Package Leaflet: Information for the user

Riastap® 1 g

Powder for solution for injection / infusion
Human fibrinogen

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

What is in this leaflet:

1. What Riastap is and what it is used for

What is Riastap?
Riastap contains human fibrinogen which is a protein important for blood clotting (coagulation). Lack of fibrinogen means that the blood does not clot as quickly as it should, which results in an increased tendency of bleeding. The replacement of human fibrinogen with Riastap will correct the coagulation defect.

What is Riastap used for?
Riastap is used for treatment of bleeding in patients with a congenital lack of fibrinogen (hypo- or afibrinogenaemia) with bleeding tendency.

2. What you need to know before you use Riastap

The following sections contain information that your doctor should consider before you are given Riastap.

Do not use Riastap:
- if you are allergic to human fibrinogen or any of the other ingredients of this medicine (listed in section 6).

Please inform your doctor if you are allergic to any medicine or food.

Warnings and precautions:

- if you have experienced allergic reactions to Riastap in the past. You should take antihistamines and corticosteroids prophylactically if advised by your doctor.
- when allergic or anaphylactic-type reactions occur (a serious allergic reaction that causes severe difficulty in breathing or dizziness). **The administration of Riastap should be stopped immediately (i.e. discontinue injection).**
- because of an increased risk of blood clots in a blood vessel (thrombosis), particularly:
  - in case of a high dose or repeated dosing
  - if you have had a heart attack (a history of coronary heart disease or myocardial infarction)
  - if you suffer from liver disease
  - if you have just had surgery (patients postoperatively)
  - if you will be having surgery soon (patients preoperatively)
  - in newborn infants (neonates)
  - if you are more likely to suffer from blood clots than normal (patients at risk of thromboembolic phenomena or disseminated intravascular coagulation)

Your doctor will consider carefully the benefit of treatment with Riastap compared with the risk of these complications.

Virus safety

When medicines are made from human blood or plasma, certain measures are put in place to prevent infections being passed on to patients. These include:

- careful selection of blood and plasma donors to make sure those at risk of carrying infections are excluded, and
- the testing of each donation and pools of plasma for signs of virus/infections.

Manufacturers of these products also include steps in the processing of the blood or plasma that can inactivate or remove viruses. Despite these measures, when medicines prepared from human blood or plasma are administered, the possibility of passing on infection cannot be totally excluded. This also applies to any unknown or emerging viruses or other types of infections.

The measures taken are considered effective for enveloped viruses such as human immunodeficiency virus (HIV, the AIDS virus), hepatitis B virus and hepatitis C virus (inflammation of the liver), and for the non-enveloped hepatitis A virus (inflammation of the liver).

The measures taken may be of limited value against non-enveloped viruses such as parvovirus B19.

Parvovirus B19 infection may be serious:

- for pregnant women (infection of the unborn child) and
- for individuals whose immune system is depressed or who have some types of anaemia (e.g. sickle cell disease or haemolytic anaemia).

Your doctor may recommend that you consider vaccination against hepatitis A and B if you regularly/repeatedly receive human plasma-derived products.

It is strongly recommended that every time that Riastap is given, your doctor should record the date of administration, the batch number and the injected volume.

Other medicines and Riastap
- Please tell your doctor or pharmacist if you are using, have recently used or might use any other medicines.
- Riastap must not be mixed with other medicinal products except those mentioned in section "*The following information is intended for healthcare professionals only / Reconstitution*".

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 or pharmacist for advice before taking this medicine.
- During pregnancy and breast-feeding Riastap should be given only if it is clearly needed.

Driving and using machines
Riastap has no or negligible influence on the ability to drive and use machines.

Important information about some of the ingredients in Riastap
Riastap contains up to 164 mg (7.1 mmol) sodium per vial. This correlates with 11.5 mg (0.5 mmol) sodium per kg body weight of the patient if the recommended initial dose of 70 mg/kg body weight is applied. Please take this into account if you are on a controlled sodium diet.

3. How to use Riastap

Treatment should be initiated and supervised by a physician who is experienced in this type of disorder.

Dosage
The amount of human fibrinogen you need and the duration of treatment depend on:
- the severity of your disease,
- the site and intensity of the bleeding,
- your clinical condition.

If you use more Riastap than you should
Your doctor should regularly check your blood clot status during the treatment. In case of overdosage, the risk of development of thromboembolic complications is enhanced.

Method of administration
If you have any further questions on the use of this product, ask your doctor or pharmacist (see section *"The following information is intended for medical or healthcare professionals only"*).

4. Possible side effects

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

Please contact your doctor immediately:
- **if any of the side effects occur**
- **if you notice any side effects not listed in this leaflet.**

The following side effect has been observed *very commonly* (may affect more than 1 in 10 people):

- Increase in body temperature

The following side effect has been observed *uncommonly* (may affect up to 1 in 100 people):

- A sudden allergic reaction (such as reddening of the skin, skin rash over the whole body, fall in blood pressure, difficulty in breathing).

The following side effect has been observed *commonly* (may affect up to 1 in 10 people, however incidence was higher in patients receiving no fibrinogen):

- Risk of increased formation of blood clots (see section *2 "What you need to know before you use Riastap"*).

Reporting of side effects
If you get any side effects, talk to your doctor or healthcare professional. This includes any possible side effects not listed in this leaflet. You can also report side effects directly (see details below). By reporting side effects, you can help provide more information on the safety of this medicine.

UK: Yellow Card Scheme.
Website: www.mhra.gov.uk/yellowcard
or search for MHRA Yellow Card in the Google Play or Apple App Store

Malta: ADR Reporting Website:
www.medicinesauthority.gov.mt/adrportal

Ireland:
HPRA Pharmacovigilance
Earlsfort Terrace
IRL - Dublin 2
Tel: +353 1 676 4971
Fax: +353 1 676 2517
Website: www.hpra.ie
Email: medsafety@hpra.ie

5. How to store Riastap

- 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 label and carton.
- Store in a refrigerator (2 °C – 8 °C).
- Do not freeze.
- Keep the vial in the outer carton, in order to protect from light.
- The reconstituted product should preferably be used immediately.
- If the reconstituted product is not administered immediately, storage shall not exceed 8 hours at room temperature (max. +25 °C).
- The reconstituted product should not be stored in the refrigerator.

6. Contents of the pack and other information

What Riastap contains

The active substance is:
Human fibrinogen (1 g/vial; after reconstitution with 50 ml of water for injections approx. 20 mg/ml).

See section *"The following information is intended for healthcare professionals only"* for further information.

The other ingredients are:
Human albumin, sodium chloride, L-arginine hydrochloride, sodium citrate, sodium hydroxide (for pH adjustment).
See last paragraph of section 2. "*Important information about some of the ingredients of Riastap*".

What Riastap looks like and contents of the pack
Riastap is presented as a white powder.
After reconstitution with water for injections the product should be clear or slightly opalescent, i.e. it might sparkle when held up to the light but must not contain any obvious particles.

Presentation
Pack with 1 g (Figure 1)
1. One vial containing 1 g human fibrinogen
2. Filter: Pall® Syringe Filter
3. Dispensing pin: Mini-Spike® Dispensing Pin

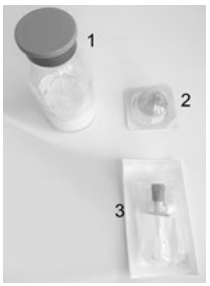

Figure 1

Marketing Authorisation Holder and Manufacturer
CSL Behring GmbH
Emil-von-Behring-Strasse 76
35041 Marburg
Germany

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

United Kingdom
CSL Behring UK Ltd.
Tel: +44 (0)1444 447405

Malta
AM Mangion Ltd.
Tel: +356 2397 6333

Ireland
CSL Behring GmbH
Tel: +49 69 30517254

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The following information is intended for healthcare professionals only

Posology

The (functional) fibrinogen level should be determined in order to calculate individual dosage and the amount and frequency of administration should be determined on an individual patient basis by regular measurement of plasma fibrinogen level and continuous monitoring of the clinical condition of the patient and other replacement therapies used.

Normal plasma fibrinogen level is in the range of 1.5 – 4.5 g/l. The critical plasma fibrinogen level below which haemorrhages may occur is approximately 0.5 – 1.0 g/l. In case of major surgical intervention, precise monitoring of replacement therapy by coagulation assays is essential.

Initial Dose
If the patient's fibrinogen level is not known, the recommended dose is 70 mg per kg body weight administered intravenously.

Subsequent Dose
The target level (1 g/l) for minor events (e.g. epistaxis, intramuscular bleeding, or menorrhagia) should be maintained for at least three days. The target level (1.5 g/l) for major events (e.g. head trauma, or intracranial haemorrhage) should be maintained for seven days.

$$\text{Dose of fibrinogen (mg/kg body weight)} = \frac{\text{[Target level (g/l) - measured level (g/l)]}}{\text{0.017 (g/l per mg/kg body weight)}}$$

Dosage for neonates, infants and children
Limited data from clinical studies regarding the dosage of Riastap in children are available. Resulting from these studies, as well as from long lasting clinical experience with fibrinogen products, dosage recommendations in the treatment of children are the same as for adults.

Method of Administration

General instructions
- Reconstitution and withdrawal should be carried out under aseptic conditions.
- Reconstituted products should be inspected visually for particulate matter and discoloration prior to administration.
- The solution should be almost colourless to yellowish, clear to slightly opalescent and of neutral pH. Do not use solutions that are cloudy or have deposits.

Reconstitution
- Warm both the solvent and the powder in unopened vials to room or body temperature (not above 37 °C).
- Riastap should be reconstituted with water for injections (50 ml, not provided).
- Wash hands or use gloves before reconstituting the product.
- Remove the cap from the Riastap vial to expose the central portions of the infusion stoppers.
- Treat the surface of the infusion stopper with antiseptic solution and allow it to dry.
- Transfer the solvent into the vial using an appropriate transfer device. Ensure complete wetting of the powder.

- Gently swirl the vial until the powder is reconstituted and the solution is ready for administration. Avoid strong shaking which causes formation of foam. Generally, the powder dissolves within approximately 5 minutes. It should not take longer than 15 minutes to completely dissolve.
- Open the plastic blister containing the dispensing pin (Mini-Spike® Dispensing Pin) provided with Riastap (Figure 2).


Figure 2

- Take the provided dispensing pin and insert it into the stopper of the vial with the reconstituted product (Figure 3).


Figure 3

- After the dispensing pin is inserted, remove the cap. After the cap is removed, do not touch the exposed surface.
- Open the blister with the filter (Pall® Syringe Filter) provided with Riastap (Figure 4).

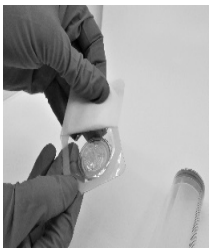
Figure 4

- Screw the syringe onto the filter (Figure 5).

Figure 5

- Screw the syringe with the mounted filter onto the dispensing pin (Figure 6).

Figure 6

- Draw the reconstituted product into the syringe (Figure 7).


Figure 7

- When completed, **remove the filter, dispensing pin and empty vial from the syringe,** dispose of properly, and proceed with administration as usual.
- Reconstituted product should be administered immediately by a separate injection/infusion line.
- Take care that no blood enters syringes filled with product.

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

Administration

A standard infusion set is recommended for intravenous application of the reconstituted solution at room temperature. The reconstituted solution should be injected or infused slowly at a rate which the patient finds comfortable. The injection or infusion rate should not exceed approx. 5 ml per minute.