



## Starting Disease-modifying Therapies for Multiple Sclerosis

**The AAN is the world's largest association of neurologists and neuroscience professionals and is dedicated to promoting the highest quality patient-centered neurologic care. Neurologists are doctors who identify and treat diseases of the brain and nervous system.**

Experts from the AAN carefully reviewed the available scientific studies on use of disease-modifying therapy, or DMT, for treating multiple sclerosis, or MS. The following information is a summary of the evidence from those studies and other key information.

### Overview

In MS, the immune system attacks the brain and spinal cord. This damages nerves and the tissue that covers and protects nerve fibers. Damage to this protective tissue changes how the nerves deliver signals from the brain and spinal cord.

DMTs help slow the disease process and might help keep your condition stable. Several DMTs have either strong or moderate evidence supporting their use.

Using a DMT can be better than letting MS run its course without treatment. This is because MS usually gets worse over time. However, all medicines have possible risks.

Before deciding to start DMT, be sure to think about both the benefits and the risks.

For information on the AAN's levels of evidence, see the Key to Evidence Levels at the end of this sheet.

## Types of Multiple Sclerosis

### Relapsing

#### Relapsing-remitting MS (RRMS)

- Most Common MS Type
- Relapses—New or Worsening Symptoms
- Remission—Stable Between Relapses

### Progressive

#### Secondary Progressive MS (SPMS)

- Started as RRMS
- Now Slowly, Steadily Getting Worse
- Some Relapses But Less Often

#### Primary Progressive MS (PPMS)

- Gradual Worsening from the Beginning
- Usually No Relapses

### Clinically Isolated Syndrome (CIS)

#### CIS may become MS

- One or More Symptoms That Are Like MS Symptoms
- Symptoms Last 24 Hours or Longer
- At Higher Risk of MS
- Amount of Risk Depends on Clinical Exam and MRI Results

# Treatment for Multiple Sclerosis

## Disease-Modifying Therapies

**Disease-modifying therapies (DMTs) for MS help slow the disease process to help keep your condition stable.**

### Lesions

DMTs lessen the number of new lesions that form or keep existing lesions from getting larger. These are abnormal spots on the brain or spinal cord.

### Relapses

DMTs lessen the number of relapses that happen.

## Symptom Management

**DMTs are not prescribed to treat MS symptoms.**

### Dizziness, Fatigue, Pain

- Dizziness
- Feeling lightheaded
- Chronic pain
- Tiredness and lack of energy

### Emotional Problems

- Depression, or a state of sadness that can last a short or long time
- Anxiety, or a state of fear that can last a short or long time

### Vision

- Blurred vision
- Pain with eye movement

### Thinking and Memory

- Trouble learning and remembering new information
- Trouble organizing and problem solving

### Muscle/Movement

- Spasticity, or muscle tightness that makes it hard to move normally
- Weakness
- Numbness or tingling

### Bladder/Bowel Problems

- Difficulty emptying bladder
- Difficulty moving or emptying bowels

## Choosing Whether to Start DMT

If you have MS, a careful discussion with your clinician about DMT is important. You need to decide whether DMT is right for you. If you choose to use DMT, be sure to talk with your clinician about how to choose the DMT for your needs. Also, be sure to check whether your insurance plan covers your choice of DMT.

People who do not have an MS diagnosis should discuss DMT use with their clinicians if they have experienced the following things:

- One event of MS-like symptoms
- Two or more brain lesions shown on an MRI scan

The decision whether to start a DMT depends on the risks and benefits and your specific situation.

## FDA Approval for DMTs and Evidence for DMTs in MS

The US Food and Drug Administration (FDA) has approved all the medicines described here. The FDA bases its decisions about medicines on well-designed clinical studies. These studies test whether a medicine helps treat a certain condition.

For FDA approval for MS, a medicine must be shown to help treat the disease.

However, some medicines help treat MS better than others. Thus, each DMT has a level of evidence to show whether it helps slow certain disease processes. Your clinician will take the evidence into account when discussing treatment choices with you.

Several DMTs have either strong evidence or moderate evidence supporting their use for slowing certain disease processes. The table at the end of this sheet shows the evidence for lowering risk of relapse in relapsing-remitting multiple sclerosis (RRMS).

## Pregnancy and Reproductive Health

Most DMTs have health risks for pregnant women with MS or their unborn babies. Some DMTs also can affect reproductive health for men with MS.

Tell your clinician if you are or plan to become pregnant. Your plans may affect your decisions about DMT use and choice.

## Tracking Your MS While Using DMT

DMTs can help slow the disease process. But not every DMT may work for you. Also, these medicines have risks, and some risks can be serious.

While using a DMT, it is important to track your MS and general health in the following ways:

- Follow the directions for DMT use as shown on the prescription label. Consistent use of your medicine is important for managing your MS.
- Be sure to watch carefully over time for any side effects that develop. Learn the risks of the DMT you use. Tell your clinician about side effects.
- Work with your clinician to be checked regularly for new MS activity on MRI scans. The results will help when you make treatment decisions.

DMT	Evidence for Lowering Relapse Rate	Serious Side Effects	How Medicine Taken	Date of FDA Approval
Alemtuzumab	Strong	<ul style="list-style-type: none"> <li>• Kidney problems</li> <li>• Severe immune system responses</li> <li>• Severe infections</li> <li>• Skin cancer</li> <li>• Thyroid problems</li> </ul>	By IV needle into a vein	November 14, 2014
Azathioprine	Moderate	<ul style="list-style-type: none"> <li>• Cancer risk long-term</li> <li>• Liver problems</li> <li>• Pancreas problems</li> </ul>	By mouth	Not approved specifically for use in MS
Cladribine	Strong	<ul style="list-style-type: none"> <li>• Infection brought on by suppressed immune system</li> </ul>	By mouth or IV needle into a vein	Not approved specifically for use in MS
Corticosteroids	Very Low	<ul style="list-style-type: none"> <li>• Several</li> </ul>	Usually by IV needle into a vein	Not approved specifically for slowing the MS disease process
Cyclophosphamide	Low	<ul style="list-style-type: none"> <li>• Bladder tumors</li> </ul>	Usually by IV needle into a vein	Not approved specifically for use in MS
Dimethyl Fumarate	Strong	<ul style="list-style-type: none"> <li>• Low number of white blood cells</li> <li>• PML, a severe brain infection</li> </ul>	By mouth two times a day	March 27, 2013
Fingolimod	Strong	<ul style="list-style-type: none"> <li>• Heart problems</li> <li>• Herpes infection</li> <li>• Liver problems</li> <li>• Low number of white blood cells</li> <li>• PML, a severe brain infection</li> </ul>	By mouth	September 21, 2010
Glatiramer Acetate	Strong	<ul style="list-style-type: none"> <li>• Reaction in several body systems right after treatment</li> </ul>	By shot through skin three times a week	First brand name forms: 1996, 2014; first generic form: April 16, 2015
Immunoglobulins	Very Low	<ul style="list-style-type: none"> <li>• Too much fluid in the body</li> </ul>	By IV needle into a vein	Not approved specifically for use in MS
Interferon beta-1a	Strong	<ul style="list-style-type: none"> <li>• Liver problems</li> <li>• Low number of white blood cells</li> <li>• Severe skin problems</li> </ul>	By shot into muscle once per week	1996; pen version February 2012
Interferon beta-1a	Strong	<ul style="list-style-type: none"> <li>• Liver problems</li> <li>• Low number of white blood cells</li> <li>• Severe skin problems</li> </ul>	By shot through skin once per week	March 2002
Interferon beta-1a	Strong	<ul style="list-style-type: none"> <li>• Liver problems</li> <li>• Low number of white blood cells</li> <li>• Severe skin problems</li> </ul>	By shot through skin three times per week	March 2002
Interferon beta-1b	Moderate	<ul style="list-style-type: none"> <li>• Liver problems</li> <li>• Low number of white blood cells</li> <li>• Severe skin problems</li> </ul>	By shot through skin every other day	July 23, 1993
Methotrexate	Very Low	<ul style="list-style-type: none"> <li>• Chronic and worsening lung disease</li> <li>• Liver injury</li> </ul>	By mouth or shot through skin	Not approved specifically for use in MS
Mitoxantrone	Strong	<ul style="list-style-type: none"> <li>• Heart problems</li> <li>• Bone marrow cancer</li> <li>• Damage to certain sex organs</li> </ul>	By IV needle into a vein	October 2000

DMT	Evidence for Lowering Relapse Rate	Serious Side Effects	How Medicine Taken	Date of FDA Approval
Mycophenolate Mofetil	Low	<ul style="list-style-type: none"> <li>• Infection brought on by suppressed immune system</li> </ul>	Varies	Not approved specifically for use in MS
Natalizumab	Strong	<ul style="list-style-type: none"> <li>• Liver problems</li> <li>• PML, a severe brain infection</li> </ul>	By IV needle into a vein	November 23, 2004
Ocrelizumab	Strong	<ul style="list-style-type: none"> <li>• Infection brought on by suppressed immune system</li> <li>• PML, a severe brain infection</li> <li>• Triggering of hepatitis B infection</li> </ul>	By IV needle into a vein	March 28, 2017
Pegylated Interferon	Strong	<ul style="list-style-type: none"> <li>• Liver problems</li> <li>• Low number of white blood cells</li> <li>• Severe skin problems</li> </ul>	By shot through skin every 14 days	August 2014
Rituximab	Very Low	<ul style="list-style-type: none"> <li>• Infection brought on by suppressed immune system</li> <li>• PML, a severe brain infection</li> <li>• Triggering of hepatitis B infection</li> </ul>	By IV needle into a vein	Not approved specifically for use in MS
Teriflunomide	Strong	<ul style="list-style-type: none"> <li>• Liver problems</li> <li>• Risk of birth defects in unborn baby, if pregnant</li> </ul>	By mouth	September 12, 2012

Note: DMTs compared with placebo, a sugar pill with no active medicine.

To read the full guideline, visit [AAN.com/guidelines](http://AAN.com/guidelines).

**This practice guideline was endorsed by the Consortium of Multiple Sclerosis Centers, the Multiple Sclerosis Association of America, and the National Multiple Sclerosis Society.**

#### Key to Evidence Levels

After the experts review all of the published research studies, they describe the strength of the evidence supporting each recommendation:

Strong evidence = Future studies very unlikely to change the conclusion

Moderate evidence = Future studies unlikely to change the conclusion

Low evidence = Future studies likely to change the conclusion

Very low evidence = Future studies very likely to change the conclusion

This statement is provided as an educational service of the American Academy of Neurology. It is based on an assessment of current scientific and clinical information. It is not intended to include all possible proper methods of care for a particular neurologic problem or all legitimate criteria for choosing to use a specific procedure. Neither is it intended to exclude any reasonable alternative methodologies. The AAN recognizes that specific patient care decisions are the prerogative of the patient and the physician caring for the patient, based on all of the circumstances involved.

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