

MEDICATION GUIDE

AVONEX[®]
Interferon beta-1a

(Including appendix with instructions for using AVONEX[®] Vials)

Please read this guide carefully before you start to use AVONEX[®] (a-vuh-necks) and each time your prescription is refilled since there may be new information. The information in this guide does not take the place of talking with your doctor or healthcare professional.

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

AVONEX[®] will not cure multiple sclerosis (MS) but it has been shown 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[®] can cause serious side effects, so before you start taking AVONEX[®], you should talk with your doctor about the possible benefits of AVONEX[®] and its possible side effects to decide if AVONEX[®] is right for you. Potential serious side effects include:

- **Depression** - Some people treated with interferons, including AVONEX[®], have become depressed (feeling sad, feeling low or feeling bad about oneself). Some people have thought about killing themselves and a few have committed suicide. Depression is common in people with MS. If you are noticeably sadder or feeling more hopeless, you should tell a family member or friend right away and call your doctor as soon as possible. You should tell the doctor if you have ever had any mental illness, including depression, and if you take any medicines for depression.
- **Risk to pregnancy** - If you become pregnant while taking AVONEX[®], you should stop using AVONEX[®] immediately and call your doctor. AVONEX[®] may cause you to lose your baby (miscarry) or may cause harm to your unborn child. You and your doctor will need to decide whether the potential benefit of taking AVONEX[®] is greater than the risks are to your unborn child.
- **Allergic reactions** - Some patients taking AVONEX[®] have had severe allergic reactions leading to difficulty breathing. Allergic reactions can happen after your first dose or may not happen until after you have taken AVONEX[®] many times. Less severe allergic reactions such as rash, itching, skin bumps or swelling of the mouth and tongue can also happen. If you think you are having an allergic reaction, stop using AVONEX[®] immediately and call your doctor.
- **Blood problems** - You may have a drop in the levels of infection-fighting blood cells, red blood cells or cells that help to form blood clots. If the drop in levels are severe, they can lessen your ability to fight infections, make you feel tired or sluggish or cause you to bruise or bleed easily.
- **Seizures** - Some patients have had seizures while taking AVONEX[®], including some patients who have never had seizures before. It is not known whether the

seizures were related to the effects of their MS, to AVONEX[®], or to a combination of both. If you have a seizure while taking AVONEX[®], you should stop taking AVONEX[®] and call your doctor right away.

- **Heart problems** - While AVONEX[®] is not known to have 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[®]. Some of the symptoms of heart problems are swollen ankles, shortness of breath, decreased ability to exercise, fast heartbeat, tightness in chest, increased need to urinate at night, and not being able to lay flat in bed. If you develop these symptoms or any heart problems while taking AVONEX[®], you should call your doctor right away.

For more information on possible side effects with AVONEX[®], please read the section on “**What are the possible side effects of AVONEX[®]?**” in this Medication Guide.

What is AVONEX[®]?

AVONEX[®] is a form of a protein called beta interferon that occurs naturally in the body. It is used to treat relapsing forms of multiple sclerosis. It 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.

Who should not take AVONEX[®]?

Do not take AVONEX[®] if you have had an allergic reaction (difficulty breathing, itching, flushing or skin bumps spread widely over the body) to interferon beta.

Do not take the vial formulation of AVONEX[®] if you have a history of hypersensitivity to albumin (human).

If you have ever had any of the following conditions or serious medical problems, you should tell your doctor before taking AVONEX[®]:

- Depression (sinking feeling or sadness), anxiety (feeling uneasy or fearful for no reason), or trouble sleeping
- Problems with your thyroid gland
- Blood problems such as bleeding or bruising easily and anemia (low red blood cells) or low white blood cells
- Seizures (for example, epilepsy)
- Heart problems
- Liver disease
- Are planning to become pregnant

You should tell your doctor if you are taking any other prescription or nonprescription medicines. This includes any vitamin or mineral supplements, or herbal products.

You should tell your doctor if you have had a latex sensitivity since the AVONEX[®] prefilled syringe cap contains natural rubber (latex), which may cause allergic reactions.

How should I take AVONEX®?

To get the most benefit from this medicine, it is important that you take AVONEX® exactly as your doctor tells you.

AVONEX® is given by injection into the muscle (intramuscular injection) once a week, on the same day (for example, every Monday right before bedtime). 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® on two consecutive days.** Take only the dose your doctor has prescribed for you.

Do not change your dose unless you are told to by your doctor. If you take more than your prescribed dose, call your healthcare provider right away.

Your doctor may want to monitor you more closely.

You should always follow your doctor's instructions and advice about how to take this medication. If your doctor feels that you, or a family member or friend, may give you the injections, then you and/or the other person should be instructed by your doctor or other healthcare provider in how to prepare and inject your dose of AVONEX®.

Do not try to give yourself injections at home until you are sure that you (or the person who will be giving you the injections) fully understands and is comfortable with how to prepare and inject the product. At the end of this guide there are detailed instructions on how to prepare and give yourself an injection of AVONEX® that will help remind you of the instructions from your doctor or healthcare provider.

Always use a new, unopened AVONEX® vial or prefilled syringe for each injection. Never reuse the vials or syringes.

It is important that you change your injection site each week. You should always avoid injecting AVONEX® into an area of skin that is sore, red, infected, or otherwise damaged.

AVONEX® comes in two different forms (a powder in a single-use vial and a liquid in a prefilled syringe). **See the attached appendix for detailed instructions for preparing and giving a dose of AVONEX®. These instructions are specific to the form of AVONEX® chosen for you by your healthcare provider.**

What should I avoid while taking AVONEX®?

- **Pregnancy** - You should avoid becoming pregnant while taking AVONEX® until you have talked with your doctor. AVONEX® can cause you to lose your baby (miscarry).
- **Breast-feeding** - You should talk to your doctor if you are breast-feeding an infant. It is not known if the interferon in AVONEX® gets into the breast milk, or if it could harm your nursing baby.

What are the possible side effects of AVONEX®?

- **Flu-like symptoms** - Most people who take AVONEX® have flu-like symptoms (fever, chills, sweating, muscle aches, and tiredness) 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 injecting your AVONEX® dose at bedtime and taking over-the-counter pain and fever reducers. For many people, these symptoms lessen or go away over time. Talk to your doctor if these symptoms continue longer than the first few months of therapy, or if they are difficult to manage.

- **Depression** - Some patients taking interferons have become severely depressed and/or anxious. If you feel sad or hopeless you should tell a friend or family member right away and call your doctor immediately. Your doctor or healthcare provider may ask that you stop taking AVONEX[®], and/or may recommend that you take a medication to treat your depression. **(See “What is the most important information I should know about AVONEX[®]?”)**
- **Blood problems** - A drop in the levels of white (infection-fighting) blood cells, red blood cells, or a part of your blood that helps to form blood clots (platelets) can happen. If this drop in blood levels is severe, it can lessen your ability to fight infections, make you feel very tired or sluggish, or cause you to bruise or bleed easily. Your doctor may ask you to have periodic blood tests. **(See “What is the most important information I should know about AVONEX[®]?”)**
- **Liver problems** - Your liver function may be affected. Symptoms of changes in your liver include yellowing of the skin and whites of the eyes and easy bruising.
- **Thyroid problems** - Some people taking AVONEX[®] develop changes in the function of their thyroid. Symptoms of these changes include feeling cold or hot all the time, a change in your weight (gain or loss) without a change in your diet or amount of exercise you get, or feeling emotional.
- **Seizures** - Some patients have had seizures while taking AVONEX[®], including patients who have never had seizures before. It is not known whether the seizures were related to the effects of their MS, to AVONEX[®], or to a combination of both. If you have a seizure while taking AVONEX[®], you should call your doctor right away. **(See “What is the most important information I should know about AVONEX[®]?”)**
- **Heart problems** - 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[®]. Some of the symptoms of heart problems are swollen ankles, shortness of breath, decreased ability to exercise, fast heartbeat, tightness in chest, increased need to urinate at night, and not being able to lay flat in bed. If you develop these symptoms or any heart problems while taking AVONEX[®], you should call your doctor right away. **(See “What is the most important information I should know about AVONEX[®]?”)**

If you get any of the symptoms listed in this section or any listed in the section “**What is the most important information I should know about AVONEX[®]?**”, you should call your doctor right away. Whether you experience any side effects or not, you and your doctor should periodically discuss your general health. Your doctor may want to monitor you more closely or may ask you to have blood tests more frequently.

General advice about prescription medicines

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. This medication has been prescribed for your particular condition. Do not use it for another condition or give this drug to anyone else. If you have questions you should speak with your doctor or healthcare professional. You may also ask your doctor or pharmacist for a copy of the information provided to them with the product.

Keep this and all drugs out of the reach of children.

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

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Medication Guide Appendix: Instructions for Preparing and Giving a Dose with an AVONEX[®] Vial

Storing AVONEX[®] Vials

Prior to use, AVONEX[®] should be refrigerated (36-46°F or 2-8°C) but can be kept for up to 30 days at room temperature (77°F or 25°C). You should avoid exposing AVONEX[®] to high temperatures and freezing. After mixing, AVONEX[®] solution should be used immediately, within 6 hours when stored refrigerated at 36-46°F or 2-8°C. Do not freeze the AVONEX[®] solution.

How do I prepare and inject a 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. You may want to take one AVONEX[®] Administration Dose Pack out of the refrigerator about 30 minutes before you plan on injecting your dose to allow it to reach room temperature. A room temperature solution is more comfortable to inject.

You will need the following supplies:

- vial of AVONEX[®] (white to off-white powder or cake)
- vial of diluent, single-use (Sterile Water for Injection, USP)
- 3 mL syringe
- blue MICRO PIN[®] (vial access pin)
- sterile needle
- alcohol wipes
- gauze pad
- adhesive bandage
- a puncture resistant container for disposal of used syringes, needles, and MICRO PINS.

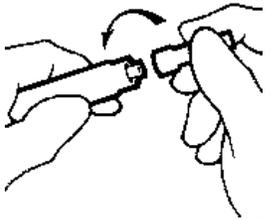
Preparing the AVONEX[®] solution

It is important to keep your work area, your hands, and your injection site clean to minimize risk of infection. You should wash your hands prior to preparing the medication.

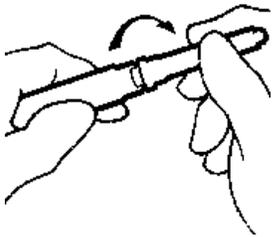
1. Check the expiration date on the AVONEX[®] vial and the vial of diluent; do not use if the medication or diluent is expired.
2. Remove the caps from the vial of AVONEX[®] and the vial of diluent, and clean the rubber stopper on the top of each vial with an alcohol wipe.



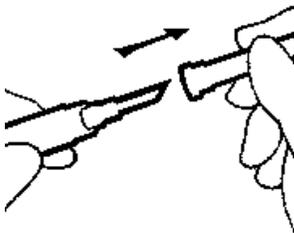
3. Remove the small light blue protective cover from the end of the syringe barrel with a counterclockwise turn.



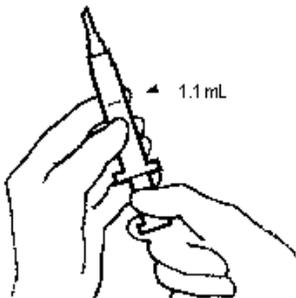
4. Attach the blue MICRO PIN[®] to the syringe by turning clockwise until secure.
NOTE: Over-tightening can make the MICRO PIN[®] difficult to remove.



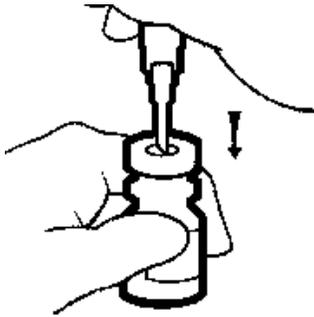
5. Pull the MICRO PIN[®] cover straight off; do not twist. Save the cover for later use.



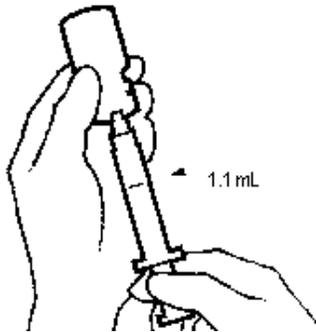
6. Pull back the syringe plunger to the 1.1 mL mark.



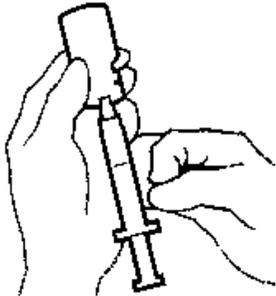
7. Firmly push the MICRO PIN[®] down through the **center** of the rubber stopper of the diluent vial.



8. Inject the air in the syringe into the diluent vial by pushing down on the plunger until it cannot be pushed any further.
9. Keeping the MICRO PIN[®] in the vial, turn the diluent vial and syringe upside down.
10. While keeping the MICRO PIN[®] in the fluid, slowly pull back on the plunger to withdraw 1.1 mL of diluent into the syringe.

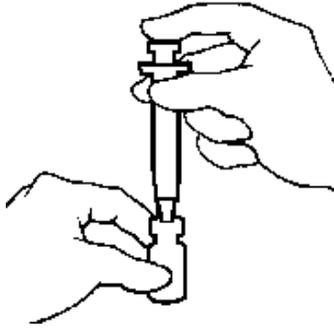


11. Gently tap the syringe with your finger to make any air bubbles rise to the top. If bubbles are present, slowly press the plunger in (to push just the bubbles out through the needle). Make sure there is still 1.1 mL of diluent in the syringe.

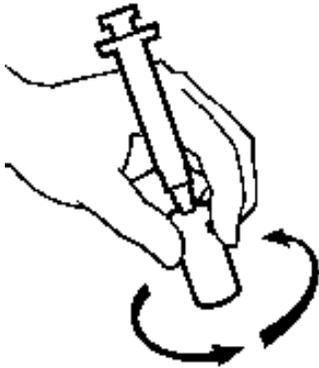


12. Slowly pull the MICRO PIN[®] out of the diluent vial.
13. Carefully insert the MICRO PIN[®] through the **center** of the rubber stopper of the vial of AVONEX[®]. *NOTE: Off-center punctures can push the stopper into the vial. If the stopper falls into the vial, do not use.*
14. **Slowly** inject the diluent into the vial of AVONEX[®]. **DO NOT** aim the stream of diluent directly on the AVONEX[®] powder. Too direct or forceful a stream of

diluent onto the powder may cause foaming, and make it difficult to withdraw AVONEX[®].

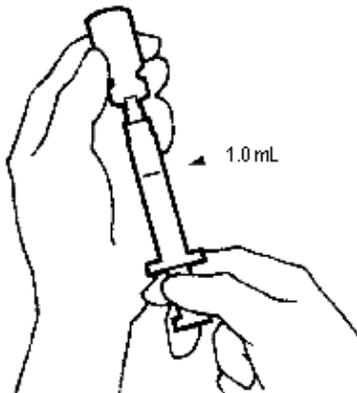


15. Without removing the syringe, **gently** swirl the vial until the AVONEX[®] is dissolved. **DO NOT SHAKE.**

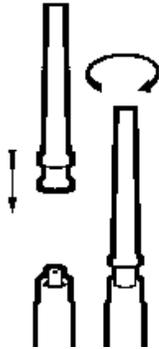


16. Check to see that all of the AVONEX[®] is dissolved. Check the solution in the vial of AVONEX[®]. It should be clear to slightly yellow in color and should not have any particles. Do not use the vial if the solution is cloudy, has particles in it or is a color other than clear to slightly yellow.

17. Turn the vial and syringe upside down. Slowly pull back on the plunger to withdraw 1.0 mL of AVONEX[®]. If bubbles appear, push solution slowly back into the vial and withdraw the solution again.



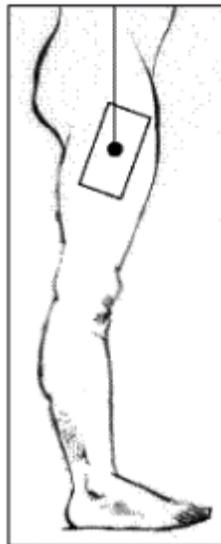
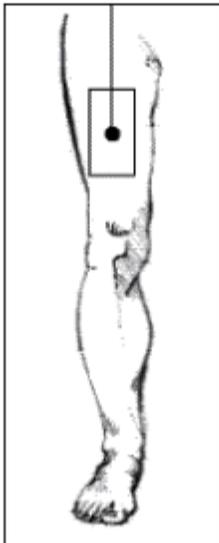
18. With the vial still upside down, tap the syringe **gently** to make any air bubbles rise to the top. Then press the plunger in until the AVONEX[®] is at the top of the syringe. Check the volume (should be 1.0 mL) and withdraw more medication if necessary. Withdraw the MICRO PIN[®] and syringe from the vial.
19. Replace the cover on the MICRO PIN[®] and remove from the syringe with a counterclockwise turn.
20. Attach the sterile needle for injection to the syringe turning clockwise until the needle is secure. A secure attachment will prevent leakage during the injection.



Selecting an injection site

The best sites for intramuscular injection are the thigh and upper arm:

- thigh



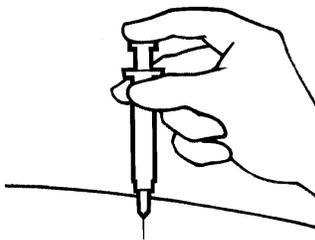
- upper arm



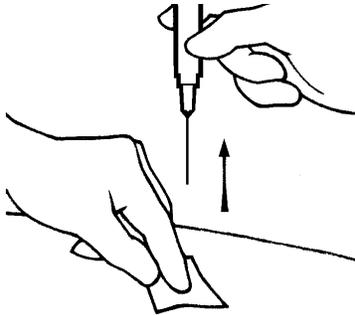
You should rotate injection sites each week. This can be as simple as switching between thighs (if you are always injecting yourself). If another person is helping you, you can rotate among your thighs and upper arms. Make sure that the site you choose is free from any skin irritations.

Injecting the AVONEX[®] dose

1. Use a new alcohol wipe to clean the skin at one of the recommended intramuscular injection sites. Then, pull the protective cover **straight** off the needle; do not twist the cover off.
2. With one hand, stretch the skin out around the injection site. Hold the syringe like a pencil with the other hand, and using a quick motion insert the needle at a 90° angle, through the skin and into the muscle.
3. Once the needle is in, let go of the skin and use that hand to gently pull back slightly on the plunger. If you see blood come into the syringe, withdraw the needle from the injection site and put pressure on the site with a gauze pad. You will need to replace the needle and choose and clean a new site for an injection.
4. If no blood came into the syringe, slowly push the plunger in until the syringe is empty.



5. Hold a gauze pad near the needle at the injection site and pull the needle straight out. Use the pad to apply pressure to the site for a few seconds or rub gently in a circular motion.



6. If there is bleeding at the site, wipe it off and, if necessary, apply an adhesive bandage.
7. Dispose of the used syringe, needle and blue MICRO PIN[®] in your puncture resistant container. DO NOT USE a syringe, MICRO PIN[®], or needle more than once. The AVONEX[®] and diluent vials should be put in the trash.

Disposal of syringes and needles

There may be special state and/or local laws for disposing of used needles and syringes. Your doctor, nurse or pharmacist should provide you with instructions on how to dispose of your used needles and syringes.

- **Always keep your disposal container out of the reach of children.**
- **DO NOT** throw used needles and syringes into the household trash and **DO NOT RECYCLE.**

Appendix Revision Date: 05/2003