Patient leaflet according to the Pharmacists' Regulations (Products), 1986
The medicine is marketed according to a physician's prescription only.

Firazyr 30 mg
Solution for injection

Composition:
The active ingredient and its quantity:

Icatibant (as acetate) 30 mg/3 ml

*For inactive ingredients, see section 6 (additional information) in this leaflet.

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

This medicine has been prescribed for the treatment of your ailment. Do not pass it on to others. It may harm them, even if it seems to you that their ailment is similar.

1. What is this medicine intended for?

Firazyr contains the active ingredient icatibant.

Firazyr is used for treating 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 therefore 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:

- If you are allergic to its active ingredient (Icatibant) or to any of its additional ingredients (listed in section 6).

Special warnings regarding the use of this medicine:

Before taking Firazyr, tell your physician if:

- if you are suffering from angina (reduced blood flow to the heart muscle)
- if 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.
- Immediately after you self-inject or your caregiver injects you while you are experiencing an attack accompanied by upper respiratory tracks blocking, you must seek medical care in a medical institution.
- 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 safety and efficacy of using this medicine in children under 2 years of age or weighing less than 12 kg.

Drug interactions
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, you should inform your physician before receiving Firazyr.

Pregnancy and breast-feeding:
If you are pregnant or breast-feeding or plan becoming pregnant, 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 machinery if you feel tired or dizzy as a result of your HAE attack or after using Firazyr.

Important information on some of this medicine's ingredients
The solution for Injection contains less than 1 mmol (23 mg) of sodium per syringe, and thus considered sodium free.

3. How to use this medicine?

Always use this medicine exactly as your physician has told you.
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 previously, your first dose will always be injected by your physician or nurse. Your physician will tell you when it is safe for you to go home.
After receiving guidance from your physician or nurse and after training in subcutaneous (under the skin) injection technique, you will be able to Inject yourself with Firazyr (or your caregiver will be able to Inject Firazyr to 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.
Your healthcare provider will teach you and your caregiver how to safely inject Firazyr by following the instructions detailed in the Package Leaflet.

When and how often should you use Firazyr?

The dosage and manner of treatment will be decided by the physician only. The usual acceptable dose is:

Adults
- The recommended dose is one injection of Firazyr (3 ml, 30 mg), subcutaneously (under the skin), at the moment symptoms of an angioedema attack are Identified (such as swelling of the skin, especially in the face and neck area, or increasing abdomen 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 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 symptoms of an angioedema attack (for example: increased skin swelling, particularly affecting the face and neck, or increasing tummy pain).

- See section on instructions for use 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, refer immediately to a physician or to a hospital emergency room and bring the package of the medicine with

you.

You should complete the treatment recommended by the doctor.

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

If you have further questions regarding the use of this medicine, consult the physician or pharmacist.

Firazyr - instructions for use

Firazyr should be injected subcutaneously (under the skin).
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 Information
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 solution
5) Disposal of the injection material

Step-by-Step Instructions for Injection

1) General information:

- Clean the work area (surface) to be used 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
- Put down the pre-filled syringe after unscrewing the cap.

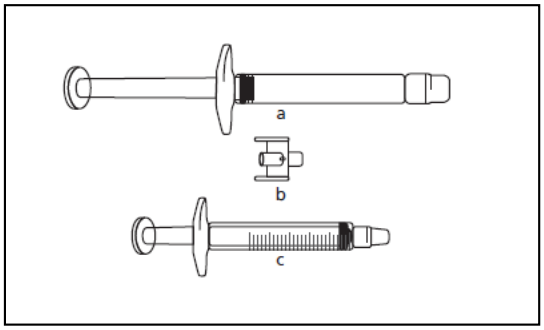
2a) Preparing the syringe for children and adolescents (2-17 years) weighing 65 kg or less:

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 in an 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**

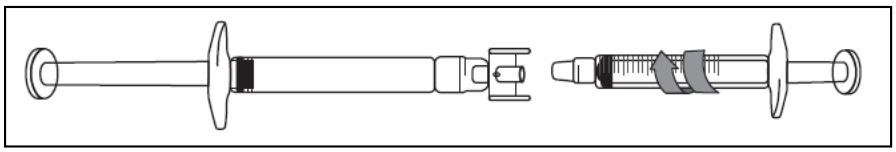
Patients weighing **more than 65 kg** will use the full contents of the pre-filled syringe (3 ml).

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

1) Remove the caps on each end of the connector.

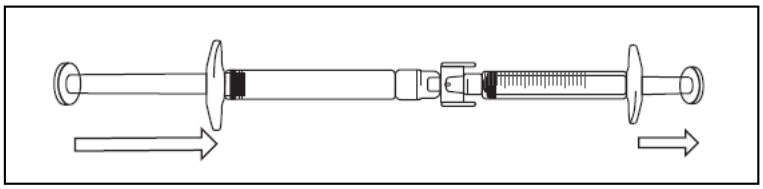
Avoid touching the ends of the connector and syringe tips, to prevent contamination.

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.

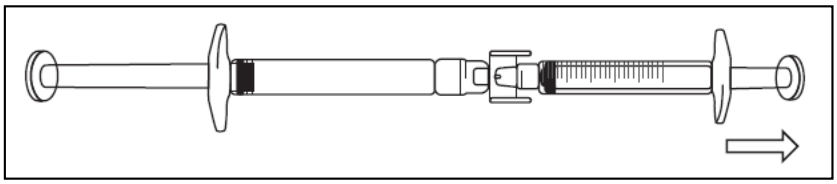


Transferring the icatibant solution to the graduated syringe:

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



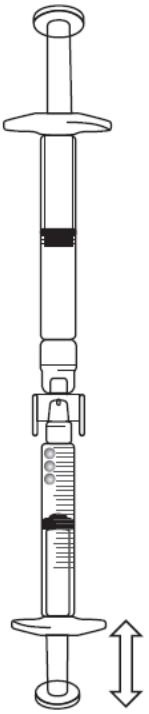
2) If the icatibant solution does not begin to transfer to the graduated syringe, pull slightly on the graduated syringe plunger until the icatibant solution starts to flow into the graduated syringe (see below image).



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).

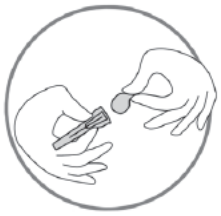


- Push the plunger of the graduated syringe so that any air is transferred back into the pre-filled syringe (this step may need to be repeated several times).
- Withdraw the required volume of icatibant solution.

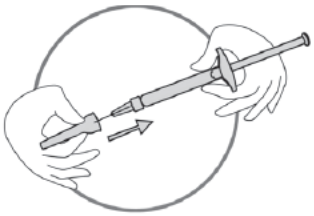
4) Remove the pre-filled syringe and connector from the graduated syringe.

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

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



- Remove the needle cap from the blister.
- Remove the seal from the needle cap (the needle should be still in the needle cap).



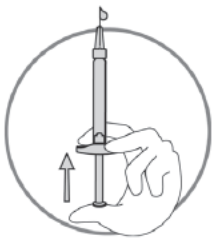
- Grip the syringe firmly. Carefully attach the needle to the syringe containing the colourless solution.
- Screw the syringe on the needle, still fixed in the needle cap.
- Remove the needle from the needle cap by pulling the syringe. Do not pull up the plunger.
- The syringe is now ready for injection.

3. Preparing the injection site

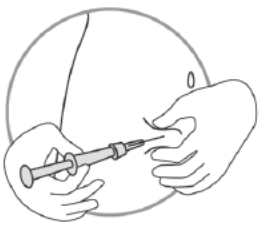
- Choose the injection site. The injection site should be a skin fold on your abdomen, approximately 5-10 cm below your navel on either side. The area should be at least 5 cm away from any scars. Do not choose an area that is bruised, swollen or painful.

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

4. Injecting the solution



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



- Hold syringe between 45-90 degrees angle to skin with needle facing the skin.
- Keeping the syringe in one hand, use your other hand to gently hold 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 fluid is injected into the skin and no liquid remain 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 the injection material

- Discard the syringe, needle and needle cap into the sharp container for throwing away waste that might hurt others if not handled properly.

4. Side Effects:

Like with any medicine, using Firazyr may lead to side effects in some of the users. Do not be alarmed following reading the list of side effects. You may experience none 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.

If you feel an aggravation of the attack symptoms after injecting **Firazyr**, refer to the physician immediately.

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

Common side effects (may affect up to 1 in 10 people): Feeling sick, headache, dizziness, fever, Itching, rash, reddening of the skin, abnormal liver function test.

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

If any of the side effects appears, if any of of the side effects gets worse, or when you suffer from a side effect not mentioned in the leaflet, consult the physician.

Reporting of side effects
Side effects can be reported to the Ministry of Health by clicking on the link "Reporting side effects following drug treatment" that appears on the home page of the Ministry of Health web site (www.health.gov.il), which leads to an online form for reporting side effects. Alternatively, you can use the following link:
https://sideeffects.health.gov.il/

5. How to Store this Medicine?

- Avoid poisoning! This medicine and all other medicines should be kept 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 relates 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 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 waste water 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 injection.

- **What Firazyr looks like and contents of the pack**

  Firazyr is a colorless clear solution, intended to be injected in a prefilled glass syringe containing 3 ml.

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

- License holder and address: Takeda Israel Ltd., 25 Efal st., Petach Tikva 4951125
- Manufacturer and address:
  Shire Pharmaceuticals Ireland Ltd, Block 2&3 Miesian Plaza, 50-58 Baggot Street Lower, Dublin 2, D02 Y754 Ireland

- This leaflet was updated in October 2020

- Drug registration number at the national medicines registry of the Ministry of Health: 142.99.33003