AAN Summary for Public Comment
Immunization and Multiple Sclerosis

Overview
This document is a summary of the American Academy of Neurology (AAN) practice guideline “Immunization and Multiple Sclerosis.” This is a summary of a draft guideline manuscript. The draft guideline is still in development and has not yet been approved by the AAN Board of Directors.

Immunization helps to strengthen your immune system. This can happen naturally. When you have certain infections, your body fights off the germ that causes the infection. By doing this, your body learns how to fight the germ better if you are infected again in the future.

Immunization can also happen through vaccination. Vaccination is a process of putting a weakened or dead form of a germ in your body through a vaccine. The vaccine teaches your body to fight the germ without infecting you with the germ.

Multiple sclerosis (MS) is a disease that affects your brain and spinal cord. In MS, damage occurs to a substance called myelin, which coats certain parts of your brain cells. Myelin helps that the electrical signals that travel along these cells move quickly and in a stable manner. Damage to myelin can slow or disrupt these signals. These signals may control your body’s movement, vision, and speech. As a result, many people with MS have a loss of muscle strength and muscle coordination as well as problems seeing and talking.

Although the cause of MS is not definitely known, it is thought that one possible cause is that certain immune cells in people with MS attack the myelin. That is why many of the types of drugs used to treat people with MS work on reducing the effect of the immune system on myelin. These drugs modify your immune cells to help keep them from attacking the myelin or attack it less. However, weakened immune cells may also be less able to fight germs that cause infections

This guideline was written to help provide recommendations for clinicians when they talk about vaccination for immunization with their patients who have MS. The guideline addresses what is known about benefits and risks according to evidence from studies about how infections, vaccines to prevent infections, and MS drugs all affect people with MS.

What is a practice guideline?
Guidelines are summaries of what we know about different tests and treatments for health problems.
Guidelines are based on research. When we develop guidelines, we include steps for others to weigh in. These include experts like doctors, patients, and other health providers.

Because no two people are the same, guidelines do not tell doctors the best way to treat any one person.

This guideline is still a draft and is still being changed. This draft has not yet been reviewed or approved by the AAN Board of Directors and therefore does not represent the official position of the AAN.

This information helps doctors and patients to weigh what might be good or bad about choices for care. It helps the doctor and patient to work together to make the best decision.

What are guideline recommendations and how are they determined?

Guideline recommendations are meant to help guide clinicians when they are partnering with patients or patients and families to make decisions about medical care.

When guideline authors write recommendations, they consider:

- the best medical research evidence available.
- the balance of potential benefit and potential harm of following the recommendation.
- the anticipated result of following the recommendation (how important is the outcome that will result from following the recommendation).
- the cost and availability of the test, therapy, or other subject of the recommendation.
- patients’ values and preferences.

Terms used in this guideline

- **Immunization**—Immunization is the process of your immune system reacting to a foreign substance in your body, like a germ, in a way that helps teach your immune system to identify and fight the substance more quickly the next time it gets into your body. Immunization can happen naturally, like when a germ gets into your body, you get sick, and your body fights off the germ. Immunization can also happen when you get a vaccination (throughout the guideline “immunization” and “vaccination” are used interchangeably to refer to vaccination).

- **Immunomodulatory medication**—These are drugs that have an effect on your immune system. They may make your immune system weaker.

- **Immunomodulatory and immunosuppressive medication (ISIM)**—ISIM, like immunomodulatory drugs, affect your immune system.

- **Live attenuated vaccines**—Live attenuated vaccines are vaccines made of live germs that have been weakened.

- **Vaccination**—Vaccination is the process of putting a dead or weakened virus into your body through a vaccine to cause immunization.
What the research shows
The recommendations are summarized in the following sections. The strength of the recommendations is based on the factors listed in Table 1.

Discussions about immunization
Clinicians should talk with their patients who have MS about the evidence regarding the relationship between immunization and MS with their patients (Level B) and ask these patients about their opinions and preferences and questions they have about immunizations to help form the best immunization strategy according to their patients’ MS status, values, and preferences (Level B).

Recommendations for immunizations
Clinicians should recommend that patients with MS follow all local vaccine standards, such as standards from the Centers for Disease Control and Prevention, the World Health Organization, and local regulatory bodies, unless there is a specific reason not to. For example, they are currently receiving treatment with immunomodulatory medication (Level B).

Clinicians should think about local risks of vaccine-preventable diseases when talking with patients who have MS about vaccination (Level B) and recommend that patients with MS receive the influenza vaccination annually, unless there is a specific reason not to, like a negative reaction to an influenza vaccination in the past (Level B).

MS drugs and immunization
Clinicians should talk with patients who have MS about infection risks associated with specific ISIM drugs and vaccination guidance according to the prescribing instructions for any ISIMs that are being considered MS treatment (Level B).

Physicians should review which vaccines their patients who have MS have had (if any) before prescribing ISIM therapy and should vaccinate patients with MS, according to local regulatory standards and guided by treatment-specific infectious risks, at least 4–6 weeks before starting ISIM therapy as advised by specific prescribing information (Level B). Clinicians may discuss the advantage of vaccination with patients as soon as possible after MS diagnosis, regardless of their plans for initial MS treatment, to prevent future delays in beginning MS treatment with ISIM drugs (LEVEL C).

Screening and treating for infection before treatment with MS drugs
Clinicians must screen for tuberculosis, according to the prescribing information for teriflunomide before starting MS treatment with that drug (Level A) and should treat patients for tuberculosis (when they have positive test results) before treating them for MS with teriflunomide (Level B).
Clinicians must also screen for latent tuberculosis before starting MS treatment with ISIM medications other than teriflunomide, particularly in high-risk populations or in countries where tuberculosis is more likely (Level A) and should treat patients for tuberculosis (when they have positive test results) before treating them with ISIM drugs other than teriflunomide (Level B).

**Immunization with live vaccines**
Clinicians should recommend against live attenuated vaccines in people with MS who are receiving or recently stopped receiving treatment with ISIM drugs (Level B). When the risk of infection is high, clinicians may recommend using live attenuated vaccines, if killed vaccines are unavailable, in people with MS who are receiving ISIM therapies (Level C).

**Immunization and MS relapse**
Clinicians may delay vaccination of people with MS who are experiencing a relapse until the relapse goes away after treatment or stops on its own, often many weeks after relapse onset (Level C).

**Table 1. Definitions for Recommendation Levels**

<table>
<thead>
<tr>
<th>Recommendation Level</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A</strong> (Strong)</td>
<td>There are very strong and compelling reasons to follow this recommendation, it possible to follow this recommendation in almost all circumstances, and in almost all circumstances, patients would want the course of action described in the recommendation to be followed.</td>
</tr>
<tr>
<td><strong>B</strong> (Moderate)</td>
<td>There are good and compelling reasons to follow this recommendation, it is generally possible to follow this recommendation, and in most circumstances, patients would want the course of action described in the recommendation to be followed.</td>
</tr>
<tr>
<td><strong>C</strong> (Weak)</td>
<td>There are reasons to follow this recommendation, but the research supporting this recommendation is weak, the benefits relative to the risks is less certain, the test or treatment is costly, or only some patients would want the course of action described in the recommendation to be followed. Recommendations can be “weak” for a variety of different reasons and these reasons are described in the complete guideline.</td>
</tr>
<tr>
<td><strong>U</strong> (None Made)</td>
<td>There is not enough research to make a recommendation and/or the balance of the benefits, harms, and costs is unknown.</td>
</tr>
</tbody>
</table>
There is not enough research to make a recommendation and/or the balance of the benefits, harms, and costs is unknown, but there is a good reason to think that more research should be done. Only patients in a research study would receive the course of action.

Clinical practice guidelines, practice advisories, systematic reviews and other guidance published by the American Academy of Neurology and its affiliates are assessments of current scientific and clinical information provided as an educational service. The information: 1) should not be considered inclusive of all proper treatments, methods of care, or as a statement of the standard of care; 2) is not continually updated and may not reflect the most recent evidence (new evidence may emerge between the time information is developed and when it is published or read); 3) addresses only the question(s) specifically identified; 4) does not mandate any particular course of medical care; and 5) is not intended to substitute for the independent professional judgment of the treating provider, as the information does not account for individual variation among patients. In all cases, the selected course of action should be considered by the treating provider in the context of treating the individual patient.

Use of the information is voluntary. AAN provides this information on an “as is” basis, and makes no warranty, expressed or implied, regarding the information. AAN specifically disclaims any warranties of merchantability or fitness for a particular use or purpose. AAN assumes no responsibility for any injury or damage to persons or property arising out of or related to any use of this information or for any errors or omissions.