

Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) - 1986

This medicine is dispensed with a physician's prescription only

Avonex Solution for Injection

Solution for injection in a pre-filled pen/pre-filled syringe

Composition:

Each 0.5 ml syringe/ pen contains interferon beta-1a 30 µg

* See inactive ingredients in section 6 ("Additional information") in this leaflet

Read this package insert in its entirety before using this medicine. This leaflet includes concise information about this medicine. If you have additional questions, please consult your doctor or pharmacist. This medicine was prescribed for the treatment of your ailment. Do not pass it to others as it may harm them even if they seem to have a similar disease.

Avonex Solution for Injection is not intended for use in children and adolescents under the age of 16.

1. Introduction:

The active ingredient in **Avonex Solution for Injection** is a protein called interferon beta 1a. Interferons are substances that are naturally produced by the human body to protect it from infections and diseases. The protein in **Avonex Solution for Injection** is made from the same ingredients as interferon beta-1a found in the human body.

What is Avonex Solution for Injection used for?

Avonex Solution for Injection is used to treat symptoms of relapsing multiple sclerosis.

Avonex Solution for Injection can help reduce the occurrence of relapses and slow down the disabling effects of the disease.

This medicine works best when injected regularly at the same time, once a week. Do not stop treatment with **Avonex Solution for Injection** without first consulting your neurologist.

Therapeutic group: interferons.

2. Before you use this medicine:

Do not use this medicine if:

- You are sensitive (allergic) to interferon beta or to any of the other ingredients in **Avonex Solution for Injection** (see section 6, 'Additional information')
- You have severe depression or suicidal thoughts.

Special warnings concerning use of this medicine:

Consult your doctor if you are suffering or have previously suffered from:

- depression or problems affecting your mood
- thoughts about committing suicide
- epilepsy or other seizure disorders not controlled by medical treatment
- serious kidney or liver problems

- low white blood cell or platelet count (may increase the risk of infection, bleeding, or anemia).
- heart problems associated with symptoms such as chest pain particularly after activity (angina); swollen ankles; shortness of breath (congestive heart failure) or heart rhythm problems (arrhythmia).

Tell your doctor immediately if you are experiencing mood changes, suicidal thoughts or unusual feelings of sadness, anxiety or worthlessness.

Tell your doctor if you have any of the above-mentioned conditions or if they became worse while taking **Avonex Solution for Injection**.

Blood clots in 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 Solution for Injection**.

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

If you are currently taking medicines that may harm your liver or if you are drinking excessive quantities of alcohol, your doctor may ask you to take blood tests to make sure that your liver is still functioning properly.

Tell your doctor or the medical staff that you are taking **Avonex Solution for Injection** before taking a blood test, as this medicine may interfere with the results of the test.

Inform the medical staff that you are taking **Avonex Solution for Injection** if you are prescribed additional medications.

Use in children:

Avonex Solution for Injection is not intended for children and adolescents under the age of 16.

Tests and follow-up:

During treatment you may be asked to take a complete and a differential white blood cell count, a blood test - chemistry including liver function.

Drug interactions:

If you are using or have recently used other medicines, including non-prescription medicines and dietary supplements, tell your doctor or pharmacist. Particularly if you are taking:

- Medicines for the treatment of epilepsy or depression.

Using the medicine and food:

Treatment with **Avonex Solution for Injection** is not affected by food or the time of the meal.

Pregnancy and breastfeeding:

If you are or could become 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 are anticipated. **Avonex Solution for Injection** can be used during breastfeeding.

Driving and using machines:

If you feel dizzy, do not drive. **Avonex Solution for Injection** may cause dizziness in some people. If you experience dizziness or if you experience anything else that may affect your abilities, do not drive or operate machines.

Important information about some of the medicine's ingredients:

Avonex Solution for Injection is essentially 'sodium-free'. Each weekly dose of **Avonex Solution for Injection** contains less than 23 mg (1 mmol) sodium.

3. How should this medicine be used?

Always use according to the doctor's instructions.

Check with your doctor or pharmacist if you are unsure about the dosage and method of using the medicine.

- Dosage and form of treatment will be determined by the physician only. **The usual dose** for adults and adolescents over 16 years old is **one injection of Avonex Solution for Injection, once a week.**
- **Do not exceed the recommended dose.**
- It is advisable to use **Avonex Solution for Injection** on the same day of the week and at the same time a of day.
- Your doctor/nurse may gradually increase the dosage of **Avonex Solution for Injection** at the beginning of treatment in order to help reduce flu-like symptoms.
- **Not to be used in children** - this medicine must not be used in children under the age of 16.
- **Self-injection** - you can inject **Avonex Solution for Injection** yourself without medical assistance, if you have been trained to do so. The instructions for self-injection can be found at the end of this leaflet (see section 6).
If you are having trouble injecting, ask your doctor to advise you who may be able to help.

Duration of treatment:

Your doctor will tell you how long you need to take this medicine. It is important to continue using **Avonex Solution for Injection** regularly. Do not make any changes unless your doctor tells you to.

If you accidentally injected an overdose - use one dose of **Avonex Solution for Injection** once a week. If you used more than one injection within three days, contact your doctor or pharmacist immediately.

If you have taken an overdose or if a child has accidentally swallowed some medicine, go to a doctor or a hospital emergency room and bring the medicine package with you.

If you missed the weekly injection of Avonex Solution for Injection - if you missed your weekly injection, inject a dose as soon as possible and wait one week before injecting another injection of **Avonex Solution for Injection**. From now on continue injecting once a week on the new day.

Do not use a double dose to make up for a missed injection.

Continue treatment as recommended by your doctor.

Even if your health improves, do not stop taking this medicine without consulting your doctor or pharmacist.

If you stop taking this medicine, its beneficial effect will disappear.

Discontinuous treatment may prevent you from getting the desired result.

Do not take medicines in the dark! Check the label and dose every time you take a medicine. Wear glasses if you need them.

If you have additional questions about using this medicine, consult your doctor or pharmacist.

4. Possible side effects:

Like all medicines, using of **Avonex Solution for Injection** can cause side effects in some patients. Do not be alarmed by the list of side effects; you may not experience any of them.

Stop using this medicine and consult your doctor immediately, if you get any of the following side effects which may indicate an allergic reaction:

- swelling of the face, lips or tongue
- breathing difficulties
- rash

See your doctor immediately. Do not use an additional dose of **Avonex Solution for Injection** until you have consulted your doctor.

Consult your doctor immediately if you feel:

- symptoms of depression – unexplained sadness, anxiety or feeling of worthlessness.
- liver problems - yellowing of the skin or the white of your eye (jaundice), itching over your entire body, nausea, vomiting, bruising. These symptoms may be signs of a possible liver problem.

Additional side effects:

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

- Flu-like symptom: headache, muscle aches, chills or fever.
These symptoms are not really flu. They are more common when you first start using **Avonex Solution for Injection**. To avoid their appearance the medical staff may increase your dose gradually when you start treatment. These symptoms will wear off eventually.
- Headache.

Ways to help cope with flu-like symptoms:

1. Inject this medicine before bedtime.
2. Take paracetamol or ibuprofen about half an hour before injecting this medicine and continue taking it throughout the day. Consult your doctor or pharmacist about the suitable dose.
3. If you have fever, drink plenty of water to prevent dehydration.

Common side effects (may affect 1 - 10 in 100 people)

loss of appetite, weakness and fatigue, difficulty sleeping, depression, flushing, runny nose, diarrhea, nausea, vomiting, numbness or tingling of the skin, rash, bruising, increased sweating, night sweats, muscle/joint/leg/neck pain, muscle cramps, muscle and joint stiffness, pain and redness at the injection site, changes in blood tests which may cause fatigue, recurrent infections, bruising or bleeding.

Uncommon side effects (may affect up to 1-10 in 1,000 people)

hair loss, changes in the menstrual cycle, burning sensation at the injection site.

Rare side effects (may affect up to 1-10 in 10,000 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.
- Increased bruising, bleeding, fever, extreme weakness, headache, or dizziness may occur if blood clots in the small blood vessels affect your kidneys (thrombotic thrombocytopenic purpura or hemolytic uremic syndrome).

Side effects of unknown frequency (side effects whose frequency has not been determined yet)

- An underactive or overactive thyroid
- Agitation or anxiety, emotional instability, irrational thoughts or hallucinations, confusion or suicidal thoughts
- Numbness of the senses, dizziness, convulsions, and migraines
- Rapid or irregular heartbeat or heart problems that are experienced as reduced ability to exercise, inability to lie flat in bed, shortness of breath or swollen heels
- Liver problems as described above
- Nettle rash or blister-like rash, itching or worsening of psoriasis
- Swelling or bleeding at the injection site or chest pain after the injection
- Gaining or losing weight
- Changes in laboratory test results, including changes in liver function
- 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 over the course of treatment, including several years after starting treatment with interferon beta products.

Effects of injecting:

- Your first injection of **Avonex Solution for Injection** will be given to you by a healthcare professional. The injection may make you feel faint the first time. This is unlikely to happen again.
- After the injection you may feel tension or looseness in your muscles like with a seizure. This only happens during the injection and will pass soon after.
- If you notice any irritation or skin problems after the injection, talk to your doctor.

Consult your doctor if any of these side effects get worse or if you notice any side effect not mentioned in this leaflet.

You can report side effects to the Ministry of Health by following the link 'Reporting Side Effects of Drug Treatment' on the Ministry of Health home page (www.health.gov.il) which links to an online form for reporting side effects. You can also use this link: <https://sideeffects.health.gov.il>

5. How to store this medicine:

- Avoid poisoning! This medicine and all other medicines must be kept in a closed place, out of the reach and sight of children and/or babies; by this you will avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by your doctor.
- Do not use this medicine after the expiry date (exp. date) stated on the package. The expiry date refers to the last day of that month.
- **Storage conditions:** Store in a refrigerator (2°C-8°C: this is the temperature range in most domestic refrigerators).
Take the pre-filled syringe out of the refrigerator about half an hour before the injection. Do not freeze, protect from light. The syringe can be stored at a temperature of 15°C-30°C for up to one week, after which it cannot be used.

Do not use Avonex Solution for Injection if you notice any of the following signs:

- The liquid in the syringe is not colorless and transparent or you see any particles in it.
- The white cap of the syringe is open or appears to have been opened.
- The pen is broken.
- The sealed plastic tray is damaged or opened.

Medicines should not be disposed of via wastewater. Ask your pharmacist how to dispose of medicines that are no longer being used.

6. Additional information:

- In addition to the active ingredient this medicine also contains:
sodium acetate trihydrate, glacial acetic acid, arginine hydrochloride, polysorbate 20, water for injections.
- What this medicine looks like and what the package contains:
 - **Avonex Solution for Injection in a syringe** – the box contains four or twelve doses. Each dose is individually packed in a hermetically-sealed plastic tray. Inside there is a pre-filled syringe which contains 0.5 ml of a transparent liquid and a separate needle.
 - **Avonex Solution for Injection in a pen** – the box contains four or twelve doses. Each dose is individually packed and contains a pen, needle, and a pen cover. The pen contains a pre-filled syringe with 0.5 ml of transparent liquid.

Not all packages may be marketed.

- Name and address of the manufacturer:
Biogen (Denmark) Manufacturing ApS, Biogen Allé 1, DK-3400 Hillerød, Denmark
- Name and address of the license holder: Medison Pharma LTD, 10 Ha`Shiloach st.
P.O.Box 7090, Petach Tikva.
- This leaflet was reviewed and approved by the Ministry of Health in March 2016 and revised on December 2019 in accordance with Ministry of Health guidelines.
- Registration number in the Ministry of Health's National Drug Registry: 148-95-33434-00

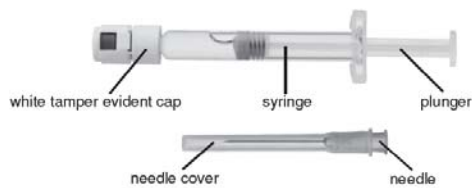
How to inject Avonex Solution for Injection

You may self-inject this medicine only if you have been properly trained with the injection technique. The following explanations serve as a guide; if you are unsure please check with your physician or pharmacist.

- **Avonex Solution for Injection** is intended for injection into the muscle, for example the upper thigh muscle. Injection into the buttocks is not recommended.
- It is recommended to change the injection site every week to reduce the risk of skin or muscle irritation.
- Avoid injecting into damaged, irritated, or infected skin areas or around open wounds.

Avonex Solution for Injection in a syringe:

Contents of the plastic tray



Early preparation stage:

1. Remove the plastic tray from the box.

Check the expiry date on the tray itself; do not use it if it has expired.

Pull back the cap and check that the blister contains:



- One syringe
- One injection needle

2. Leave the syringe out of the refrigerator for about half an hour. Injection is easier this way rather than straight from the refrigerator.

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

4. Prepare alcohol wipes and plasters (these are not supplied with the kit) if you need them. Find a clean and hard surface to lay out the items needed for injection. Lay the tray down on it.

Preparing for injection

	<p>1. Check the liquid in the syringe – the liquid should be transparent. Do not use if the solution appears cloudy, is not transparent, or it contains particles.</p>
	<p>2. Remove the white syringe cap – Make sure that the cap is whole and that there is no evidence of opening. If it seems that the cover has been opened do not use the syringe. Hold the syringe so that the white cap is facing upwards. Bend the cap at a right angle until it snaps off. Do not touch the connection port; do not push the plunger.</p>



3. Attaching the needle – Open the needle to expose the connection port. Leave the cover on the needle. **Press the needle onto the syringe and rotate clockwise until locked.**

Tip: Make sure that the needle is firmly attached to the syringe otherwise it may leak. **Now pull off the needle cover. Do not rotate it.**

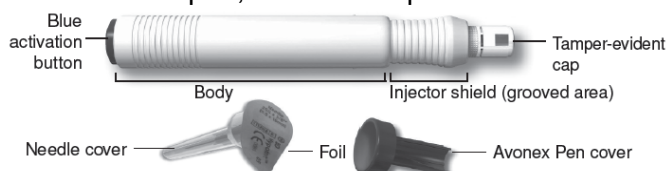
Tip: If you rotate the needle cover to remove it you may accidentally also remove the needle.

Giving the injection

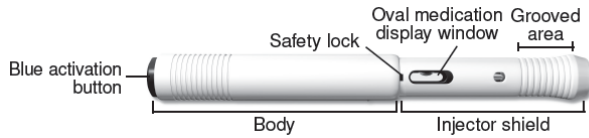
	<p>1. Clean the injection site (if necessary, use an alcohol wipe), let the skin dry. Using one hand stretch the skin around the injection site. Relax the muscle.</p>
	<p>2. Insert the injection needle with a quick dart-like thrust at 90° angles to the skin, into the muscle. The needle must go all the way in. Press the plunger slowly to inject the solution, until the syringe has emptied.</p>
	<p>3. Keep the skin tightly stretched, or press the skin surrounding the injection site and pull out the needle. Use an alcohol wipe if you need to and press it against the injection site. Put a plaster over the injection site if needed.</p>
	<p>4. Once you are finished with the injection, place the needle, syringe, and bottle in a suitable container intended for the safe collection of used needles. You may dispose of waste paper and used wipes using the regular disposal container.</p>

Avonex Solution for Injection in a pen

Pack content: pen, needle and pen cover



Pen after preparation for injection



Pen after injection



Early preparation phase

1. Take one pen package out of the box.

Check the expiry date on the pen's package, do not use if it has expired.

Check that the package contains:

- pen
- needle
- pen cover




2. Leave the pen outside of the refrigerator for about half an hour. Injecting is made easier this way rather than injecting straight from the refrigerator.

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



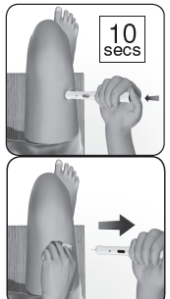
4. Prepare alcohol wipes and plasters (not supplied with the kit) if needed. Find a clean, hard surface to place the items needed for the injection.



Preparing the pen

	<p>1. Remove the cover - Make sure the cover is intact and has not been opened. If it looks like it has been opened, do not use the pen.</p> <ul style="list-style-type: none"> • Hold the pen so that the cover is pointing upwards. • Bend the cover at a right angle until it snaps off. • Do not touch the glass tip. <p>Tip: Place the pen down on the table before beginning step 2.</p>
	<p>2. Attaching the needle -</p> <ul style="list-style-type: none"> • The pen has been designed to function using the supplied needle only. • Peel off the foil from the base of the needle cover. • Attach the needle by pressing it into the pen's glass tip. Keep the pen upright with the needle pointing up. • Do not remove the needle cover. • Gently turn the needle clockwise until it is firmly locked, otherwise the needle may leak. You may not get the full dose if it leaks. <p>Tip: The needle cover will come off automatically during step 3.</p>

 <p>Before</p> <p>After</p>	<p>3. Extend the injector shield -</p> <ul style="list-style-type: none"> • 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 (the grooved area) over the needle until the needle is fully covered. • The plastic needle cover will disconnect and fall off. <p>Tip: Do not press the blue activation button.</p>
	<p>4. Check the injector shield is completely extended. A small rectangular area will be visible next to the oval display window. This is the safety mechanism.</p>
	<p>5. Check the liquid. Look through the oval display window. The liquid should be transparent. Do not use if the solution is cloudy, not transparent or contains particles. It is normal to see air bubbles.</p>

Giving the injection

	<p>1. Clean the injection site (use alcohol wipes, if needed), allow the skin to dry. Using one hand stretch the skin around the injection site. Relax the muscle.</p>
 <p>Safety lock visible Safety lock released</p>	<p>2. Place the pen on the skin -</p> <ul style="list-style-type: none"> • Hold the pen at a right angle to the injection site using one hand. Make sure the pen windows are visible. • Press the body of the pen against the skin to release the safety mechanism. • Check that the safety lock is released. The small rectangle will disappear. The pen is now ready for injection.
 <p>10 secs</p>	<p>3. Inject the medicine -</p> <ul style="list-style-type: none"> • 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 move the pen away from your body. • Continue to hold the pen close to your skin and count slowly for a full 10 seconds.

	<ul style="list-style-type: none"> • 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 wipe off the area.
	<p>4. Confirm injection delivery -</p> <ul style="list-style-type: none"> • Check the circular display window. The window will appear yellow when the full dose has been injected. • Do not re-use the pen. It is for single use only.
	<p>5. Preparation for disposal-</p> <ul style="list-style-type: none"> • Place the pen cover on a flat and hard surface. <p>Tip: Do not hold the pen cover. You may be injured by the needle.</p> <ul style="list-style-type: none"> • Insert the needle directly into the cover of the pen. • Firmly press until you hear a “click” which locks the needle. You may need to use both hands. Once the pen is locked there is no danger of injury. • Dispose of the waste using a designated container.