

Package leaflet: Information for the user

AVONEX 30 micrograms/0.5ml solution for injection in pre-filled pen (interferon beta-1a) Pre-filled pen

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

Even if you have used Avonex before, some of the information may have changed.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

(Notes information)

This leaflet is changed from time to time.

Please check every time you get your prescription refilled to see if the leaflet has been updated.

(Notes information)

If there's anything you're not sure about, ask your doctor or pharmacist.

What is in this leaflet

1. What AVONEX is and what it is used for
2. What you need to know before you use AVONEX
3. How to use AVONEX PEN
4. Possible side effects
5. How to store AVONEX PEN
6. Contents of the pack and other information
7. How to inject AVONEX PEN

1 What AVONEX is and what it is used for

(Notes information)

Avonex works best when you use it:

- **at the same time**
- **once a week**
- **on a regular basis**

Do not stop your Avonex treatment without speaking to your doctor.

What AVONEX is

Avonex Pen is used to inject Avonex. The active substance in Avonex is a protein called *interferon beta-1a*. Interferons are natural substances made in your body to help protect you from infections and diseases. The protein in Avonex is made up of exactly the same ingredients as interferon beta that is found in the human body.

What AVONEX is used for

Avonex is used to treat Multiple Sclerosis (MS). Treatment with Avonex can help to prevent you from getting worse, although it will not cure MS.

Everyone has their own set of MS symptoms. These can include:

- Feeling off-balance or light headed, walking problems, stiffness and muscle spasms, tiredness, numbness in the face, arms or legs
- Acute or chronic pain, bladder and bowel problems, sexual problems and problems seeing things
- Difficulty in thinking and concentrating, depression.

MS also tends to flare up from time to time: this is called a relapse.

Avonex can help to reduce the number of relapses that you have and slow down the disabling effects of MS. Your doctor will advise you for how long you can use Avonex or when to stop.

How AVONEX works

Multiple sclerosis is linked to nerve (brain or spinal cord) damage. In MS, your body's defence system reacts against its own myelin – the 'insulation' that surrounds nerve fibres. When myelin is damaged, the messages between the brain and other parts of the body are disrupted. This is what causes the symptoms of MS. Avonex seems to work by stopping your body's defence system from attacking the myelin.

2. What you need to know before you use AVONEX

(Notes information)

Avonex and allergic reactions

Because Avonex is based on a protein, there is a small chance of an allergic reaction.

More about depression

If you have severe depression or thoughts about suicide, you must not use Avonex.

If you have depression, your doctor may still prescribe Avonex for you, but it's important to let your doctor know if you have had depression or any similar problems affecting your moods.

Do not use AVONEX:

- **If you are allergic** to interferon beta or any of the other ingredients of this medicine (listed in section 6)
- **If you have severe depression** or think about committing suicide.

Talk to a doctor straight away if any of these apply to you.

Warnings and precautions

Talk to your doctor before using Avonex if you have or have had in the past:

- **Depression** or problems affecting your moods
- **Thoughts about committing suicide.**

Changes to your mood, thoughts about suicide, feeling unusually sad, anxious or worthless, should be reported to your doctor immediately.

- **Epilepsy** or other seizure disorders not controlled by medication
- **Serious kidney or liver problems**
- **A low number of white blood cells or platelets**, which can cause an increased risk of infection, bleeding or anaemia

- **Heart problems**, which can cause symptoms such as chest pain (*angina*), particularly after any activity; swollen ankles, shortness of breath (*congestive heart failure*); or an irregular heartbeat (*arrhythmias*).
- Irritation at an injection site, which can lead to skin and tissue damage (injection site necrosis). When you are ready to inject, carefully follow the instructions in section 7 “How to inject AVONEX PEN”, at the end of this leaflet. This is to reduce the risk of injection site reactions.

Talk to your doctor if you have any of these conditions, or if they worsen whilst taking Avonex.

Blood clots in the small blood vessels may occur during your treatment. These blood clots could affect your kidneys. This might happen several weeks to several years after starting Avonex.

Your doctor may want to check your blood pressure, blood (platelet count) and the function of your kidneys.

Tell your doctor you are using Avonex:

- **If you are having a blood test.** Avonex may interfere with the results.

(Notes information)

Sometimes you will need to remind other medical staff that you are being treated with Avonex.

For example, if you are prescribed other medicines, or if you have a blood test, Avonex may affect the other medicines or the test result.

Paediatric population

Avonex is not recommended for use in children and adolescents because there is limited data on the use of Avonex in this population. Avonex should not be used in children below 10 years of age because it is yet to be established whether it would work for them and whether it would be safe.

Other medicines and AVONEX

Tell your doctor if you are using, have recently used or might use any other medicines, especially those used to treat epilepsy or depression. Avonex may affect other medicines or be affected by them. This includes any medicines obtained without a prescription.

Pregnancy and breast-feeding

If you are pregnant, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

No harmful effects on the breastfed newborn/infant are anticipated. Avonex can be used during breast-feeding.

Driving and using machines

If you feel dizzy, do not drive. Avonex makes some people feel dizzy. If this happens to you, or if you get any other side effects that could affect your ability, do not drive or use machines.

Important information about some of the ingredients of Avonex

This medicine is essentially ‘sodium-free’. It contains less than 23 mg (1 mmol) sodium in each weekly dose.

3. How to use AVONEX PEN

(Notes information)

There are more details on how to inject using the Avonex Pen on the back of this leaflet.

The recommended weekly dose

One injection using Avonex Pen, once a week.

Try to use Avonex at the same time on the same day each week.

Injecting yourself

You can inject Avonex yourself using the Avonex Pen without the help of your doctor, if they have trained you to do this. The instructions on how to inject yourself are at the end of this leaflet (see section 7, *How to inject AVONEX PEN*).

If you have trouble handling the Avonex Pen, ask your doctor who may be able to help.

How long to use AVONEX

Your doctor will tell you how long you need to keep using Avonex. It is important to continue using Avonex regularly. Do not make changes unless your doctor tells you.

If you inject more than you should

You should inject using only one Avonex Pen, once a week. If you have used more than one Avonex Pen in a three-day period, **contact your doctor or pharmacist straight away for advice.**

If you miss an injection

If you miss your usual weekly dose, inject a dose as soon as you can. Then leave a week before using Avonex Pen again. Continue injecting on this new day every week. If you have a preferred day for using Avonex, talk to your doctor about managing the dose, to get back to your preferred day. Do not use two injections to make up for a missed injection.

4. Possible side effects

(Notes information)

Although the list of possible side effects can seem worrying, it's possible that you may not have any of them.

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Serious side effects: get medical help

Serious allergic reactions

If you get any of these:

- Swelling of the face, lips or tongue
- Difficulty breathing
- A rash.

Call a doctor immediately. Do not use any more Avonex until you have spoken to a doctor.

Depression

If you get any symptoms of depression:

- Feeling unusually sad, anxious or worthless.

Call a doctor immediately.

Liver problems

If you get any of these symptoms:

- Yellowing of your skin or the whites of your eyes (*jaundice*)
- Itching all over
- Feeling sick, being sick (*nausea and vomiting*)
- Easy bruising of the skin.

Call a doctor immediately as they may be signs of a possible liver problem.

Side effects seen in clinical trials

(Notes information)

Side effects seen in clinical trials.

These are the side effects that people reported when Avonex was being tested. The figures are based on how many people said they'd had them. It gives you an idea how likely you are to get similar side effects.

Very common side effects (*may affect more than 1 in 10 people*)

- Flu-like symptoms – headache, muscle aches, chills or a fever: see *Flu-like symptoms*
- Headache.

Common side effects (*may affect up to 1 in 10 people*)

- Loss of appetite
- Feeling weak and tired
- Difficulty sleeping
- Depression
- Flushing
- Runny nose
- Diarrhoea (*loose stools*)
- Feeling or being sick (*nausea or vomiting*)
- Numbness or tingling of skin
- Rash, bruising of the skin
- Increased sweating, night sweats
- Pain in your muscles, joints, arms, legs or neck
- Muscle cramps, stiffness in the joints and muscles
- Pain, bruising and redness at the injection site
- Changes to blood tests. Symptoms you might notice are tiredness, repeated infection, unexplained bruising or bleeding.

Uncommon side effects (*may affect up to 1 in 100 people*)

- Hair loss
- Changes to your monthly period
- Burning feeling at the site of injection.

Rare side effects (*may affect up to 1 in 1,000 people*)

- Difficulty breathing
 - Kidney problems including scarring that may reduce your kidney function
- If you get some or all of these symptoms:

- Foamy urine
- Fatigue
- Swelling, particularly in the ankles and eyelids, and weight gain.

Tell your doctor as they may be signs of a possible kidney problem.

- Blood clots in the small blood vessels that can affect your kidneys (thrombotic thrombocytopenic purpura or haemolytic uremic syndrome). Symptoms may include increased bruising, bleeding, fever, extreme weakness, headache, dizziness or light-headedness. Your doctor may find changes in your blood and the function of your kidneys.

If any of the effects trouble you, talk to your doctor.

Other side effects

(Notes information)

These effects have been seen in people using Avonex, but we do not know how likely they are to happen.

If you feel dizzy, do not drive.

- An underactive or overactive thyroid
- Nervousness or anxiety, emotional instability, irrational thoughts or hallucinations (seeing or hearing things that are not real), confusion or suicide
- Numbness, dizziness, seizures or fits and migraines
- An awareness of your heartbeat (*palpitations*), a rapid or irregular heartbeat, or heart problems which would have the following symptoms: a reduced ability to exercise, inability to lie flat in bed, shortness of breath or swollen ankles
- Liver problems as described above
- Nettle rash or blister-like rash, itching, worsening of psoriasis if you have it
- Swelling or bleeding at the site of injection, tissue destruction (necrosis) or chest pain after an injection
- Gaining or losing weight
- Changes to test results, including changes to liver function tests
- Pulmonary arterial hypertension: A disease of severe narrowing of the blood vessels in the lungs resulting in high blood pressure in the blood vessels that carry blood from the heart to the lungs. Pulmonary arterial hypertension has been seen at various time points during treatment, including several years after starting treatment with interferon beta-products.

If any of the effects trouble you, talk to your doctor.

Effects of the injection

- **Feeling faint:** Your first injection of Avonex may be given by your doctor. It may make you feel faint. You may even actually faint. This is unlikely to happen again.
- **Just after an injection, your muscles may feel tense or very weak** – as though you are having a relapse. This is rare. It only happens when you inject and the effects soon pass. They may happen any time after starting on Avonex.
- **If you notice any irritation or skin problems** after an injection, talk to your doctor.

Flu-like symptoms

(Notes information)

Three simple ways to help reduce the impact of flu-like symptoms:

1. **Use your Avonex Pen injection just before bedtime.** This may allow you to sleep through the effects.

2. **Take paracetamol or ibuprofen half an hour before** your Avonex Pen injection and continue taking it for up to a day. Speak to your doctor or pharmacist about a suitable dose.
3. **If you have a fever, drink plenty of water** to keep you hydrated.

Some people find that after using Avonex Pen, they feel like they have flu. Signs are:

- Headache
- Muscle aches
- Chills or a fever.

These symptoms are not really flu

You can't pass it on to anyone else. They are more common when you first start using Avonex. As you keep using your injections, the flu-like symptoms gradually decrease.

Children (10 years of age and above) and adolescents

In clinical trials, some side effects were reported more frequently in children and adolescents than in adults, e.g., muscle pain, pain in extremity, fatigue, and joint pain.

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.

You can also report side effects directly via the Yellow Card Scheme.

Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

By reporting side effects you can help provide more information on the safety of this medicine.

In order to improve the traceability of this medicine, your doctor or pharmacist should record the name and the lot number of the product you have been given in your patient file. You may also wish to make a note of these details in case you are asked for this information in the future.

5. How to store AVONEX PEN

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date stated on the label.

Avonex Pen contains a pre-filled syringe of Avonex. Store in the original package in order to protect from light.

Store in a refrigerator (between 2°C and 8°C). Do not freeze.

Avonex Pen can be stored at room temperature (between 15°C and 30°C) for up to one week.

Do not use Avonex Pen if you notice:

- The pen is broken.
- The solution is coloured or you can see particles floating in it.
- The tamper evident cap has been broken.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What AVONEX PEN contains

The active substance is: Interferon beta-1a 30 micrograms/0.5 ml

The other ingredients are: Sodium acetate, trihydrate; acetic acid glacial, arginine hydrochloride, polysorbate 20 and water for injections.

What AVONEX PEN looks like and contents of the pack

Each individual pack contains one Avonex Pen, one needle and one pen cover. Avonex Pen contains a pre-filled syringe of Avonex and should only be used following adequate training. Avonex Pens are provided in packs of four or twelve for one or three months of injections.

Marketing Authorisation Holder and Manufacturer

The Marketing Authorisation Holder is:

Biogen Netherlands B.V.
Prins Mauritslaan 13
1171 LP Badhoevedorp
The Netherlands

Avonex is made by:

FUJIFILM Diosynth Biotechnologies Denmark ApS,
Biotek Allé 1,
DK-3400 Hillerød,
Denmark

Biogen Netherlands B.V.
Prins Mauritslaan 13
1171 LP Badhoevedorp
The Netherlands

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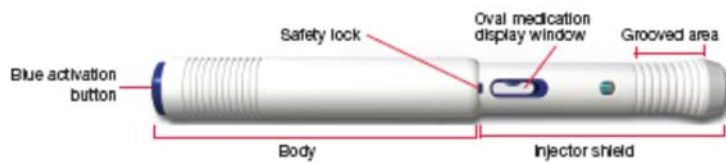
7. How to inject AVONEX PEN

Avonex Pen (single use)

Pack contents – Avonex Pen, needle and Avonex Pen cover



Avonex Pen – prepared for injection



**Avonex Pen – after injection
(prepared for disposal)**



You should have had training in how to use your Avonex Pen.

These notes are a reminder. If there's anything you're not sure about or you have a problem, check with your doctor or pharmacist.

Where to inject

Use a different injection site each week

The best area is the upper, outer thigh muscle.

Alternate the left and right thighs.

Keep a note of where you have injected each week.



- **Avonex is injected into a muscle**, the best area is the **upper, outer thigh** muscle as shown in the diagram above. Injection of Avonex into the buttocks is not recommended.
- **Use a different injection site each week.** This means less risk of irritation to your skin and muscle.
- **Do not use** any area of skin that is bruised, sore, or infected, or if there is an open wound.

A. Getting ready

1. Take one Avonex Pen out of the refrigerator

Check the pack contains one Avonex Pen, one needle and one pen cover.

Do not shake Avonex Pen.

Check the expiry date on the Avonex Pen label.

Do not use if it is out-of-date.

2. Leave Avonex Pen to warm up

Leave it at room temperature for half an hour. This makes the injection more comfortable than using straight from the refrigerator.

Tip: Do not use external heat sources such as hot water to warm Avonex Pen.

3. Wash your hands thoroughly with soap and water and dry them.

4. Prepare alcohol wipes and sticking plasters (not supplied) if you need them.

5. Find a clean, hard surface to lay out the items needed for your injection.

B. Preparing Avonex Pen



1 Remove the tamper-evident cap

Make sure the cap is intact and has not been opened. If it looks like it has been opened, do not use that Avonex Pen.

- Hold Avonex Pen so that the cap is pointing up.
- **Bend the cap at a right angle until it snaps off.**
- **Do not touch the exposed glass tip.**

Tip: Place the pen down on the table before beginning step 2.



2 Fit the needle

- Avonex Pen has been designed to function only with the supplied needle.
- **Peel off the foil** from the base of the needle cover.
- Attach the needle by pressing it onto the glass pen tip. Keep the pen upright.
- **Do not remove the needle cover.**
- Gently, turn the needle clockwise until it is firmly attached, otherwise the needle may leak. You may not get the full dose if it leaks.

Tip: The needle cover will come off automatically during step 3, below.



3 Extend the injector shield

- Hold the body of the pen firmly with one hand. Point the needle cover away from you and anyone else.
- Use your other hand, and with one quick motion **pull up the injector shield (grooved area) over the needle** until the needle is fully covered.
- **The plastic needle cover will “pop” off.**

Tip: **Do not press** the blue activation button at the same time.



4 Check the injector shield is extended correctly

- Check the injector shield is fully extended. A small rectangular area will be visible next to the oval display window. This is the safety lock.



5 Check the liquid

- Look through the oval display window. The liquid should be clear and colourless.

If the solution is cloudy, coloured or contains any floating particles, **do not use this pen.**

Air bubble(s) are normal.

C. Using Avonex Pen



1 Clean the injection site

If you need to, use an alcohol wipe to clean the skin at the injection site you've chosen. Allow the skin to dry.

Tip: The best area is the upper, outer thigh.



2 Place Avonex Pen on the skin

- Hold the body of the pen at a right angle to the injection site with one hand. Make sure the windows of the pen are visible.

Tip: Take care not to press the blue activation button too early.

- Firmly press the body of the pen down onto the skin to **release the safety lock.**

- Check the safety lock is released. The small rectangular window area will disappear. Avonex Pen is now ready to inject.

Tip: Continue to hold the pen firmly on the skin.



Safety lock visible

Safety lock released



3 Give the injection

- **Press the blue activation button with your thumb to start the injection.**

You will hear a “click” indicating the injection process has begun.

Do not lift the pen away from your skin.

- Continue to hold the pen on your skin and count slowly for a **full 10 seconds.**

- After 10 seconds pull the pen straight out to remove the needle from the injection site.

- Apply pressure to the injection site for a few seconds. If there is any blood at the site, wipe it off.



4 Confirm injection delivery

- **Check the circular display window.** The window will now appear **yellow** when the full dose has been delivered.

- Do not re-use the Avonex Pen. It is for a **single use** only.





5 Disposal

- Place the pen cover on a flat, hard surface.

Tip: **Do not hold the pen cover.** You may get a needle injury.

- Insert needle directly into the pen cover.
- **Firmly** press until you hear a “click” to seal the needle. You may need to use both hands. Once the pen is sealed there is no risk of injury.
- Dispose of rubbish properly. Your doctor, nurse or pharmacist should provide you with instructions on how to dispose of your used Avonex Pen, for example into a sharps bin. Always follow your local guidelines.