PATIENT PACKAGE INSERT ACCORDING TO PHARMACISTS' REGULATIONS (PREPARATIONS) – 1986

The medicine is dispensed with a doctor's prescription only

ASPAVELI

Solution for infusion

Active ingredient:

1 ml of Aspaveli contains 54 mg of pegcetacoplan

Inactive and allergenic ingredients in the product – see section 2 "Important information about some of the ingredients of the medicine" and section 6 "Further information".

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

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

In addition to the leaflet, **Aspaveli** has a Patient Safety Information Card. This card contains important safety information, which you must know and act upon before starting and during treatment with **Aspaveli**. Read the Patient Safety Information Card and the patient leaflet before starting to use the product. Keep the card for further reading if necessary.

1. WHAT IS THE MEDICINE INTENDED FOR?

Aspaveli is indicated for the treatment of adult patients with paroxysmal nocturnal hemoglobinuria (PNH) who are still anemic even after treatment with a C5 inhibitor for at least 3 months.

Therapeutic group: Selective immunosuppressants.

Aspaveli works by binding to complement protein C3, which is part of the body's defense system called the 'complement system'.

In patients with PNH, the 'complement system' is overactive and attacks the red blood cells, which may lead to a low blood count (anemia), tiredness, difficulty in functioning, pain, abdominal pain, dark urine, shortness of breath, difficulty swallowing, erectile dysfunction and blood clots. By attaching to and blocking the C3 protein, Aspaveli can stop the complement system from attacking red blood cells and so control symptoms of the disease. Use of Aspaveli has been shown to increase the number of red blood cells (reduce anemia), which may improve those symptoms.

2. BEFORE USING THE MEDICINE

Do not use the medicine if:

- you are sensitive (allergic) to the active ingredient pegcetacoplan or to any of the additional ingredients contained in the medicine (see section 6 "Further information").
- you have an infection caused by an encapsulated bacterium (see below).
- you are not vaccinated against *Neisseria meningitidis*, *Streptococcus pneumoniae* and *Haemophilus influenzae*.

  See section "Special warnings regarding use of the medicine".

Special warnings regarding use of the medicine

Before and during treatment with Aspaveli, inform the doctor:

Symptoms of infection

Before starting treatment with Aspaveli, inform the doctor if you have any infections.

Because the medicine targets the complement system, which is part of the body's defence against infection, use of this medicine increases the risk of infections, including those caused by encapsulated bacteria, such as *Streptococcus pneumoniae*, *Neisseria meningitidis* and *Haemophilus influenzae*. These are severe infections affecting the nose, throat and lungs or the linings of the brain and can spread throughout the blood and body.

Talk to the doctor before starting treatment with Aspaveli to be sure that you receive a vaccination against *Streptococcus pneumoniae*, *Neisseria meningitidis* and *Haemophilus influenza*, if you have not been vaccinated against them in the past. Even if you have been vaccinated in the past, you might still need to be vaccinated before starting treatment with the medicine. These vaccinations should be given at least 2 weeks before beginning treatment. If you cannot be vaccinated 2 weeks before starting treatment, the doctor will prescribe you antibiotics for 2 weeks to reduce the risk of infection after you have been vaccinated. Following vaccination, you may be more closely monitored by the doctor for symptoms of infection.

Infection symptoms

If you experience any of the following symptoms, inform the doctor immediately:

- headache or fever
- fever and rash
- fever with or without chills
- shortness of breath
- high heart rate
- clammy skin
- headache with a stiff neck or back
- headache with nausea or vomiting
- eyes sensitive to light
- muscle aches with flu-like symptoms
- confusion
- extreme pain or discomfort.

Make sure that you keep your vaccinations up to date. You should be aware that vaccines reduce the risk of serious infections, but do not prevent all serious infections. In accordance with vaccination recommendations by the healthcare professionals, the doctor might consider supplementary measures for you to prevent infection, such as antibacterial medicines.

Allergic reactions

Allergic reactions may appear in some patients. In case of severe allergic reaction, discontinue Aspaveli infusion and seek medical treatment immediately. Severe allergic reaction may present as difficulty breathing, chest pain or tightness, and/or dizziness/fainting, severe itching of the skin or raised lumps on the skin, swelling of the face, lips, tongue and/or throat, which may cause difficulty in swallowing or collapse.

Injection site reactions

Injection site reactions have been observed with use of Aspaveli. You should undergo appropriate training in proper injection technique before self-administering.

Children and adolescents

Aspaveli is not intended for children and adolescents under 18 years of age, as no data are available on its safety and effectiveness in this age group.

Tests and follow-up

During the treatment with Aspaveli the doctor will perform regular check-ups, including blood tests for lactate dehydrogenase (LDH) levels and tests of renal function, and may adjust your dose if needed.

Effects on laboratory tests

Use of silica reagents in coagulation tests should be avoided as it can artificially result in prolonged activated partial thromboplastin time (aPTT).

Drug interactions

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

Pregnancy, breastfeeding and fertility

Women of childbearing age

The effects of the medicine on the fetus are unknown. Use of effective contraceptive methods is recommended during treatment and for up to 8 weeks afterward, for women of childbearing age who may become pregnant. Consult with the doctor before using the medicine.

Pregnancy/Breastfeeding

The use of Aspaveli is not recommended during pregnancy and breastfeeding. If you are pregnant, breastfeeding, think you may be pregnant, or are planning a pregnancy, consult with the doctor before using the medicine.

Driving and using machines

This medicine has no or negligible effect on the ability to drive or use machines.

Important information about some of the ingredients of the medicine

Aspaveli contains sorbitol.

Sorbitol is a source of fructose. If the doctor has told you that you have an intolerance to certain sugars or if you have been diagnosed with hereditary fructose intolerance (HFI), a rare genetic disorder in which a person cannot break down fructose, talk with the doctor before taking or receiving the medicine.

Aspaveli contains less than 1 millimole of sodium (23 mg) per dose; therefore, it is essentially "sodium-free".

3. HOW SHOULD YOU USE THE MEDICINE?

Always use the product according to the doctor's instructions. Check with the doctor or pharmacist if you are unsure about the dosage and treatment regimen of the product.

At least two weeks before starting treatment with the medicine, the doctor will review your medical records and may administer one or more vaccines. If you cannot be vaccinated at least two weeks before starting Aspaveli, in order to reduce the risk of infection, the doctor may prescribe antibiotics for 2 weeks after you have been vaccinated.

The dosage and treatment regimen will be determined by the doctor only. The usual recommended dosage is:

The recommended initial dose for adults with PNH is 1,080 mg twice a week in addition to the current dose prescribed for you for the C5 inhibitor, for 4 weeks. You should take the bi-weekly dose on days 1 and 4 of each treatment week.

After 4 weeks, you should stop taking the C5 inhibitor.

Do not change the dose or dosing intervals without consulting the doctor. The doctor may adjust your dose to 1,080 mg every third day (e.g., day 1, day 4, day 7, day 10, day 13, etc.) if necessary. If you think you missed a dose, contact the doctor as soon as possible.

Do not exceed the recommended dose.

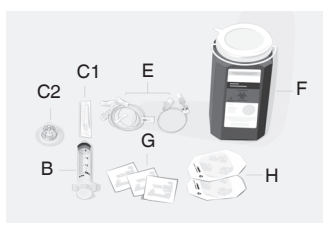
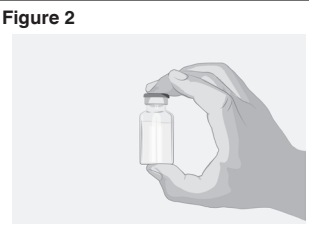
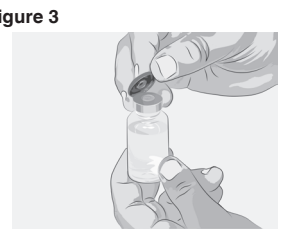
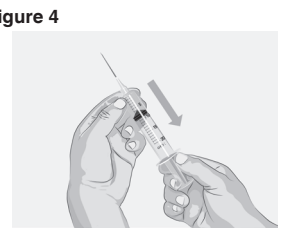
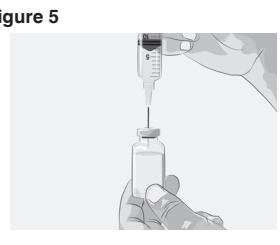
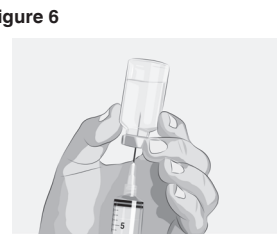
Method of use

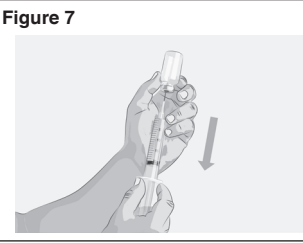
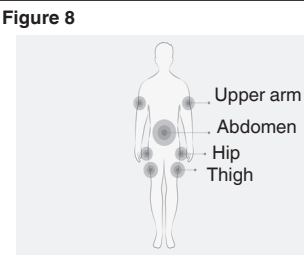
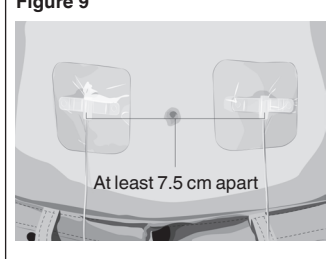
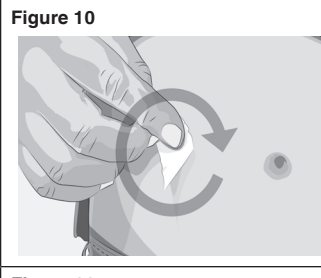
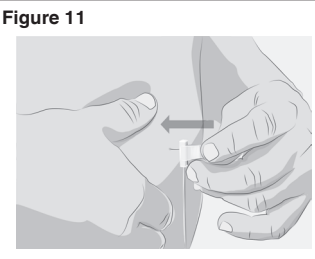
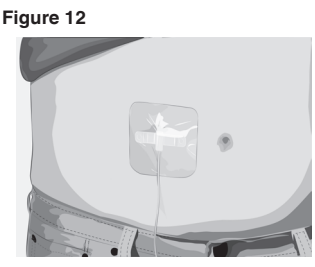
Aspaveli is intended to be given as a subcutaneous infusion (drip) using an infusion pump. The initial doses of the medicine will be administered to you by healthcare professionals in a clinic or treatment center. If the treatment progresses normally, the doctor may discuss the option of self-administration at home. If this is appropriate, a healthcare professional will train you or a caregiver how to give the infusion.

Infusion rate(s)

The infusion duration is typically around 30 minutes if using two infusion sites or 60 minutes if using one infusion site. Begin the infusion immediately after drawing the medicine into the syringe (and complete it within two hours after preparing the syringe).

Instructions for use

Step 1	**Prepare the infusion** Before you start: 1. Remove a single vial carton from the refrigerator. Keep the vial in the carton at room temperature and allow it to warm up for approximately 30 minutes. A. Do not try to speed up the warming process using a microwave or any other heat source. 2. Find a well-lit, flat work surface area, like a table. 3. Gather your supplies (Figure 1): A. Syringe system infusion pump and manufacturer's instructions (not shown). B. Compatible syringe. C. 1. Transfer needle **OR** 2. Needleless transfer device to draw up the medicine from the vial. D. Infusion set (not shown; varies according to device manufacturer's instructions). E. Infusion tubing and Y-connector (if required). F. Sharps container. G. Alcohol wipes. H. Gauze pad and tape, or transparent dressing. Thoroughly clean the work surface using an alcohol wipe. Wash your hands thoroughly with soap and water. Dry your hands.	**Figure 1 Example of Supplies** 
Step 2	**Check the vial and liquid** Remove the vial from the carton. Carefully look at the liquid in the vial. Aspaveli is a clear, colorless to slightly yellowish liquid. Check for particles or color changes (Figure 2). **Do not use the vial if:** • The liquid looks cloudy, contains particles, or is dark yellow. • The protective flip cap is missing or damaged. • The expiry date (EXP) on the label has passed.	**Figure 2** 
Step 3	**Prepare and fill the syringe** Remove the protective flip cap from the vial to expose the central portion of the gray rubber stopper of the vial (Figure 3). Throw the protective cap away. Clean the stopper with a new alcohol wipe and allow the stopper to dry. Option 1: If using a needleless transfer device (such as a vial adapter), follow the instructions provided by the device manufacturer. **OR** Option 2: If transfer is done using a transfer needle and a syringe, follow the instructions below: A. Attach a sterile transfer needle to a sterile syringe. B. Pull back the plunger to fill the syringe with approximately 20 ml of air (Figure 4). C. Make sure the vial is in an upright position. Do not turn the vial upside down. Push the air-filled syringe, with transfer needle attached, through the center of the vial stopper. D. The tip of the transfer needle should not be in the solution to avoid creating bubbles. (Figure 5). E. Gently push the air from the syringe into the vial. This will inject the air from the syringe into the vial. F. Turn the vial upside down (Figure 6).	**Figure 3**  **Figure 4**  **Figure 5**  **Figure 6** 

	G. With the transfer needle tip in the solution, gently pull the plunger to fill the syringe with all the liquid (Figure 7). H. Remove the filled syringe and the transfer needle from the vial. I. **Do not recap the transfer needle.** Unscrew the needle and throw it away in the sharps container.	**Figure 7** 
Step 4	**Prepare syringe system infusion pump and tubing** Gather the infusion pump supplies and follow the device manufacturer's instructions to prepare the pump and tubing.	
Step 5	**Prepare the infusion site(s)** A. Select an infusion site(s) on your abdomen (except for the five centimeters area around the belly button), thighs, hips, or upper arms region (Figure 8). B. Use a different site(s) from the one you used for your last infusion. If there is more than one infusion site, they must be at least 7.5 cm apart from one another. Rotate between infusion sites at each infusion (Figure 9). C. **Avoid the following infusion areas:** **1) Do not infuse into areas where the skin is tender, bruised, red or hard.** **2) Avoid tattoos, scars or areas with stretch marks.** D. Clean the skin at each infusion site with a new alcohol wipe, starting at the centre and working outward in a circular motion (Figure 10). E. Let the skin dry.	**Figure 8**  **Figure 9**  **Figure 10** 
Step 6	**Insert and secure the infusion needle(s)** A. Pinch the skin between your thumb and forefinger around the infusion site (where you intend to place the needle). Insert the needle into the skin (Figure 11). Follow the device manufacturer's instructions regarding the angle of the needle. B. Secure the needle(s) using sterile gauze pad and tape or a transparent dressing placed over the infusion site(s) (Figure 12).	**Figure 11**  **Figure 12** 
Step 7	**Start infusion** Follow the device manufacturer's instructions to start the infusion. Start the infusion promptly after drawing the solution into the syringe.	
Step 8	**Complete the infusion** Follow the device manufacturer's instructions to complete the infusion.	
Step 9	**Record the infusion** Record the treatment as directed by the healthcare professional.	
Step 10	**Clean up** A. After the infusion is completed, remove the dressing and slowly take out the needle(s). Cover the infusion site with a new dressing. B. Disconnect the infusion set from the pump and discard into the sharps container (Figure 13). C. Throw away all used disposable supplies as well as any unused medicine and the empty vial per the instructions of the healthcare professionals. D. Clean and store the syringe system infusion pump according to the device manufacturer's instructions.	**Figure 13** 

If you accidentally take a higher dosage

If you accidentally used an excessive amount of Aspaveli or if a child accidentally swallows the medicine, refer immediately to the doctor or go to the hospital emergency room and bring the package of the medicine with you.

If you forget to take the medicine

If you forget a dose, take it as soon as you remember and continue with the next dose at the scheduled time.

Adhere to the treatment as recommended by the doctor. Even if there is an improvement in your health condition, do not stop treatment with the medicine without consulting the doctor. If you think you skipped a dose, refer to the doctor as soon as possible.

If you stop using the medicine

PNH is a chronic condition, so it is expected that you will use the medicine for an extended period. If you wish to discontinue the use of the medicine, please discuss it with the doctor beforehand.

If you suddenly stop taking the medicine, you may be at risk of worsening symptoms.

If the doctor decides to discontinue the treatment with this medicine, follow his instructions regarding the cessation of treatment. The doctor will closely monitor any sign of red blood cells destruction (hemolysis) due to your medical condition, for at least 8 weeks after discontinuing the treatment. Symptoms or problems that may occur due to red blood cell destruction include:

- fatigue
- shortness of breath
- blood in urine
- abdominal pain
- decreased red blood cell count
- blood clots (thrombosis)
- swallowing difficulties
- erection disturbances in men.

Refer to the doctor if you have any of these signs or symptoms.

Do not take medicines in the dark! Check the label and the dose each time you take medicine. Wear glasses if you need them. If you have further questions regarding use of the medicine, consult the doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, use of Aspaveli may cause side effects in some users.

Do not be alarmed when reading the list of side effects. You may not suffer from any of them.

The doctor will discuss possible side effects with you, and will explain to you the risks and benefits of Aspaveli therapy, before starting treatment.

The most serious side effect is severe infection.

Inform the doctor immediately if you experience any symptoms of infection (see section 2 "Infection symptoms").

If you are not sure what the side effects below are, ask the doctor to explain them to you.

Very common side effects (occur in more than one user out of ten):

- injection site reactions: including redness (erythema), swelling, itching, bruising and pain. These effects usually disappear within a few days
- infection of the nose, throat or airways (upper respiratory tract infection)
- diarrhea
- destruction of red blood cells (hemolysis)
- abdominal pain
- headache
- tiredness (fatigue)
- fever
- cough
- urinary tract infection
- complications related to the mandatory vaccinations
- dizziness
- arm and leg pain (pain in extremities)
- joint pain
- back pain
- nausea.

Common side effects (occur in 1-10 users out of 100):

- injection site reactions, such as redness, or hardening of the skin
- infection in the ear, mouth or skin
- throat pain
- fewer platelets in the blood (thrombocytopenia) which may cause bleeding or bruising more easily than normal
- nosebleed
- skin redness
- muscle pain
- infection of the stomach and intestines, which may cause symptoms of mild to severe nausea, vomiting, cramps, diarrhea (gastrointestinal infection)
- elevated liver function in blood test results
- difficulty breathing
- decreased levels of potassium in the blood
- fewer number of white blood cells (neutropenia)
- impaired kidney function
- anxiety
- different color of the urine
- high blood pressure
- muscle spasms
- stuffy nose (nasal congestion)
- rash
- infection in the blood (sepsis)
- fungal infection
- respiratory tract infection
- viral infection
- bacterial infection
- eye stye.

Uncommon side effects (occur in 1-10 users out of 1,000):

- COVID-19 (coronavirus disease 2019)
- inflammation of the cervix
- groin infection
- pocket of pus in nose (nasal abscess)
- viral eye infection (ophthalmic herpes zoster)
- pneumonia
- vaginal yeast infection
- urticaria.

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

Side effects can be reported to the Ministry of Health by clicking on the link "Reporting Side Effects of Drug Treatment" found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the link: https://sideeffects.health.gov.il

5. HOW SHOULD THE MEDICINE BE STORED?

Avoid poisoning! This medicine and any other medicine should be kept in a safe place out of the reach and sight of children and/or infants in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.

Do not use the medicine after the expiry date (exp. date) that appears on the package. The expiry date refers to the last day of that month.

Storage conditions:

- Store in the refrigerator at 2°C-8°C.
- Store in the original carton package to protect from light.
- Do not dispose of medicines in wastewater. Ask the pharmacist how to dispose of medicines you no longer use. These measures will help protect the environment.

6. FURTHER INFORMATION

In addition to the active ingredient, the medicine also contains:

sorbitol, sodium acetate trihydrate, glacial acetic acid, sodium hydroxide, water for injection.

What does the medicine look like and what is the content of the package:

Aspaveli is a clear, colorless to slightly yellowish aqueous solution with a pH of 5.0 intended for subcutaneous infusion (54 mg pegcetacoplan/1 mL in a 20 mL vial). Solutions that are cloudy or have particles or color change should not be used.

Package size:

Aspaveli comes in a pack of 1 vial or a pack of 8 vials.

Please note that alcohol wipes, needles, and other supplies or equipment are not included in the package.

Not all package sizes may be marketed.

Name of Registration Holder and its address:

TrueMed Ltd., 10 Beni Gaon St., Poleg Industrial Park P.O. Box 8105, Netanya 4250499.

Name of Manufacturer and its address:

Swedish Orphan Biovitrum AB, SE-112 76 Stockholm, Sweden

Revised in September 2024.

Registration number of the medicine in the Ministry of Health National Drug Registry: 176-68-37797-99

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