Taking action against relapsing MS, one week at a time

Welcome to AVONEX® (interferon beta-1a)
To help you track your treatment and experience with AVONEX, we’ve created this helpful journal

This journal will help you:

► Keep track of your injection date, time, and location on your body
► Remember the steps prior to and following your injections with a useful checklist
► Discuss your treatment experience with your healthcare team and loved ones
► Capture questions to discuss with your doctor at your next appointment
► Make note of your thoughts and feelings along the way

Be sure to take this journal with you to your next doctor appointment to use in discussing your treatment, any symptoms, and questions that you have.

Manage your treatment with AVONEX

![Track the date, time, and site of each injection](image)

![Monitor your health over time](image)

![Record your comments and feelings](image)

![Collect any questions you have for your doctor](image)

And remember, the Above MS™ program is here to help throughout the MS journey, offering one-on-one MS support over the phone, relevant disease education, and healthy lifestyle information. Just call 1-800-456-2255, Monday through Friday, 8:30 AM to 8:00 PM ET.

Indication

AVONEX is approved by FDA to treat relapsing forms of multiple sclerosis (MS) to decrease the number of flare-ups and slow the occurrence of some of the physical disability that is common in people with MS. AVONEX is approved for use in people who have experienced a first attack and have lesions consistent with MS on their MRI.

Please see Important Safety Information on pages 38-39 and accompanying full Prescribing Information, Medication Guide, and Instructions for Use.
Preparing for your weekly injections

It’s normal to feel a little nervous about your injections, especially when you first begin treatment. But it’s important to take your AVONEX® as prescribed. Try to think of your injection as a weekly reminder that you are taking action against relapsing MS.

Get ready for your injection:

► Set aside a regular day and time each week for your injection
► Bring AVONEX to room temperature before taking it, but don’t use an external heat source, like hot water, to warm it up. Try taking it out of the refrigerator 30 minutes before you plan to take your injection. It’s ok to wait a little longer if necessary to bring it to room temperature
► Review your journal history to check the location of your last injection, so you can choose a different site for the next injection
► Some people find that icing the skin around the injection site makes the injection more comfortable
► Take steps to help manage flu-like symptoms (see page 6)
► If it is the first time you are taking AVONEX, your doctor may recommend you gradually build up to a full dose of AVONEX over the first month. This is a process called “titration”
► Before your first AVONEX injection, set up a training session with your doctor. You can get additional training from a Nurse Educator

Selected Important Safety Information

Do not take AVONEX if you are allergic to interferon beta, albumin, or any of the ingredients in AVONEX.

Please see additional Important Safety Information on pages 38-39 and accompanying full Prescribing Information, Medication Guide, and Instructions for Use.
Preparing for your weekly injections (cont’d)

Prepare your injection:

AVONEX® is available in 2 different forms, given once a week by injection into the muscle (intramuscular injection).

Prefilled syringe can be used with the AVOSTARTGRIP™ Titration Kit

The injection process and recommended injection sites are different for each of these forms. Make sure that you or your care partner follow the Injection Guide or Instructions for Use for whichever form you’re using. Inject AVONEX exactly as your healthcare provider tells you.

After your injection:

- Record your injection using this journal
- Properly dispose of all used AVONEX PENS and needles

Enjoy knowing you don’t have to take your AVONEX injection again for another week.

Questions? You can call us Monday through Friday between 8:30 AM and 8:00 PM ET at 1-800-456-2255.
Helping manage flu-like symptoms

Most people experience flu-like symptoms (FLS) when they first start treatment. These usually last for about a day after the injection and can include fever, chills, muscle aches, or tiredness. However, for many people they get milder or go away over time. Your body needs to adjust to AVONEX®, and as you continue to regularly take your treatment, you may see your FLS start to lessen.

Checklist for managing FLS each week:

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>✓</td>
<td>Talk to your doctor about over-the-counter pain relievers that you can take before and after your injection</td>
</tr>
<tr>
<td>✓</td>
<td>Drink plenty of water on the days around your injection</td>
</tr>
<tr>
<td>✓</td>
<td>Experiment to find the time of day that works best for you. Some people find it best to take their AVONEX in the morning, while others prefer to take it later in the day</td>
</tr>
<tr>
<td>✓</td>
<td>Keep track of your injections to help you discover which strategies work best for you. Use the AVONEX journal provided in this kit to record the details of your injections</td>
</tr>
</tbody>
</table>

Remember, you’re not alone

Whether you’re just starting treatment or have been on treatment for a while, Nurse Educators are available by phone 24/7 to provide extra support and to answer your questions.

The Above MS™ program from Biogen also provides additional training for people taking an injectable Biogen treatment for relapsing MS.

Please keep in mind that your healthcare provider is always your primary resource when it comes to your relapsing MS and your treatment.
Using your AVONEX journal

Keep track of your injections and treatment experience. Follow the examples on these pages to see how to use your AVONEX® journal each week.

Make sure you only use the injection sites for the form of AVONEX you’re taking. Always refer to the Instructions for Use prior to taking your AVONEX.

Nurse Educators can provide additional support to you and your care partner with injection technique and to respond to questions related to MS and treatment. They are available by phone 24/7.

Questions? You can call us Monday through Friday between 8:30 AM and 8:00 PM ET at 1-800-456-2255.

Please see Important Safety Information on pages 38-39 and accompanying full Prescribing Information, Medication Guide, and Instructions for Use.
BEFORE MY INJECTION, I…

- Brought AVONEX® to room temperature
- Prepared my AVONEX using the appropriate Injection Guide
- Drank plenty of water
- Took a pain or fever reducer approved by my doctor
- Other:

Injection notes:

AFTER MY INJECTION, I…

- Drank plenty of water
- Took a pain or fever reducer approved by my doctor
- Rewarded myself for taking my once-weekly AVONEX
- Other:

Other notes about this week:

Nurse Educators can provide additional support to you and your care partner with injection technique and to respond to questions related to relapsing MS and treatment. Call 1-800-456-2255 to connect with a Nurse Educator 24/7.
BEFORE MY INJECTION, I…

- Brought AVONEX® to room temperature
- Prepared my AVONEX using the appropriate Injection Guide
- Drank plenty of water
- Took a pain or fever reducer approved by my doctor
- Other:

Injection notes:

__________________________________________

AFTER MY INJECTION, I…

- Drank plenty of water
- Took a pain or fever reducer approved by my doctor
- Rewarded myself for taking my once-weekly AVONEX
- Other:

Other notes about this week:

__________________________

We’re here to help

To talk to an Above MS™ Support Coordinator, call 1-800-456-2255. They can be reached Monday through Friday from 8:30 AM until 8:00 PM ET.

Please see Important Safety Information on pages 38-39 and accompanying full Prescribing Information, Medication Guide, and Instructions for Use.
BEFORE MY INJECTION, I…

☐ Brought AVONEX® to room temperature

☐ Prepared my AVONEX using the appropriate Injection Guide

☐ Drank plenty of water

☐ Took a pain or fever reducer approved by my doctor

☐ Other:

Injection notes:

AFTER MY INJECTION, I…

☐ Drank plenty of water

☐ Took a pain or fever reducer approved by my doctor

☐ Rewarded myself for taking my once-weekly AVONEX

☐ Other:

Other notes about this week:

Nurse Educators can provide additional support to you and your care partner with injection technique and to respond to questions related to relapsing MS and treatment. Call 1-800-456-2255 to connect with a Nurse Educator 24/7.
Before my injection, I...

- Brought AVONEX® to room temperature
- Prepared my AVONEX using the appropriate Injection Guide
- Drank plenty of water
- Took a pain or fever reducer approved by my doctor
- Other:

Injection notes:


After my injection, I...

- Drank plenty of water
- Took a pain or fever reducer approved by my doctor
- Rewarded myself for taking my once-weekly AVONEX
- Other:

Other notes about this week:


We’re here to help

To talk to an Above MS™ Support Coordinator, call 1-800-456-2255. They can be reached Monday through Friday from 8:30 AM until 8:00 PM ET.

Please see Important Safety Information on pages 38-39 and accompanying full Prescribing Information, Medication Guide, and Instructions for Use.
WEEK 5

Date ____________________________ Time ____________________________ AM PM
Day S M T W T F S

BEFORE MY INJECTION, I...

☐ Brought AVONEX® to room temperature

☐ Prepared my AVONEX using the appropriate Injection Guide

☐ Drank plenty of water

☐ Took a pain or fever reducer approved by my doctor

☐ Other:

Injection notes:

______________________________

______________________________

AFTER MY INJECTION, I...

☐ Drank plenty of water

☐ Took a pain or fever reducer approved by my doctor

☐ Rewarded myself for taking my once-weekly AVONEX

☐ Other:

Other notes about this week:

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______________________________

Nurse Educators can provide additional support to you and your care partner with injection technique and to respond to questions related to relapsing MS and treatment. Call 1-800-456-2255 to connect with a Nurse Educator 24/7.

Please see Important Safety Information on pages 38-39 and accompanying full Prescribing Information, Medication Guide, and Instructions for Use.
### BEFORE MY INJECTION, I…

- Brought AVONEX® to room temperature
- Prepared my AVONEX using the appropriate Injection Guide
- Drank plenty of water
- Took a pain or fever reducer approved by my doctor
- Other:

### AFTER MY INJECTION, I…

- Drank plenty of water
- Took a pain or fever reducer approved by my doctor
- Rewarded myself for taking my once-weekly AVONEX
- Other:

### Injection notes:

<table>
<thead>
<tr>
<th>Site/Location of injection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outer thigh</td>
</tr>
<tr>
<td>Front thigh</td>
</tr>
<tr>
<td>Upper arm</td>
</tr>
</tbody>
</table>

**We’re here to help**

To talk to an Above MS™ Support Coordinator, call 1-800-456-2255. They can be reached Monday through Friday from 8:30 AM until 8:00 PM ET.
Date ________________ Time ________________ AM  PM

Day  S  M  T  W  T  F  S

BEFORE MY INJECTION, I…

☐ Brought AVONEX® to room temperature

☐ Prepared my AVONEX using the appropriate Injection Guide

☐ Drank plenty of water

☐ Took a pain or fever reducer approved by my doctor

☐ Other:

Injection notes:

AFTER MY INJECTION, I…

☐ Drank plenty of water

☐ Took a pain or fever reducer approved by my doctor

☐ Rewarded myself for taking my once-weekly AVONEX

☐ Other:

Other notes about this week:

Nurse Educators can provide additional support to you and your care partner with injection technique and to respond to questions related to relapsing MS and treatment. Call 1-800-456-2255 to connect with a Nurse Educator 24/7.

Please see Important Safety Information on pages 38-39 and accompanying full Prescribing Information, Medication Guide, and Instructions for Use.
BEFORE MY INJECTION, I…

- Brought AVONEX® to room temperature
- Prepared my AVONEX using the appropriate Injection Guide
- Drank plenty of water
- Took a pain or fever reducer approved by my doctor
- Other:

Injection notes:


AFTER MY INJECTION, I…

- Drank plenty of water
- Took a pain or fever reducer approved by my doctor
- Rewarded myself for taking my once-weekly AVONEX
- Other:

Other notes about this week:


We’re here to help
To talk to an Above MS™ Support Coordinator, call 1-800-456-2255. They can be reached Monday through Friday from 8:30 AM until 8:00 PM ET.

Please see Important Safety Information on pages 38-39 and accompanying full Prescribing Information, Medication Guide, and Instructions for Use.
Before my injection, I...

- Brought AVONEX® to room temperature
- Prepared my AVONEX using the appropriate Injection Guide
- Drank plenty of water
- Took a pain or fever reducer approved by my doctor
- Other:

Injection notes:

After my injection, I...

- Drank plenty of water
- Took a pain or fever reducer approved by my doctor
- Rewarded myself for taking my once-weekly AVONEX
- Other:

Other notes about this week:

Nurse Educators can provide additional support to you and your care partner with injection technique and to respond to questions related to relapsing MS and treatment. Call 1-800-456-2255 to connect with a Nurse Educator 24/7.
Before my injection, I…

- Brought AVONEX® to room temperature
- Prepared my AVONEX using the appropriate Injection Guide
- Drank plenty of water
- Took a pain or fever reducer approved by my doctor

Other:

Injection notes:

After my injection, I…

- Drank plenty of water
- Took a pain or fever reducer approved by my doctor
- Rewarded myself for taking my once-weekly AVONEX

Other:

Other notes about this week:

We’re here to help

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WEEK 11

Date_________________ Time_________________

Day S M T W T F S

BEFORE MY INJECTION, I...

☐ Brought AVONEX® to room temperature

☐ Prepared my AVONEX using the appropriate Injection Guide

☐ Drank plenty of water

☐ Took a pain or fever reducer approved by my doctor

☐ Other:

Injection notes:

__________________________________________________________

__________________________________________________________

_______________________________ __________________________

AFTER MY INJECTION, I...

☐ Drank plenty of water

☐ Took a pain or fever reducer approved by my doctor

☐ Rewarded myself for taking my once-weekly AVONEX

☐ Other:

Other notes about this week:

__________________________________________________________

__________________________________________________________

Nurse Educators can provide additional support to you and your care partner with injection technique and to respond to questions related to relapsing MS and treatment. Call 1-800-456-2255 to connect with a Nurse Educator 24/7.
### BEFORE MY INJECTION, I...

- [ ] Brought AVONEX® to room temperature
- [ ] Prepared my AVONEX using the appropriate Injection Guide
- [ ] Drank plenty of water
- [ ] Took a pain or fever reducer approved by my doctor

**Other:**
______________________________

**Injection notes:**
______________________________

### AFTER MY INJECTION, I...

- [ ] Drank plenty of water
- [ ] Took a pain or fever reducer approved by my doctor
- [ ] Rewarded myself for taking my once-weekly AVONEX

**Other:**
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**Other notes about this week:**
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**We’re here to help**

To talk to an Above MS™ Support Coordinator, call 1-800-456-2255. They can be reached Monday through Friday from 8:30 AM until 8:00 PM ET.

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Please see Important Safety Information on pages 38-39 and accompanying full Prescribing Information, Medication Guide, and Instructions for Use.
Your 3-month checkpoint

Congratulations, you’re off to a great start! You’ve completed your first 3 months of treatment with AVONEX®. This is a good point to check in and see how you are feeling.

Stay on track:

Keep these helpful tips in mind as you move beyond your first 3 months of treatment with AVONEX:

- Make the most of your doctor appointments. Bring any questions or relevant information, such as this journal, with you. Speak up if you don’t understand or if you disagree with something. Take notes to help you remember information, or consider bringing a family member or close friend with you.

Above MS™ from Biogen gives you access to Nurse Educators who are here to support you with additional injection training in your home or at another agreed-upon location. They can also follow up with your healthcare provider about your injection experience. Call 1-800-456-2255 to connect with a Nurse Educator 24/7.

Please keep in mind that your healthcare provider is always your primary resource when it comes to your relapsing MS and your treatment.

Selected Important Safety Information

The most common side effects of AVONEX are flu-like symptoms (fever, chills, muscle aches, and tiredness) early during the course of therapy. Usually, these symptoms last for a day after the injection.

Please see additional Important Safety Information on pages 38-39 and accompanying full Prescribing Information, Medication Guide, and Instructions for Use.
Questions for your doctor:

__________________________________________________________________________
__________________________________________________________________________
__________________________________________________________________________
__________________________________________________________________________
__________________________________________________________________________

Notes:

__________________________________________________________________________
__________________________________________________________________________
__________________________________________________________________________
__________________________________________________________________________
__________________________________________________________________________

Questions? You can call us Monday through Friday between 8:30 AM and 8:00 PM ET at 1-800-456-2255.

Please see Important Safety Information on pages 38-39 and accompanying full Prescribing Information, Medication Guide, and Instructions for Use.
Week 13

Date __________________ Time ___________________ AM PM

Day S M T W T F S

BEFORE MY INJECTION, I…

☐ Brought AVONEX® to room temperature

☐ Prepared my AVONEX using the appropriate Injection Guide

☐ Drank plenty of water

☐ Took a pain or fever reducer approved by my doctor

☐ Other:

Injection notes:

________________________

________________________

AFTER MY INJECTION, I…

☐ Drank plenty of water

☐ Took a pain or fever reducer approved by my doctor

☐ Rewarded myself for taking my once-weekly AVONEX

☐ Other:

Other notes about this week:

________________________

________________________

Nurse Educators can provide additional support to you and your care partner with injection technique and to respond to questions related to relapsing MS and treatment. Call 1-800-456-2255 to connect with a Nurse Educator 24/7.

Please see Important Safety Information on pages 38-39 and accompanying full Prescribing Information, Medication Guide, and Instructions for Use.
BEFORE MY INJECTION, I…

- Brought AVONEX® to room temperature
- Prepared my AVONEX using the appropriate Injection Guide
- Drank plenty of water
- Took a pain or fever reducer approved by my doctor
- Other:

Injection notes:

AFTER MY INJECTION, I…

- Drank plenty of water
- Took a pain or fever reducer approved by my doctor
- Rewarded myself for taking my once-weekly AVONEX
- Other:

Other notes about this week:

We’re here to help

To talk to an Above MS™ Support Coordinator, call 1-800-456-2255. They can be reached Monday through Friday from 8:30 AM until 8:00 PM ET.
Date ___________________ Time ___________________ AM   PM
Day S  M  T  W  T  F  S

BEFORE MY INJECTION, I...

☐ Brought AVONEX® to room temperature

☐ Prepared my AVONEX using the appropriate Injection Guide

☐ Drank plenty of water

☐ Took a pain or fever reducer approved by my doctor

☐ Other:

Injection notes:

AFTER MY INJECTION, I...

☐ Drank plenty of water

☐ Took a pain or fever reducer approved by my doctor

☐ Rewarded myself for taking my once-weekly AVONEX

☐ Other:

Other notes about this week:

Nurse Educators can provide additional support to you and your care partner with injection technique and to respond to questions related to relapsing MS and treatment. Call 1-800-456-2255 to connect with a Nurse Educator 24/7.

Please see Important Safety Information on pages 38-39 and accompanying full Prescribing Information, Medication Guide, and Instructions for Use.
BEFORE MY INJECTION, I...

- Brought AVONEX® to room temperature
- Prepared my AVONEX using the appropriate Injection Guide
- Drank plenty of water
- Took a pain or fever reducer approved by my doctor
- Other:

Injection notes:

________________________________________________________________________

AFTER MY INJECTION, I...

- Drank plenty of water
- Took a pain or fever reducer approved by my doctor
- Rewarded myself for taking my once-weekly AVONEX
- Other:

Other notes about this week:

________________________________________________________________________

We’re here to help

To talk to an Above MS™ Support Coordinator, call 1-800-456-2255. They can be reached Monday through Friday from 8:30 AM until 8:00 PM ET.

Please see Important Safety Information on pages 38-39 and accompanying full Prescribing Information, Medication Guide, and Instructions for Use.
BEFORE MY INJECTION, I…

- Brought AVONEX® to room temperature
- Prepared my AVONEX using the appropriate Injection Guide
- Drank plenty of water
- Took a pain or fever reducer approved by my doctor

Other:

Injection notes:

AFTER MY INJECTION, I…

- Drank plenty of water
- Took a pain or fever reducer approved by my doctor
- Rewarded myself for taking my once-weekly AVONEX

Other:

Other notes about this week:

Nurse Educators can provide additional support to you and your care partner with injection technique and to respond to questions related to relapsing MS and treatment. Call 1-800-456-2255 to connect with a Nurse Educator 24/7.
WEEK 18

Date _______________ Time ______________ AM  PM
Day  S  M  T  W  T  F  S

BEFORE MY INJECTION, I...

- Brought AVONEX® to room temperature
- Prepared my AVONEX using the appropriate Injection Guide
- Drank plenty of water
- Took a pain or fever reducer approved by my doctor
- Other:

Injection notes:

AFTER MY INJECTION, I...

- Drank plenty of water
- Took a pain or fever reducer approved by my doctor
- Rewarded myself for taking my once-weekly AVONEX
- Other:

Other notes about this week:

We’re here to help

To talk to an Above MS™ Support Coordinator, call 1-800-456-2255.
They can be reached Monday through Friday from 8:30 AM until 8:00 PM ET.

Please see Important Safety Information on pages 38-39 and accompanying full Prescribing Information, Medication Guide, and Instructions for Use.
BEFORE MY INJECTION, I…

- Brought AVONEX® to room temperature
- Prepared my AVONEX using the appropriate Injection Guide
- Drank plenty of water
- Took a pain or fever reducer approved by my doctor
- Other:

Injection notes:

AFTER MY INJECTION, I…

- Drank plenty of water
- Took a pain or fever reducer approved by my doctor
- Rewarded myself for taking my once-weekly AVONEX
- Other:

Other notes about this week:

Nurse Educators can provide additional support to you and your care partner with injection technique and to respond to questions related to relapsing MS and treatment. Call 1-800-456-2255 to connect with a Nurse Educator 24/7.
BEFORE MY INJECTION, I…

- Brought AVONEX® to room temperature
- Prepared my AVONEX using the appropriate Injection Guide
- Drank plenty of water
- Took a pain or fever reducer approved by my doctor
- Other:

Injection notes:

________________________

AFTER MY INJECTION, I…

- Drank plenty of water
- Took a pain or fever reducer approved by my doctor
- Rewarded myself for taking my once-weekly AVONEX
- Other:

Other notes about this week:

________________________

We’re here to help

To talk to an Above MS™ Support Coordinator, call 1-800-456-2255. They can be reached Monday through Friday from 8:30 AM until 8:00 PM ET.
BEFORE MY INJECTION, I…

☐ Brought AVONEX® to room temperature

☐ Prepared my AVONEX using the appropriate Injection Guide

☐ Drank plenty of water

☐ Took a pain or fever reducer approved by my doctor

☐ Other:

Injection notes:

AFTER MY INJECTION, I…

☐ Drank plenty of water

☐ Took a pain or fever reducer approved by my doctor

☐ Rewarded myself for taking my once-weekly AVONEX

☐ Other:

Other notes about this week:

Nurse Educators can provide additional support to you and your care partner with injection technique and to respond to questions related to relapsing MS and treatment. Call 1-800-456-2255 to connect with a Nurse Educator 24/7.
BEFORE MY INJECTION, I...

- Brought AVONEX® to room temperature
- Prepared my AVONEX using the appropriate Injection Guide
- Drank plenty of water
- Took a pain or fever reducer approved by my doctor
- Other:

Injection notes:

AFTER MY INJECTION, I...

- Drank plenty of water
- Took a pain or fever reducer approved by my doctor
- Rewarded myself for taking my once-weekly AVONEX
- Other:

Other notes about this week:

We’re here to help

To talk to an Above MS™ Support Coordinator, call 1-800-456-2255. They can be reached Monday through Friday from 8:30 AM until 8:00 PM ET.
WEEK 23

Date __________________ Time __________________ AM  PM
Day  S  M  T  W  T  F  S

BEFORE MY INJECTION, I...

☐ Brought AVONEX® to room temperature

☐ Prepared my AVONEX using the appropriate Injection Guide

☐ Drank plenty of water

☐ Took a pain or fever reducer approved by my doctor

☐ Other:

Injection notes:

AFTER MY INJECTION, I...

☐ Drank plenty of water

☐ Took a pain or fever reducer approved by my doctor

☐ Rewarded myself for taking my once-weekly AVONEX

☐ Other:

Other notes about this week:

Nurse Educators can provide additional support to you and your care partner with injection technique and to respond to questions related to relapsing MS and treatment. Call 1-800-456-2255 to connect with a Nurse Educator 24/7.

Please see Important Safety Information on pages 38-39 and accompanying full Prescribing Information, Medication Guide, and Instructions for Use.
We're here to help
To talk to an Above MS™ Support Coordinator, call 1-800-456-2255.
They can be reached Monday through Friday from 8:30 AM until 8:00 PM ET.

BEFORE MY INJECTION, I…

☐ Brought AVONEX® to room temperature
☐ Prepared my AVONEX using the appropriate Injection Guide
☐ Drank plenty of water
☐ Took a pain or fever reducer approved by my doctor
☐ Other:

Injection notes:

AFTER MY INJECTION, I…

☐ Drank plenty of water
☐ Took a pain or fever reducer approved by my doctor
☐ Rewarded myself for taking my once-weekly AVONEX
☐ Other:

Other notes about this week:

We’re here to help
To talk to an Above MS™ Support Coordinator, call 1-800-456-2255.
They can be reached Monday through Friday from 8:30 AM until 8:00 PM ET.
Your 6-month checkpoint

Congratulations, you’ve reached an important milestone!
With 6 months of AVONEX® treatment now complete, it’s a good time to check in again and see how you’re feeling.

Continue to take action against relapsing MS:

Keep the momentum going. If you haven’t already, order a new journal to continue keeping track of your weekly injections and recording your symptoms and feelings. Call 1-800-456-2255 to order a new journal.

Stay on track:

Keep these helpful tips in mind as you move beyond your first 6 months of treatment with AVONEX:

► Make the most of your doctor appointments. Bring any questions or relevant information, such as this journal, with you. Speak up if you don’t understand or if you disagree with something. Take notes to help you remember information, or consider bringing a family member or close friend with you.

Above MS™ from Biogen gives you access to Nurse Educators who are here to support you with additional injection training in your home or at another agreed-upon location. They can also follow up with your healthcare provider about your injection experience. Call 1-800-456-2255 to connect with a Nurse Educator 24/7.

Please keep in mind that your healthcare provider is always your primary resource when it comes to your relapsing MS and your treatment.
Questions for your doctor:

____________________________________________________________________________________

____________________________________________________________________________________

____________________________________________________________________________________

____________________________________________________________________________________

____________________________________________________________________________________

Notes:

____________________________________________________________________________________

____________________________________________________________________________________

____________________________________________________________________________________

____________________________________________________________________________________

____________________________________________________________________________________

Questions? You can call us Monday through Friday between 8:30 AM and 8:00 PM ET at 1-800-456-2255.

Please see Important Safety Information on pages 38-39 and accompanying full Prescribing Information, Medication Guide, and Instructions for Use.
Important contacts

**Neurologist:**
- Address:
- Phone:
- Email:

**Primary care doctor:**
- Address:
- Phone:
- Email:

**Pharmacy:**
- Phone:

**Specialty pharmacy:**
- Phone:

**Hospital:**
- Phone:

**Health insurance company:**
- Phone:

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Above MS
Phone: 1-800-456-2255
Hours: Monday through Friday
from 8:30 AM until 8:00 PM ET

Please see Important Safety Information on pages 38-39 and accompanying full Prescribing Information, Medication Guide, and Instructions for Use.
Important contacts (cont’d)

**National Multiple Sclerosis Society (NMSS)**  
Phone: 1-800-FIGHT-MS (1-800-344-4867)  
Website: NationalMSSociety.org

**Local NMSS chapter**  
Phone:  
Email:  

**Multiple Sclerosis Association of America (MSAA)**  
Phone: 1-800-532-7667  
Website: MyMSAA.org  
Email: MSquestions@mymsaa.org

**Multiple Sclerosis Foundation (MSF)**  
Phone: 1-888-MSFOCUS (1-888-673-6287)  
Website: MSFocus.org  
Email: support@msfocus.org

**Other important contacts**

**Name:**  
Address:  
Phone:  
Email:  

**Name:**  
Address:  
Phone:  
Email:  

**Name:**  
Address:  
Phone:  
Email:  

Please see Important Safety Information on pages 38-39 and accompanying full Prescribing Information, Medication Guide, and Instructions for Use.
Indication

AVONEX® (interferon beta-1a) is approved by FDA to treat relapsing forms of multiple sclerosis (MS) to decrease the number of flare-ups and slow the occurrence of some of the physical disability that is common in people with MS. AVONEX is approved for use in people who have experienced a first attack and have lesions consistent with MS on their MRI.

Important Safety Information

Do not take AVONEX if you are allergic to interferon beta, albumin (human), or any of the ingredients in AVONEX.

Before beginning treatment, you should discuss with your healthcare provider the potential benefits and risks associated with AVONEX.

AVONEX can cause serious side effects. Tell your healthcare provider right away if you have any of the symptoms listed below while taking AVONEX.

- **Behavioral health problems including depression, suicidal thoughts or hallucinations.** Some people taking AVONEX may develop mood or behavior problems including irritability (getting upset easily), depression (feeling hopeless or feeling bad about yourself), nervousness, anxiety, aggressive behavior, thoughts of hurting yourself or suicide, and hearing or seeing things that others do not hear or see (hallucinations).

- **Liver problems, or worsening of liver problems including liver failure and death.** Symptoms may include nausea, loss of appetite, tiredness, dark colored urine and pale stools, yellowing of your skin or the white part of your eye, bleeding more easily than normal, confusion, and sleepiness. During your treatment with AVONEX you will need to see your healthcare provider regularly and have regular blood tests to check for side effects.

- **Serious allergic reactions and skin reactions.** Symptoms may include itching, swelling of the face, eyes, lips, tongue or throat, trouble breathing, anxiousness, feeling faint, and skin rash, hives, sores in your mouth, or your skin blisters and peels.

AVONEX will not cure your MS but may decrease the number of flare-ups of the disease and slow the occurrence of some of the physical disability that is common in people with MS. MS is a life-long disease that affects your nervous system by destroying the protective covering (myelin) that surrounds your nerve fibers.

The way AVONEX works in MS is not known. It is not known if AVONEX is safe and effective in children.

Before taking AVONEX, tell your healthcare provider if you:

- are being treated for a mental illness, or had treatment in the past for any mental illness, including depression and suicidal behavior.

- have or had bleeding problems or blood clots, have or had low blood cell counts, have or had liver problems, have or had seizures (epilepsy), have or had heart problems, have or had thyroid problems, have or had any kind of autoimmune disease (where the body’s immune system attacks the body’s own cells), such as psoriasis, systemic lupus erythematosus, or rheumatoid arthritis.

- drink alcohol.

- are pregnant or plan to become pregnant. It is not known if AVONEX will harm your unborn baby. Tell your healthcare...
Important Safety Information (cont’d)

provider if you become pregnant during your treatment with AVONEX.

- are breastfeeding or plan to breastfeed. It is not known if AVONEX® passes into your breast milk. You and your healthcare provider should decide if you will use AVONEX or breastfeed. You should not do both.

Tell your healthcare provider about all the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements.

AVONEX can cause serious side effects including:

- Heart problems, including heart failure. While AVONEX is not known to have any direct effects on the heart, a few patients who did not have a history of heart problems developed heart muscle problems or congestive heart failure after taking AVONEX. If you already have heart failure, AVONEX may cause your heart failure to get worse. Call your healthcare provider right away if you have worsening symptoms of heart failure such as shortness of breath or swelling of your lower legs or feet while using AVONEX.
  - Some people using AVONEX may have other heart problems including low blood pressure, fast or abnormal heart beat, chest pain, and heart attack or heart muscle problem (cardiomyopathy).

- Blood problems. AVONEX can affect your bone marrow and cause low red and white blood cell, and platelet counts. In some people, these blood cell counts may fall to dangerously low levels. If your blood cell counts become very low, you can get infections and problems with bleeding and bruising.

- Seizures. Some patients have had seizures while taking AVONEX, including patients who have never had seizures before.

- Infections. Some people who take AVONEX may get an infection. Symptoms of an infection may include fever, chills, pain or burning with urination, urinating often, bloody diarrhea, and coughing up mucus.

- Thyroid problems. Some people taking AVONEX develop changes in their thyroid function. Symptoms of thyroid changes include problems concentrating, feeling cold or hot all the time, weight changes, and skin changes.

Tell your healthcare provider right away if you have any of the symptoms listed above.

The most common side effects of AVONEX include:

- Flu-like symptoms. Most people who take AVONEX have flu-like symptoms early during the course of therapy. Usually, these symptoms last for a day after the injection. You may be able to manage these flu-like symptoms by taking over-the-counter pain and fever reducers. For many people, these symptoms lessen or go away over time. Symptoms may include muscle aches, fever, tiredness, and chills.

Call your healthcare provider for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

Please see accompanying full Prescribing Information, Medication Guide, and Instructions for Use.

This information is not intended to replace discussions with your healthcare provider.
Sometimes it helps to know that you’re not alone facing relapsing MS. Your healthcare provider is your first source of information, but Biogen is also here to support you through its Above MS™ services.

Get tips, tools, and personalized assistance for your MS—and more.

Call 1-800-456-2255 to speak with a Support Coordinator. They can be reached Monday through Friday from 8:30 AM until 8:00 PM ET.

Please see Important Safety Information on pages 38-39 and accompanying full Prescribing Information, Medication Guide, and Instructions for Use.
AVONEX (interferon beta-1a) injection, for intramuscular injection

Initial U.S. Approval: 1996

AVONEX is an interferon beta indicated for the treatment of patients with relapsing forms of multiple sclerosis to slow the accumulation of physical disability and decrease the frequency of clinical exacerbations. Patients with multiple sclerosis in whom efficacy has been demonstrated include patients who have experienced a first clinical episode and have MRI features consistent with multiple sclerosis. (1)

Dosage and Administration

For intramuscular use only (2.1)

Recommended dose: 30 micrograms once a week (2.1)

AVONEX may be titrated, starting with 7.5 micrograms for first week, to reduce flu-like symptoms (2.1)

Increase dose by 7.5 micrograms each week for next 3 weeks until recommended dose of 30 micrograms (2.1)

See patient instructions for use for complete administration instructions (2.2)

Perform first injection under the supervision of an appropriately qualified health care professional (2.2)

Premedication for Flu-like Symptoms

Analgesics and/or antipyretics on treatment days may help ameliorate flu-like symptoms (2.3)

Dosage Forms and Strengths

For Injection: 30 micrograms lyophilized powder in a single-use vial (3)

Injection: 30 micrograms per 0.5 mL solution in single-use prefilled syringe (3)

Injection: Single-use prefilled autoinjector containing 0.5 mL solution with 30 mcg (3)

Warnings and Precautions

Thrombotic Microangiopathy (5.6) - Cases of thrombotic microangiopathy have been reported. Discontinue AVONEX if clinical symptoms and laboratory findings consistent with TMA occur (5.6)

Autoimmune Disorders: consider discontinuation of AVONEX if new autoimmune disorder occurs (5.8, 5.9)

Contraindications

History of hypersensitivity to natural or recombinant interferon beta, albumin or any other component of the formulation (4)

Depression, Suicide, and Psychotic Disorders: advise patients to immediately report any symptoms of depression, suicidal ideation, and/or psychosis; consider discontinuation of AVONEX if depression occurs (5.1)

Hepatic Injury: monitor liver function tests; monitor patients for signs and symptoms of hepatic injury; consider discontinuation of AVONEX if hepatic injury occurs (5.2, 5.9)

Anaphylaxis and Other Allergic-Reactions: Discontinue if occurs (5.3)

Congestive Heart Failure: monitor patients with pre-existing significant cardiac disease for worsening of cardiac symptoms (5.4)

Decreased Peripheral Blood Counts: monitor complete blood count (5.5, 5.9)

Thrombotic Microangiopathy: Cases of thrombotic microangiopathy have been reported. Discontinue AVONEX if clinical symptoms and laboratory findings consistent with TMA occur (5.6)

Autoimmune Disorders: consider discontinuation of AVONEX if new autoimmune disorder occurs (5.8, 5.9)

Adverse Reactions

The most common adverse reactions (at least 5% more frequent on AVONEX than on placebo) were flu-like symptoms including chills, fever, myalgia, and asthenia. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Biogen at 1-800-456-2255 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Use in Specific Populations

Pregnancy: Based on animal data, may cause fetal harm (8.1)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Full Prescribing Information: Contents

1 Indications and Usage

2 Dosage and Administration

2.1 Dosing Information

2.1.1 Important Administration Instructions (All Dosage Forms)

2.2 Premedication for Flu-like Symptoms

3 Dosage Forms and Strengths

4 Contraindications

5 Warnings and Precautions

5.1 Depression, Suicide, and Psychotic Disorders

5.2 Hepatic Injury

5.3 Anaphylaxis and Other Allergic-Reactions

5.4 Congestive Heart Failure

5.5 Decreased Peripheral Blood Counts

5.6 Thrombotic Microangiopathy

5.7 Seizures

5.8 Autoimmune Disorders

5.9 Laboratory Tests

6 Adverse Reactions

6.1 Clinical Trials Experience

6.2 Postmarketing Experience

8 Use in Specific Populations

8.1 Pregnancy

8.2 Nursing Mothers

8.3 Pediatric Use

8.4 Geriatric Use

*Sections or subsections omitted from the Full Prescribing Information are not listed.
AVONEX® (interferon beta-1a) Intramuscular Injection

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

AVONEX (interferon beta-1a) is indicated for the treatment of patients with relapsing forms of multiple sclerosis to slow the accumulation of physical disability and decrease the frequency of clinical exacerbations. Patients with multiple sclerosis in whom efficacy has been demonstrated include patients who have experienced a first clinical episode and have MRI features consistent with multiple sclerosis.

2 DOSAGE AND ADMINISTRATION

2.1 Dosing Information

AVONEX is administered intramuscularly.

The recommended dose is 30 micrograms once a week. To reduce the incidence and severity of flu-like symptoms that may occur when initiating AVONEX therapy at a dose of 30 micrograms, AVONEX may be started at a dose of 7.5 micrograms and the dose may be increased by 7.5 micrograms each week for the next three weeks until the recommended dose of 30 micrograms is achieved (see Table 1). An AVOSTARTGRIP™ kit containing 3 titration devices can be used for titration and is to be used only with AVONEX Prefilled Syringes.

Table 1: Schedule for Dose Titration

<table>
<thead>
<tr>
<th>Week</th>
<th>AVONEX Dose</th>
<th>Recommended Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7.5 micrograms</td>
<td>1/4 dose</td>
</tr>
<tr>
<td>2</td>
<td>15 micrograms</td>
<td>1/2 dose</td>
</tr>
<tr>
<td>3</td>
<td>22.5 micrograms</td>
<td>3/4 dose</td>
</tr>
<tr>
<td>4+</td>
<td>30 micrograms</td>
<td>full dose</td>
</tr>
</tbody>
</table>

*Dosed once a week, intramuscularly

2.2 Important Administration Instructions (All Dosage Forms)

All AVONEX dosage forms are single-use (injection of reconstituted solution, prefilled syringe, and prefilled autoinjector). See Patient’s Instructions for Use for complete administration instructions.

The first AVONEX injection should be performed under the supervision of an appropriately qualified healthcare professional. If patients or caregivers are to administer AVONEX, train them in the proper intramuscular injection technique and assess their ability to inject intramuscularly to ensure the proper administration of AVONEX.

Advise patients and caregivers to:
- Rotate sites for intramuscular injections with each injection to minimize the likelihood of injection site reactions
- NOT inject into an area of the body where the skin is irritated, reddened, bruised,
Check the injection site after 2 hours for redness, swelling, or tenderness
Contact their healthcare provider if they have a skin reaction and it does not clear up in a few days

A 25 gauge, 1” needle for intramuscular injection with AVONEX prefilled syringe or injection of reconstituted solution may be substituted for the 23 gauge, 1 ¼” needle by the healthcare provider, if deemed appropriate. A 25 gauge, 5/8” needle specific to the prefilled autoinjector is supplied with the AVONEX PEN® Administration Dose Pack. DO NOT use any other needle with the autoinjector.

Use safe disposal procedures for needles and syringes. Do not re-use needles, syringes, prefilled syringes, or autoinjectors. Following the administration of each titrated dose, discard any remaining product.

2.3 Premedication for Flu-like Symptoms

Concurrent use of analgesics and/or antipyretics on treatment days may help ameliorate flu-like symptoms associated with AVONEX use.

3 DOSAGE FORMS AND STRENGTHS

- For injection: 30 micrograms lyophilized powder in a single-use vial
- Injection: 30 micrograms per 0.5 mL solution in a single-use prefilled syringe
- Injection: 30 micrograms per 0.5 mL solution in a single-use prefilled autoinjector

4 CONTRAINDICATIONS

AVONEX is contraindicated in patients with a history of hypersensitivity to natural or recombinant interferon beta, or any other component of the formulation [see Warnings and Precautions (5.3)].

The lyophilized vial formulation of AVONEX is contraindicated in patients with a history of hypersensitivity to albumin (human).

5 WARNINGS AND PRECAUTIONS

5.1 Depression, Suicide, and Psychotic Disorders

Patients treated with AVONEX and their caregivers should be advised to report immediately any symptoms of depression, suicidal ideation, and/or psychosis to their prescribing physicians. If a patient develops depression or other severe psychiatric symptoms, cessation of AVONEX therapy should be considered.

Depression and suicide have been reported to occur with increased frequency in patients receiving AVONEX. In Study 1, the incidence of depression was similar in placebo-treated and in AVONEX-treated patients, but suicidal tendency was seen more frequently in AVONEX-treated patients (4% in AVONEX group vs. 1% in placebo group). In Study 2, there was a greater incidence of depression in AVONEX-treated patients than in placebo-treated patients (20% in AVONEX group vs. 13% in placebo group) [see Clinical Studies (14)].
Additionally, there have been postmarketing reports of depression, suicidal ideation, and/or
development of new or worsening of other pre-existing psychiatric disorders, including
psychosis. For some of these patients, symptoms of depression improved upon cessation of
AVONEX.

5.2 Hepatic Injury

Severe hepatic injury, including cases of hepatic failure, has been reported rarely in patients
taking AVONEX. Asymptomatic elevation of hepatic transaminases has also been reported,
and in some patients has recurred upon rechallenge with AVONEX. In some cases, these
events have occurred in the presence of other drugs that have been associated with hepatic
injury. The potential risk of AVONEX used in combination with known hepatotoxic drugs or
other products (e.g., alcohol) should be considered prior to starting AVONEX, or before starting
hepatotoxic drugs. Patients should be monitored for signs of hepatic injury [see Warnings and
Precautions (5.9)].

5.3 Anaphylaxis and Other Allergic-Reactions

Anaphylaxis has been reported as a rare complication of AVONEX use. Other allergic reactions
have included dyspnea, orolingual edema, skin rash and urticaria. Discontinue AVONEX if
anaphylaxis or other allergic reactions occur.

5.4 Congestive Heart Failure

Patients with pre-existing congestive heart failure should be monitored for worsening of their
cardiac condition during initiation of and continued treatment with AVONEX. While beta
interferons do not have any known direct cardiac toxicity, during the postmarketing period cases
of congestive heart failure, cardiomyopathy, and cardiomyopathy with congestive heart failure
have been reported in patients without known predisposition to these events, and without other
etiologies being established. In some cases, these events have been temporally related to the
administration of AVONEX. In some of these instances recurrence upon rechallenge was
observed.

5.5 Decreased Peripheral Blood Counts

Decreased peripheral blood counts in all cell lines, including rare pancytopenia and
thrombocytopenia, have been reported from postmarketing experience in AVONEX-treated
patients [see Adverse Reactions (6.2)]. In some cases, platelet counts were below
10,000/microliter. Some cases recurred with rechallenge [see Adverse Reactions (6.2)].
Patients should be monitored for symptoms or signs of decreased blood counts.

5.6 Thrombotic Microangiopathy

Cases of thrombotic microangiopathy (TMA), including thrombotic thrombocytopenic
purpura and hemolytic uremic syndrome, some fatal, have been reported with interferon
beta products, including AVONEX. Cases have been reported several weeks to years
after starting interferon beta products. Discontinue AVONEX if clinical symptoms and
laboratory findings consistent with TMA occur, and manage as clinically indicated.
5.7 Seizures

Seizures have been temporally associated with the use of beta interferons in clinical trials and postmarketing safety surveillance. In the two placebo-controlled studies in multiple sclerosis (Studies 1 and 2), 4 patients receiving AVONEX experienced seizures, while no seizures occurred in the placebo group [see Clinical Studies (14)]. Three of these 4 patients had no prior history of seizure [see Adverse Reactions (6.1)]. It is not known whether these events were related to the effects of multiple sclerosis alone, to AVONEX, or to a combination of both.

5.8 Autoimmune Disorders

Postmarketing reports of autoimmune disorders of multiple target organs in AVONEX-treated patients included idiopathic thrombocytopenia, hyper- and hypothyroidism, and rare cases of autoimmune hepatitis. If AVONEX-treated patients develop a new autoimmune disorder, consider stopping the therapy.

5.9 Laboratory Tests

In addition to those laboratory tests normally required for monitoring patients with multiple sclerosis, complete blood and differential white blood cell counts, platelet counts, and blood chemistries, including liver function tests, are recommended during AVONEX therapy [see Warnings and Precautions (5.2, 5.5, 5.8)]. Patients with myelosuppression may require more intensive monitoring of complete blood cell counts, with differential and platelet counts. Thyroid function should be monitored periodically. If patients have or develop symptoms of thyroid dysfunction (hypo- or hyperthyroidism), thyroid function tests should be performed according to standard medical practice.

6 ADVERSE REACTIONS

The following serious adverse reactions are discussed in more detail in other sections of labeling:

- Depression, Suicide, and Psychotic Disorders [see Warnings and Precautions (5.1)]
- Hepatic Injury [see Warnings and Precautions (5.2)]
- Anaphylaxis and Other Allergic-Reactions [see Warnings and Precautions (5.3)]
- Congestive Heart Failure [see Warnings and Precautions (5.4)]
- Decreased Peripheral Blood Counts [see Warnings and Precautions (5.5)]
- Thrombotic Microangiopathy [see Warnings and Precautions (5.6)]
- Seizures [see Warnings and Precautions (5.7)]
- Autoimmune Disorders [see Warnings and Precautions (5.8)]
- Laboratory Tests [see Warnings and Precautions (5.9)]

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of AVONEX cannot be directly compared to rates in clinical trials of other drugs and may not reflect the rates observed in practice.

Among 351 patients with relapsing forms of MS treated with AVONEX 30 micrograms (including 319 patients treated for 6 months and 288 patients treated for greater than one year) the most commonly reported adverse reactions (at least 5% more frequent on AVONEX than on placebo)
were flu-like symptoms. Symptoms can include chills, fever, myalgia and asthenia occurring within hours to days following an injection. Most people who take AVONEX have flu-like symptoms early during the course of therapy. Usually, these symptoms last for a day after the injection. For many people, these symptoms lessen or go away over time. The most frequently reported adverse reactions resulting in clinical intervention (for example, discontinuation of AVONEX or the need for concomitant medication to treat an adverse reaction symptom) were flu-like symptoms and depression.

Table 2 enumerates adverse reactions that occurred with AVONEX-treated patients at an incidence of at least 2% more than that observed in the placebo-treated patients in the pooled placebo-controlled studies in patients with relapsing forms of MS [see Clinical Studies (14)].
<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>Placebo (N = 333)</th>
<th>AVONEX (N = 351)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Body as a Whole</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>55%</td>
<td>58%</td>
</tr>
<tr>
<td>Flu-like symptoms (otherwise unspecified)</td>
<td>29%</td>
<td>49%</td>
</tr>
<tr>
<td>Pain</td>
<td>21%</td>
<td>23%</td>
</tr>
<tr>
<td>Asthenia</td>
<td>18%</td>
<td>24%</td>
</tr>
<tr>
<td>Fever</td>
<td>9%</td>
<td>20%</td>
</tr>
<tr>
<td>Chills</td>
<td>5%</td>
<td>19%</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>6%</td>
<td>8%</td>
</tr>
<tr>
<td>Injection site pain</td>
<td>6%</td>
<td>8%</td>
</tr>
<tr>
<td>Infection</td>
<td>4%</td>
<td>7%</td>
</tr>
<tr>
<td>Injection site inflammation</td>
<td>2%</td>
<td>6%</td>
</tr>
<tr>
<td>Chest pain</td>
<td>2%</td>
<td>5%</td>
</tr>
<tr>
<td>Injection site reaction</td>
<td>1%</td>
<td>3%</td>
</tr>
<tr>
<td>Toothache</td>
<td>1%</td>
<td>3%</td>
</tr>
<tr>
<td><strong>Nervous System</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depression</td>
<td>14%</td>
<td>18%</td>
</tr>
<tr>
<td>Dizziness</td>
<td>12%</td>
<td>14%</td>
</tr>
<tr>
<td><strong>Respiratory System</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper respiratory tract infection</td>
<td>12%</td>
<td>14%</td>
</tr>
<tr>
<td>Sinusitis</td>
<td>12%</td>
<td>14%</td>
</tr>
<tr>
<td>Bronchitis</td>
<td>5%</td>
<td>8%</td>
</tr>
<tr>
<td><strong>Digestive System</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>19%</td>
<td>23%</td>
</tr>
<tr>
<td><strong>Musculoskeletal System</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myalgia</td>
<td>22%</td>
<td>29%</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>6%</td>
<td>9%</td>
</tr>
<tr>
<td><strong>Urogenital</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>15%</td>
<td>17%</td>
</tr>
<tr>
<td>Urine constituents abnormal</td>
<td>0%</td>
<td>3%</td>
</tr>
<tr>
<td><strong>Skin and Appendages</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alopecia</td>
<td>2%</td>
<td>4%</td>
</tr>
<tr>
<td><strong>Special Senses</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eye disorder</td>
<td>2%</td>
<td>4%</td>
</tr>
<tr>
<td><strong>Hemic and Lymphatic System</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Injection site ecchymosis</td>
<td>4%</td>
<td>6%</td>
</tr>
<tr>
<td>Anemia</td>
<td>1%</td>
<td>4%</td>
</tr>
<tr>
<td><strong>Cardiovascular System</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Migraine</td>
<td>3%</td>
<td>5%</td>
</tr>
<tr>
<td>Vasodilation</td>
<td>0%</td>
<td>2%</td>
</tr>
</tbody>
</table>
**Immunogenicity**

Anaphylaxis and other allergic reactions have occurred in AVONEX-treated patients [see Warnings and Precautions (5.3)]. As with all therapeutic proteins, there is a potential for immunogenicity. In studies assessing immunogenicity in multiple sclerosis patients administered AVONEX for at least 1 year, 5% (21 of 390 patients) showed the presence of neutralizing antibodies at one or more times.

These data reflect the percentage of patients whose test results were considered positive for antibodies to AVONEX using a two-tiered assay (ELISA binding assay followed by an antiviral cytopathic effect assay), and are highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of neutralizing activity in an assay may be influenced by several factors including sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to AVONEX with the incidence of antibodies to other products may be misleading.

### 6.2 Postmarketing Experience

The following additional adverse reactions have been identified during post-approval use of AVONEX. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

- Menorrhagia and metrorrhagia
- Rash (including vesicular rash)
- Rare cases of injection site abscess or cellulitis requiring surgical intervention

### 8 USE IN SPECIFIC POPULATIONS

#### 8.1 Pregnancy

*Pregnancy Category C:* There are no adequate and well-controlled studies in pregnant women. AVONEX should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

In pregnant monkeys given interferon beta at 100 times the recommended weekly human dose (based upon a body surface area [mg/m²] comparison), no teratogenic or other adverse effects on fetal development were observed. Abortifacient activity was evident following 3 to 5 doses at this level. No abortifacient effects were observed in monkeys treated at 2 times the recommended weekly human dose (based upon mg/m²).

#### 8.3 Nursing Mothers

It is not known whether AVONEX is excreted in human milk.

#### 8.4 Pediatric Use

Safety and effectiveness in pediatric patients have not been established.
8.5 Geriatric Use

Clinical studies of AVONEX did not include sufficient numbers of patients aged 65 and over to determine whether they respond differently than younger patients.

11 DESCRIPTION

AVONEX is a 166 amino acid glycoprotein with a molecular weight of approximately 22,500 daltons. It is produced by recombinant DNA technology using genetically engineered Chinese Hamster Ovary cells into which the human interferon beta gene has been introduced. The amino acid sequence of AVONEX is identical to that of natural human interferon beta.

Using the World Health Organization (WHO) International Standard for Interferon, AVONEX has a specific activity of approximately 200 million international units of antiviral activity per mg of interferon beta-1a determined specifically by an in vitro cytopathic effect bioassay using lung carcinoma cells (A549) and Encephalomyocarditis virus (ECM). AVONEX 30 micrograms contains approximately 6 million international units of antiviral activity using this method. The activity against other standards is not known. Comparison of the activity of AVONEX with other interferon betas is not appropriate, because of differences in the reference standards and assays used to measure activity.

11.1 AVONEX Lyophilized Powder Vial

A vial of AVONEX is a sterile, white to off-white lyophilized powder for intramuscular injection after reconstitution with supplied diluent (Sterile Water for Injection, USP). Each vial of reconstituted AVONEX contains 30 micrograms of interferon beta-1a; 15 mg Albumin (Human), USP; 5.8 mg Sodium Chloride, USP; 5.7 mg Dibasic Sodium Phosphate, USP; and 1.2 mg Monobasic Sodium Phosphate, USP, in 1.0 mL at a pH of approximately 7.3.

11.2 AVONEX Single-Use Prefilled Syringe

A prefilled syringe of AVONEX is a sterile liquid for intramuscular injection. Each 0.5 mL (30 microgram dose) of AVONEX in a prefilled glass syringe contains 30 micrograms of interferon beta-1a, 0.79 mg Sodium Acetate Trihydrate, USP; 0.25 mg Glacial Acetic Acid, USP; 15.8 mg Arginine Hydrochloride, USP; and 0.025 mg Polysorbate 20 in Water for Injection, USP at a pH of approximately 4.8.

11.3 AVONEX PEN Single-Use Prefilled Autoinjector

AVONEX PEN is a sterile liquid for intramuscular injection in a prefilled glass syringe surrounded by an autoinjector. Each 0.5 mL (30 microgram dose) in the AVONEX PEN contains 30 micrograms of interferon beta-1a, 0.79 mg Sodium Acetate Trihydrate, USP; 0.25 mg Glacial Acetic Acid, USP; 15.8 mg Arginine Hydrochloride, USP; and 0.025 mg Polysorbate 20 in Water for Injection, USP at a pH of approximately 4.8.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action
The mechanism of action by which AVONEX exerts its effects in patients with multiple sclerosis is unknown.

12.2 Pharmacodynamics

Interferons (IFNs) are a family of naturally occurring proteins, produced by eukaryotic cells in response to viral infection and other biologic agents. Three major types of interferons have been defined: type I (IFN-alpha, beta, epsilon, kappa and omega), type II (IFN–gamma) and type III (IFN-lambda). Interferon-beta is a member of the type I subset of interferons. The type I interferons have considerably overlapping but also distinct biologic activities. The bioactivities of all IFNs, including IFN-beta, are induced via their binding to specific receptors on the membranes of human cells. Differences in the bioactivities induced by the three major subtypes of IFNs likely reflect differences in the signal transduction pathways induced by signaling through their cognate receptors.

Interferon beta exerts its biological effects by binding to specific receptors on the surface of human cells. This binding initiates a complex cascade of intracellular events that leads to the expression of numerous interferon-induced gene products and markers. These include 2', 5'-oligoadenylate synthetase, β2-microglobulin, and neopterin. These products have been measured in the serum and cellular fractions of blood collected from patients treated with AVONEX.

Clinical studies conducted in multiple sclerosis patients showed that interleukin 10 (IL-10) levels in cerebrospinal fluid were increased in patients treated with AVONEX compared to placebo. Serum IL-10 levels maximally were increased by 48 hours after intramuscular injection of AVONEX and remained elevated for 1 week. However, no relationship has been established between absolute levels of IL-10 and clinical outcome in multiple sclerosis.

12.3 Pharmacokinetics

Pharmacokinetics of AVONEX in multiple sclerosis patients have not been evaluated. The pharmacokinetic and pharmacodynamic profiles of AVONEX in healthy subjects following doses of 30 micrograms through 75 micrograms have been investigated. Serum levels of AVONEX as measured by antiviral activity are slightly above detectable limits following a 30 microgram intramuscular dose, and increase with higher doses.

After an intramuscular dose, serum levels of AVONEX generally peak at 15 hours post-dose (range: 6-36 hours) and then decline at a rate consistent with a 19 (range: 8-54) hour elimination half-life.

Subcutaneous administration of AVONEX should not be substituted for intramuscular administration as there is no data establishing that subcutaneous and intramuscular administration of AVONEX result in equivalent pharmacokinetic and pharmacodynamic parameters.

Biological response markers (e.g., neopterin and β2-microglobulin) are induced by AVONEX following parenteral doses of 15 micrograms through 75 micrograms in healthy subjects and treated patients. Biological response marker levels increase within 12 hours of dosing and remain elevated for at least 4 days. Peak biological response marker levels are typically observed 48 hours after dosing. The relationship of serum AVONEX levels or levels of these
induced biological response markers to the mechanisms by which AVONEX exerts its effects in multiple sclerosis is unknown.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, and Impairment of Fertility

Carcinogenesis: The carcinogenic potential of AVONEX has not been tested in animals.

Mutagenesis: Interferon beta was not mutagenic when tested in an in vitro bacterial reverse mutation (Ames) test or in an in vitro cytogenetic assay in human lymphocytes.

Impairment of Fertility: In monkeys administered interferon beta by subcutaneous injection (8 to 15 doses of 1.25 mcg/kg or 50 mcg/kg) over the course of one menstrual cycle, menstrual irregularities, anovulation, and decreased serum progesterone levels were observed at the higher dose. These effects were reversible after discontinuation of drug. The no-effect dose (1.25 mcg/kg) is approximately 2 times the recommended weekly dose in humans (30 mcg) on a mg/m² basis.

14 CLINICAL STUDIES

The clinical effects of AVONEX in patients with relapsing forms of multiple sclerosis (MS) were studied in two randomized, multicenter, double-blind, placebo-controlled studies in patients with MS (Studies 1 and 2). Safety and efficacy of treatment with AVONEX beyond 3 years is not known.

In Study 1, 301 patients received either 30 micrograms of AVONEX (n=158) or placebo (n=143) by intramuscular injection once weekly. Patients received injections for up to 2 years, and continued to be followed until study completion. Two hundred eighty-two patients completed 1 year on study, and 172 patients completed 2 years on study. There were 144 patients treated with AVONEX for more than 1 year, 115 patients for more than 18 months and 82 patients for 2 years.

All patients had a definite diagnosis of multiple sclerosis of at least 1 year duration and had at least 2 exacerbations in the 3 years prior to study entry (or 1 per year if the duration of disease was less than 3 years). At entry, study participants were without exacerbation during the prior 2 months and had Kurtzke Expanded Disability Status Scale (EDSS³) scores ranging from 1.0 to 3.5. The EDSS is a scale that quantifies disability in patients with MS and ranges from 0 (normal neurologic exam) to 10 (death due to MS). Patients with chronic progressive multiple sclerosis were excluded from this study.

Disability
The primary outcome assessment was time to progression in disability, measured as an increase in the EDSS score of at least 1 point that was sustained for at least 6 months. An increase in EDSS score reflects accumulation of disability. This endpoint was used to help distinguish permanent increase in disability from a transient increase due to an exacerbation.

As shown in Figure 1, the time to onset of sustained progression in disability was significantly longer in AVONEX-treated patients than in placebo-treated patients in Study 1 (p = 0.02). The percentage of patients progressing by the end of 2 years was 35% for placebo-treated patients
and 22% for AVONEX-treated patients. This represents a 37% relative reduction in the risk of accumulating disability in the AVONEX-treated group compared to the placebo-treated group.

Figure 1: Time to Onset of Sustained Disability Progression in Patients with MS in Study 1

1Kaplan-Meier Methodology; Disability progression was defined as at least a 1 point increase in EDSS score sustained for at least 6 months.

The distribution of confirmed EDSS change from study entry (baseline) to the end of the study is shown in Figure 2. There was a statistically significant difference between the AVONEX and placebo groups in confirmed change for patients with at least 2 scheduled visits (p = 0.006).
**Exacerbations**
The rate and frequency of MS exacerbations were secondary outcomes. For all patients included in the study, irrespective of time on study, the annual exacerbation rate was 0.67 per year in the AVONEX-treated group and 0.82 per year in the placebo-treated group (p = 0.04).

AVONEX treatment significantly decreased the frequency of exacerbations in the subset of patients who were enrolled in the study for at least 2 years (87 placebo-treated patients and 85 AVONEX-treated patients; p = 0.03; see Table 3).

**MRI Results**
Gadolinium (Gd)-enhanced and T2-weighted magnetic resonance imaging (MRI) scans of the brain were obtained in most patients at baseline and at the end of 1 and 2 years of treatment. Secondary outcomes included Gd-enhanced lesion number and volume, and T2-weighted lesion volume. Gd-enhancing lesions seen on brain MRI scans represent areas of breakdown of the blood brain barrier thought to be secondary to inflammation. AVONEX-treated patients demonstrated significantly lower Gd-enhanced lesion number after 1 and 2 years of treatment than placebo-treated patients (p ≤ 0.05; see Table 3). The volume of Gd-enhanced lesions showed similar treatment effects in the AVONEX and placebo groups (p ≤ 0.03). Percentage change in T2-weighted lesion volume from study entry to Year 1 was significantly lower in AVONEX-treated than placebo-treated patients (p = 0.02). A significant difference in T2-weighted lesion volume change was not seen between study entry and Year 2 in the AVONEX and placebo groups.
The exact relationship between MRI findings and the clinical status of MS patients is unknown. The prognostic significance of MRI findings in these studies has not been evaluated.

**Summary of Effects of Clinical and MRI Endpoints in Study 1**

A summary of the effects of AVONEX on the clinical and MRI endpoints of this study is presented in **Table 3**.

**Table 3: Clinical and MRI Endpoints in Patients with MS in Study 1**

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Placebo</th>
<th>AVONEX</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PRIMARY ENDPOINT:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time to sustained progression in disability (N: 143, 158)¹</td>
<td>--- See Figure 1 ---</td>
<td></td>
<td>0.02²</td>
</tr>
<tr>
<td>Percentage of patients progressing in disability at 2 years (Kaplan-Meier estimate)¹</td>
<td>35%</td>
<td>22%</td>
<td></td>
</tr>
<tr>
<td><strong>SECONDARY ENDPOINTS:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>DISABILITY</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean confirmed change in EDSS from study entry to end of study (N: 136, 150)¹</td>
<td>0.50</td>
<td>0.20</td>
<td>0.006³</td>
</tr>
<tr>
<td><strong>EXACERBATIONS</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of exacerbations in subset completing 2 years (N: 87, 85)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>26%</td>
<td>38%</td>
<td>0.03³</td>
</tr>
<tr>
<td>1</td>
<td>30%</td>
<td>31%</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>11%</td>
<td>18%</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>14%</td>
<td>7%</td>
<td></td>
</tr>
<tr>
<td>≥ 4</td>
<td>18%</td>
<td>7%</td>
<td></td>
</tr>
<tr>
<td>Percentage of patients exacerbation-free in subset completing 2 years (N: 87, 85)</td>
<td>26%</td>
<td>38%</td>
<td>0.10⁴</td>
</tr>
<tr>
<td>Annual exacerbation rate (N: 143, 158)¹</td>
<td>0.82</td>
<td>0.67</td>
<td>0.04⁵</td>
</tr>
</tbody>
</table>
Table 3 (continued): Clinical and MRI Endpoints in Study 1

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Placebo</th>
<th>AVONEX</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MRI</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of Gd-enhanced lesions:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At study entry (N: 132, 141)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (Median)</td>
<td>2.3 (1.0)</td>
<td>3.2 (1.0)</td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>0-23</td>
<td>0-56</td>
<td></td>
</tr>
<tr>
<td>Year 1 (N: 123, 134)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (Median)</td>
<td>1.6 (0)</td>
<td>1.0 (0)</td>
<td>0.02³</td>
</tr>
<tr>
<td>Range</td>
<td>0-22</td>
<td>0-28</td>
<td></td>
</tr>
<tr>
<td>Year 2 (N: 82, 83)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (Median)</td>
<td>1.6 (0)</td>
<td>0.8 (0)</td>
<td>0.05³</td>
</tr>
<tr>
<td>Range</td>
<td>0-34</td>
<td>0-13</td>
<td></td>
</tr>
<tr>
<td>T2 lesion volume:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percentage change from study entry to Year 1 (N: 116, 123)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>-3.3%</td>
<td>-13.1%</td>
<td>0.02³</td>
</tr>
<tr>
<td>Percentage change from study entry to Year 2 (N: 83, 81)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>-6.5%</td>
<td>-13.2%</td>
<td>0.36³</td>
</tr>
</tbody>
</table>

Note: *(N: , ) denotes the number of evaluable placebo and AVONEX patients, respectively.*
³Patient data included in this analysis represent variable periods of time on study.
³Analyzed by Mantel-Cox (logrank) test.
³Analyzed by Mann-Whitney rank-sum test.
³Analyzed by Cochran-Mantel-Haenszel test.
³Analyzed by likelihood ratio test.

In Study 2, 383 patients who had recently experienced an isolated demyelinating event involving the optic nerve, spinal cord, or brainstem/cerebellum, and who had lesions typical of multiple sclerosis on brain MRI, received either 30 micrograms of AVONEX *(n = 193)* or placebo *(n = 190)* by intramuscular injection once weekly. Patients were enrolled into the study over a two-year period and followed for up to three years or until they developed a second clinical exacerbation in an anatomically distinct region of the central nervous system.

Exacerbations
In Study 2, the primary outcome measure was time to development of a second exacerbation in an anatomically distinct region of the central nervous system. Time to development of a second exacerbation was significantly delayed in AVONEX-treated compared to placebo-treated patients *(p = 0.002)*. The Kaplan-Meier estimates of the percentage of patients developing an exacerbation within 24 months were 39% in the placebo group and 21% in the AVONEX group (see Figure 3). The relative rate of developing a second exacerbation in the AVONEX group was 0.56 of the rate in the placebo group (95% confidence interval 0.38 to 0.81).
**MRI Findings**

Secondary outcomes were brain MRI measures, including the cumulative increase in the number of new or enlarging T2 lesions, T2 lesion volume at baseline compared to results at 18 months, and the number of Gd-enhancing lesions at 6 months. See Table 4 for the MRI results.
Table 4: Brain MRI Results in Study 2

<table>
<thead>
<tr>
<th></th>
<th>AVONEX</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHANGE FROM BASELINE IN T2</td>
<td>N = 119</td>
<td>N = 109</td>
</tr>
<tr>
<td>VOLUME OF LESIONS AT 18 MONTHS:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Actual Change (mm$^3$)$^{1*}$</td>
<td>Median (25th%, 75th%)</td>
<td>28 (-576, 397)</td>
</tr>
<tr>
<td>Percentage Change$^{1*}$</td>
<td>Median (25th%, 75th%)</td>
<td>1 (-24, 29)</td>
</tr>
</tbody>
</table>

NUMBER OF NEW OR ENLARGING T2 LESIONS AT 18 MONTHS$^{1}$:

<table>
<thead>
<tr>
<th></th>
<th>N = 132</th>
<th>N = 119</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>62 (47)</td>
<td>22 (18)</td>
</tr>
<tr>
<td>1-3</td>
<td>41 (31)</td>
<td>47 (40)</td>
</tr>
<tr>
<td>&gt;4</td>
<td>29 (22)</td>
<td>50 (42)</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>2.13 (3.2)</td>
<td>4.97 (7.7)</td>
</tr>
</tbody>
</table>

NUMBER OF GD-ENHANCING LESIONS AT 6 MONTHS$^{2}$:

<table>
<thead>
<tr>
<th></th>
<th>N = 165</th>
<th>N = 152</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>115 (70)</td>
<td>93 (61)</td>
</tr>
<tr>
<td>1</td>
<td>27 (16)</td>
<td>16 (11)</td>
</tr>
<tr>
<td>&gt;1</td>
<td>23 (14)</td>
<td>43 (28)</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>0.87 (2.3)</td>
<td>1.49 (3.1)</td>
</tr>
</tbody>
</table>

1 $P$ value <0.001
2 $P$ value <0.03
* $P$ value from a Mann-Whitney rank-sum test

16 HOW SUPPLIED/STORAGE AND HANDLING

16.1 AVONEX Lyophilized Powder Vial

A vial of AVONEX is supplied as a lyophilized powder in a single-use vial containing 33 micrograms (6.6 million international units) of interferon beta-1a; 16.5 mg Albumin (Human), USP; 6.4 mg Sodium Chloride, USP; 6.3 mg Dibasic Sodium Phosphate, USP; and 1.3 mg Monobasic Sodium Phosphate, USP, and is preservative-free. Diluent is supplied in a single-use vial (Sterile Water for Injection, USP).

AVONEX lyophilized vials are available in the following package configuration (NDC 59627-111-03): A package containing four Administration Dose Packs (each containing one vial of AVONEX, one 10 mL diluent vial, two alcohol wipes, one gauze pad, one 3 mL syringe, one MICRO PIN® vial access pin, one 23 gauge, 1¼ inch needle, and one adhesive bandage).

Vials of AVONEX should be stored in a 2°C to 8°C (36°F to 46°F) refrigerator. Should refrigeration be unavailable, vials of AVONEX can be stored at 25°C (77°F) for a period of up to 30 days. DO NOT EXPOSE TO HIGH TEMPERATURES. DO NOT FREEZE. Protect from light. Do not use beyond the expiration date stamped on the vial. Following reconstitution, it is
recommended the product be used as soon as possible within 6 hours stored at 2°C to 8°C (36°F to 46°F). DO NOT FREEZE RECONSTITUTED AVONEX.

16.2 AVONEX Single-Use Prefilled Syringe

A prefilled syringe of AVONEX is supplied as a sterile liquid albumin-free formulation containing 30 micrograms of interferon beta-1a, 0.79 mg Sodium Acetate Trihydrate, USP; 0.25 mg Glacial Acetic Acid, USP; 15.8 mg Arginine Hydrochloride, USP; and 0.025 mg Polysorbate 20 in Water for Injection, USP. Each prefilled glass syringe contains 0.5 mL for Intramuscular injection.

AVONEX prefilled syringes are available in the following package configuration (NDC 59627-222-05): A package containing four Administration Dose Packs (each containing one single-use syringe of AVONEX and one 23 gauge, 1¼ inch needle), and a recloseable accessory pouch containing 4 alcohol wipes, 4 gauze pads, and 4 adhesive bandages.

AVONEX in prefilled syringes should be stored in a 2°C to 8°C (36°F to 46°F) refrigerator. Once removed from the refrigerator, AVONEX in a prefilled syringe should be allowed to warm to room temperature (about 30 minutes). Do not use external heat sources such as hot water to warm AVONEX in a prefilled syringe. Should refrigeration be unavailable, AVONEX in a prefilled syringe can be stored at ≤ 25°C (77°F) for a period up to 7 days. Once the product is removed from the refrigerator, it must not be stored above 25°C (77°F). If the product has been exposed to conditions other than those recommended, DISCARD THE PRODUCT and DO NOT USE. DO NOT EXPOSE TO HIGH TEMPERATURES. DO NOT FREEZE. Protect from light. Do not use beyond the expiration date stamped on the syringe.

16.3 AVONEX PEN Single-Use Prefilled Autoinjector

AVONEX PEN is supplied as a sterile liquid albumin-free formulation containing 30 micrograms of interferon beta-1a, 0.79 mg Sodium Acetate Trihydrate, USP; 0.25 mg Glacial Acetic Acid, USP; 15.8 mg Arginine Hydrochloride, USP; and 0.025 mg Polysorbate 20 in Water for Injection, USP. Each single-use prefilled autoinjector contains 0.5 mL for intramuscular injection.

AVONEX PEN single-use prefilled autoinjectors are available in the following package configuration (NDC 59627-333-04): A package containing four AVONEX PEN Administration Dose Packs (each containing one AVONEX PEN autoinjector, one 25 gauge, 5/8 inch needle and an AVONEX PEN cover), and a recloseable accessory pouch containing 4 alcohol wipes, 4 gauze pads, and 4 adhesive bandages.

AVONEX PEN should be stored in a 2°C to 8°C (36°F to 46°F) refrigerator. Once removed from the refrigerator, AVONEX PEN should be allowed to warm to room temperature (about 30 minutes). Do not use external heat sources such as hot water to warm AVONEX. Should refrigeration be unavailable, AVONEX PEN can be stored at ≤ 25°C (77°F) for a period up to 7 days. Once the product is removed from the refrigerator, it must not be stored above 25°C (77°F). If the product has been exposed to conditions other than those recommended, DISCARD THE PRODUCT and DO NOT USE. DO NOT EXPOSE TO HIGH TEMPERATURES. DO NOT FREEZE. Protect from light. Do not use beyond the expiration date stamped on the prefilled autoinjector.
See FDA-approved patient labeling (Medication Guide and Patient’s Instructions for Use).

Instruct patients to carefully read the supplied AVONEX Medication Guide and caution patients not to change the AVONEX dose or schedule of administration without medical consultation.

Inform patients that the Prefilled Syringe tip cap of this product contains natural rubber latex which may cause allergic reactions.

**Instruction on Self-injection Technique and Procedures**

Provide appropriate instruction for reconstitution of AVONEX and methods of self-injection, including careful review of the AVONEX Medication Guide. Instruct patients in the use of aseptic technique when administering AVONEX.

Inform patients that their healthcare provider should show them or their caregiver how to prepare and inject AVONEX before administering the first dose. Their healthcare provider should watch the first AVONEX injection given. Tell patients not to re-use needles or syringes and instruct patients on safe disposal procedures. Inform patients to dispose of used needles and syringes in a puncture-resistant container and instruct the patient regarding safe disposal of full containers.

Advise patients:
- of the importance of rotating areas of injection with each dose to minimize the likelihood of injection site reactions. [see Choose an Injection Site section of the Medication Guide].
- NOT to inject area of the body where the skin is irritated, reddened, bruised, infected or scarred in any way
- to check the injection site after 2 hours for redness, swelling, or tenderness
- contact their healthcare provider if they have a skin reaction and it does not clear up in a few days

**Pregnancy**

Advise patients that AVONEX should not be used during pregnancy unless the potential benefit justifies the potential risk to the fetus [see Use in Special Population (8.1)].

**Depression**

Advise patients of the symptoms of depression, suicidal ideation, or psychotic disorders as they have been reported with the use of AVONEX and instruct patients to report them immediately to their physician [see Warnings and Precautions (5.1)].

**Liver Disease**

Advise patients that severe hepatic injury, including hepatic failure, has been reported during the use of AVONEX. Advise patients of symptoms of hepatic dysfunction, and instruct patients to report them immediately to their physician [see Warnings and Precautions (5.2)].

**Allergic Reactions and Anaphylaxis**

Advise patients of the symptoms of allergic reactions and anaphylaxis, and instruct patients to seek immediate medical attention if these symptoms occur [see Warnings and Precautions (5.3)].

**Congestive Heart Failure**
Advise patients that worsening of pre-existing congestive heart failure has been reported in patients using AVONEX. Advise patients of symptoms of worsening cardiac condition, and instruct patients to report them immediately to their physician [see Warnings and Precautions (5.4)].

Seizures
Advise patients that seizures have been reported in patients using AVONEX. Instruct patients to report seizures immediately to their physician [see Warnings and Precautions (5.7)].

Flu-like Symptoms
Inform patients that flu-like symptoms are common following initiation of therapy with AVONEX [see Dosage and Administration (2.3) and Adverse Reactions (6)]. Advise patients that starting with a lower dose than 30 micrograms and increasing the dose over 3 weeks reduces the incidence and severity of flu-like symptoms.

Manufactured by:
Biogen Inc.
Cambridge, MA 02142 USA
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1-800-456-2255

*MICRO PIN® is the trademark of B. Braun Medical Inc.*
Read this Medication Guide before you start using AVONEX, and each time you get a refill. There may be new information. This information does not take the place of talking with your healthcare provider about your medical condition or your treatment.

What is the most important information I should know about AVONEX?

**AVONEX can cause serious side effects.** Tell your healthcare provider right away if you have any of the symptoms listed below while taking AVONEX.

1. **Behavioral health problems including depression, suicidal thoughts or hallucinations.** Some people taking AVONEX may develop mood or behavior problems including:
   - irritability (getting upset easily)
   - depression (feeling hopeless or feeling bad about yourself)
   - nervousness
   - anxiety
   - aggressive behavior
   - thoughts of hurting yourself or suicide
   - hearing or seeing things that others do not hear or see (hallucinations)

2. **Liver problems, or worsening of liver problems including liver failure and death. Symptoms may include:**
   - nausea
   - loss of appetite
   - tiredness
   - dark colored urine and pale stools
   - yellowing of your skin or the white part of your eye
   - bleeding more easily than normal
   - confusion
   - sleepiness

During your treatment with AVONEX you will need to see your healthcare provider regularly and have regular blood tests to check for side effects.

3. **Serious allergic reactions and skin reactions. Symptoms may include:**
   - itching
   - swelling of the face, eyes, lips, tongue or throat
• trouble breathing
• anxiousness
• feeling faint
• skin rash, hives, sores in your mouth, or your skin blisters and peels

What is AVONEX?

AVONEX is a form of a protein called beta interferon that occurs naturally in the body. AVONEX is a prescription medicine used to treat adults with relapsing forms of multiple sclerosis (MS). This includes people who have had their first symptoms of multiple sclerosis and have an MRI consistent with multiple sclerosis.

AVONEX will not cure your MS but may decrease the number of flare-ups of the disease and slow the occurrence of some of the physical disability that is common in people with MS. MS is a life-long disease that affects your nervous system by destroying the protective covering (myelin) that surrounds your nerve fibers.

The way AVONEX works in MS is not known.

It is not known if AVONEX is safe and effective in children.

Who should not use AVONEX?

Do not take AVONEX if you:

• are allergic to interferon beta, albumin (human), or any of the ingredients in AVONEX. See the end of this Medication Guide for a complete list of ingredients in AVONEX.

What should I tell my healthcare provider before using AVONEX?

Before taking AVONEX, tell your healthcare provider if you:

• are being treated for a mental illness or had treatment in the past for any mental illness, including depression and suicidal behavior
• have or had bleeding problems or blood clots
• have or had low blood cell counts
• have or had liver problems
• have or had seizures (epilepsy)
• have or had heart problems
• have or had thyroid problems
• have or had any kind of autoimmune disease (where the body’s immune system attacks the body’s own cells), such as psoriasis, systemic lupus erythematosus, or rheumatoid arthritis
• drink alcohol
are pregnant or plan to become pregnant. It is not known if AVONEX will harm your unborn baby. Tell your healthcare provider if you become pregnant during your treatment with AVONEX.

are breastfeeding or plan to breastfeed. It is not known if AVONEX passes into your breast milk. You and your healthcare provider should decide if you will use AVONEX or breastfeed. You should not do both.

Tell your healthcare provider about all the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements.

How should I use AVONEX?

- Your healthcare provider should show you how to prepare and measure your dose of AVONEX and how to inject your AVONEX before you use AVONEX for the first time.
- Your healthcare provider or nurse should watch the first AVONEX injection you give yourself.
- AVONEX is given once a week by injection into the muscle (intramuscular injection).
- Inject AVONEX exactly as your healthcare provider tells you.
- Your healthcare provider will tell you how much AVONEX to inject and how often to inject AVONEX. Do not inject more than your healthcare provider tells you to.
- If you miss a dose, you should take your next dose as soon as you remember. You should continue your regular schedule the following week. Do not take AVONEX 2 days in a row.
- Do not change your dose unless your healthcare provider tells you to.
- Change (rotate) your injection site you choose with each injection. This will help decrease the chance that you will have an injection site reaction.
- Do not inject into an area of the body where the skin is irritated, reddened, bruised, infected or scarred in any way.
- AVONEX comes as a:
  - Vial with freeze-dried (lyophilized) powder
  - Prefilled syringe (can be used with the AVOSTARTGRIP™ titration kit)
  - Single-Use Prefilled Autoinjector Pen (AVONEX PEN®)

Your healthcare provider will decide which one is best for you. See the Instructions for Use for detailed instructions for preparing and injecting your dose of AVONEX.

- Always use a new, unopened AVONEX vial, prefilled syringe, or single-use prefilled autoinjector pen for each intramuscular injection.
What are the possible side effects of AVONEX?

AVONEX can cause serious side effects including:

- See “What is the most important information I should know about AVONEX?”

- **Heart problems, including heart failure.** While AVONEX is not known to have any direct effects on the heart, a few patients who did not have a history of heart problems developed heart muscle problems or congestive heart failure after taking AVONEX. If you already have heart failure, AVONEX may cause your heart failure to get worse. Call your healthcare provider right away if you have worsening symptoms of heart failure such as shortness of breath or swelling of your lower legs or feet while using AVONEX.
  - Some people using AVONEX may have other heart problems including:
    - low blood pressure
    - fast or abnormal heart beat
    - chest pain
    - heart attack or a heart muscle problem (cardiomyopathy)

- **Blood problems.** AVONEX can affect your bone marrow and cause low red and white blood cell, and platelet counts. In some people, these blood cell counts may fall to dangerously low levels. If your blood cell counts become very low, you can get infections and problems with bleeding and bruising.

- **Seizures.** Some patients have had seizures while taking AVONEX, including patients who have never had seizures before.

- **Infections.** Some people who take AVONEX may get an infection. Symptoms of an infection may include:
  - fever
  - chills
  - pain or burning with urination
  - urinating often
  - bloody diarrhea
  - coughing up mucus

- **Thyroid problems.** Some people taking AVONEX develop changes in their thyroid function. Symptoms of thyroid changes include:
  - problems concentrating
  - feeling cold or hot all the time
  - weight changes (gain or loss)
  - skin changes

Tell your healthcare provider right away if you have any of the symptoms listed above.
The most common side effects of AVONEX include:

- **Flu-like symptoms.** Most people who take AVONEX have flu-like symptoms early during the course of therapy. Usually, these symptoms last for a day after the injection. You may be able to manage these flu-like symptoms by taking over-the-counter pain and fever reducers. For many people, these symptoms lessen or go away over time. Symptoms may include:
  - muscle aches
  - fever
  - tiredness
  - chills

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

**How should I store AVONEX?**

- Store AVONEX in the refrigerator at 36°F to 46°F (2°C to 8°C).
- **Do not** freeze AVONEX. **Do not** use AVONEX that has been frozen.
- **Do not** store AVONEX above 77°F (25°C).
- Keep AVONEX away from light.
- **Do not** use AVONEX past the expiration date.
- If you cannot refrigerate your AVONEX vials, you can store your AVONEX vials at 77°F (25°C) for up to 30 days. After mixing, the AVONEX solution should be used immediately, within 6 hours when stored refrigerated at 36°F to 46°F (2°C to 8°C).
- If you cannot refrigerate your AVONEX PEN and AVONEX prefilled syringes, you can store your AVONEX PEN and AVONEX prefilled syringes up to 77°F (25°C) for up to 7 days.

Keep AVONEX vials, prefilled syringes, pens and all other medicines out of the reach of children.

**General advice about the safe and effective use of AVONEX**

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. **Do not** use AVONEX for a condition for which it was not prescribed. **Do not** give AVONEX to other people, even if they have the same symptoms that you have, it may harm them.

This Medication Guide summarizes the most important information about AVONEX. If you would like more information, talk with your healthcare provider. You may ask your healthcare provider or pharmacist for information about AVONEX that is written for healthcare professionals.
What are the ingredients in AVONEX?

Active ingredient: interferon beta-1a

Inactive ingredients:

- **Vial with freeze-dried (lyophilized) powder**: albumin (human), sodium chloride, dibasic sodium phosphate, and monobasic sodium phosphate.

- **Single-Use Prefilled Syringe**: sodium acetate trihydrate, glacial acetic acid, arginine hydrochloride, polysorbate 20 in water for injection.

- **Single-Use Prefilled Autoinjector Pen**: sodium acetate trihydrate, glacial acetic acid, arginine hydrochloride, polysorbate 20 in water for injection.

This Medication Guide has been approved by the U.S. Food and Drug Administration.

Manufactured by:

Biogen Inc.

Cambridge, MA 02142 USA

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1-800-456-2255

Revised: 03/2016
For people with relapsing forms of multiple sclerosis (MS)

Injection Guide for Treatment with the AVONEX PEN®

For important safety information, please see pages 15-17 and the enclosed full Prescribing Information, Medication Guide and Instructions for Use.

Questions? You can call us any time at 1-800-456-2255.
Table of contents

Introduction ..........................................................................................................................3

Three forms ..........................................................................................................................4

AVONEX PEN
Getting started .....................................................................................................................5
Preparing the AVONEX PEN .............................................................................................5
Preparing the AVONEX PEN injection .............................................................................7
Giving your AVONEX injection .........................................................................................9
After your AVONEX injection .........................................................................................13

Important Safety Information about AVONEX ...............................................................15
Introduction

This injection training guide is designed to help you feel comfortable with the AVONEX® (interferon beta-1a) injection technique when using the AVONEX PEN. It provides detailed instructions and the do’s and don’ts you need to know to ensure the proper use and administration of AVONEX.

The Above MS™ program from Biogen provides additional training for people taking an injectable Biogen treatment. If a Nurse Educator is coming to your home, please keep this guide handy so you can go through it together. Nurse Educators are there to provide additional support to you and your care partner with injection technique and to respond to questions you may have. You can always decide to request an additional in-home visit from a Nurse Educator any time while you are taking AVONEX.

Please read through this guide carefully. Should you not wish to receive supplemental training by a Nurse Educator, you can always change your mind and decide to have an in-home visit.

Questions may arise at any time while you are taking AVONEX and your healthcare provider should be your first source of information. The Above MS™ program is always here to assist you with any questions you may have. You can speak with a Nurse Educator 24 hours a day, 7 days a week by calling 1-800-456-2255.
Three forms

AVONEX® (interferon beta-1a) is approved by FDA to treat relapsing forms of multiple sclerosis (MS) to decrease the number of flare-ups and slow the occurrence of some of the physical disability that is common in people with MS. AVONEX is approved for use in people who have experienced a first attack and have lesions consistent with MS on their MRI.

AVONEX is available in 3 forms: pen, prefilled syringe, and a powder that must be mixed before injection.

While all methods deliver the same effective dose of AVONEX, the steps for preparing and injecting each one are different:

AVONEX PEN®

AVONEX Prefilled Syringe

AVONEX Powder Form
Getting started with the AVONEX PEN

Read the Instructions for Use before you start using AVONEX PEN and each time you get a refill. There may be new information. This information does not take the place of talking with your healthcare provider about your medical condition or your treatment.

Your healthcare provider should show you or your caregiver how to prepare the dose of AVONEX and how to inject with your AVONEX PEN the right way before it is used for the first time. Your healthcare provider or nurse should watch you inject the dose of AVONEX the first time AVONEX PEN is used.

General information about the safe and effective use of AVONEX PEN

- Always use a new AVONEX PEN and needle for each injection. Do not re-use your AVONEX PEN or needle.
- Do not share your AVONEX PEN or needles.
- Keep AVONEX PEN and needles out of the reach of children.

Preparing the AVONEX PEN

- Find a well-lit, clean, flat work surface like a table and collect all the supplies you will need to give yourself or receive an injection.
- Take 1 AVONEX PEN Administration Dose Pack out of the refrigerator about 30 minutes before you plan on injecting the AVONEX dose to allow it to reach room temperature. Do not use external heat sources such as hot water to warm the AVONEX PEN.
- Check the expiration date printed on the AVONEX PEN, AVONEX PEN Administration Dose Pack carton, and the outer carton. Do not use the AVONEX PEN past the expiration date.
- Wash your hands with soap and water.
Preparing the AVONEX PEN (cont’d)

Supplies you will need to give the AVONEX PEN injection:

- 1 AVONEX Administration Dose Pack that contains:
  - 1 AVONEX PEN
  - a 25 gauge, 5/8 inch long sterile needle
  - 1 AVONEX PEN cover
- 1 alcohol wipe
- 1 gauze pad
- 1 adhesive bandage
- a puncture resistant container for disposal of used AVONEX PEN and needle

Identifying parts of the AVONEX PEN

Single-Use Administration Dose Pack Contents: AVONEX PEN, Supplied Needle and AVONEX PEN Cover

Body

Tamper-evident cap

Blue activation button

Injector shield (grooved area)

Needle cover

Foil

AVONEX PEN® cover

Figure A
Preparing the AVONEX PEN injection

Step 1: Hold the AVONEX PEN with the white tamper-evident cap (cap) pointing up (See Figure B).

➤ Check that the cap is intact and has not been removed. If the cap has been removed or is not tightly attached, **do not** use it, throw it away and get a new AVONEX PEN.

Step 2: With your other hand, grasp the cap and bend it at a 90° angle until the cap snaps off (See Figure C).

➤ After the cap comes off, you will see the glass tip of the syringe. **Do not** touch the glass tip of the syringe (See Figure D).

Step 3: Place the AVONEX PEN down on a flat work surface.

Step 4: Pull off the sterile foil from the needle cover (See Figure E).

➤ Only use the needle that comes with your AVONEX PEN.

Step 5: Hold the AVONEX PEN with the glass syringe tip pointing up. Press the needle onto the AVONEX PEN glass syringe tip (See Figure F).
Preparing the AVONEX PEN injection (cont’d)

Step 6: Gently turn the needle clockwise until it is firmly attached (See Figure G).

- If the needle is not firmly attached, it may leak, and you may not get your full dose of AVONEX.
- Do not remove the plastic cover from the needle (See Figure H).

Step 7: Hold the body of the AVONEX PEN in 1 hand with the needle and needle cover pointing away from you and other people. Do not remove the plastic cover from the needle (See Figure I).

Step 8: Using your other hand, hold onto the injector shield (grooved area) tightly and quickly pull up on the injector shield until the injector shield covers the needle all the way.

- The plastic needle cover will “pop” off after the injector shield has been fully extended (See Figure J).
- When the injector shield is extended the right way, you will see a small blue rectangular area next to the oval medication display window (See Figure K).

Step 9: Check the oval medication display window and make sure the AVONEX is clear and colorless (See Figure L). You might see air bubbles in the oval display window. This is normal and will not affect your dose.

- Do not use AVONEX PEN if the liquid is colored, cloudy, or contains any lumps or particles. Throw away the AVONEX PEN and get a new one, then repeat steps 1 to 9.
Giving your AVONEX injection

Choosing an injection site

▶ Your healthcare provider should show you or your caregiver how to prepare the dose of AVONEX and how to inject your AVONEX PEN the right way before AVONEX PEN is used for the first time. Your healthcare provider or nurse should watch you inject the dose of AVONEX the first time AVONEX PEN is used.

▶ Inject your AVONEX PEN exactly as your healthcare provider has shown you.

▶ AVONEX PEN is injected into the muscle (intramuscularly).

▶ AVONEX PEN should be injected into the upper, outer thigh (See Figure M).

▶ Change (rotate) injection sites for each dose. Do not use the same injection site for each injection.

▶ Do not inject into an area of the body where the skin is irritated, reddened, bruised, infected or scarred in any way.

▶ Do not push down on the injector shield and the blue activation button at the same time until you are ready to give your injection.

Figure M
Giving your AVONEX injection (cont’d)

**Step 10:** Choose an injection site and wipe the skin with an alcohol wipe (See Figure N). Let the injection site dry before injecting the dose.

▶ Do not touch this area again before giving the injection.

**Step 11:** Place the AVONEX PEN on the injection site (See Figure O).

**Step 12:** Hold the body of the AVONEX PEN at a 90° angle to the injection site, and make sure you can see the windows (See Figure P).

**Step 13:** Keeping your fingers away from the blue activation button, firmly push the body of the AVONEX PEN down against the thigh to release the safety lock (See Figure Q). Do not lift the AVONEX PEN off of the injection site.

▶ Check to make sure the safety lock has been released. You will know the safety lock is released when the small blue rectangular area above the oval medication display window is gone (See Figure R).

For important safety information, please see pages 15-17 and the enclosed full Prescribing Information, Medication Guide and Instructions for Use.

Questions? You can call us any time at 1-800-456-2255.
Giving your AVONEX injection (cont’d)

**Step 14:** Continue to firmly maintain pressure and push down on the AVONEX PEN against the injection site, then push down on the blue activation button with your thumb (See Figure S). Keep the AVONEX PEN pushed down against the injection site and slowly count to 10.

- You will hear a “click” when the injection starts.
  - If you do not hear a “click,” your injection was not given the right way.
    - If this happens, make sure that the injector shield is extended, the safety lock is completely released, and that you are firmly maintaining pressure and pushing down against the injection site. Press the blue activation button with your thumb again. If you still do not hear a “click,” call Biogen® at 1-800-456-2255.

**Step 15:** After you count to 10, pull the AVONEX PEN straight out of the skin (See Figure T). Use the gauze pad to apply pressure to the injection site for a few seconds or rub gently in a circular motion.

- If you see blood after you press the injection site for a few seconds, wipe it off with gauze and apply an adhesive bandage.

**Step 16:** Check the circular display window on the AVONEX PEN to make sure that it is yellow. This is to be sure that you have been given your full dose (See Figure U).

- If you did not receive your full dose of AVONEX, throw away the AVONEX PEN and call your doctor. Do not re-use the AVONEX PEN.
For important safety information, please see pages 15-17 and the enclosed full Prescribing Information, Medication Guide and Instructions for Use. Questions? You can call us any time at 1-800-456-2255.

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**Giving your AVONEX injection (cont’d)**

**Step 17:** Do not hold the AVONEX PEN cover with your hands. Place the AVONEX PEN cover on a flat work surface. **Line up the exposed needle with the hole of the AVONEX PEN cover,** and insert directly into the opening (See Figure V).

![Figure V]

**Step 18:** Firmly press the AVONEX PEN down until you hear a “click” to seal the needle (See Figure W). You may need to hold both hands around the AVONEX PEN body to snap the AVONEX PEN cover into place.

![Figure W]

*If you are not sure you received the full dose, contact your healthcare provider.*

*We are always here to help if you have problems with your injection. Call us at 1-800-456-2255.*
After your AVONEX injection

- Throw away the used AVONEX PENS and needles in a sharps container or some type of hard plastic or metal container with a screw cap such as a detergent bottle or coffee can. Check with your healthcare provider about the right way to throw away the container. There may be local or state laws about how to throw away used AVONEX PENS and needles. Do not throw away used AVONEX PENS and needles in household trash or recycling bins.

- After 2 hours, check the injection site for redness, swelling or tenderness. If you have a skin reaction and it does not clear up in a few days, contact your healthcare provider.
For important safety information, please see pages 15-17 and the enclosed full Prescribing Information, Medication Guide and Instructions for Use.

Questions? You can call us any time at 1-800-456-2255.
Indication and Important Safety Information

**Indication**

AVONEX (interferon beta-1a) is approved by FDA to treat relapsing forms of multiple sclerosis (MS) to decrease the number of flare-ups and slow the occurrence of some of the physical disability that is common in people with MS. AVONEX is approved for use in people who have experienced a first attack and have lesions consistent with MS on their MRI.

**Important Safety Information**

Before beginning treatment, you should discuss with your healthcare provider the potential benefits and risks associated with AVONEX.

**AVONEX can cause serious side effects.** Tell your healthcare provider right away if you have any of the symptoms listed below while taking AVONEX.

- **Behavioral health problems including depression, suicidal thoughts or hallucinations.** Some people taking AVONEX may develop mood or behavior problems including irritability (getting upset easily), depression (feeling hopeless or feeling bad about yourself), nervousness, anxiety, aggressive behavior, thoughts of hurting yourself or suicide, and hearing or seeing things that others do not hear or see (hallucinations).

- **Liver problems, or worsening of liver problems including liver failure and death.** Symptoms may include nausea, loss of appetite, tiredness, dark colored urine and pale stools, yellowing of your skin or the white part of your eye, bleeding more easily than normal, confusion, and sleepiness. During your treatment with AVONEX you will need to see your healthcare provider regularly and have regular blood tests to check for side effects.

- **Serious allergic reactions and skin reactions.** Symptoms may include itching, swelling of the face, eyes, lips, tongue or throat, trouble breathing, anxiousness, feeling faint, and skin rash, hives, sores in your mouth, or your skin blisters and peels.

**AVONEX will not cure your MS but may decrease the number of flare-ups of the disease and slow the occurrence of some of the physical disability that is common in people with MS. MS is a life-long disease that affects your nervous system by destroying the protective covering (myelin) that surrounds your nerve fibers.**

The way AVONEX works in MS is not known. It is not known if AVONEX is safe and effective in children.

**Do not take AVONEX if you are allergic to interferon beta, albumin (human), or any of the ingredients in AVONEX.**

For important safety information, please see pages 15-17 and the enclosed full Prescribing Information, Medication Guide and Instructions for Use.

Questions? You can call us any time at 1-800-456-2255.
Important Safety Information (cont’d)

Before taking AVONEX, tell your healthcare provider if you:

▪ are being treated for a mental illness, or had treatment in the past for any mental illness, including depression and suicidal behavior.

▪ have or had bleeding problems or blood clots, have or had low blood cell counts, have or had liver problems, have or had seizures (epilepsy), have or had heart problems, have or had thyroid problems, have or had any kind of autoimmune disease (where the body’s immune system attacks the body’s own cells), such as psoriasis, systemic lupus erythematosus, or rheumatoid arthritis.

▪ drink alcohol.

▪ are pregnant or plan to become pregnant. It is not known if AVONEX will harm your unborn baby. Tell your healthcare provider if you become pregnant during your treatment with AVONEX.

▪ are breastfeeding or plan to breastfeed. It is not known if AVONEX passes into your breast milk. You and your healthcare provider should decide if you will use AVONEX or breastfeed. You should not do both.

Tell your healthcare provider about all the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements.

AVONEX can cause serious side effects including:

▪ Heart problems, including heart failure.

While AVONEX is not known to have any direct effects on the heart, a few patients who did not have a history of heart problems developed heart muscle problems or congestive heart failure after taking AVONEX. If you already have heart failure, AVONEX may cause your heart failure to get worse. Call your healthcare provider right away if you have worsening symptoms of heart failure such as shortness of breath or swelling of your lower legs or feet while using AVONEX.

▪ Some people using AVONEX may have other heart problems including low blood pressure, fast or abnormal heart beat, chest pain, and heart attack or heart muscle problem (cardiomyopathy).
Blood problems. AVONEX can affect your bone marrow and cause low red and white blood cell, and platelet counts. In some people, these blood cell counts may fall to dangerously low levels. If your blood cell counts become very low, you can get infections and problems with bleeding and bruising.

Seizures. Some patients have had seizures while taking AVONEX, including patients who have never had seizures before.

Infections. Some people who take AVONEX may get an infection. Symptoms of an infection may include fever, chills, pain or burning with urination, urinating often, bloody diarrhea, and coughing up mucus.

Thyroid problems. Some people taking AVONEX develop changes in their thyroid function. Symptoms of thyroid changes include problems concentrating, feeling cold or hot all the time, weight changes, and skin changes.

Tell your healthcare provider right away if you have any of the symptoms listed above.

The most common side effects of AVONEX include:

Flu-like symptoms. Most people who take AVONEX have flu-like symptoms early during the course of therapy. Usually, these symptoms last for a day after the injection. You may be able to manage these flu-like symptoms by taking over-the-counter pain and fever reducers. For many people, these symptoms lessen or go away over time. Symptoms may include muscle aches, fever, tiredness, and chills.

Call your healthcare provider for medical advice about side effects.
You may report side effects to FDA at 1-800-FDA-1088.

Please see the enclosed Prescribing Information and Medication Guide for additional important safety information. This information is not intended to replace discussions with your healthcare provider.
For important safety information, please see pages 15-17 and the enclosed full Prescribing Information, Medication Guide and Instructions for Use.

Questions? You can call us any time at 1-800-456-2255.
Instructions for Use

AVONEX PEN® (a-vuh-necks) (pen)
(interferon beta-1a)

injection for intramuscular use
single-use prefilled autoinjector pen

Read the Instructions for Use before you start using AVONEX and each time you get a refill. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or your treatment.

Your healthcare provider should show you or your caregiver how to prepare the dose of AVONEX and how to inject your AVONEX PEN the right way before AVONEX PEN is used for the first time. Your healthcare provider or nurse should watch you inject the dose of AVONEX the first time AVONEX PEN is used.

Preparing the AVONEX PEN:

- Find a well lit, clean, flat work surface like a table and collect all the supplies you will need to give yourself or receive an injection.
- Take 1 AVONEX PEN Administration Dose Pack out of the refrigerator about 30 minutes before you plan on injecting the AVONEX dose to allow it to reach room temperature. Do not use external heat sources such as hot water to warm the AVONEX PEN.
- Check the expiration date printed on the AVONEX PEN, AVONEX PEN Administration Dose Pack carton, and the outer carton. Do not use the AVONEX PEN past the expiration date.
- Wash your hands with soap and water.

Supplies you will need to give the AVONEX PEN injection:

- 1 AVONEX Administration Dose Pack that contains:
  - 1 AVONEX PEN
  - a 25 gauge, 5/8 inch long sterile needle
  - 1 AVONEX PEN cover
- 1 alcohol wipe
- 1 gauze pad
- 1 adhesive bandage
- a puncture resistant container for disposal of used AVONEX PEN and needle

Identifying parts of the AVONEX PEN (See Figure A).

Single-Use Administration Dose Pack Contents – AVONEX PEN, Supplied Needle and AVONEX PEN Cover
Preparing the AVONEX PEN injection:

**Step 1:** Hold the AVONEX PEN with the white tamper-evident cap (cap) pointing up (See Figure B).
- Check that the cap is intact and has not been removed. If the cap has been removed or is not tightly attached, do not use it, throw it away and get a new AVONEX PEN.

**Step 2:** With your other hand, grasp the cap and bend it at a 90° angle until the cap snaps off (See Figure C).
- After the cap comes off, you will see the glass tip of the syringe. Do not touch the glass tip of the syringe (See Figure D).
<table>
<thead>
<tr>
<th>Step 3:</th>
<th>Place the AVONEX PEN down on a flat work surface.</th>
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<tbody>
<tr>
<td>Step 4:</td>
<td>Pull off the sterile foil from the needle cover (See Figure E).</td>
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<tr>
<td></td>
<td>Only use the needle that comes with your AVONEX PEN.</td>
</tr>
<tr>
<td>Step 5:</td>
<td>Hold the AVONEX PEN with the glass syringe tip pointing up. Press the needle onto the AVONEX PEN glass syringe tip (See Figure F).</td>
</tr>
<tr>
<td>Step 6:</td>
<td>Gently turn the needle clockwise until it is firmly attached (See Figure G).</td>
</tr>
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<td>If the needle is not firmly attached, it may leak, and you may not get your full dose of AVONEX.</td>
</tr>
<tr>
<td></td>
<td><strong>Do not</strong> remove the plastic cover from the needle (See Figure H).</td>
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</tbody>
</table>

(Figure D)  
(Figure E)  
(Figure F)  
(Figure G)  
(Figure H)
Step 7: Hold the body of the AVONEX PEN in 1 hand with the needle and needle cover pointing away from you and other people. Do not remove the plastic cover from the needle (See Figure I).

![Before (Figure I)]

Step 8: Using your other hand, hold onto the injector shield (grooved area) tightly and quickly pull up on the injector shield until the injector shield covers the needle all the way.

- The plastic needle cover will “pop” off after the injector shield has been fully extended (See Figure J).

![After (extended) (Figure J)]

- When the injector shield is extended the right way, you will see a small blue rectangular area next to the oval medication display window (See Figure K).

![Safety Lock (visible) (Figure K)]
## Step 9: Check the oval medication display window and make sure the AVONEX is clear and colorless (See Figure L).

You might see air bubbles in the oval display window. This is normal and will not affect your dose.

- **Do not** use AVONEX PEN if the liquid is colored, cloudy, or contains any lumps or particles. Throw away the AVONEX PEN and get a new one, then repeat steps 1 to 9.

![Oval Medication Display Window](Figure L)

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### Giving the AVONEX injection:

- Your healthcare provider should show you or your caregiver how to prepare the dose of AVONEX and how to inject your AVONEX PEN the right way before AVONEX PEN is used for the first time. Your healthcare provider or nurse should watch you inject the dose of AVONEX the first time AVONEX PEN is used.

- Inject your AVONEX PEN exactly as your healthcare provider has shown you.

- AVONEX PEN is injected into the muscle (intramuscularly).

- AVONEX PEN should be injected into the upper, outer thigh (See Figure M).

- Change (rotate) injection sites for each dose. **Do not** use the same injection site for each injection.

- **Do not** inject into an area of the body where the skin is irritated, reddened, bruised, infected or scarred in any way.

- **Do not** push down on the injector shield and the blue activation button at the same time until you are ready to give your injection.

![Figure M]
skin with an alcohol wipe (See Figure N). Let the injection site dry before injecting the dose.

• Do not touch this area again before giving the injection.

<table>
<thead>
<tr>
<th>Step 11: Place the AVONEX PEN on the injection site (See Figure O).</th>
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<td><img src="image" alt="Figure N" /></td>
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<th>Step 12: Hold the body of the AVONEX PEN at a 90° angle to the injection site, and make sure you can see the windows (See Figure P).</th>
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<tbody>
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<td><img src="image" alt="Figure O" /></td>
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</table>

| Step 13: Keeping your fingers away from the blue activation button, firmly push the body of the AVONEX PEN down against the thigh to release the safety lock (See Figure Q). Do not lift the AVONEX PEN off of the injection site.  
  • Check to make sure the safety lock has been released. You will know the safety lock is released when the small blue rectangular area above the oval medication display window is gone (See Figure R). |
<table>
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<tbody>
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<td><img src="image" alt="Figure P" /></td>
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</table>

| ![Figure Q](image) |

| ![Safety Lock (visible)](image) ![Safety Lock (released)](image) |

| ![Figure R](image) |
Step 14: Continue to firmly maintain pressure and push down on the AVONEX PEN against the injection site, then push down on the blue activation button with your thumb (See Figure S). Keep the AVONEX PEN pushed down against the injection site and slowly count to 10.

- **You will hear a “click” when the injection starts.** If you do not hear a “click”, your injection was not given the right way.
  - If this happens, make sure that the injector shield is extended, the safety lock is completely released, and that you are firmly maintaining pressure and pushing down against the injection site. Press the blue activation button with your thumb again. If you still do not hear a “click”, call Biogen Inc. at 1-800-456-2255.

Step 15: After you count to 10, pull the AVONEX PEN straight out of the skin (See Figure T). Use the gauze pad to apply pressure to the injection site for a few seconds or rub gently in a circular motion.

- If you see blood after you press the injection site for a few seconds, wipe it off with gauze and apply an adhesive bandage.

Step 16: Check the circular display window on the AVONEX PEN to make sure that it is yellow. This is to be sure that you have been given your full dose (See Figure U).

- If you did not receive your full dose of AVONEX, throw away the AVONEX PEN and call your doctor. **Do not** re-use the AVONEX PEN.
Step 17: **Do not** hold the AVONEX PEN cover with your hands. Place the AVONEX PEN cover on a flat work surface. **Line up the exposed needle with the hole of the AVONEX PEN cover**, and insert directly into the opening (See Figure V).

(Figure V)

Step 18: Firmly press the AVONEX PEN down until you hear a “click” to seal the needle (See Figure W). You may need to hold both hands around the AVONEX PEN body to snap the AVONEX PEN cover into place.

(Figure W)

After the AVONEX injection:

- Throw away the used AVONEX PENS and needles in a sharps container or some type of hard plastic or metal container with a screw cap such as a detergent bottle or coffee can. Check with your healthcare provider about the right way to throw away the container. There may be local or state laws about how to throw away used AVONEX PENS and needles. **Do not** throw away used AVONEX PENS and needles in household trash or recycling bins.

- After 2 hours, check the injection site for redness, swelling or tenderness. If you have a skin reaction and it does not clear up in a few days, contact your healthcare provider.

General information about the safe and effective use of AVONEX PEN

- Always use a new AVONEX PEN and needle for each injection. **Do not** re-use your AVONEX PEN or needle.

- **Do not** share your AVONEX PEN or needles.

- Keep AVONEX PEN and needles out of the reach of children.

This Instructions for Use has been approved by the U.S. Food and Drug Administration.

Manufactured by:

Biogen Inc.

Cambridge, MA 02142 USA

U.S. License # 1697

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1-800-456-2255
For people with relapsing forms of multiple sclerosis (MS)

Injection Guide for Treatment with the AVONEX Prefilled Syringe
Table of contents

Introduction ..................................................................................................................3

Three forms .................................................................................................................4

AVONEX Prefilled Syringe
Getting started .........................................................................................................5
Preparing the AVONEX dose ..................................................................................5
Preparing the AVONEX injection .........................................................................7
Giving your AVONEX injection ............................................................................9
After your AVONEX injection ..............................................................................11

Important Safety Information about AVONEX ..................................................13
Introduction

This injection training guide is designed to help you feel comfortable with the AVONEX® (interferon beta-1a) injection technique when using the AVONEX prefilled syringe. It provides detailed instructions and the do’s and don’ts you need to know to ensure the proper use and administration of AVONEX.

The Above MS™ program from Biogen provides additional training for people taking an injectable Biogen treatment. If a Nurse Educator is coming to your home, please keep this guide handy so you can go through it together. Nurse Educators are there to provide additional support to you and your care partner with injection technique and to respond to questions you may have. You can always decide to request an additional in-home visit from a Nurse Educator any time while you are taking AVONEX.

Please read through this guide carefully. Should you not wish to receive supplemental training by a Nurse Educator, you can always change your mind and decide to have an in-home visit.

Questions may arise at any time while you are taking AVONEX and your healthcare provider should be your first source of information. The Above MS™ program is always here to assist you with any questions you may have. You can speak with a Nurse Educator 24 hours a day, 7 days a week by calling 1-800-456-2255.
Three forms

AVONEX® (interferon beta-1a) is approved by FDA to treat relapsing forms of multiple sclerosis (MS) to decrease the number of flare-ups and slow the occurrence of some of the physical disability that is common in people with MS. AVONEX is approved for use in people who have experienced a first attack and have lesions consistent with MS on their MRI.

AVONEX is available in 3 forms: pen, prefilled syringe, and a powder that must be mixed before injection.

While all methods deliver the same effective dose of AVONEX, the steps for preparing and injecting each one are different:

AVONEX PEN®

AVONEX Prefilled Syringe

AVONEX Powder Form
Getting started with the AVONEX Prefilled Syringe

Read the Instructions for Use before you start using the AVONEX prefilled syringe and each time you get a refill. There may be new information. This information does not take the place of talking with your healthcare provider about your medical condition or your treatment.

General information about the safe and effective use of AVONEX

▷ Always use a new AVONEX prefilled syringe and needle for each injection. Do not re-use your AVONEX prefilled syringe or needles.
▷ Do not share your AVONEX prefilled syringe or needles.
▷ Keep the AVONEX prefilled syringe and needles out of the reach of children.

Preparing the AVONEX dose

▷ Find a well-lit, clean, flat work surface like a table and collect all the supplies you will need to give yourself or receive an injection.
▷ Take 1 AVONEX Administration Dose Pack out of the refrigerator about 30 minutes before you plan on injecting the AVONEX dose to allow it to reach room temperature. Do not use external heat sources such as hot water to warm the AVONEX prefilled syringe.
▷ Check the expiration date printed on the AVONEX prefilled syringe, AVONEX prefilled syringe Administration Dose Package carton, and the outer carton. Do not use the AVONEX prefilled syringe past the expiration date.
▷ Wash your hands with soap and water.
Preparing the AVONEX dose (cont’d)

Supplies you will need for the AVONEX injection:

- 1 AVONEX Administration Dose Pack that contains:
  - 1 AVONEX prefilled syringe
  - 23 gauge, 1¼ inch long sterile needle
- 1 alcohol wipe
- 1 gauze pad
- 1 adhesive bandage
- a puncture resistant container for disposal of used syringes and needles

Identifying parts of the AVONEX prefilled syringe

- Syringe
- Cap
- Protective rubber cover
Preparing the AVONEX injection

**Step 1:** Hold the AVONEX prefilled syringe with the cap pointing down and with the 0.5 mL mark at eye level (See Figure A).

- **Check the syringe:**
  - The syringe should not have any cracks or damage.
  - Check that the cap is intact and has not been removed.
  - The amount of liquid in the syringe should be at or very close to the 0.5 mL mark.
  - AVONEX should look clear, colorless, and should not have any particles in it.

- **Do not** use the AVONEX prefilled syringe if:
  - the syringe is cracked or damaged
  - the solution is cloudy, colored, or has lumps or particles in it
  - the cap has been removed or is not tightly attached
  - there is not enough liquid in the syringe

**Do not** use that syringe. Get a new syringe. Contact Above MS™ at 1-800-456-2255.
Preparing the AVONEX injection (cont’d)

**Step 2:** With 1 hand, hold the AVONEX prefilled syringe right under the cap and with the cap pointing up (See Figure B).
- Make sure you are holding the AVONEX prefilled syringe by the ridged part, directly under the cap.

**Figure B**

**Step 3:** With the other hand, grasp the cap and bend it at a 90° angle until the cap snaps off (See Figure C and Figure D).

**Figure C**  **Figure D**

**Step 4:** Open the sterile needle package and take out the covered needle. Hold the AVONEX prefilled syringe with the glass syringe tip pointing up. Press the needle on the AVONEX prefilled syringe glass tip (See Figure E).

**Figure E**

**Step 5:** Gently turn the needle forward (clockwise) until it is tight and firmly attached (See Figure F).
- If the needle is not firmly attached, it may leak and you may not get your full dose of AVONEX.
- **Do not** remove the plastic cover from the needle.

**Figure F**
Giving your AVONEX injection

Choosing an injection site

► Your healthcare provider should show you or a caregiver how to prepare and inject the dose of AVONEX before AVONEX prefilled syringe is used for the first time. Your healthcare provider or nurse should watch you inject the dose of AVONEX the first time AVONEX prefilled syringe is used.

► Inject your AVONEX exactly as your healthcare provider has shown you.

► AVONEX is injected into the muscle (intramuscularly).

► AVONEX should be injected into the thigh or upper arm (See Figures G and H).

► Change (rotate) your injection sites for each dose. Do not use the same injection site for each injection.

Do not inject into an area of the body where the skin is irritated, reddened, bruised, infected, or scarred in any way.

Step 6: Choose an injection site and wipe the skin with an alcohol wipe (See Figures G and H). Let the injection site dry before injecting the dose.

• Do not touch this area again before giving the injection.

Step 7: Pull the protective cover straight off the needle (See Figure I). Do not twist the cover off.
Giving your AVONEX injection (cont’d)

Step 8: With 1 hand, stretch the skin out around the injection site. With the other hand, hold the syringe like a pencil. Use a quick dart-like motion and insert the needle at a 90 degree angle, through the skin and into the muscle (See Figure J). Once the needle is in, let go of the skin.

Step 9: Slowly push the plunger down until the syringe is empty (See Figure K).

Step 10: Pull the needle out of the skin (See Figure L). Press down on the injection site with the gauze pad for a few seconds or rub gently in a circular motion.

• If you see blood after you press the injection site for a few seconds, wipe it off with gauze and apply an adhesive bandage.

If you are not sure you received the full dose, contact your healthcare provider.

We are always here to help if you have problems with your injection. Call us at 1-800-456-2255.
After your AVONEX injection

▷ Do not recap the needle. Recapping the needle can lead to a needle stick injury.

▷ Throw away the used AVONEX prefilled syringes and needles in a sharps container or some type of hard plastic or metal container with a screw cap such as a detergent bottle or coffee can. Check with your healthcare provider about the right way to throw away the container. There may be local or state laws about how to throw away used AVONEX prefilled syringes and needles. Do not throw away used AVONEX prefilled syringes and needles in household trash or recycling bins.

▷ After 2 hours, check the injection site for redness, swelling or tenderness. If you have a skin reaction and it does not clear up in a few days, contact your healthcare provider.
AVONEX prefilled syringe

Notes

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For important safety information, please see pages 13-15 and the enclosed full Prescribing Information, Medication Guide and Instructions for Use.

Questions? You can call us any time at 1-800-456-2255.
Indication and Important Safety Information

Indication

AVONEX (interferon beta-1a) is approved by FDA to treat relapsing forms of multiple sclerosis (MS) to decrease the number of flare-ups and slow the occurrence of some of the physical disability that is common in people with MS. AVONEX is approved for use in people who have experienced a first attack and have lesions consistent with MS on their MRI.

Important Safety Information

Before beginning treatment, you should discuss with your healthcare provider the potential benefits and risks associated with AVONEX.

AVONEX can cause serious side effects. Tell your healthcare provider right away if you have any of the symptoms listed below while taking AVONEX.

- Behavioral health problems including depression, suicidal thoughts or hallucinations. Some people taking AVONEX may develop mood or behavior problems including irritability (getting upset easily), depression (feeling hopeless or feeling bad about yourself), nervousness, anxiety, aggressive behavior, thoughts of hurting yourself or suicide, and hearing or seeing things that others do not hear or see (hallucinations).

- Liver problems, or worsening of liver problems including liver failure and death. Symptoms may include nausea, loss of appetite, tiredness, dark colored urine and pale stools, yellowing of your skin or the white part of your eye, bleeding more easily than normal, confusion, and sleepiness. During your treatment with AVONEX you will need to see your healthcare provider regularly and have regular blood tests to check for side effects.

- Serious allergic reactions and skin reactions. Symptoms may include itching, swelling of the face, eyes, lips, tongue or throat, trouble breathing, anxiousness, feeling faint, and skin rash, hives, sores in your mouth, or your skin blisters and peels.

AVONEX will not cure your MS but may decrease the number of flare-ups of the disease and slow the occurrence of some of the physical disability that is common in people with MS. MS is a life-long disease that affects your nervous system by destroying the protective covering (myelin) that surrounds your nerve fibers.

The way AVONEX works in MS is not known. It is not known if AVONEX is safe and effective in children.

Do not take AVONEX if you are allergic to interferon beta, albumin (human), or any of the ingredients in AVONEX.
Important Safety Information (cont’d)

Before taking AVONEX, tell your healthcare provider if you:

► are being treated for a mental illness, or had treatment in the past for any mental illness, including depression and suicidal behavior.

► have or had bleeding problems or blood clots, have or had low blood cell counts, have or had liver problems, have or had seizures (epilepsy), have or had heart problems, have or had thyroid problems, have or had any kind of autoimmune disease (where the body’s immune system attacks the body’s own cells), such as psoriasis, systemic lupus erythematosus, or rheumatoid arthritis.

► drink alcohol.

► are pregnant or plan to become pregnant. It is not known if AVONEX will harm your unborn baby. Tell your healthcare provider if you become pregnant during your treatment with AVONEX.

► are breastfeeding or plan to breastfeed. It is not known if AVONEX passes into your breast milk. You and your healthcare provider should decide if you will use AVONEX or breastfeed. You should not do both.

Tell your healthcare provider about all the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements.

AVONEX can cause serious side effects including:

► Heart problems, including heart failure.
While AVONEX is not known to have any direct effects on the heart, a few patients who did not have a history of heart problems developed heart muscle problems or congestive heart failure after taking AVONEX. If you already have heart failure, AVONEX may cause your heart failure to get worse. Call your healthcare provider right away if you have worsening symptoms of heart failure such as shortness of breath or swelling of your lower legs or feet while using AVONEX.

► Some people using AVONEX may have other heart problems including low blood pressure, fast or abnormal heart beat, chest pain, and heart attack or heart muscle problem (cardiomyopathy).
Important Safety Information (cont’d)

- **Blood problems.** AVONEX can affect your bone marrow and cause low red and white blood cell, and platelet counts. In some people, these blood cell counts may fall to dangerously low levels. If your blood cell counts become very low, you can get infections and problems with bleeding and bruising.

- **Seizures.** Some patients have had seizures while taking AVONEX, including patients who have never had seizures before.

- **Infections.** Some people who take AVONEX may get an infection. Symptoms of an infection may include fever, chills, pain or burning with urination, urinating often, bloody diarrhea, and coughing up mucus.

- **Thyroid problems.** Some people taking AVONEX develop changes in their thyroid function. Symptoms of thyroid changes include problems concentrating, feeling cold or hot all the time, weight changes, and skin changes.

Tell your healthcare provider right away if you have any of the symptoms listed above.

The most common side effects of AVONEX include:

- **Flu-like symptoms.** Most people who take AVONEX have flu-like symptoms early during the course of therapy. Usually, these symptoms last for a day after the injection. You may be able to manage these flu-like symptoms by taking over-the-counter pain and fever reducers. For many people, these symptoms lessen or go away over time. Symptoms may include muscle aches, fever, tiredness, and chills.

Call your healthcare provider for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

Please see the enclosed full Prescribing Information and Medication Guide for additional important safety information. This information is not intended to replace discussions with your healthcare provider.
Instructions for Use
AVONEX® (a-vuh-necks)
(interferon beta-1a)
injection for intramuscular use
single-use prefilled syringe

Read the Instructions for Use before you start using AVONEX and each time you get a refill. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or your treatment.

Supplies you will need for the AVONEX injection:
• 1 AVONEX Administration Dose Pack that contains:
  • 1 AVONEX prefilled syringe
  • 23 gauge, 1¼ inch long sterile needle
• 1 alcohol wipe
• 1 gauze pad
• 1 adhesive bandage
• a puncture resistant container for disposal of used syringes and needles

Preparing the dose of AVONEX:
• Find a well-lit, clean, flat work surface like a table and collect all the supplies you will need to give yourself or receive an injection.
• Take 1 AVONEX Administration Dose Pack out of the refrigerator about 30 minutes before you plan on injecting the AVONEX dose to allow it to reach room temperature. Do not use external heat sources such as hot water to warm the AVONEX prefilled syringe.
• Check the expiration date printed on AVONEX prefilled syringe, AVONEX Administration Dose Pack, and the outer carton. Do not use AVONEX prefilled syringe past the expiration date.
• Wash your hands with soap and water.

Identifying parts of the AVONEX prefilled syringe (See Figure A):

Preparing the AVONEX injection:
### Step 1: Hold the AVONEX prefilled syringe with the cap pointing down and with the 0.5 mL mark at eye level (See Figure A).
- Check the syringe:
  - The syringe should not have any cracks or damage.
  - Check that the cap is intact and has not been removed.
  - The amount of liquid in the syringe should be at or very close to the 0.5 mL mark.
  - AVONEX should look clear, colorless, and should not have any particles in it.
- **Do not** use the AVONEX prefilled syringe if:
  - the syringe is cracked or damaged
  - the solution is cloudy, colored, or has lumps or particles in it
  - the cap has been removed or is not tightly attached or
  - there is not enough liquid in the syringe

**Do not** use that syringe. Get a new syringe. Contact MS ACTIVESOURCE at 1-800-456-2255.

<table>
<thead>
<tr>
<th>Syringe</th>
<th>Cap</th>
<th>Protective rubber cover</th>
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<tbody>
<tr>
<td>(Figure A)</td>
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### Step 2: With 1 hand, hold the AVONEX prefilled syringe right under the cap and with the cap pointing up (See Figure B).
- Make sure you are holding the AVONEX prefilled syringe by the ridged part, directly under the cap.

<table>
<thead>
<tr>
<th>Hand holding syringe</th>
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<td>(Figure B)</td>
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### Step 3: With the other hand, grasp the cap and bend it at a 90° angle until the cap snaps off (See Figure C and Figure D).
Step 4: Open the sterile needle package and take out the covered needle. Hold the AVONEX prefilled syringe with the glass syringe tip pointing up. Press the needle on the AVONEX prefilled syringe glass tip (See Figure E).

Step 5: Gently turn the needle forward (clockwise) until it is tight and firmly attached (See Figure F).
- If the needle is not firmly attached, it may leak and you may not get your full dose of AVONEX.
- Do not remove the plastic cover from the needle.

Giving the AVONEX injection:
- Your healthcare provider should show you or a caregiver how to prepare and inject the dose of AVONEX before AVONEX prefilled syringe is used for the first time. Your healthcare provider or nurse should watch you inject the dose of AVONEX the first time AVONEX prefilled syringe is used.
- Inject your AVONEX exactly as your healthcare provider has shown you.
- AVONEX is injected into the muscle (intramuscularly).
- AVONEX should be injected into the thigh or upper arm (See Figures G and H).
- Change (rotate) your injection sites for each dose. **Do not** use the same injection site for each injection.
- **Do not** inject into an area of the body where the skin is irritated, reddened, bruised, infected or scarred in any way.

**Step 6:** Choose an injection site and wipe the skin with an alcohol wipe (See Figures G and H). Let the injection site dry before injecting the dose.
- **Do not** touch this area again before giving the injection.

**Step 7:** Pull the protective cover straight off the needle (See Figure I). **Do not** twist the cover off.

**Step 8:** With 1 hand, stretch the skin out around the injection site. With the other hand, hold the syringe like a pencil. Use a quick dart-like motion and insert the needle at a 90 degree angle, through the skin and into the muscle (See Figure J). Once the needle is in, let go of the skin.

**Step 9:** Slowly push the plunger down until the syringe is empty (See Figure K).
Step 10: Pull the needle out of the skin (See Figure L). Press down on the injection site with the gauze pad for a few seconds or rub gently in a circular motion.

- If you see blood after you press the injection site for a few seconds, wipe it off with gauze and apply an adhesive bandage.

After the AVONEX injection:

- **Do not** recap the needle. Recapping the needle can lead to a needle stick injury.

- Throw away the used AVONEX prefilled syringes and needles in a sharps container or some type of hard plastic or metal container with a screw cap such as a detergent bottle or coffee can. Check with your healthcare provider about the right way to throw away the container. There may be local or state laws about how to throw away used AVONEX prefilled syringes and needles. **Do not** throw away used AVONEX prefilled syringes and needles in household trash or recycling bins.

- After 2 hours, check the injection site for redness, swelling or tenderness. If you have a skin reaction and it does not clear up in a few days, contact your healthcare provider.

General information about the safe and effective use of AVONEX

- Always use a new AVONEX prefilled syringe and needle for each injection. **Do not** re-use your AVONEX prefilled syringe or needles.

- **Do not** share your AVONEX prefilled syringe or needles.

- Keep the AVONEX prefilled syringe and needles out of the reach of children.

This Instructions for Use has been approved by the U.S. Food and Drug Administration.

Manufactured by: Biogen Inc.
Instructions for Use

AVOSTARTGRIP® Titration Kit

Use with AVONEX® (interferon beta-1a) Prefilled Syringe Only

Read the Instructions for Use before you start using AVONEX and each time you get a refill. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or your treatment.

Preparing the AVONEX Prefilled Syringe:

- Find a well lit, clean, flat work surface like a table and collect all the supplies you will need to give yourself or receive an injection.

- Take 1 AVONEX Administration Dose Pack out of the refrigerator about 30 minutes before you plan on injecting the AVONEX dose to allow it to reach room temperature. **Do not** use external heat sources such as hot water to warm the AVONEX prefilled syringe.

- Check the expiration date printed on the AVONEX prefilled syringe, AVONEX prefilled syringe Administration Dose Package carton, and the outer carton. **Do not** use the AVONEX prefilled syringe past the expiration date.

- Wash your hands with soap and water.

Supplies you will need for the AVONEX injection:

- 1 AVONEX Administration Dose Pack that contains:
  - 1 AVONEX prefilled syringe
  - 23 gauge, 1¼ inch long sterile needle

- 1 alcohol wipe

- 1 gauze pad

- 1 adhesive bandage

- a puncture resistant container for disposal of used syringes and needles
Identifying parts of the AVONEX prefilled syringe (See Figure A):

Preparing the AVONEX injection:

**Step 1:** Hold the AVONEX prefilled syringe with the cap pointing down and with the 0.5 mL mark at eye level (See Figure A).

- Check the syringe:
  - The syringe should not have any cracks or damage.
  - Check that the cap is intact and has not been removed.
  - The amount of liquid in the syringe should be at or very close to the 0.5 mL mark.
  - AVONEX should look clear, colorless, and should not have any particles in it.

- **Do not** use the AVONEX prefilled syringe if:
  - the syringe is cracked or damaged
  - the solution is cloudy, colored, or has lumps or particles in it
  - the cap has been removed or is not tightly attached or
  - there is not enough liquid in the syringe

*Do not* use that syringe. Get a new syringe. Contact MS ActiveSource at 1-800-456-2255.
**Step 2:** With 1 hand, hold the AVONEX prefilled syringe right under the cap and with the cap pointing up (See Figure B).
  - Make sure you are holding the AVONEX prefilled syringe by the ridged part, directly under the cap.

(Figure B)

**Step 3:** With the other hand, grasp the cap and bend it at a 90º angle until the cap snaps off (See Figure C and Figure D).

(Figure C)

(Figure D)

**Step 4:** Open the sterile needle package and take out the covered needle. Hold the AVONEX prefilled syringe with the glass syringe tip pointing up. Press the needle on the AVONEX prefilled syringe glass tip (See Figure E).

(Figure E)
**Step 5:** Gently turn the needle forward (clockwise) until it is tight and firmly attached (See Figure F).

- If the needle is not firmly attached, it may leak and you may not get your full dose of AVONEX.
- **Do not** remove the plastic cover from the needle.

**Using the AVONEX prefilled syringe with the AVOSTARTGRIP titration kit:**

- Your AVONEX dose may be titrated over 3 weeks by using AVONEX prefilled syringe with the AVOSTARTGRIP titration kit. The AVOSTARTGRIP is used for giving the week 1, 2, and 3 (¼, ½, ¾) injections.
  - **Week 1:** ¼ dose (white device)
  - **Week 2:** ½ dose (yellow device)
  - **Week 3:** ¾ dose (purple device)
  - **Week 4:** a full dose

- The 3 AVOSTARTGRIP devices are for single-use only with the AVONEX prefilled syringe. **Do not** re-use the AVONEX prefilled syringe and AVOSTARTGRIP devices.

- You must prepare the AVONEX prefilled syringe and needle before you put it into the AVOSTARTGRIP device. **Follow steps 1 to 5 above to prepare the AVONEX prefilled syringe.**
Identifying the parts of AVOSTARTGRIP titration kit (See Figure G):

- AVOSTARTGRIP has a “collar” on top of the device that will stop the syringe from injecting a full dose (See Figure H). The “collar” makes sure that you do not get the full dose of AVONEX.
## Attaching the AVOSTARTGRIP device:

**Step 6:** Choose the right AVOSTARTGRIP titration device for your weekly dose.

- **Week 1 Injection:** Choose the **white** device to give ¼ dose (See Figure I).

- **Week 2 Injection:** Choose the **yellow** device to give ½ dose (See Figure J).

- **Week 3 Injection:** Choose the **purple** device to give ¾ dose (See Figure K).

**Step 7:** Put the right AVOSTARTGRIP device on a flat surface with the door open (See Figure L).

**Step 8:** Line up the AVONEX prefilled syringe over the AVOSTARTGRIP device with the plunger pointing to the left and the needle pointing to the right (See Figure M).
**Step 9:** Push the AVONEX prefilled syringe down into the AVOSTARTGRIP device until both ends “snap” into place (See Figure N).

![Figure N](image)

**Step 10:** Using two fingers, push the door down until it closes over the AVONEX prefilled syringe (See Figure O).
- You will hear a “snap” when the door is closed the right way. **Do not** open door after it is closed.

![Figure O](image)

**Step 11:** Check to make sure that the AVONEX prefilled syringe is in the AVOSTARTGRIP device the right way and that the door is tightly closed.

**Giving the AVONEX injection:**
- Your healthcare provider should show you or a caregiver how to prepare and inject the dose of AVONEX before AVONEX prefilled syringe is used for the first time. Your healthcare provider or nurse should watch you inject the dose of AVONEX the first time AVONEX prefilled syringe is used.
- Inject your AVONEX exactly as your healthcare provider has shown you.
- AVONEX is injected into the muscle (intramuscularly).
- AVONEX should be injected into the thigh or upper arm (See Figures P and Q).
- Change (rotate) your injection sites for each dose. **Do not** use the same injection site for each injection.
- **Do not** inject into an area of the body where the skin is irritated, reddened, bruised, infected or scarred in any way.
**Step 12:** Choose an injection site and wipe the skin with an alcohol wipe (See Figures P and Q). Let the injection site dry before injecting the dose.

- **Do not** touch this area again before giving the injection.

(Figure P)  (Figure Q)

**Step 13:** Pull the protective cover straight off the needle (See Figure R). **Do not** twist the cover off.

(Figure R)

**Step 14:** With 1 hand, stretch the skin out around the injection site. With the other hand, hold the syringe like a pencil. Use a quick dart-like motion and insert the needle at a 90° angle, through the skin and into the muscle (See Figure S). Once the needle is in, let go of the skin.

(Figure S)

**Step 15:** Make sure that you push the plunger all the way down until it touches the collar (See Figure T).

(Figure T)

**Step 16:** Pull the needle out of the skin (See Figure U). Press down on the injection site with the gauze pad for a few seconds or rub gently in a circular motion.

- If you see blood after you press the injection site for a few seconds, wipe it off with gauze and apply an adhesive bandage.

(Figure U)
After the AVONEX injection:

Do not recap the needle. Recapping the needle can lead to a needle stick injury.

- Throw away the used AVONEX prefilled syringes, AVOSTARTGRIP devices, and needles in a sharps container or some type of hard plastic or metal container with a screw cap such as a detergent bottle or coffee can. Check with your healthcare provider about the right way to throw away the container. There may be local or state laws about how to throw away used AVONEX prefilled syringes, AVOSTARTGRIP devices, and needles. Do not throw away used AVONEX prefilled syringes, AVOSTARTGRIP devices, and needles in household trash or recycling bins.

- After 2 hours, check the injection site for redness, swelling or tenderness. If you have a skin reaction and it does not clear up in a few days, contact your healthcare provider.

General information about the safe and effective use of AVONEX

- Always use a new AVONEX prefilled syringe, AVOSTARTGRIP device, and needle for each injection. Do not re-use your AVONEX prefilled syringe, AVOSTARTGRIP device, or needles.

- Do not share your AVONEX prefilled syringe, AVOSTARTGRIP device, or needles.

- Keep the AVONEX prefilled syringe, AVOSTARTGRIP device, and needles out of the reach of children.

- You can use the table below to keep track of your weekly injections.

<table>
<thead>
<tr>
<th>Week</th>
<th>Dose</th>
<th>Use Titration Device</th>
<th>Date/Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 1</td>
<td>¼ Dose</td>
<td>White</td>
<td></td>
</tr>
<tr>
<td>Week 2</td>
<td>½ Dose</td>
<td>Yellow</td>
<td></td>
</tr>
<tr>
<td>Week 3</td>
<td>¾ Dose</td>
<td>Purple</td>
<td></td>
</tr>
<tr>
<td>Week 4</td>
<td>Full Dose</td>
<td>None</td>
<td></td>
</tr>
</tbody>
</table>

This Instructions for Use has been approved by the U.S. Food and Drug Administration.