Package leaflet: Information for the user

Aprotinin 10,000 KIU/ml Injection BP

Aprotinin

Read all of this leaflet carefully before you are given 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 the doctor/surgeon giving you Aprotinin 10,000 KIU/ml Injection (called Aprotinin Injection in the rest of this leaflet)
- If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet.

What is in this leaflet

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

1. What Aprotinin Injection is and what it is used for

Aprotinin Injection belongs to a group of medicines called anti-fibrinolytics, i.e. medicines to prevent blood loss.

Aprotinin Injection can help to reduce the amount of blood loss you have during and after heart surgery. It is also used to reduce the need for a blood transfusion during and after heart surgery. Your doctor/surgeon has decided that you would benefit from Aprotinin Injection treatment because you are at increased risk of major blood loss since you will undergo a heart bypass operation using a circulation outside your body (heart-lung machine).

Your doctor will administer aprotinin after careful consideration of the benefits and risks, and the availability of alternative treatments.

2. What you need to know before you are given Aprotinin Injection

Do not use Aprotinin Injection

- if you are **allergic to Aprotinin Injection** or any of the other ingredients of this medicine (listed in section 6).
- if a **positive aprotinin-specific IgG antibody** test is available, showing an increased risk of an allergic reaction to **Aprotinin Injection**

- if no aprotinin specific IgG antibody test is possible prior to treatment and you have received or you suspect that you have received Aprotinin-containing medicinal products in the last 12 months.

Warnings and precautions

Talk to your doctor before receiving Aprotinin Injection.

Tell your doctor if any of these apply to you, to help him or her decide if Aprotinin Injection is suitable for you:

- **Your kidneys do not work properly.** If you have kidney problems Aprotinin Injection should only be used if your doctor/surgeon feels it will be of benefit.
- **You have or suspect you have received aprotinin or aprotinin containing fibrin sealants in the last 12 months.**

If any of these apply to you, your doctor will decide whether Aprotinin Injection is suitable for you or not.

Aprotinin Injection will only be given if your doctor has done **blood tests before** to check you are suitable (e.g. an appropriate aprotinin-specific IgG antibody test), otherwise other medicines may be a better option for you.

You will be monitored carefully for any allergic reaction to the medicine and your doctor/surgeon will treat any symptoms you may experience. Standard emergency treatment for severe allergic reactions should be readily available during treatment with Aprotinin Injection

Children and adolescents
The safety and efficacy of Aprotinin Injection in children below the age of 18 years have not been established.

Other medicines and Aprotinin Injection
Tell your doctor if you are taking, have recently taken or might take any other medicines.

You should specifically tell your doctor if you take:
- medicines used to dissolve blood clots, such as streptokinase, urokinase, alteplase (r-tPA)
- aminoglycosides (antibiotics, medicines used to treat infections)

It is recommended that your doctor/surgeon should, in addition to Aprotinin Injection administer heparin (a medicine used to prevent blood clots) before and during the operation. Your doctor will evaluate the dose of heparin based on the results from tests of your blood.

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before you are given this medicine. If you are pregnant or breast-feeding Aprotinin Injection should only be used if your doctor/surgeon finds it will be of benefit. Your doctor will discuss with you the risks and benefits of using this medicine.

3. How to use Aprotinin Injection

For adult patients the following dose regimen is recommended:

You will receive a small amount of Aprotinin Injection (1 ml) before the operation begins, to test if you are allergic to the Aprotinin Injection. Medicines used to prevent the symptoms of allergy (H_1-antagonist and a H_2-antagonist) may be administered 15 minutes prior to the test dose of Aprotinin Injection

If there are no signs of allergy, you will be given 100-200 ml Aprotinin Injection over 20 to 30 minutes, followed by 25 - 50 ml per hour (max. 5 - 10 ml/min) until the end of the operation. In general, you will not be given more than 700 ml of Aprotinin Injection at any one time.

There is no special dose recommendation for elderly patients or patients with poor kidney function

Aprotinin Injection will usually be given to you lying down by slow injection or infusion (through 'a drip') through a catheter into a larger vein in your body.

If you are given more Aprotinin Injection than the recommended dose
There is no specific substance to counteract the effects of Aprotinin Injection

4. Possible side effects

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

Although allergic reactions are rare in patients receiving an Aprotinin-containing medicinal product for the first time, patients who are given Aprotinin Injection more than once may have an increased chance of an allergic reaction. The symptoms of an allergic reaction may include:
- **breathing difficulties**
- **reduced blood pressure**
- **itching, rash and hives**
- **feeling sick**

Other side effects are:

Uncommon: may affect up to 1 in 100 patients
- chest pain (*myocardial ischaemia, coronary occlusion / thrombosis*), heart attack (*myocardial infarction*)
- leakage of heart fluid into the surrounding body cavity (*pericardial effusion*)
- blood clot (*thrombosis*)
- kidney disease (*acute renal failure, renal tubular necrosis*)
- passing less urine than is normal

Rare: may affect up to 1 in 1,000 patients
- blood clot in blood vessels (*arteries*)
- severe allergic reaction (*anaphylactic / anaphylactoid reaction*)

Very rare: may affect up to 1 in 10,000 patients
- swelling on or around the location of the injected skin (injection and infusion site reactions, infusion site (*thrombo- phlebitis*)
- blood clot in the lungs (*pulmonary embolism*)
- severe blood clotting disorder that results in tissue damage and bleeding (*disseminated intravascular coagulation*)
- inability of the blood to clot or coagulate normally (*coagulopathy*)
- severe allergic shock (*anaphylactic shock*), which is potentially life threatening

If any of these occur during administration of Aprotinin Injection your doctor/surgeon will stop treatment with the drug.

Reporting of side effects

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

You can also report side effects directly via the national reporting system in UK
Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple store.

By reporting side effects you can help provide more information on the safety of this medicine

5. How to store Aprotinin Injection

Aprotinin Injection should be stored below 25°C, protected from light. Do NOT use Aprotinin Injection if it is past the expiry date on the packaging.

Keep out of the sight and reach of children.

6. Contents of the pack and other information

What Aprotinin Injection contains

Aprotinin Injection contains the active ingredient aprotinin in water for injection.
One 50ml vial contains 500,000 Kallikrein Inactivator Units (equal to 277.8 E.P. Units) of aprotinin.

Aprotinin Injection also contains the inactive ingredient sodium chloride.

What Aprotinin Injection looks like and contents of the pack

Aprotinin Injection is a sterile, clear colourless solution. It is supplied in single glass vials of 50ml.

Marketing Authorisation Holder and Manufacturer

The marketing authorisation holder is
Nordic Group B.V., Siriusdreef 41, 2132 WT Hoofddorp, the Netherlands.
The manufacturer is Fresenius Kabi Austria GmbH (FKA), Hafnerstrasse 36, A-8055 Graz, Austria.

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INFORMATION FOR HEALTHCARE PROFESSIONALS

Name of the Medicinal Product

Aprotinin 10,000 KIU/ml Injection BP

Qualitative and Quantitative Composition

Each 50ml vial contains aprotinin solution corresponding to 500,000 Kallikrein Inactivator Units, KIU (= 277.8 European Pharmacopoeia, E.P. units) aprotinin in 0.9% sodium chloride solution.

Pharmaceutical Form

Solution for Injection

Posology and Method of Administration

An appropriate aprotinin-specific IgG antibody test may be considered before administration of aprotinin (see section 4.3 of the Summary of Product Characteristics).

Owing to the risk of allergic/anaphylactic reactions, a 1 ml (10,000 KIU) test dose should be administered to all patients at least 10 minutes prior to the remainder of the dose. After the uneventful administration of the 1 ml test dose, the therapeutic dose may be given. A H_1-antagonist and a H_2-antagonist may be administered 15 minutes prior to the test dose of aprotinin. In any case standard emergency treatments for anaphylactic and allergic reactions should be readily available (see section 4.4 of the Summary of Product Characteristics).

A loading dose of 1 - 2 million KIU is administered as a slow intravenous injection or infusion over 20 - 30 minutes after induction of anaesthesia and prior to sternotomy. A further 1 - 2 million KIU should be added to the pump prime of the heart-lung machine. To avoid physical incompatibility of aprotinin and heparin when adding to the pump prime solution, each agent must be added during recirculation of the pump prime to assure adequate dilution prior to admixture with the other component.
The initial bolus infusion is followed by the administration of a continuous infusion of 250,000 - 500,000 KIU per hour until the end of the operation.

In general, the total amount of aprotinin administered per treatment course should not exceed 7 million KIU.

Method of administration

Aprotinin should be infused using a central venous catheter. The same lumen should not be used for the administration of any other medicinal product. When using a multi-lumen central catheter a separate catheter is not required.

Aprotinin must be given only to patients in the supine position and must be given slowly (maximum 5 - 10 ml/min) as an intravenous injection or a short infusion.

Incompatibilities

Aprotinin is incompatible with antibiotics such as tetracyclines which react with proteins, corticosteroids, heparin and nutrient solutions containing amino acids or fat emulsions. The addition of aprotinin to mixed infusions (particularly with beta-lactam antibiotics) should be avoided. Electrolyte and sugar solutions are compatible with aprotinin.

Shelf Life

3 years

Special Precautions for Storage

Store below 25°C; store in the original package in order to protect from light.

Special precautions for disposal and other handling

Parenteral drug products should be inspected visually for particulate matter and colour change prior to administration. Any residual solution should not be kept for later use.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.