PATIENT LEAFLET IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) – 1986

The medicine is dispensed with a doctor's prescription only

Icatibant Teva

Solution for subcutaneous injection

Composition

Each syringe contains: Icatibant (as acetate) 30 mg / 3 ml

For information regarding inactive ingredients, see section 2 "Important information about some ingredients of the medicine" and section 6 "Additional information".

Read the entire leaflet carefully before using the medicine. This leaflet contains concise information about the medicine. If you have additional questions, refer to the doctor or the pharmacist.

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

1. WHAT IS THE MEDICINE INTENDED FOR?

Icatibant Teva is used for symptomatic treatment of acute attacks of hereditary angioedema (HAE) in adults, adolescents and children two years of age and older.

In HAE conditions, bradykinin levels in the blood increase, causing effects such as swelling, pain, nausea and diarrhea.

Icatibant Teva blocks bradykinin activity and thus stops further progression of these effects.

Therapeutic class: Other hematological agents, medicines for treatment of hereditary angioedema.

2. BEFORE USING THE MEDICINE:

Do not use this medicine if:

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

Special warnings regarding the use of the medicine:

Before treatment with Icatibant Teva, inform the doctor if:

- You have angina (decreased blood flow to the cardiac muscle).
- You had a stroke recently.

Some of the side effects associated with treatment with Icatibant Teva are similar to your illness' symptoms. Inform the doctor immediately if you observe worsening of the attack's symptoms after using Icatibant Teva.

In addition:

- You or your caregiver should be trained in subcutaneous injection technique before self-administration or before administering Icatibant Teva to a patient.
- Whether you administer the medicine yourself or receive the injection from a caregiver, in case of **an attack accompanied by obstruction of the upper airways**, go to a hospital immediately to seek medical attention.
- If the attack's symptoms do not improve following one self-injection or one injection of Icatibant Teva by the caregiver, consult a doctor regarding taking additional doses of Icatibant Teva. For adult patients, up to 2 additional injections may be administered within 24 hours.

Use in children and adolescents

No information is available regarding the safety and efficacy of using this preparation in children under two years of age or children who weigh less than 12 kg.

Drug interactions

If you are taking or have recently taken other medicines including non-prescription medicines and food supplements, tell the doctor or the pharmacist.

Icatibant Teva is not known to interact with other medicines.

If you are taking other medicines known as Angiotensin Converting Enzyme (ACE) inhibitors, e.g. captopril, enalapril, ramipril, quinapril and lisinopril, for the purpose of lowering blood pressure or for any other reason, you must consult a doctor before taking Icatibant Teva.

Pregnancy and breastfeeding:

- If you are pregnant, think you may be pregnant or are planning to become pregnant, consult a doctor before using the medicine.
- If you are breastfeeding, **do not breastfeed for 12 hours** after administering the last dose of the medicine.

Driving and operating machinery:

Do not drive or operate machinery if you feel dizziness or tiredness due to an HAE attack or after taking Icatibant Teva.

Important information about some ingredients of the medicine

The solution for injection contains less than 1 millimole (23 mg) of sodium, therefore it is considered to be sodium-free.

3. HOW SHOULD YOU USE THE MEDICINE?

Always use the medicine according to the doctor's instructions.

Check with the doctor or pharmacist if you are uncertain about the dosage and how to use the medicine.

If you have never used Icatibant Teva in the past, the first dose will always be administered by the doctor or nurse. The doctor will tell you when it is safe for you to go home.

After receiving instructions from a doctor or a nurse, and after practicing subcutaneous (under the skin) injection technique, you will be able to self-administer Icatibant Teva (or your caregiver will be able to administer Icatibant Teva to you) during an HAE attack.

It is important that the injection will be given subcutaneously as soon as the angioedema attack begins.

A healthcare professional will teach you and your caregiver how to administer Icatibant Teva safely while following the instructions in this leaflet.

How should Icatibant Teva be used and how frequently?

The dosage and treatment regimen will be determined only by the doctor. The generally accepted dosage is:

Adults

The recommended dosage is one subcutaneous injection of Icatibant Teva (3 ml / 30 mg) as soon as signs of angioedema attack are observed (e.g. increased swelling of the skin, especially in the area of the face and neck, or increasing abdominal pain).

If your condition does not improve after 6 hours, consult a doctor regarding additional injections of Icatibant Teva. For adults, up to 2 additional injections may be administered within 24 hours.

No more than 3 injections should be administered in 24 hours and if more than 8 injections of Icatibant Teva are required in one month, consult a doctor.

Children and adolescents 2-17 years of age

The recommended dosage of Icatibant Teva is 1 ml up to a maximum of 3 ml, injected subcutaneously (under the skin), according to body weight (one syringe of Icatibant Teva contains 3 ml), as soon as signs of angioedema attack develop (e.g. increased swelling of the skin, especially in the area of the face and neck, or increasing abdominal pain).

See dosages for injection in Table 1 under "Step-by-step injection instructions" further down in this leaflet.

If you are not sure what dose to administer, consult the doctor, pharmacist or nurse.

Do not exceed the recommended dose.

If your symptoms worsen or do not improve, you should seek medical attention immediately.

If you took an overdose or if a child accidentally swallowed or injected this medicine, go immediately to a doctor or to a hospital emergency room and bring the package of the medicine with you.

Follow the treatment as recommended by the doctor.

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

If you have any other questions regarding use of the medicine, consult the doctor or the pharmacist.

<u>Instructions for use of Icatibant Teva</u>

Icatibant Teva is intended for subcutaneous (under the skin) injection.

Each syringe is for a single use only.

Icatibant Teva should be injected into the fatty layer under the skin of the abdomen using a short needle.

The following instructions refer to the injection:

- **For adults (self-administration or by a caregiver/healthcare professional)**
- **For adolescents or children above the age of two (who weigh at least 12 kg) by a caregiver/healthcare professional**

The instructions include the following main steps:

a) General instructions (for all patients)
b) Preparing a syringe with the appropriate dose for children and adolescents (2-17 years of age) who weigh 12-65 kg
c) Preparing the syringe and the needle for injection (for all patients)
d) Preparing the site of injection into the body
e) Injecting the medicine
f) Discarding the injection materials after the treatment

<u>Step-by-step injection instructions</u>

a) General instructions (for all patients)

- Clean your work surface (table) before starting the procedure
- Wash your hands with water and soap
- Tear off the inner package cover completely according to the cutting line (so that the needle can also be removed)
- Remove the prefilled syringe from the package
- Unscrew the cap from the end of the prefilled syringe
- After removing the cap, place the syringe on the surface

b) Preparing a syringe with the appropriate dose for children and adolescents (2-17 years of age) who weigh 12-65 kg

Important information for medical staff and caregivers:

When the dose intended to be injected is less than 30 mg (3 ml), the following supplies are required to draw the appropriate dose for injection (see Figure 1):

- An Icatibant Teva prefilled syringe (containing the medicine) - marked by the letter a
- A connector (adapter) - marked by the letter b
- A 3-ml graduated syringe - marked by the letter c

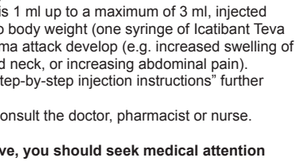

Figure 1

Draw the required amount of solution, according to body weight, into the empty 3-ml graduated syringe (see Table 1).

Patients weighing **more than 65 kg** will use the entire content of the prefilled syringe (3 ml).

⚠ **If you are not sure what volume of the solution to draw, consult the doctor, pharmacist or nurse.**

Table 1: Dosage regimen for children and adolescents

Volume of injection	Body weight
1.0 ml	12-25 kg
1.5 ml	26-40 kg
2.0 ml	41-50 kg
2.5 ml	51-65 kg

The following actions should be performed:

1. Remove the caps from both ends of the adapter.
   ⚠ **Avoid touching the ends of the adapter and the syringe, to keep them from becoming infected.**
2. Screw the adapter to the prefilled Icatibant Teva syringe (see Figure 2).

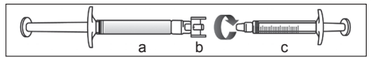

Figure 2

3. Connect the graduated syringe to the other end of the adapter, ensuring both connections are tight.

Transferring the icatibant solution to the graduated syringe

4. To start transferring the icatibant solution, push on the plunger of the prefilled syringe (see the left hand side of Figure 3).

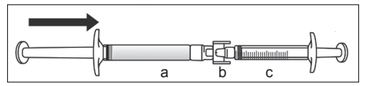

Figure 3

5. If the solution does not begin to move into the (graduated) empty syringe, pull the plunger of the graduated syringe gently until the icatibant solution begins to flow into it (see Figure 4).

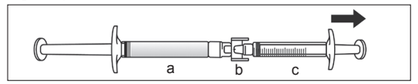

Figure 4

6. Keep pushing the plunger of the prefilled syringe until the volume needed for injection (the dose) has been transferred to the graduated syringe. See Table 1 for information regarding the required volume.

If the graduated syringe contains air:

- Pick up the connected syringes so that the prefilled syringe is on top (see Figure 5).
- Push the plunger of the graduated syringe so that all of the air will return into the prefilled syringe (you may need to repeat this step several times).
- Make sure you have drawn the required volume of icatibant solution.

7. Disconnect the prefilled syringe and the adapter from the graduated syringe.
8. Discard the prefilled syringe and the adapter into a sharps container.

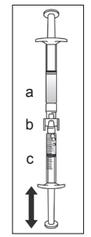

Figure 5

c) Preparing the syringe and the needle for injection for all patients (adults, adolescents and children)

- Open the needle package by rotating the cover clockwise (no need to remove the sticker to open). Do not remove the needle cap at this stage (see Figure 6).

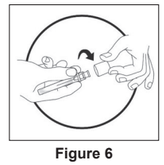

Figure 6

- Hold the syringe steadily. Without removing the needle cap, carefully screw the needle clockwise (until it stops). Make sure the needle is securely attached.
- Remove the needle cap by holding the syringe body and pulling the needle cap. <u>Do not</u> pull the syringe plunger (see Figure 7).
- The syringe is now ready for injection.

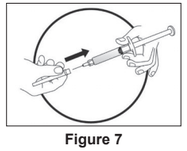

Figure 7

d) Preparing the site of injection into the body

- Choose the injection site. The site of injection should be a skin fold in the abdomen, under the bellybutton, about **5-10 cm** from it. The site should be at least 5 cm away from any scar. Do not choose a bruised, swollen or painful site.
- The site of injection should be cleaned with alcohol and allowed to dry (see Figure 8).

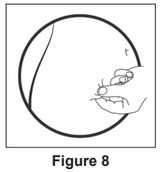

Figure 8

e) Injecting the medicine

- Hold the syringe with one hand between two fingers, with the thumb holding the plunger from below.
- Make sure that no air bubble is present in the syringe by pressing on the plunger until the first drop appears at the tip of the needle (see Figure 9).

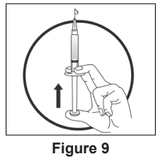

Figure 9

- Hold the syringe with the needle facing the skin at a 45-90° angle.
- With the syringe in one hand, pinch/fold the skin in the disinfected area using the thumb and fingers of your other hand.
- Hold the skin fold, bring the syringe close to the skin and quickly insert the needle into the skin fold (see Figure 10).

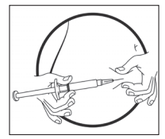

Figure 10

- Press on the syringe plunger slowly and steadily until all of the liquid has entered the skin. Make sure that no liquid remains in the syringe. The injection should take about 30 seconds.
- Release the skin and carefully pull the needle out.

f) Discarding the injection materials after the treatment

Discard the syringe, needle and needle cap into a special sharps container in order to prevent injury to others (see Figure 11).

Figure 11

4. SIDE EFFECTS

As with any medicine, using Icatibant Teva may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not experience any of them.

Most patients receiving Icatibant Teva will experience side effects at the site of injection (e.g., skin irritation, swelling, pain, itching, redness of the skin and a burning sensation). These effects are usually mild and resolve without requiring any treatment.

If you observe aggravation of the symptoms of the attack following administration of Icatibant Teva, contact the doctor immediately.

Very common side effects (occurring in more than one out of 10 patients):

Other side effects at the site of injection (pressure sensation, bruising, reduced sensation and/or numbness, itchy rash with raised skin and sensation of heat in the skin).

Common side effects (occurring in 1-10 out of 100 patients):

Nausea, headache, dizziness, fever, itching, rash, redness in the skin, abnormal results of liver function tests.

Side effect with unknown incidence (incidence cannot be estimated from existing data):

Allergic skin rash (urticaria).

If a side effect occurs, if one of the side effects worsens, or if you suffer from a side effect not mentioned in this leaflet, consult your doctor.

<u>Reporting side effects</u>

Side effects may be reported to the Ministry of Health by clicking on the link "Report side effects due to medicinal treatment" found on the Ministry of Health website homepage (<u>www.health.gov.il</u>), which will direct you to the online form for reporting side effects, or by clicking on the following link: <u>https://sideeffects.health.gov.il</u>

5. HOW TO STORE THE MEDICINE?

- Avoid poisoning! This medicine and any other medicine must be kept in a closed place out of the reach and sight of children and/or infants to avoid poisoning. Do not induce vomiting without an explicit instruction from the doctor.
- Do not use the medicine after the expiry date (exp. date) appearing on the package. The expiry date refers to the last day of that month.
- Storage conditions: store at 2-25°C. Do not freeze.
- Do not use the medicine if the package of the syringe or the needle is damaged or if there is any sign of damage to the product or signs of spoilage, for example: if the solution is cloudy or contains floating particles, or if it is discolored.
- Do not throw away any medicines via wastewater or household waste. Ask the pharmacist how to dispose of medicines no longer in 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, water for injection, nitrogen

The solution does not contain preservatives.

What does the medicine look like and what are the contents of the package

3 ml of clear and colorless solution in a prefilled glass syringe. The package also contains a sterile needle 25G.

A package of one carton and a package of three cartons are available. Each carton contains one dose of the medicine. Not all package sizes may be marketed.

Name and address of the manufacturer and license holder:

Teva Israel Ltd., 124 Dvora HaNevi'a St., Tel Aviv 6944020

The leaflet was revised in January 2024.

Registration number of the medicine in the national drug registry of the Ministry of Health: 160-88-35235

ICATIBANT SOL. PL MW0124