

AryoSeven RT

Eptacog alfa (activated)

Package leaflet: Information for the patient

AryoSeven RT 1 mg (50 KIU) Powder and solvent for solution for injection

AryoSeven RT 2 mg (100 KIU) Powder and solvent for solution for injection

AryoSeven RT 5 mg (250 KIU) Powder and solvent for solution for injection

AryoSeven RT 8 mg (400 KIU) Powder and solvent for solution for injection

Eptacog alfa (activated)

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet?

1. What AryoSeven RT is and what it is used for
2. What you need to know before you use AryoSeven RT
3. How to use AryoSeven RT
4. Possible side effects
5. How to store AryoSeven RT
6. Contents of the pack and other information

Overleaf is the instructions for preparing and giving an injection of AryoSeven RT

1. What AryoSeven RT is and what it is used for

AryoSeven RT contains the active substance called Eptacog alfa (activated), (Recombinant coagulation factor VIIa), belonging to a group of medicines called blood coagulation factors that are involved in blood clotting.

AryoSeven RT is a vitamin K-dependent and works by activating the extrinsic pathway of the coagulation. It is structurally similar to human plasma derived factor VIIa.

AryoSeven RT is used for the treatment of bleeding and prevention of bleeding during surgical operations in patients for the following indications:

- Congenital Haemophilia A or B with inhibitors (inadequate response to coagulation factor VIII or IX)
- Acquired Haemophilia
- Congenital FVII deficiency
- Glanzmann's thrombasthenia (a bleeding disorder) with past or present refractoriness to platelet transfusions.

2. What you need to know before you use AryoSeven RT

Do not use AryoSeven RT

If you have had allergic reactions to Eptacog alfa or any of the other ingredients of this medicine (listed in section 6) and if you had anaphylactic reactions to mouse, hamster or bovine proteins.

Warnings and precautions

Talk to your doctor, pharmacist or nurse before using AryoSeven RT:

- If you had any allergic, hypersensitivity or anaphylactic-type reactions to this medicine you should avoid injection of AryoSeven RT and contact your doctor immediately. You should be monitored closely.
- If you have advanced atherosclerotic disease (artery wall thickness), coronary heart disease, crush injury or have recently undergone a surgery, septicaemia (infection that has spread through your blood), severe liver disease or you are at risk of thromboembolic phenomena (like disseminated intravascular coagulation), consult with your doctor immediately to evaluate the risk and benefit of this medicine according to your complications.
- If you have severe bleeding or uncontrolled bleeding, emergency hospital care is essential and preferably you should be monitored by a physician specialized in hemophilia.
- If you are factor VII deficient and your bleeding is uncontrolled by the usual recommended dose tell your doctor. You should have an extra lab tests.
- If you have been intolerant to sucrose, fructose or glucose, or that you cannot digest them properly contact your doctor before taking AryoSeven RT.

Other medicines and AryoSeven RT

- Tell your doctor about any other medicines you are taking for other conditions.
- Taking AryoSeven RT with prothrombin complex concentrates or rFXIII should be avoided.
- Tell your doctor if you also use factor VIII or IX products before using AryoSeven RT.

- Co-administration of anti-fibrinolytics (Tranexamic acid) and AryoSeven RT should be done under your doctor supervision. Some limited experience showed they have positive effect on reducing bleeding.

Pregnancy, breast-feeding and fertility

- If you are pregnant or breast-feeding, think you may be pregnant or are planning to be pregnant ask your doctor, pharmacist or nurse for advice before taking this medicine.
- There are no adequate and well-controlled studies in pregnant women or nursing mothers.
- There are no reports of harmful effects of rFVIIa on male or female fertility.

Driving and using machines

No studies on the effect on the ability to drive and use machines have been performed.

3. How to use AryoSeven RT

Always use this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure of how to use AryoSeven RT. Based on body weight, condition and type of bleeding your doctor would recommend the appropriate dose for you.

AryoSeven RT should be administered as immediately as possible after the start of a bleeding episode. Ask your doctor about the number of injections you could have at home for mild bleedings. Without consulting with your doctor do not continue the treatment more than 24 hours at home.

In case of severe bleeding episodes you usually need hospital care.

Recommended dose:

Congenital Hemophilia A or B with inhibitors or expected to have a high anamnestic response

The recommended dose in bleeding episodes is 90 µg/kg intravenous bolus injection (over 2-5 minutes) every 2 - 3 hours until hemostasis is achieved or your doctor may recommend a single high dose in some cases. The dose, interval, and duration of therapy may be adjusted based upon the severity of bleeding and the degree of hemostasis achieved.

Congenital factor VII deficiency

The recommended dose in bleeding episodes and surgical interventions is 15-30 µg/kg every 4-6 hours until hemostasis is achieved. Dose and frequency of injections should be adapted to each individual.

Acquired Hemophilia

The recommended dose in bleeding episodes is 90

µg/kg every 2 to 3 hours until hemostasis is achieved.

Glanzmann's thrombasthenia (refractory to platelet transfusions)

The recommended dose in bleeding episodes is 90 µg/kg (range 80 - 120 µg/kg) every 2 hours. At least three doses should be administered to ensure effective haemostasis has been achieved.

Method and route of administration

AryoSeven RT powder must be reconstituted with the supplied solvent and administered as intravenous bolus injection (injection over 2-5 minutes).

If you use more AryoSeven RT than you should

Immediately get medical advise and consult with your doctor, you may need hospital care.

If you forget to use AryoSeven RT

Immediately consult with your doctor.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4- Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody experience them.

Serious side effects:

If you notice any of these serious side effects seek medical advice immediately.

Allergic reactions: Some patients may have allergic, hypersensitivity and anaphylactic reactions to AryoSeven RT. If you develop a severe rash, itching, hives, swollen face or lips, wheezing and difficulty breathing while taking AryoSeven RT, seek for urgent medical advice and immediately go to the nearest hospital.

Thromboembolic events: Formation of a clot in a blood vessel that breaks and is carried by the blood stream to clog another vessel leads to thromboembolic events. The clot may clog a vessel in the lungs (pulmonary embolism), brain (stroke), heart (heart attack or angina), gastrointestinal tract, kidneys or leg. If you develop signs including severe pain in chest, difficulty breathing, difficulty with speech, paralysis, red and painful swelling in leg, go to the nearest hospital immediately.

Inhibitory antibody formation: Probability of antibodies formation against rFVIIa have been reported specially in factor VII deficiency cases that have been previously treated with human plasma or plasma-derived factor. If you notice you have lack of response to AryoSeven RT consult with your doctor.

The above mentioned adverse effects are rare and uncommon but serious and could be life-threatening, if you notice any of the above symptoms, call your doctor

or visit the nearest hospital immediately.

The following side effects have been observed with and are listed in groups with decreasing in frequency:

Uncommon: (may affect up to 1 in 100 people)

Rash, Hives, Fever, Venous thromboembolic events, Inhibitory antibody formation, Pruritus and urticarial.

Rare: (may affect up to 1 in 1,000 people)

Disseminated intravascular coagulation, Arterial thromboembolic events, Nausea, Headache, Elevation of alanine aminotransferase, alkaline phosphatase and lactate dehydrogenase, Injection site reaction including injection site pain.

Not known: (frequency cannot be estimated from the available data)

Intracardiac thrombus, Flushing, Angioedema, Anaphylactic reactions.

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet.

You can also report side effects directly via the national reporting system fda.gov.ir or +98-21-22382641. By reporting side effects, you can help to provide more information on the safety of this medicine.

5- How to store AryoSeven RT

Storage conditions

- Keep this medicine out of the sight and reach of children.
- Do not use this medicine after the expiry date which is stated on the vial label and outer carton after "EXP". The expiry date refers to the last day of that month.
- Store powder and solvent below 25 °C.
- Do not freeze.
- Keep the vial and solvent in outer carton to protect from light.
- The reconstituted solution of AryoSeven RT is physically and chemically stable for 24 hours at 2 °C - 8 °C or for 6 hours below 25 °C. However, it is highly recommended to use the reconstituted solution of AryoSeven RT immediately to avoid microbial contamination. Store it in vial and protect from light.
- Do not use this medicine if you notice any particulate matter or discoloration before injection.
- 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 to protect the environment.

6- Contents of the pack and other information

What AryoSeven RT contains

Powder:

The active substance is recombinant coagulation factor VIIa (activated Eptacog alfa).

The other ingredients are Sodium chloride, Calcium chloride dihydrate, Glycylglycine, Polysorbate 80, D-Mannitol, Sucrose, Methionine.

Solvent:

Water for Injection and Histidine

AryoSeven RT 1 mg (50 KIU) Powder and solvent for solution for injection

Each single use vial contains 1 mg of activated Eptacog alfa that has to be dissolved in 1.1 ml of solvent. The final solution contains approximately 1 mg/ml of Eptacog alfa (rFVIIa).

AryoSeven RT 2 mg (100 KIU) Powder and solvent for solution for injection

Each single use vial contains 2 mg of activated Eptacog alfa that has to be dissolved in 2.1 ml of solvent. The final solution contains approximately 1 mg/ml of Eptacog alfa (rFVIIa).

AryoSeven RT 5 mg (250 KIU) Powder and solvent for solution for injection

Each single use vial contains 5 mg of activated Eptacog alfa that has to be dissolved in 5.2 ml of solvent. The final solution contains approximately 1 mg/ml of Eptacog alfa (rFVIIa).

AryoSeven RT 8 mg (400 KIU) Powder and solvent for solution for injection

Each single use vial contains 8 mg of activated Eptacog alfa that has to be dissolved in 8.1 ml of solvent. The final solution contains approximately 1 mg/ml of Eptacog alfa (rFVIIa).

What AryoSeven RT looks like and contents of the pack

AryoSeven RT is a white lyophilised powder for solution for injection which is supplied in a glass vial with a rubber stopper. The solvent vial contains a clear and colorless solution.

The reconstituted solution is a colorless solution.

The AryoSeven RT package contains:

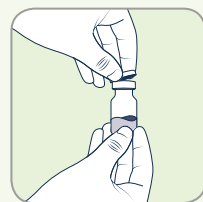
- One labeled vial with white powder (AryoSeven RT) for solution for injection
- One labeled vial with solvent (containing Histidine) for reconstitution
- One alcohol swab
- One syringe
- One scalp vein

INSTRUCTIONS ON HOW TO USE AryoSeven RT

Read these instructions carefully before using AryoSeven RT:

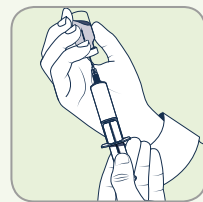
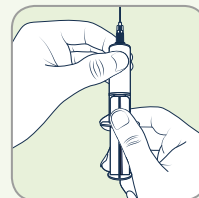
- Check the name and strength of the drug product.
- Check the expiry date of AryoSeven RT and solvent vials.
- Always use an aseptic technique.
- Wash your hands and ensure that the area around you is clean.

Reconstitution



Remove the plastic cap from the solvent vial. If the cap is loose or missing, do not use the solvent. Clean the rubber stopper on the vial with the alcohol swab and allow it to dry before use.

Pull the plunger of syringe to draw in a volume of air that is equal to the amount of solvent in the solvent vial (ml equals cc on the syringe).

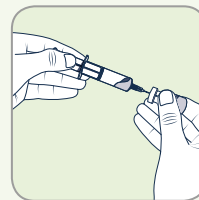


Insert the syringe needle into the solvent vial. Inject air into the vial by pushing the plunger until you feel a clear resistance.

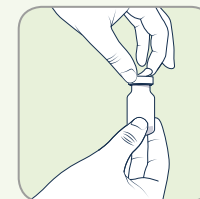
Hold the syringe with the solvent vial upside down and pull the plunger to draw the water into the syringe.

Remove the syringe from empty solvent vial, by tipping the syringe.

Remove the plastic cap from the powder vial. If the cap is loose or missing, do not use the vial content. Clean the rubber stopper on the vial with the alcohol swab and allow it to dry before use.



Insert the syringe needle into the powder vial. Hold the syringe slightly tilted with the vial facing downwards. Push the plunger slowly to inject the solvent into the powder vial. Make sure not to aim the stream of water directly at the AryoSeven RT powder as this will cause foaming.



Gently swirl the vial until all the powder is dissolved. Do not shake the vial as this will cause foaming.

AryoSeven RT reconstituted solution is colorless and should be inspected visually for particulate matter and discoloration prior to administration.

The enclosed disposable syringe is compatible with the reconstituted preparation, but do not store reconstituted AryoSeven RT in plastic syringes.

It is recommended to use AryoSeven RT immediately after reconstitution.

Administration

Administration should preferably take place immediately after reconstitution. Reconstituted AryoSeven RT should be stored in vial.

AryoSeven RT is intended for intravenous bolus injection only and should not be mixed with infusion solutions. Administration should be performed using the following procedures:

- Remove the plastic cap from the powder vial. If the cap is loose or missing, do not use the vial content. Clean the rubber stopper on the vial with the alcohol swab and allow it to dry before use.
- Hold the syringe with the vial upside down and pull the plunger to draw all the solution into the syringe. Remove the syringe from the empty vial. AryoSeven RT is now ready for injection. Rub the injection site with alcohol swab and then put the scalp vein in the appropriate vein, and slowly inject AryoSeven RT into a vein over a period of 2 - 5 minutes without removing the needle from the injection site.
- Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

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