



## FDA Drug Safety Communication

FDA warns about rare but serious risks of stroke and blood vessel wall tears with multiple sclerosis drug Lemtrada (alemtuzumab)

### Safety Announcement

**[11-29-2018]** The U.S. Food and Drug Administration (FDA) is warning that rare but serious cases of stroke and tears in the lining of arteries in the head and neck have occurred in patients with multiple sclerosis (MS) shortly after they received Lemtrada (alemtuzumab). These problems can lead to permanent disability and even death. As a result, we have added a new warning about these risks to the prescribing information in the [drug label](#) and to the patient [Medication Guide](#). We have also added the risk of stroke to the existing *Boxed Warning*, FDA's most prominent warning.

Lemtrada is one of several medicines used to treat forms of MS that get better and then worse, or relapse, and was approved in the United States in 2014. Lemtrada must be administered by intravenous (IV) infusion by health care professionals.

Alemtuzumab is also approved under the brand name Campath, which was approved in May 2001 to treat a type of cancer called B-cell chronic lymphocytic leukemia (B-CLL). The [Campath drug label](#) will also be updated to include these risks in the *Adverse Reactions* section under *Postmarketing Experience*.

**Patients or their caregivers** should seek emergency treatment as soon as possible if the patient experiences signs or symptoms of a stroke or tears in the lining of the head and neck arteries, called arterial dissection, which can include:

- Sudden numbness or weakness in the face, arms, or legs, especially if it occurs on only one side of the body
- Sudden confusion, trouble speaking, or difficulty understanding speech
- Sudden trouble seeing in one or both eyes
- Sudden trouble with walking, dizziness, or loss of balance or coordination
- Sudden severe headache or neck pain

Most patients taking Lemtrada who developed stroke or tears in the artery linings, developed symptoms within 1 day of receiving Lemtrada. One patient reported symptoms that occurred 3 days after treatment.

**Health care professionals** should advise patients at every Lemtrada infusion to seek immediate emergency medical attention if they experience symptoms of ischemic or hemorrhagic stroke or cervicocephalic arterial dissection. The diagnosis is often complicated because early symptoms such as headache and neck pain are not specific. Promptly evaluate patients who complain of symptoms consistent with these conditions.

In the nearly five years since FDA approved Lemtrada in 2014 to treat relapsing forms of MS, we identified 13 worldwide cases of ischemic and hemorrhagic stroke or arterial dissection that occurred shortly after the patient received Lemtrada (see Data Summary). This number includes only reports submitted to FDA,\* so additional cases we are unaware of may have occurred. Twelve of these cases reported symptoms within 1 day of receiving Lemtrada. As a result, we have added a new warning about this risk in the *Warnings and Precautions* section of the prescribing information in the drug label. We have also added the risk of stroke to the existing *Boxed Warning*, FDA's most prominent warning.

To help FDA track safety issues with medicines, we urge health care professionals to report side effects from Lemtrada or other medicines to the FDA MedWatch program, using the information in the "Contact FDA" box at the bottom of this page.

\*The cases were reported to the [FDA Adverse Event Reporting System \(FAERS\)](#).

### **Facts about Alemtuzumab (Lemtrada, Campath)**

- Lemtrada is one of several medicines used to treat relapsing forms of multiple sclerosis (MS). This type of MS causes "attacks" or "relapses," which are periods of time when MS symptoms worsen.
- Lemtrada is administered by intravenous infusion. It is available only through the [Lemtrada Risk Evaluation and Mitigation Strategy \(REMS\) Program](#), a restricted distribution program to help ensure that the medicine's benefits outweigh the risks.
- Because of its safety profile, Lemtrada should generally be reserved for patients who have had an inadequate response to two or more medicines indicated for MS.
- Common side effects of Lemtrada include infusion-related reactions and infections.
- Lemtrada can also cause a number of other serious adverse reactions, which are included in the [prescribing information](#) and patient [Medication Guide](#).
- Alemtuzumab is also approved as brand name Campath, a medicine approved to treat a type of cancer called B-cell chronic lymphocytic leukemia (B-CLL).

### **Additional Information for Patients and Caregivers**

- Rare but serious cases of stroke and tears in the linings of the arteries in the head and neck have been reported in patients after receiving Lemtrada.

- Most often, these problems occur within 1 day after receiving treatment, but can occur a few days after treatment. Seek emergency medical care immediately if you experience symptoms such as:
  - Sudden numbness or weakness in the face, arms, or legs, especially if it occurs on only one side of the body
  - Sudden confusion, trouble speaking, or difficulty understanding speech
  - Sudden trouble seeing in one or both eyes
  - Sudden trouble with walking, dizziness, or loss of balance or coordination
  - Sudden severe headache or neck pain
- A stroke can occur when blood flow to an area of the brain is cut off or when there is bleeding into the brain. When brain cells are deprived of blood flow and oxygen they can begin to die within minutes.
- Tears in the lining of arteries of the head and neck called arterial dissections can cause a stroke.
- It is important for you to read the patient [Medication Guide](#) that comes with your Lemtrada prescription every time you receive a course of treatment because the information may be updated.
- To help FDA track safety issues with medicines, please report side effects from Lemtrada or other medicines to the FDA MedWatch program, using the information in the “Contact FDA” box at the bottom of this page.

### **Additional Information for Health Care Professionals**

- Rare but serious cases of ischemic and hemorrhagic stroke and cervicocephalic arterial dissection have been reported to FDA.
- These events most often occurred within 1 day of Lemtrada administration but can occur a few days later.
- Instruct patients to seek emergency medical attention immediately if they experience symptoms of stroke or cervicocephalic arterial dissection.
- Lemtrada may cause other serious adverse reactions that are already described in the [prescribing information](#). These include:
  - Serious autoimmune problems, including immune thrombocytopenic purpura and anti-glomerular basement membrane disease
  - Serious infusions reactions, such as dyspnea, chest pain, or rash
  - Certain cancers, including thyroid cancer, melanoma, and lymphoproliferative disorders and lymphoma
- Encourage patients to read the patient [Medication Guide](#) they receive with each Lemtrada prescription, which explains the benefits and risks of the medicine.
- Lemtrada is available only through the [Lemtrada Risk Evaluation and Mitigation Strategy \(REMS\) Program](#), a restricted distribution program to help ensure that the medicine’s benefits outweigh the risks.
- To help FDA track safety issues with medicines, please report adverse events involving Lemtrada to the FDA MedWatch program, using the information in the “Contact FDA” box at the bottom of this page.

## Data Summary

In nearly 5 years since FDA approved Lemtrada (alemtuzumab) in 2014 to treat relapsing MS, we identified 13 worldwide cases of ischemic and hemorrhagic stroke and cervicocephalic arterial dissection. These 13 cases reported in the FDA Adverse Event Reporting System (FAERS) database occurred within 3 days of administration of the drug to patients with MS. Ten of the cases occurred in the U.S. and three occurred in Europe.

The thirteen cases reported in FAERS included seven with hemorrhagic stroke, one with both hemorrhagic stroke and dissection of both vertebral arteries, one with ischemic stroke, one with ischemic stroke and dissection of bilateral carotid and right vertebral arteries, two with dissection that involved the right carotid and left vertebral arteries, and two with unspecified type of stroke. One patient who suffered hemorrhagic stroke died. Twelve of the 13 cases reported that these adverse events occurred within one day after administration of a Lemtrada dose.

Most of the cases reported to FDA in FAERS did not provide sufficient detail to allow a full assessment of individual risk factors. However, the occurrence of these adverse events within one day of Lemtrada administration suggests an association. Although the etiology is unknown, the adverse events occurred within the same time frame as cytokine release syndrome, a systemic inflammatory response syndrome known to occur after Lemtrada administration and may contribute to these adverse events. Symptoms of cytokine release syndrome were reported in some patients, including cytokine storm in the patient who died of hemorrhagic stroke. However, in many cases, insufficient information was reported to determine whether cytokine release syndrome occurred together with stroke or arterial dissection.

Cases of ischemic stroke and intracerebral hemorrhage have also been reported in patients treated with alemtuzumab under the brand name Campath for B-cell chronic lymphocytic leukemia and other leukemias or lymphomas. These cases either had potential contributing factors, including underlying risk factors and concomitant medications, or the reports were missing this information. For these reasons, a causal association between Campath and stroke in patients being treated for hematologic cancers could not be established.

## Related Information

- [National Institute of Neurological Disorders and Stroke \(NINDS\): Stroke Information](#)
- [Centers for Disease Control and Prevention: Stroke Signs and Symptoms](#)
- [Intracranial Hemorrhage](#)
- [Cervicocephalic Arterial Dissections](#)
- [The FDA's Drug Review Process: Ensuring Drugs Are Safe and Effective](#)
- [Think It Through: Managing the Benefits and Risks of Medicines](#)