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

This medicine is dispensed with a doctor's prescription only

Firazyr 30 mg
Solution for Injection

Composition:
The active ingredient and its quantity:
icatibant (as acetate) 30 mg/3 ml

Inactive ingredients and allergens in this medicine – see section 2 under 'Important information about some of this medicine's ingredients' and section 6 'Additional information' in this leaflet.

Read this leaflet carefully in its entirety before using this medicine. This leaflet contains concise information about this medicine. If you have further questions, contact your physician or pharmacist.

This medicine has been prescribed to treat your illness. Do not pass it on to others. It may harm them, even if it seems to you that their illness is similar to yours.

1. What is this medicine intended for?

Firazyr is used to treat the symptoms of acute attacks of hereditary angioedema (HAE) in adults, adolescents and children aged 2 years and older.

In HAE levels of a substance in your bloodstream called bradykinin are increased and this leads to symptoms like swelling, pain, nausea and diarrhoea.

Firazyr blocks the activity of bradykinin and in this way ends the further progression of the symptoms.

Therapeutic group: other haematological agents, drugs used to treat hereditary angioedema.

2. Before using this medicine

Do not use this medicine if:

- You are sensitive (allergic) to the active ingredient (icatibant) or to any of the other ingredients in this medicine (listed in section 6).

Special warnings regarding the use of this medicine

Before taking Firazyr, tell your physician if:

- you are suffering from angina (reduced blood flow to the heart muscle)
- you have recently suffered a stroke

Some of the side effects connected with Firazyr are similar to the symptoms of your disease. Tell your physician immediately if you notice that your symptoms of the attack get worse after you received Firazyr.

In addition:

- You or your caregiver must be trained on subcutaneous (under the skin) injection technique, before you self-inject, or your caregiver injects you with Firazyr.
- If you self-inject or your caregiver injects you while you are experiencing **an attack with obstruction of the upper airway**, you must get immediate medical help in hospital.
- If no improvement is achieved in the attack symptoms after one self-or caregiver administered injection of Firazyr, refer to the physician regarding additional injections of Firazyr. For adult patients, up to 2 additional injections may be given within 24 hours.

Children and adolescents
There is no information regarding the safety and efficacy of using this medicine in children under 2 years of age or weighing less than 12 kg.

Interactions with other medicines
If you are taking or have taken recently other medicines, including non-prescription medicines and nutritional supplements, inform the physician or pharmacist.
Firazyr is not known to interact with other medicines.
If you are taking other medicines known as Angiotensin Converting Enzyme (ACE) inhibitors (for example: captopril, enalapril, ramipril, quinapril, lisinopril) used for lowering blood pressure or for any other reason, consult your physician before receiving Firazyr.

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, consult your physician before using Firazyr.
If you are breast-feeding, **you should not breast-feed for 12 hours** after you have last received Firazyr.

Driving and operating machines
Do not drive or use machines if you feel tired or dizzy as a result of your HAE attack or after using Firazyr.

Important information about some of this medicine's ingredients
The solution for injection contains less than 1 mmol (23 mg) of sodium per syringe, that is to say essentially “sodium free”.

3. How to use this medicine?

Always use this medicine according to your physician’s instructions.

Check with your physician or pharmacist if you are not sure about the dosage and the administration of the medicine.

If you have never received Firazyr before, your first dose will always be injected by a physician or nurse. Your physician will tell you when it is safe for you to go home.
After receiving training from your physician or nurse and after practicing subcutaneous (under the skin) injection technique, you will be able to inject yourself with Firazyr (or your caregiver will be able to inject Firazyr for you) when you have an HAE attack.

It is important that the injection will be performed subcutaneously (under the skin) as soon as the angioedema attack begins.
A healthcare professional will teach you and your caregiver how to safely inject Firazyr by following the instructions detailed in the Patient Leaflet.

How to use Firazyr and how often to use it?
The dosage and manner of treatment will be decided by the physician only. The recommended dosage is usually:

Adults
- The recommended dose is one injection of Firazyr (3 ml, 30 mg), subcutaneously (under the skin), as soon as symptoms of an angioedema attack are identified (such as increased swelling of the skin, especially in the face and neck area, or increasing abdominal pain).
- If no improvement is achieved after 6 hours, you should consult your physician regarding additional injections of Firazyr. For adults, up to 2 additional injections may be given within 24 hours.
- **You should not have more than 3 injections in a 24 hour period, and if you require more than 8 injections of Firazyr in a month, you should consult your physician.**

Children and adolescents aged 2 to 17 years
- The recommended dose of Firazyr is one injection of 1 ml up to a maximum of 3 ml based on body weight, injected subcutaneously (under the skin) as soon as you develop signs of an angioedema attack (for example: increased skin swelling, especially in the face and neck area, or increasing abdominal pain).
- See the section “Instructions for Injection” for the dose to inject.
- If you are not sure which dose to inject, ask your physician, pharmacist or nurse.

Do not exceed the recommended dose.

If your symptoms get worse or do not improve, you must seek immediate medical help.

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

Adhere to the treatment as recommended by your physician.

Do not take medicines in the dark! Check the label and dose <u>each time</u> you take medicine. Wear glasses if you need them.

If you have any further questions about using this medicine, consult your physician or pharmacist.

<u>Instructions for using Firazyr</u>
Firazyr is intended for subcutaneous (under the skin) injection.
Each syringe should only be used once.

Firazyr is injected with a short needle into the fatty tissue under the skin in the abdomen (tummy).

The following step-by step instructions are intended for:

- **self-administration (adults)**
- **administration by a caregiver or healthcare professional to adults, adolescents, or children aged over 2 years (weighing at least 12 kg).**

The instructions include the following main steps:
1) General guidelines
2a) Preparing the syringe for children and adolescents (2-17 years) weighing 65 kg or less
2b) Preparing the syringe and needle for injection (all patients)
3) Preparing the injection site
4) Injecting the medicine
5) Disposal of waste materials after treatment

Step-by-Step Instructions for Injection

1. General guidelines:

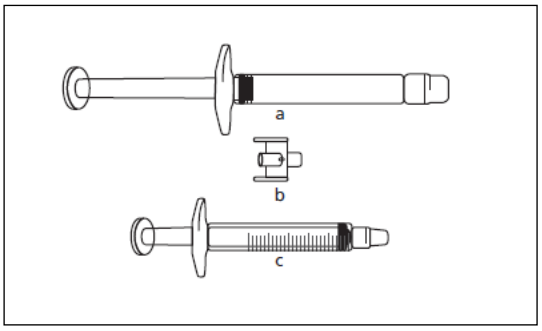
- Clean the work surface (table) before beginning the process.
- Wash your hands with soap and water.
- Open the tray by peeling back the seal.
- Remove the pre-filled syringe from the tray.
- Remove the cap from the end of the pre-filled syringe by unscrewing the cap.
- After unscrewing the cap, put down the pre-filled syringe on the surface.

2a. Preparing the syringe for children and adolescents (2-17 years) weighing 65 kg or less:

Important information for healthcare professionals and caregivers:

Where the dose is less than 30 mg (3 ml), the following equipment is required to extract the appropriate dose (see below):

a. Firazyr pre-filled syringe (containing icatibant solution)
b. Connector (adapter)
c. 3 ml graduated syringe



The required injection volume (in ml) should be drawn up into the empty 3 ml graduated syringe (see table below).

Table 1: Dosage regimen for children and adolescents

Body Weight	Injection Volume
12 kg to 25 kg	1.0 ml
26 kg to 40 kg	1.5 ml
41 kg to 50 kg	2.0 ml
51 kg to 65 kg	2.5 ml

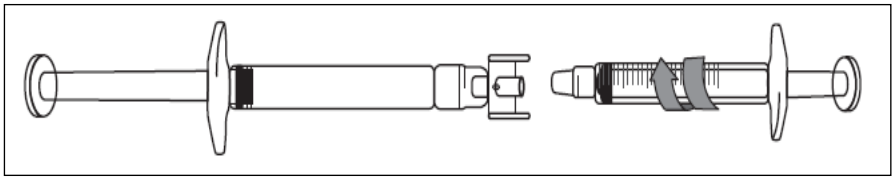
Patients weighing **more than 65 kg** will use the full contents of the pre-filled syringe (3 ml).

If you are not sure which volume of solution to extract, ask your physician, pharmacist or nurse.

1) Remove the caps on both ends of the connector.

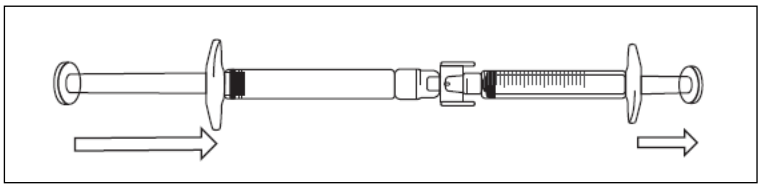
Avoid touching the ends of the connector and syringe tips, to prevent contamination.

2) Screw the connector onto the pre-filled syringe.
3) Attach the graduated syringe to the other end of the connector ensuring that both connections fit securely.

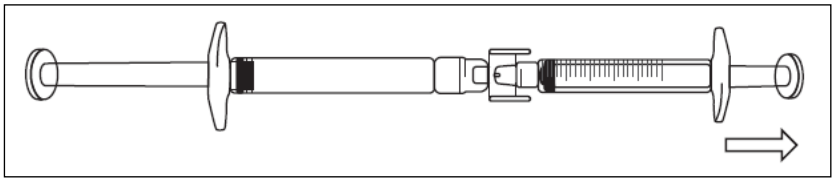


Transferring the icatibant solution to the graduated syringe:

1) To start transfer of icatibant solution, push the pre-filled syringe plunger (on far left of below image).



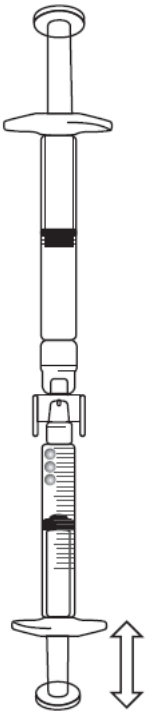
2) If the icatibant solution does not begin to transfer to the graduated syringe, pull slightly on the graduated syringe plunger until the icatibant solution starts to flow into the graduated syringe (see below image).



3) Continue to push on the pre-filled syringe plunger until the required injection volume (dose) is transferred to the graduated syringe. Refer to Table 1 for dosage information.

If there is air in the graduated syringe:

- Turn the connected syringes so that the pre-filled syringe is on top (see below image).

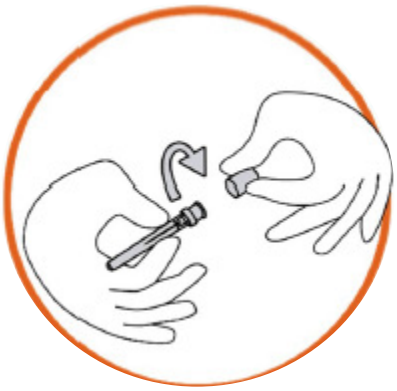


- Push the plunger of the graduated syringe so that any air is transferred back into the pre-filled syringe (this step may need to be repeated several times).
- Withdraw the required volume of icatibant solution.

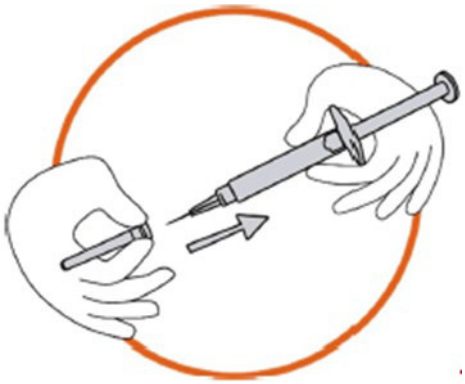
4) Remove the pre-filled syringe and connector from the graduated syringe.

5) Discard the pre-filled syringe and connector into a sharps container.

2b. Preparing the syringe and needle for injection: All patients (adults, adolescents, and children)



- Remove the needle cap from the blister.
- Twist the lid of the needle cap to break the seal (keep the needle in the needle cap).



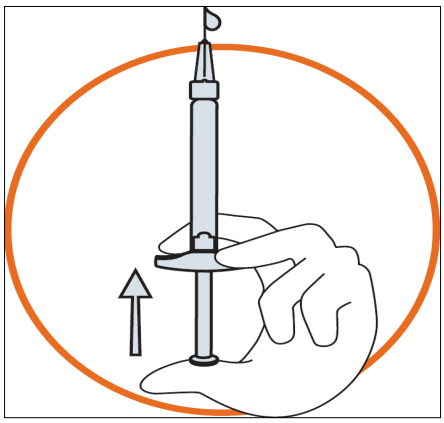
- Grip the syringe firmly. Carefully attach the needle to the syringe containing the colourless solution.
- Screw the syringe onto the needle, with the needle still covered by the needle cap.
- Remove the needle from the needle cap by pulling on the syringe. Do not pull up on the plunger.
- The syringe is now ready for injection.

3. Preparing the injection site

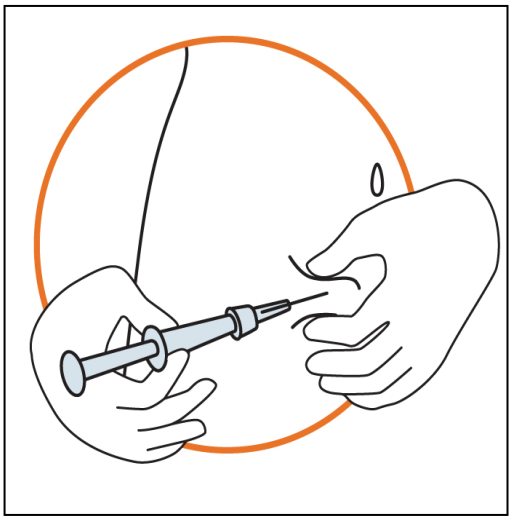
- Choose the injection site. The injection site should be a skin fold on your abdomen, approximately **5-10 cm** below your navel on either side. The area should be at least 5 cm away from any scars. Do not choose an area that is bruised, swollen or painful.

- Clean the injection site with alcohol and allow it to dry.

4. Injecting the medicine



- Hold the syringe in one hand between two fingers with your thumb at the bottom of the plunger.
- Make sure that there are no air bubbles in the syringe by pressing the plunger until the first drop appears on the tip of the needle.



- Hold the syringe at an angle of 45-90 degrees to your skin with the needle facing the skin.
- Keeping the syringe in one hand, use your other hand to take up a fold of skin between your thumb and fingers at the previously disinfected injection site.
- Hold the fold of skin, bring the syringe to the skin and quickly insert the needle into the skin fold.
- Slowly push the plunger of the syringe with a steady hand until all the liquid is injected into the skin. Make sure no liquid remains in the syringe.
- Press slowly so that this takes approximately 30 seconds.
- Release the skin fold and gently pull the needle out.

5. Disposal of waste materials after treatment

- Discard the syringe, needle, and needle cap into a sharps container to prevent harm to others.

4. Side Effects

Like with any medicine, using Firazyr may lead to side effects in some of the users. Do not be alarmed by this list of side effects. You may not experience any of them.

Most of the patients receiving Firazyr will experience side effects at the site of the injection (such as skin irritation, swelling, pain, itchiness, redness of the skin and burning sensation). These side effects are usually moderate and transient, with no need for any additional treatment.

Contact your physician immediately if you notice that the symptoms of your attack get worse after your Firazyr injection.

Very common side effects (may affect more than 1 in 10 users):
Additional injection site reactions (pressure sensation, bruising, reduced sensation and/or numbness, raised itchy skin rash with a sensation of hot skin).

Common side effects (may affect 1-10 in 100 users):
Nausea, headache, dizziness, fever, itching, rash, skin redness, abnormal results of a liver function test.

Side effects of unknown frequency (frequency of side effects cannot be estimated from the available data):
Hives (urticaria)

If you experience any side effect, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet, consult your physician.

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

5. How to store this medicine?

- Prevent poisoning! Keep this and all other medicines in a closed place out of the sight and reach of children and/or infants to avoid poisoning.
  Do not induce vomiting unless explicitly instructed to do so by the physician.

- Do not use this medicine after the expiry date (exp. date) stated on the package/label. The expiry date refers to the last day of that month.

- **Storage conditions:** Store at a temperature below 25°C. Do not freeze.

- Do not use this medicine if you notice that the syringe or needle packaging is damaged or if there are any visible signs of damage or deterioration, for example if the solution is cloudy, if it has floating particles, or if the colour of the solution has changed.

  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. Additional information

- In addition to the active ingredient the medicine also contains:
  sodium chloride, glacial acetic acid, sodium hydroxide and water for injections.

- **What this medicine looks like and contents of the pack**
  Firazyr is a colourless clear solution for injection in a prefilled glass syringe containing 3 ml.

  A hypodermic needle (25G, 16 mm) is included in the package.

- **Registration holder and importer's name and address:** Takeda Israel Ltd., 25 Efal St., Petach Tikva 4951125

- This leaflet was revised in June 2023 according to MOH guidelines.

- Registration number of the medicine in the Ministry of Health's National Drug Registry: 142 99 33003