to help you plan and remember your monitoring schedule. Refer to Section 6 of this guide, 'Planning your monitoring schedule'.



Side effects

As mentioned earlier in this guide, treatment with LEMTRADA can put you at risk of contracting serious infections, experiencing side effects that mainly occur during or shortly after the infusion (within 1–3 days), or later, and developing delayed side effects that can occur months to years after treatment with alemtuzumab.

Potentially serious infusion-associated side effects that usually occur during or shortly after the infusion include

- Heart attack
- Stroke
- Tears in blood vessels supplying the brain
- Bleeding in the lung
- Thrombocytopenia

Delayed side effects that may occur with a delay of months to years after infusion:

- Thyroid disorders
- Immune thrombocytopenic purpura (ITP)
- Kidney problems, including nephropathies such as anti-Glomerular Basement Membrane disease (anti-GBM disease)
- Autoimmune hepatitis
- Haemophagocytosis lymphohistiocytosis (HLH)
- Acquired haemophilia A
- Thrombotic thrombocytopenic purpura (TTP)
- Adult onset still disease (AOSD)
- Autoimmune encephalitis (AIE)

Early identification of these conditions is vital, as delays in diagnosis and treatment increases the risk of complications. This is why it is so important to recognise and immediately report any signs or symptoms of these conditions to your doctor or go to the hospital.

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

Serious infections

Receiving treatment with LEMTRADA can put you at risk of getting a serious infection. If you develop symptoms of a serious infection such as persistent fever, chills, fatigue or not feeling well, you may have to go to hospital for treatment.

You should also report symptoms like shortness of breath, cough, wheezing, chest pain or tightness and coughing up blood to your doctor, as these may be caused by pneumonitis

When attending hospital with any symptoms of infection, it's important that you tell doctors that you have received treatment with LEMTRADA.

Make sure you tell your doctor if you are suffering from a serious infection before you start your LEMTRADA treatment. Your doctor should delay the treatment until the infection has been resolved

Rare brain infection (PML)

There have been cases of a rare brain infection called PML (progressive multifocal leukoencephalopathy) in patients who have been given LEMTRADA. 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 like progressive weakness or clumsiness of limbs, disturbance of vision, speech difficulties or changes in thinking, memory, and orientation leading to confusion and personality changes.

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

Serious side effects occurring shortly after LEMTRADA infusion

When prescribed LEMTRADA, 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 LEMTRADA infusion, but

some may occur weeks later. Tell your doctor right away if you develop any of the following symptoms: trouble breathing, chest pain, facial drooping, sudden severe headache, weakness on one side of the body, difficulty with speech, neck pain or coughing up blood.

Delayed autoimmune side effects

Treatment with LEMTRADA may increase the risk of autoimmune conditions. These are conditions in which your immune system mistakenly attacks your body and these can occur many years after treatment. Therefore, regular blood and urine tests are needed until 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.

1. Thyroid disorders

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.

LEMTRADA 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 LEMTRADA, 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.

What are the signs and symptoms of an overactive thyroid?

Symptoms may include:

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

What are the signs and symptoms of an underactive thyroid?

Symptoms may include:

- 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 opposite.

Depending on the type of thyroid disorder you are experiencing, your doctor will decide 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 LEMTRADA, 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 taken in case of pregnancy.

2. Immune thrombocytopenic purpura (ITP)

ITP is a condition which results in a low number of platelets in the blood. Serious ITP occurs in approx. 1% of patients taking LEMTRADA. 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 LEMTRADA treatment, and on a monthly basis which continues for at least 48 months following your last treatment course.

It's important to note that ITP can start quickly and may occur in between the blood tests. It's therefore essential that you remain vigilant for signs and symptoms.

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 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

Take a look at Figure 2 which shows examples of bruises and rashes caused by ITP.

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.

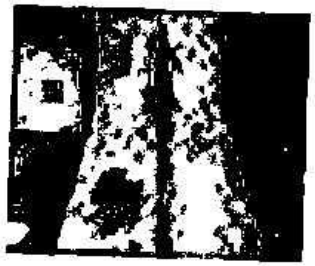
If you notice any of the signs or symptoms described above, contact your doctor right away to report the symptoms. If you cannot reach your doctor, seek immediate medical attention and show them your LEMTRADA Patient Alert Card.

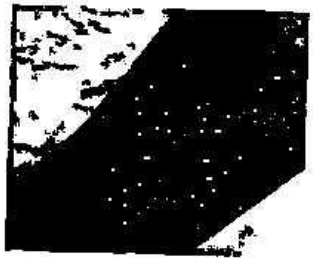
If detected early, ITP is usually treatable. If you develop ITP, you and your doctor will decide which treatment is best for you.

Figure 2 - Examples of bruises and rashes caused by ITP

Example of arms with easy or excessive bruising.

Where on the body? Bruises may occur anywhere on your body, not just on your arms.





Example of a leg with scattered spots under the skin that are red, pink or purple. They might look like pin pricks (petechial) or they can be a little bigger (purpura).

Where on the body? These spots can occur anywhere on your body, not just on your legs.

Example of spots due to bleeding under the tongue.

Where on the body? This may 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 petechiae. The patient may have less severe type of bruise or petechiae than these pictures and still have ITP.

3. Kidney problems, including nephropathies such as anti-GBM disease

LEMTRADA can sometimes cause kidney problems, including 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. 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 LEMTRADA, 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.

What are the signs and symptoms of kidney problems, 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.

4. Autoimmune hepatitis

Some people have developed liver inflammation, also known as autoimmune hepatitis, after receiving LEMTRADA. If you experience unexplained nausea, vomiting, abdominal pain and/or swelling, fatigue, loss of appetite, yellow skin and eyes and/or dark urine, or bleeding or bruising more easily than normal, report this to your doctor.

5. Haemophagocytic lymphohistiocytosis (HLH)

HLH is a life-threatening condition that occurs when specific immune cells become overactive, causing too much inflammation. Ordinarily, these cells should destroy infected, 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. If you experience unexplained high fever, severe headache, stiff neck, lymph node enlargement, yellow skin, or skin rash you must call your doctor right away to report the symptoms.

6. Acquired haemophilia A

When treated with LEMTRADA it's possible that you may develop a disorder called acquired haemophilia A. 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. This condition must be diagnosed and treated immediately. If you experience spontaneous bruising, nose bleeds, painful or swollen joints, other types of bleeding, or bleeding from a cut that may take longer than usual to stop, you must call your doctor right away to report the symptoms.

7. Thrombotic Thrombocytopenic Purpura (TTP)

TTP is a disease where blood clots form inside blood vessels and can occur with LEMTRADA. 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: purplish spots on the skin or in the mouth, yellow skin and eyes and/or dark urine, tiredness or weakness, very pale skin, fever, fast heartbeat or short of breath, headache, speech changes, confusion, coma, stroke, seizure, stomach area pain, nausea, vomiting or diarrhoea, vision changes, or persistent low sugar symptoms.

8. Adult onset still disease (AOSD)

AOSD is a rare condition that has the potential to cause multi-organ inflammation with several symptoms such as fever >39°C or 102.2°F lasting more than 1 week, pain, stiffness with or without swelling in multiple joints and/or a skin rash. If you experience a combination of these symptoms, contact your healthcare provider immediately.

9. Autoimmune encephalitis (AIE)

This autoimmune condition (an immune mediated brain disorder) can occur after receiving LEMTRADA. This condition may include symptoms such as behavioural and/or psychiatric changes, movement disorders, short term memory loss or seizures as well as other symptoms which may resemble an MS relapse. If you experience one or more of these symptoms, contact your healthcare providers.

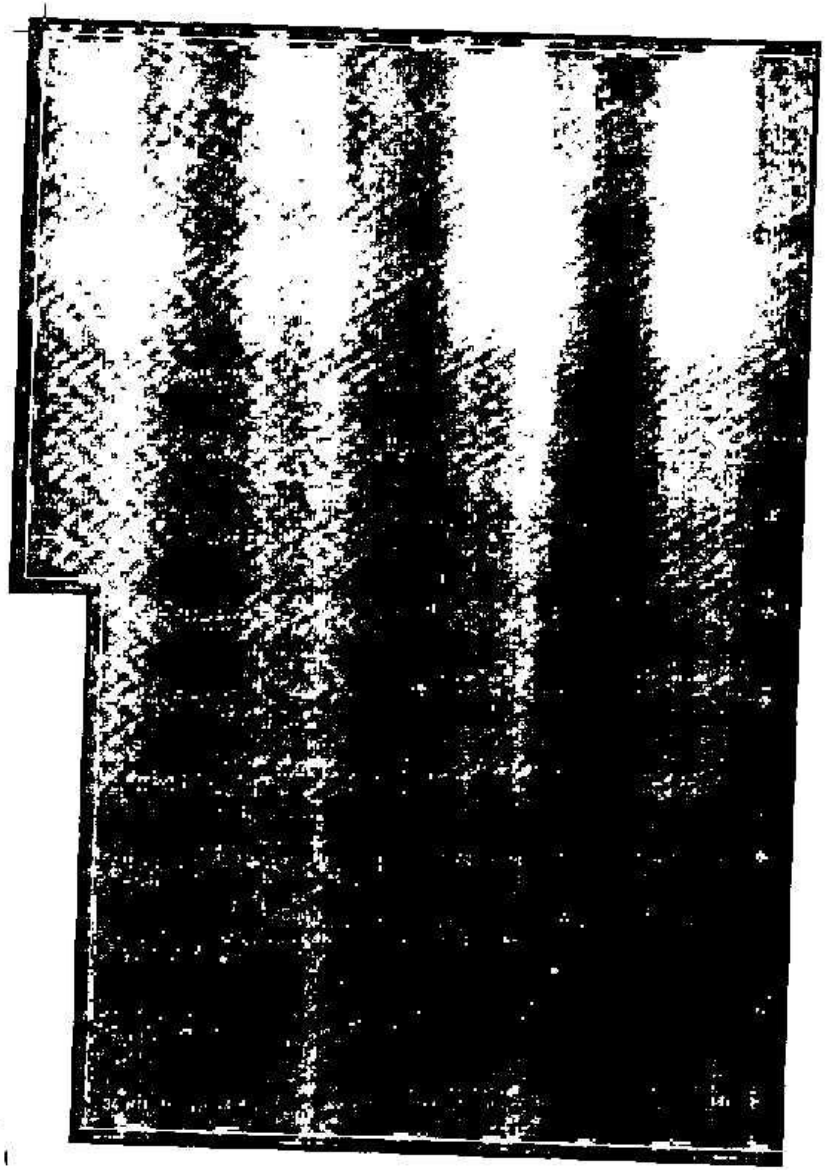
IMPORTANT!

Since all of these delayed side effects can occur long after you received a course of treatment with LEMTRADA, it's very important that you continue to have your monthly tests (even if you are feeling well).

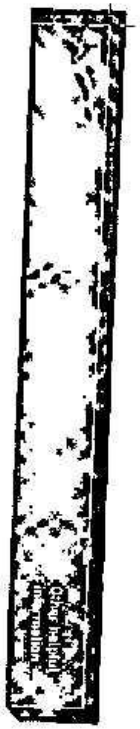
You must also continue to watch out for signs and symptoms for at least 48 months after your last course of treatment with LEMTRADA.

- Early detection and diagnosis may give you the best opportunity for recovery
- Carry your Patient Alert Card with you and show it to any healthcare providers who are providing you treatment (including for non-MS conditions) and in the event of a medical emergency

[Add local information with regard to MS One to One and Lemcheck]



Other helpful information



Vaccinations

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 vaccination to start your LEMTRADA treatment. Tell your doctor if you have had a vaccination within the last 6 weeks.

Fertility

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

Pregnancy and contraception

It is not known if LEMTRADA could harm an unborn child. You should use effective contraception during treatment with LEMTRADA and for 4 months after each course of treatment to ensure there is no LEMTRADA 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 LEMTRADA.

Tell your doctor right away if you become pregnant during your treatment course or within 4 months of receiving a LEMTRADA infusion.

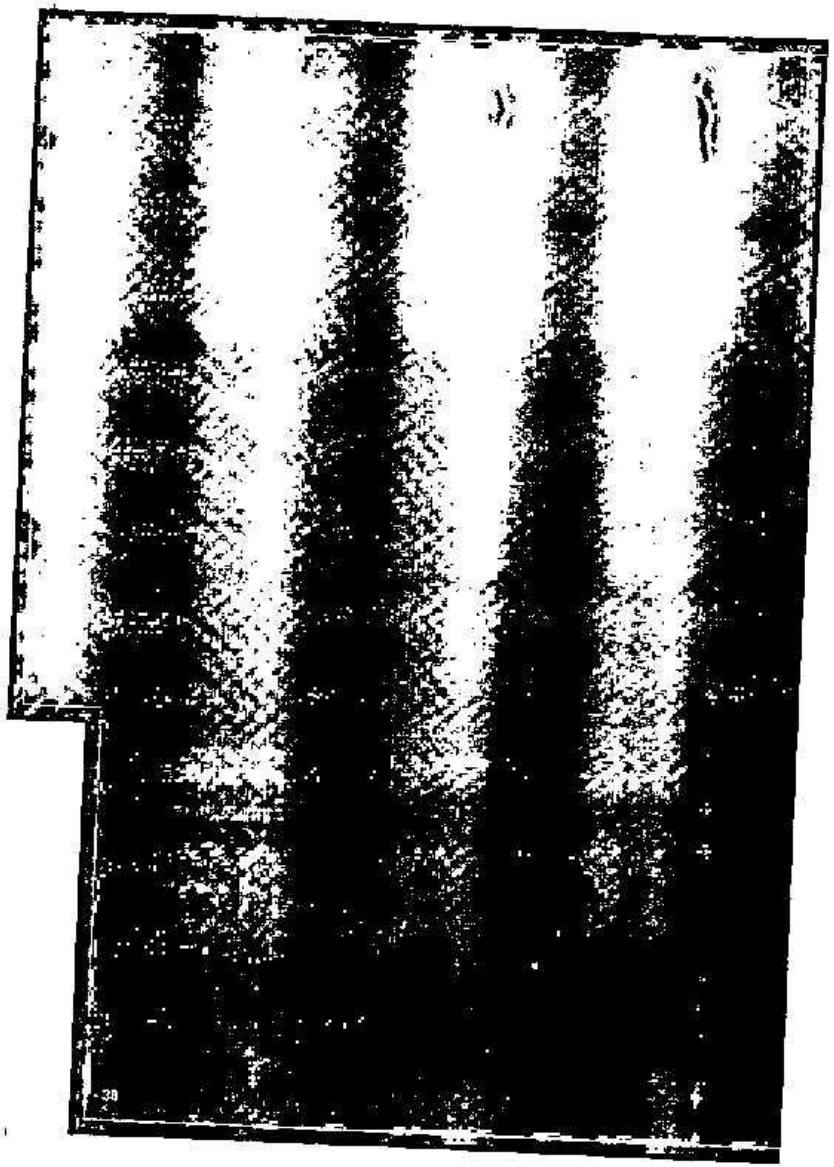
If you become pregnant after treatment with LEMTRADA and experience a thyroid disorder during pregnancy, extra caution is needed as thyroid disorders can be harmful to an unborn baby.

Breastfeeding

It's unknown if LEMTRADA 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 LEMTRADA 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.

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



Planning your monitoring schedule

The autoimmune conditions described in this guide may occur long after you received a course of treatment with LEMTRADA. It's very important that you continue to have your monthly tests for at least 48 months after your last treatment course, even if you're feeling well.

[Note: Determined + appropriate accor... + ...nal practices/ circumstances]

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

The following tools can help you remember your monitoring tests.

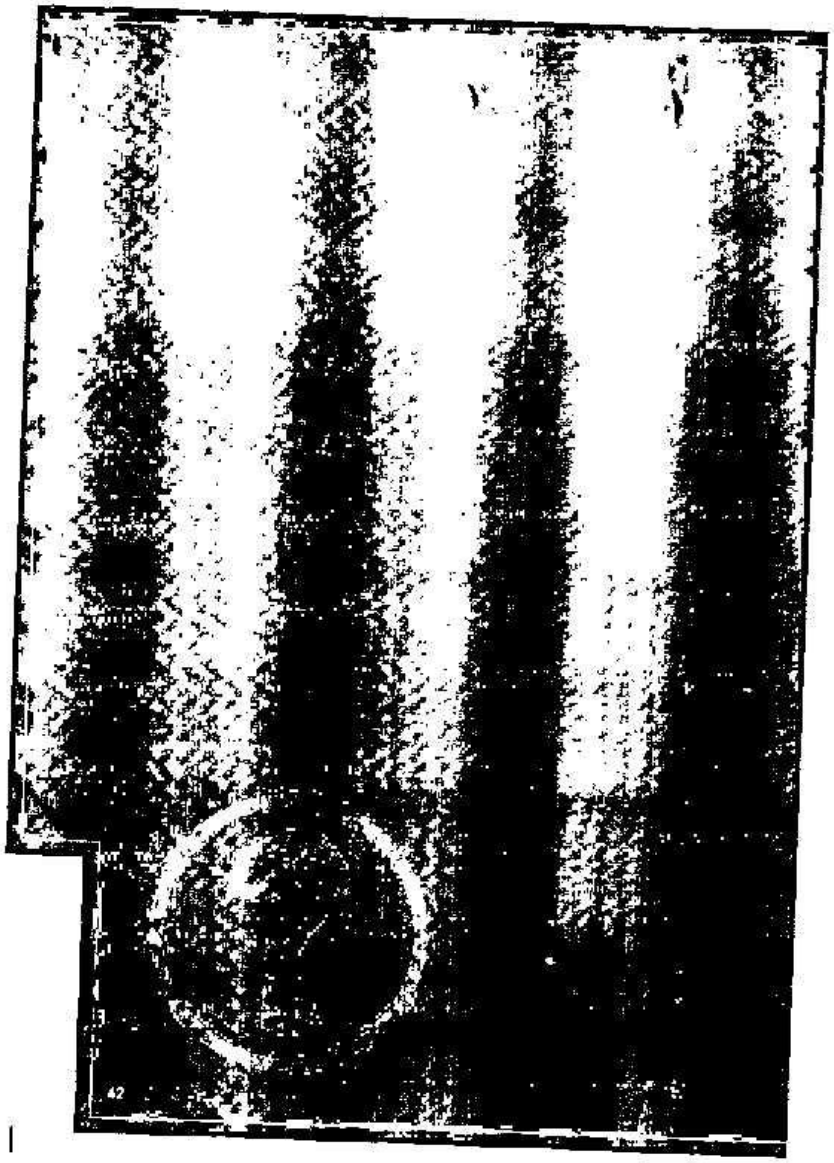
You can use as many, or as few, of them as you like.

- **Web-based reminder:**
  Through www.msonetoone.eu 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 through the website at any anytime or just contact [insert contact details of selected vendor]

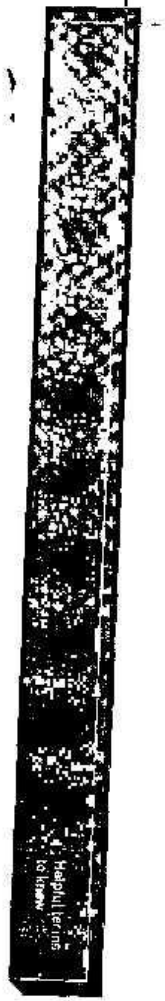
These services are offered through a third party, who will collect and process your personal data in accordance with appropriate data protection legislation. Your personal data will be stored securely and will not be shared with others, including the manufacturer of LEMTRADA. Again, these services are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

- Lemcheck (not available in all European countries)
  An MS One to One application to help support your adherence to your monitoring programme when prescribed LEMTRADA
- Ot... MS One to One voice assistant:
  A Google assistant designed to help you plan and prepare for your appointments with your neurologist or MS nurse

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 recovery.



Helpful terms to know



Acquired haemophilia A: A bleeding disorder that occurs in people with a personal and family history negative for haemorrhages. In acquired haemophilia A, the body produces antibodies that attack clotting factors, specialised proteins required for the blood to clot normally. Affected individuals develop complications associated with abnormal, uncontrolled bleeding into the muscles, skin and soft tissue and during surgery or following trauma.

AIE (Autoimmune encephalitis): Autoimmune condition which may include symptoms such as behavioural and or psychiatric changes, movement disorders, short term memory loss or seizures as well as other symptoms which may resemble an MS relapse.

Anti-Glomerular Basement Membrane disease (anti-GBM): A disease caused by the immune system turning against the kidneys and in some cases, 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.

AOSD (Adult onset still disease): Rare condition that has the potential to cause multi-organ inflammation.

Autoimmune conditions/disorders: The immune system usually protects the body from bacteria, viruses, and other harmful agents. When 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 hepatitis: A certain type of liver inflammation that occurs when the body's immune system, which ordinarily attacks pathogens (e.g. viruses and bacteria), targets the liver. This attack on your liver can lead to inflammation and cause serious damage to liver cells. If you develop one or more of the following symptoms report this to your doctor: nausea, vomiting, abdominal pain, fatigue, loss of appetite, yellow skin or eyes, dark urine, or bleeding or bruising more easily than normal.

Autoimmune thyroid disorder: A disorder that occurs when the immune system mistakenly attacks the thyroid gland. Autoimmune thyroid disorders are treatable. They can come in different types.

- Hyperthyroidism: when the thyroid produces too much hormone
- Hypothyroidism: when the thyroid does not produce enough hormones

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

Haemophagocytic lymphohistiocytosis (HLH): A life-threatening condition that occurs when certain types of immune cells don't work properly. These cells become overactive, causing too much inflammation. In HLH the immune system begins 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. Signs and symptoms of HLH may include: persistent fever, skin rash, swollen glands.

Immune system: Your body's defence system against infection, foreign substances, and abnormal cells.

Infusion: A method of administering a treatment whereby a solution (a liquid containing a medicine) is slowly passed into a vein through a needle.

Immune thrombocytopenic purpura (ITP): A condition which results in a low number of platelets in the blood. Platelets are necessary for normal blood clotting, therefore ITP can cause severe bleeding. ITP is treatable if detected promptly, but if left untreated it can lead to serious health problems and may be fatal.

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

Progressive Multifocal Leukoencephalopathy (PML): A rare infection of the brain. You should contact your doctor immediately if you develop any symptoms like progressive weakness or clumsiness of limbs, disturbance of vision, speech difficulties or changes in thinking, memory, and orientation leading to confusion and personality changes.

TTP (Thrombotic thrombocytopenic purpura): A blood clotting disease where blood clots form in blood vessels and can occur anywhere in the body.

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

How to reach your doctors

LEMTRADA® (alemtuzumab)
Healthcare professional checklist

Timing	Activity		Detail
Initial patient screening	Contraindications	☐	**Assess patient to ensure they don't hold any of the following contraindications:** • Hypersensitivity to alemtuzumab or to any of the excipients listed in Summary of Product Characteristics (SmPC) section 6.1 • Human Immunodeficiency Virus (HIV) infection • Severe active infections until complete resolution • Uncontrolled hypertension • History of arterial dissection of the cervicocephalic arteries • History of stroke • History of angina pectoris or myocardial infarction • Known coagulopathy, or anti-platelet or anti-coagulant therapy • Other concomitant autoimmune diseases (besides multiple sclerosis (MS))
	Precautions for use	☐	**Consider combined effects on the patient's immune system if LEMTRADA is used concomitantly with antineoplastic or immunosuppressive therapies**
	Recommended screening	☐	**Evaluate for active and inactive ("latent") tuberculosis (as per local guidelines)**
		☐	Evaluate MRI scan for any sign suggestive of progressive multifocal leukoencephalopathy (PML) prior to initiation and readministration of alemtuzumab treatment
		☐	**Consider screening patients at high risk of hepatitis B virus (HBV) and/or hepatitis C virus (HCV) infection. Exercise caution in prescribing LEMTRADA to patients identified as carriers of HBV and/or HCV**
		☐	**Consider screening for Human Papillomavirus (HPV) in female patients prior to treatment and annually thereafter**
		☐	**Consider evaluation of cytomegalovirus (CMV) immune serostatus (as per local guidelines)**
	Baseline lab tests and measurements	☐	**Obtain baseline electrocardiogram (ECG) and vital signs, including heart rate and blood pressure (BP) measurements**
		☐	**Complete blood count with differential**
		☐	**Test serum transaminases and serum creatinine levels**
		☐	**Perform thyroid function tests, such as thyroid stimulating hormone (TSH) level**
		☐	**Perform urinalysis with microscopy**
	Understanding of benefits and risks	☐	**Ensure the patient has been informed about and understands the potential safety events associated with LEMTRADA (including serious autoimmune disorders, infections and malignancies), the monitoring requirement and the measures to minimise risk (e.g. watching for symptoms, carrying the Patient Alert Card and the need to commit to periodic monitoring for at least 48 months after the last treatment)**
4 weeks prior to treatment, if needed	Vaccinations	☐	**Recommend that patients complete local immunisation requirements**
		☐	**Consider varicella zoster virus vaccination of antibody negative patients before initiating a course of LEMTRADA treatment**
2 weeks prior to, during, and for at least 1 month after treatment	Diet		Recommend that patients avoid ingestion of uncooked or undercooked meats, soft cheeses and unpasteurised dairy products 2 weeks prior to, during, and for at least 1 month after treatment

Timing	Activity		Detail
Immediately prior to treatment	General health	☐	Delay initiation of LEMTRADA administration in patients with severe active infection until the infection is fully controlled
	Pretreatment for infusion-associated reactions	☐	Pretreat with corticosteroids immediately prior to LEMTRADA infusion on each of the first 3 days of any treatment course
		☐	Pretreat with antihistamines and/or antipyretics prior to LEMTRADA administration may also be considered
	Oral prophylaxis for herpes	☐	Administer 200 mg acicloviir (or equivalent) twice a day from first day of treatment and continuing for a minimum of 1 month following treatment with LEMTRADA
	Pregnancy and contraception	☐	Ensure women of childbearing potential use effective contraceptive measures when receiving a course of treatment with LEMTRADA and for 4 months following the course of treatment
Infusion administration	Pre-infusion evaluations	☐	Obtain a baseline ECG and vital signs, including heart rate and BP measurements
		☐	Perform laboratory tests (complete blood count with differential, serum transaminases, serum creatinine, thyroid function test and urinalysis with microscopy)
	During infusion	☐	Monitor heart rate, BP, and overall clinical status of the patient at least once every hour
		☐	Discontinue the infusion: • in the case of a severe adverse event • if the patient shows clinical symptoms suggesting development of a serious adverse event associated with the infusion (myocardial ischaemia, haemorrhagic stroke, cervicocephalic arterial dissection or pulmonary alveolar haemorrhage)
		☐	Flush lines to ensure the entire dosage has been administered to the patient
		☐	Observe patients for a minimum of 2 hours after each infusion. Patients displaying clinical symptoms that may indicate a serious adverse event should be closely monitored until complete resolution of the symptoms and observation time extended as appropriate
	Post-infusion	☐	Educate patients about the potential for a delayed onset of infusion-associated reactions and instruct them to report symptoms immediately and seek appropriate medical care if they arise
		☐	Obtain a platelet count on Days 3 and 5 of the first infusion course, and after infusion on Day 3 of any subsequent course. Follow clinically significant thrombocytopenia until resolution and consider referral to a haematologist for management
For 4 years, 48 months after last treatment	Monitoring activities	☐	Complete blood count with differential and serum creatinine: monthly
		☐	Perform urinalysis with microscopy: monthly
		☐	Perform thyroid function tests: every 3 months
		☐	Perform liver function testing: monthly

Patient name:

Patient medical record number:

Patient date of birth:

Prescriber name:

Date: