

# AryoSeven™

Eptacog alfa (activated)

AryoSeven™ 1.2 mg (60 KIU) Powder and solvent for solution for injection

AryoSeven™ 2.4 mg (120 KIU) Powder and solvent for solution for injection

AryoSeven™ 4.8 mg (240 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™ is and what it is used for
2. What you need to know before you use AryoSeven™
3. How to use AryoSeven™
4. Possible side effects
5. How to store AryoSeven™
6. Contents of the pack and other information

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

## 1. What AryoSeven™ is and what it is used for

AryoSeven™ 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™ 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™ is used for the treatment and prevention of bleedings during surgical operations 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™

### Do not use AryoSeven™

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 have ever had anaphylactic reactions to mouse or bovine proteins.

### Warnings and precautions

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

- If you had any allergic, hypersensitivity or anaphylactic-type reactions to this medicine you should avoid injection of AryoSeven™ 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), immediately consult with your doctor to evaluate the risk and benefit of this medicine according to your complications.
- If you have severe bleeding or the bleeding is not kept under control, emergency hospital care is essential and you should preferably 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 test.

### Children and Adolescents

The use of this medicine in children and adolescents is similar to adult patients.

### Other medicines and AryoSeven™

- Tell your doctor about any other medicines you are taking for other conditions.
- Taking AryoSeven™ with prothrombin complex concentrates or rFXIII should be avoided.
- Tell your doctor if you also use factor VIII or IX products before using AryoSeven™.
- Co-administration of anti-fibrinolytics (Tranexamic acid) and AryoSeven™ should be done under your doctor's supervision. Limited data shows that 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 is 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™

Always use this medicine exactly as your doctor or pharmacist have told you. Check with your doctor or pharmacist if you are not sure. Your doctor will recommend the appropriate dose for you, depending on your body weight, condition and type of bleeding.

AryoSeven™ should be administered as immediately as possible after a bleeding episode starts. 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 severe bleedings 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.

### Acquired Hemophilia

The recommended dose in bleeding episodes is 90 µg/kg every 2 to 3 hours until hemostasis is 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.

### 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 secure achievement of effective haemostasis.

## Use in children and adolescents

The dose of AryoSeven™ in children and adolescents is same as the dose given to adult patients. However, because this medicine might be cleared faster in children and adolescents, the dosing frequency might be increased which will be decided by the physician.

## Method and route of administration

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

## If you use more AryoSeven™ than you should

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

## If you forget to use AryoSeven™

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 gets them.

## Serious side effects:

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

**Allergic reactions:** Some patients may have allergic, hypersensitivity and anaphylactic reactions to AryoSeven™. If you develop a severe rash, itching, hives, swollen face or lips, wheezing and difficulty breathing while taking AryoSeven™, 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 plug another vessel cause thromboembolic events. The clot may plug a vessel in the lungs (pulmonary embolism), brain (stroke), heart (heart attack or angina), gastrointestinal tract, kidneys or leg. If you develop symptoms including severe pain in chest, difficulty breathing, difficulty with speech, paralysis, red and painful swelling in leg, immediately go to the nearest hospital.

**Inhibitory antibody formation:** Probability of antibodies formation against rFVIIa have been reported specially in factor VII deficiency cases that previously have been treated with human plasma or plasma-derived factor. If you notice you have lack of response to AryoSeven™ 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, immediately call your doctor or visit the nearest hospital.

The following side effects have been observed with AryoSeven™ 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 urticaria

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

Disseminated intravascular coagulation, Arterial thromboembolic events, Nausea, Headache, Increase of alanine aminotransferase, alkaline phosphatase, lactate dehydrogenase, Increase of prothrombin, 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 [fdagov.ir](http://fdagov.ir). By reporting side effects, you can help provide more information on the safety of this medicine.

#### 5. How to store AryoSeven™

- 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 in a refrigerator (2°C - 8°C).
- Do not freeze.
- Keep the vial and solvent in outer carton to protect from light.
- The reconstituted solution of AryoSeven™ is physically and chemically stable for 24 hours at 2°C - 8°C or for 6 hours below 25°C. Although, it is highly recommended to use the reconstituted solution of AryoSeven™ 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

protect the environment.

#### 6. Contents of the pack and other information

##### What AryoSeven™ 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 and D-Mannitol.

###### Solvent:

Sterile water for injections

##### AryoSeven™ 1.2 mg (60 KIU) Powder and solvent for solution for injection

Each single use vial contains 1.2 mg of activated Eptacog alfa that has to be dissolved in 2.2 ml of sWFI. The final solution contains (approximately) 0.6 mg/ml of Eptacog alfa (rFVIIa).

##### AryoSeven™ 2.4 mg (120 KIU) Powder and solvent for solution for injection

Each single use vial contains 2.4 mg of activated Eptacog alfa that has to be dissolved in 4.3 ml of sWFI. The final solution contains (approximately) 0.6 mg/ml of Eptacog alfa (rFVIIa).

##### AryoSeven™ 4.8 mg (240 KIU) Powder and solvent for solution for injection

Each single use vial contains 4.8 mg of activated Eptacog alfa that has to be dissolved in 8.5 ml of sWFI. The final solution contains (approximately) 0.6 mg/ml of Eptacog alfa (rFVIIa).

##### What AryoSeven™ looks like and contents of the pack

AryoSeven™ 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™ package contains:

- One labeled vial with white powder (AryoSeven™) for solution for injection.
- One labeled vial with solvent (sterile water for injections) for reconstitution.
- One alcohol swab.
- One syringe

#### INSTRUCTIONS ON HOW TO USE ARYOSEVEN™

##### Read these instructions carefully before using AryoSeven™:

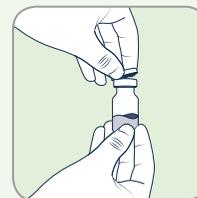
- Check the name and strength of the drug product.
- Check the expiry date of AryoSeven™ and solvent vials.
- Always use an aseptic technique.
- Wash your hands and ensure that the area around you is clean.

##### Reconstitution

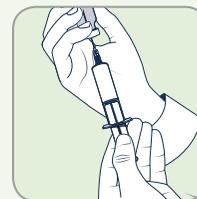
Wash your hands with soap and warm water.

Bring AryoSeven™ powder and solvent vials to room temperature (25°C). It can be done by holding them in palms.

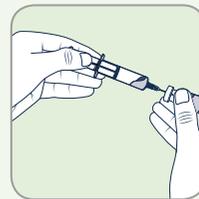
Remove the plastic cap from the solvent vial. If the cap is loose or missing, do not use the vial. Clean the rubber stopper on the vial with the alcohol swab and allow it to dry before use.



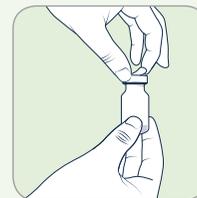
Pull the plunger of syringe to draw in a volume of air that is equal to the amount of solvent in the solvent vial (ml equals to cc on the syringe).



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. 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 water into the powder vial. Make sure not to aim the stream of water directly at the AryoSeven™ 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™ 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™ in plastic syringes.

It is recommended to use AryoSeven™ immediately after reconstitution.

##### Administration

Administration should preferably take place immediately after reconstitution. Reconstituted AryoSeven™ should be stored in vial. AryoSeven™ 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. 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™ is now ready for injection. Put scalp vein in the appropriate vein, and slowly inject AryoSeven™ 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 off in accordance with local requirements.

**ARYOGEN**  
آریوژن فارمد

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