PATIENT LEAFLET IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) - 1986
This medicine is dispensed with a doctor's prescription only

Cablivi 10 mg

Powder and solvent for solution for subcutaneous/ intravenous injection

Active ingredient: each powder vial contains caplacizumab 10 mg
Inactive and allergenic ingredients in the preparation: see section 6.

Read the entire leaflet carefully before you start using this medicine.
This leaflet contains concise information about this medicine.
If you have any further questions, consult your doctor, pharmacist or nurse.
This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar to yours.

In addition to the patient information leaflet, Cablivi also has a patient safety information card. This card contains important safety information that you need to know and that you should follow before you start treatment and during the treatment with Cablivi. Carefully read the patient safety information card and patient information leaflet before using this medicine. Keep the card in case you need to read it again.

1. WHAT CABLIVI IS INTENDED FOR?

Cablivi is indicated for the treatment of adults and adolescents of 12 years of age and older weighing at least 40 kg, suffering from acquired thrombotic thrombocytopenic purpura (aTTP), in conjunction with plasma exchange and immunosuppression.

aTTP is a rare blood clotting disorder in which clots form in small blood vessels. These blood clots may block blood vessels and damage the brain, heart, kidneys, or other organs. Cablivi prevents the formation of these blood clots by stopping platelets in the blood from clumping together. By doing so, Cablivi reduces the risk of experiencing another episode of aTTP soon after the first episode.

Therapeutic group: antithrombotic agents.

2. BEFORE USING THIS MEDICINE

Do not use this medicine:
if you are sensitive (allergic) to caplacizumab or any of the other ingredients in this medicine (see section 6).

Special warnings regarding use of the medicine
Tell your doctor if:
- you bleed excessively or experience unusual symptoms such as headache, shortness of breath, tiredness or fainting which may indicate serious internal bleeding. Your doctor may ask you to stop the treatment. The doctor will say when you can start your treatment again.
- you are using medicines that prevent or treat blood clots, such as warfarin, heparin, rivaroxaban, apixaban. Your doctor will decide how you should be treated.
- you are using anti-platelet agents such as aspirin, or low molecular weight heparin (which prevents formation of blood clots). Your doctor will decide how you should be treated.
- you have a bleeding disorder such as haemophilia. Your doctor will decide how you should be treated.
- you have severely reduced liver function. Your doctor will decide how you should be treated.
- you are going to have an operation or dental treatment. Your doctor will decide if it can be postponed or if you should stop Cablivi before your surgery or dental treatment.

Children and adolescents
This medicine is not intended for children under 12 years and below 40 kg body weight.
There is no information about the safety and efficacy of this medicine in children and adolescents under the age of 18 years.

Drug interactions
If you are taking, or have recently taken, or might take other medicines, including non-prescription medicines and dietary supplements, tell your doctor or pharmacist. Particularly if you are taking:
an anticoagulant medicine such as a vitamin K antagonist, rivaroxaban or apixaban, which treat blood clots or anti-platelet agents, such as aspirin, or low molecular weight heparin which prevent formation of blood clots.

Pregnancy, breastfeeding and fertility
Pregnancy
Tell your doctor if you are pregnant or plan to get pregnant. Use of Cablivi is not recommended during pregnancy.
Breastfeeding
Tell your doctor if you are breastfeeding. Your doctor will advise you whether to discontinue breastfeeding or not to use Cablivi, considering the benefit of breastfeeding for the baby and the benefit of Cablivi for you.

Driving and using machines
Cablivi is not expected to influence your ability to drive or use machines.

Important information about some of this medicine's ingredients
This medicine contains less than 1 mmol sodium (23 mg) per dose, i.e., it is essentially 'sodium-free'.

3. HOW TO USE THIS MEDICINE?

Always use this medicine according to your doctor's instructions.
Check with your doctor or pharmacist if you are not sure about your dose or about how to take this medicine.
Only your doctor will determine your dose and how you should take this medicine.
Treatment with Cablivi is started by a doctor experienced in blood disorders.
The recommended dose is usually:
- **First dose**
  - 1 vial injected into a vein by a healthcare professional.
  - the medicine will be given before starting plasma exchange.
- **Subsequent doses**
  - 1 vial once daily as a subcutaneous injection (under the skin of the belly).
  - the subcutaneous injection will be given after each daily plasma exchange.
  - after the daily plasma exchange finishes, your treatment with Cablivi will continue for at least 30 days with injection of 1 vial once daily.

Your doctor may instruct you to continue daily treatment for a maximum of 28 additional days.

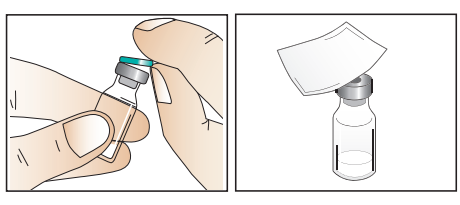
Do not exceed the recommended dose.
Your doctor may decide that you or your caregiver may inject Cablivi. In this case, your doctor or healthcare provider will train you or your caregiver on how to use Cablivi.

Instructions for use
The first injection of Cablivi into your vein must be given by a healthcare professional. Instructions for healthcare professionals on how to inject Cablivi into your vein are at the end of the leaflet.
For each injection, use a new kit package to prepare the injection solution. Do not try to inject Cablivi until you have been taught how to do so by a healthcare professional. Never use the kit for another injection.

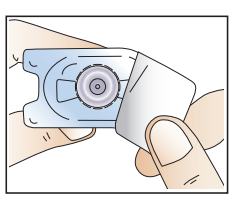
Step 1 - Cleaning
- Wash your hands thoroughly with soap and water.
- Prepare a clean flat surface for placing the kit package.
- Make sure you have a disposal container at hand.

Step 2 - Before use
- Make sure the kit package is complete.
- **Check the expiry date.** Do not use if the expiry date has passed.
- Do not use the kit if the packaging or the items in it are damaged in any way.
- Place all components of the kit on the clean flat surface.
- If the kit was not stored at room temperature, allow the vial and the syringe to reach room temperature (15°C–25°C) by letting them stand at room temperature for a few minutes. Do not warm them up in any other way.

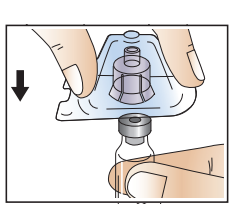
Step 3 - Disinfect the rubber stopper
- Remove the plastic cap from the vial. Do not use the vial if the green plastic cap is missing.
- Clean the exposed rubber stopper using one of the alcohol pads provided and allow it to dry for a few seconds.
- After cleaning, do not touch the rubber stopper or allow it to touch any surface.



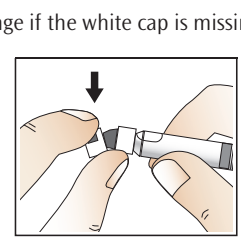
Step 4 - Attaching the adapter
- Take the packed vial adapter and remove the paper cover. Leave the adapter in its opened plastic packaging. Do not touch the adapter itself.



- Place the adapter over the vial, while keeping the adapter in its plastic packaging.
- Press down firmly until the adapter snaps into place, with the adapter spike going through the vial stopper. Leave the adapter attached to the vial, **still in its outer packaging**.

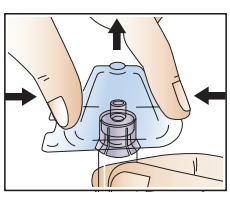


Step 5 - Prepare the syringe
- Holding the syringe in your hand, break off the white cap with your other hand.
- Do not use the syringe if the white cap is missing, loose or damaged.

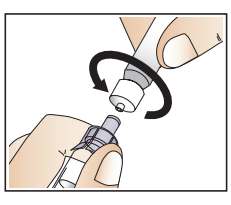


- **Do not touch** the syringe tip or allow it to come into contact with any surfaces.
- Place the syringe on the clean flat surface.

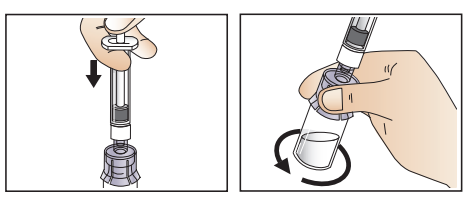
Step 6 - Connect syringe with adapter and vial
- Take the vial with the attached adapter.
- Remove the plastic packaging from the adapter by holding the vial with one hand, pressing the sides of the adapter packaging with your other hand, and then lifting the packaging upwards.
  Take care that the adapter does not come away from the vial.



- Hold the adapter with the attached vial with one hand. Place the tip of the syringe on the connector part of the vial adapter.
- Gently lock the syringe onto the vial by turning it clockwise until resistance is felt.

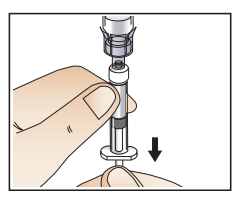


Step 7 - Prepare the solution
- Keep the vial standing vertically on the surface with the syringe pointing downwards.
- Slowly push the syringe's plunger down until the syringe is empty. Do not remove the syringe from the vial.
- With the syringe still connected to the vial adapter, gently swirl the vial with connected syringe until the powder is dissolved. Avoid foaming. **Do not shake** the vial.

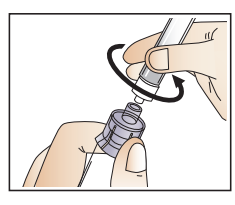


- Allow the vial with connected syringe to stand on the surface for **5 minutes** at room temperature to allow the solution to completely dissolve. The plunger may rise up by itself again - this is normal.
- Go to step 8 immediately after these 5 minutes.

Step 8 - Draw up the solution
- **Check the solution for particles.** All powder must be dissolved and the solution must be clear.
- Slowly press the syringe plunger fully down.
- Turn the whole - vial, adapter and syringe - upside down.
- While keeping it vertical, slowly pull the plunger to transfer all the solution into the syringe. Do not shake it.

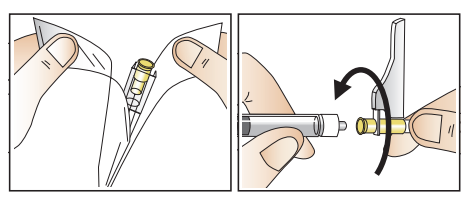


Step 9 - Prepare the syringe for administration



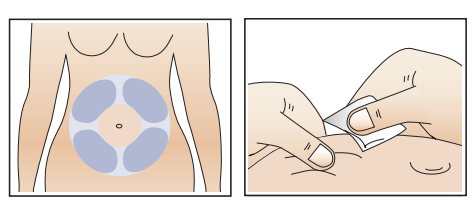
- Turn the whole - vial, adapter and syringe - upwards (with the syringe at the top).
  Disconnect the filled syringe from the adapter by holding the adapter in one hand and gently turning the syringe counter-clockwise.
- Put the vial and the attached adapter into the supplied disposal container.
- **Do not touch** the syringe tip or allow it to touch the surface. Place the syringe on the clean flat surface.
- Go to step 10 to inject caplacizumab under the skin of the belly. Instructions for healthcare professionals on how to inject Cablivi into your vein are at the end of the leaflet.

Step 10 - Attach the needle
- Unpack the needle by tearing the paper cover off the needle packaging and removing the needle with protective cap.



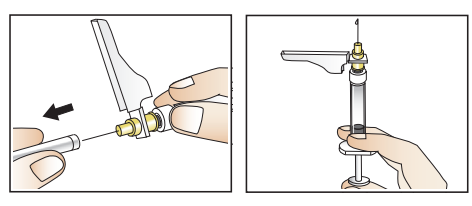
- Without removing the needle cap, attach the needle to the syringe by turning clockwise until resistance is felt.
- Pull back the needle safety shield.
- **Check the content of the syringe.** Do not use the medicine if you see any cloudiness, clumps or anything else that looks abnormal. Contact your doctor or nurse if this happens.

Step 11 - Prepare the injection site for under the skin injection

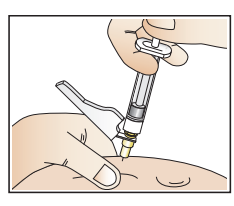


- Select a suitable place ('injection site') on your belly for injection under your skin. Avoid the area around the belly button.
- Select a different injection site from the one you used on the previous day to help the skin to recover after the injection.
- Use the second alcohol pad to clean the injection site you have chosen.

Step 12 - Administration of the medicine
- Carefully remove the needle protection cap from the needle and throw it away. Make sure the needle does not touch anything before the injection.
- Hold the syringe at eye level with the needle pointing upwards.
- Remove any air bubbles by tapping the side of the syringe with your finger to make the bubbles rise towards the tip. Then, slowly push the plunger until a small amount of liquid comes out of the needle.
- Gently pinch the cleaned skin between your thumb and forefinger to make a fold.

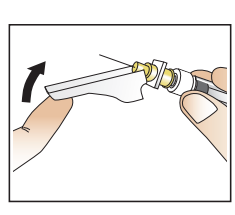


- Hold this skin fold during the entire injection.
- Insert the full length of the needle into the skin fold at an angle as shown in the illustration.
- Press the plunger down as far as it goes.



- Pull out the needle at the same angle you inserted it. Do not rub the injection site.

Step 13 - After administration of the medicine
- Immediately after the injection, move the needle safety shield over the needle, until it clicks into place.



- Place the syringe with the needle in a disposal container.

If you use more Cablivi than you should
An overdose is unlikely since one vial contains only a single dose. Tell your doctor if you think you have had an overdose.
If a child has accidentally swallowed some medicine, immediately see a doctor or go to a hospital emergency room and bring the medicine package with you.

If you forget to use Cablivi
If you forgot to inject the medicine, you should still inject it if it is within 12 hours of the scheduled time. If more than 12 hours have passed since the dose should have been injected, do not take the missed dose, but inject the next dose at the usual time.
Adhere to the treatment as recommended by your doctor.

If you stop using Cablivi
To get the most benefit from your treatment, it is important to use Cablivi as prescribed and for as long as your doctor decides. Please talk to your doctor before you stop the treatment because stopping it too early may cause your condition to come back.

Do not take medicines in the dark! Check the label and dose <u>every time</u> you take a medicine. Wear glasses if you need them.
If you have any further questions about using this medicine, consult your doctor or pharmacist.

4. SIDE EFFECTS

Like with all medicines, using Cablivi may cause side effects in some users. Do not be alarmed by the list of side effects; you may not experience any of them.

Contact your doctor immediately if any of the following serious side effects occur:
Long or excessive bleeding.
Your doctor may decide to keep you under closer observation or change your treatment.

Side effects in a clinical study were reported with the following frequencies:

Very common side effects, may affect more than 1 in 10 patients:
- bleeding gums
- fever
- tiredness
- headache
- nosebleeds
- hives

Common side effects, may affect up to 1 in 10 patients:
- bleeding from eye
- vomiting blood
- blood in the stools
- black, tarry stools
- bleeding from the stomach
- bleeding hemorrhoids
- rectal bleeding
- injection site reactions: rash, itching and bleeding
- bleeding in brain manifested by severe headache of rapid onset, vomiting, decreased level of consciousness, fever, sometimes seizures and neck stiffness or neck pain
- muscle pain
- stroke
- blood in urine
- excessive bleeding during periods
- vaginal bleeding
- coughing blood
- shortness of breath
- hematoma (bruise)

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 doctor.

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 (<u>www.health.gov.il</u>) which links to an online form for reporting side effects. You can also use this link:
<u>https://sideeffects.health.gov.il</u>

5. HOW TO STORE THE MEDICINE

Avoid poisoning! To avoid poisoning, keep this, and all other medicines, in a closed place, out of the reach and sight of children and/or infants. Do not induce vomiting unless explicitly instructed to do so by a doctor.
Do not use the medicine after the expiry date (exp. date) which is stated on the package, label and carton. The expiry date refers to the last day of that month.

Storage conditions:
Store in a refrigerator (2°C-8°C). Do not freeze.
Store in the original package in order to protect from light.
Cablivi may be stored at a temperature not above 25°C for a single period of up to 2 months, but not beyond the expiry date. Do not return Cablivi to refrigerated storage after storage at room temperature.
Do not use Cablivi if you notice any particulate matter or discolouration prior to administration.
<u>Storage condition after product reconstitution</u>:
The reconstituted solution is stable for 4 hours at 25°C. However, from the perspective of microbiological cleanliness, unless the method of reconstitution precludes the risk of microbial contamination, the product should be used immediately.
If the reconstituted solution is not used immediately, storage times and conditions are at the responsibility of user.
Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer need. These measures will help protect the environment.

6. ADDITIONAL INFORMATION

In addition to the active ingredient, each powder vial contains the following inactive ingredients:
Sucrose, trisodium citrate dihydrate (See also in section 2 "Important information about some of this medicine's ingredients"), citric acid anhydrous, and polysorbate 80.

Each pre-filled syringe contains:
1 ml of water for injections

What the medicine looks like and contents of the pack:
- a glass vial containing a white powder for solution for injection
- water for injections in a pre-filled syringe to dissolve the powder

After dissolving the powder in the solvent, the solution is clear, colourless or slightly yellowish.

Cablivi is available in a single pack containing 1 vial with caplacizumab powder, 1 pre-filled syringe with solvent, 1 vial adapter, 1 needle and 2 alcohol swabs,
or in a pack containing 7 vials with caplacizumab powder, 7 pre-filled syringes with solvent, 7 vial adapters, 7 needles and 14 alcohol swabs.
Not all pack sizes may be marketed.

This leaflet does not contain the entire information about the medicine. If you have any question or are not sure about anything, please contact the doctor.

Registration holder's name and address: sanofi-aventis Israel ltd., 10 Beni Gaon St., Netanya.
Registration number of the medicine in the National Drug Registry of the Ministry of Health: 165-25-36110.
Revised in March 2024 according to MOH guidelines.

The following information is intended for healthcare professionals only:

The intravenous bolus injection of Cablivi given at the start of the treatment must be administered by a healthcare professional. Preparing a dose of Cablivi for intravenous injection should be done in the same way as for a subcutaneous injection (see Instructions for Use, steps 1 to 9, in section 3).

Cablivi can be intravenously administered by connecting the prepared syringe to standard Luer locks of intravenous lines or using a suitable needle. The line can be flushed with sodium chloride 9 mg/ml (0.9%) solution for injection.

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