Package leaflet: Information for the user

Berinert 1500
1500 IU
Powder and solvent for solution for injection.
Human C1-esterase inhibitor

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

1. What Berinert is and what it is used for

What is Berinert?
Berinert is presented as powder and solvent. The made up solution is to be given by injection into a vein.

Berinert is made from human plasma (this is the liquid part of the blood). It contains the protein human C1-esterase inhibitor as active ingredient.

What is Berinert used for?
Berinert is used for the treatment and pre-procedure prevention of the hereditary angioedema type I and II (HAE, oedema = swelling). HAE is a congenital disease of the vascular system. It is a non-allergic disease. HAE is caused by deficiency, absence or defective synthesis of C1-esterase inhibitor, an important protein. The illness is characterised by the following symptoms:
- swelling of the hands and feet that occurs suddenly,
- facial swelling with tension sensation that occurs suddenly
- eyelid swelling, lip swelling, possibly laryngeal (voice-box) swelling with difficulty in breathing,
- tongue swelling,

- colic pain in abdominal region
Generally, all parts of the body can be affected.

2. What you need to know before you use Berinert

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

Do not use Berinert:
- if you are allergic to the protein C1-esterase inhibitor or any of the other ingredients of this medicine listed in section *6.*
  Please inform your doctor or pharmacist if you are allergic to any medicine or food.

Warnings and precautions:
- if you have experienced allergic reactions on Berinert 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 Berinert should then be stopped immediately (e.g. discontinue injection).**
- if you suffer from laryngeal swelling (laryngeal oedema). You should be carefully monitored with emergency treatment in stand-by.
- during unlicensed use beyond the approved indications and posology (e.g. Capillary Leak Syndrome, CLS). See section *4. "Possible side effects"*.

Your doctor will consider carefully the benefit of treatment with Berinert 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, hepatitis C virus (inflammation of the liver) and for the non-enveloped viruses hepatitis A (inflammation of the liver) and parvovirus B19.

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 Berinert is given, the date of administration, the batch number and the injected volume should be recorded.

Other medicines and Berinert
- Please tell your doctor or pharmacist if you are taking or have recently taken any medicines, including medicines obtained without a prescription.
- Berinert should not be mixed with other medicinal products and diluents in the syringe.

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 Berinert should be given only if it is clearly needed.

Driving and using machines
No studies on the effects on the ability to drive and use machines have been performed.

Important information about some of the ingredients of Berinert
Berinert contains less than 1 mmol sodium (23mg) per vial, that is to say essentially „sodium-free“.

3. How to use Berinert

Treatment should be started and supervised by a doctor who is experienced in the treatment of C1-esterase inhibitor deficiency.

Dosage

Adults
Treatment of acute angioedema attacks:
20 IU per kilogram body weight (20 IU/kg b.w.).

Pre-procedure prevention of angioedema attacks:
1000 IU less than 6 hours prior to a medical, dental, or surgical procedure.

Paediatric population
Treatment of acute angioedema attacks:
20 IU per kilogram body weight (20 IU/kg b.w.).

Pre-procedure prevention of angioedema attacks:
15 to 30 IU per kilogram body weight (15-30 IU/kg b.w.) less than 6 hours prior to a medical, dental or surgical procedure. Dose should be selected taking into account clinical circumstances (e.g. type of procedure and disease severity).

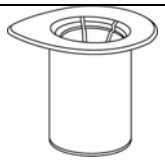
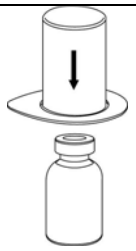
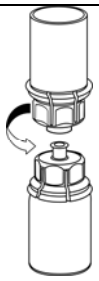
Overdose
No case of overdose has been reported.

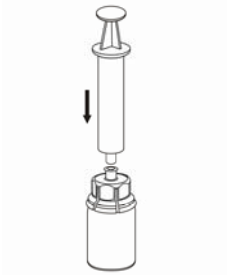
Reconstitution and method of administration

Berinert is usually injected into a vein (intravenously) by your doctor or nurse. You or your carer might also administer Berinert as an injection, but only after receiving adequate training. If your doctor decides that you may be suitable for such home-treatment, he/she will give you detailed instructions. You will be required to keep a diary in order to document each treatment received at home and to bring it to each of your visits to the doctor. Regular review of your/your carer's injection technique will be performed to ensure continued appropriate handling.

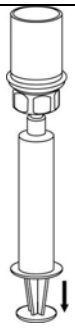
General instructions
- The powder must be dissolved and withdrawn from the vial under aseptic conditions. Use the syringe provided with the product.
- The made up solution should be colourless and clear to slightly opalescent. After filtering or withdrawal (see below) the solution should be checked by eye for small particles and discoloration, before it is administered.
- Do not use the solution if it is visibly cloudy or if it contains flakes or particles.
- Any unused product or waste material should be disposed of in accordance with local requirements and as instructed by your doctor.

Reconstitution
Without opening either vial, warm the Berinert powder and the solvent to room temperature. This can be done either by leaving the vials at room temperature for about an hour, or by holding them in your hands for a few minutes. DO NOT expose the vials to direct heat. The vials must not be heated above body temperature (37°C).
Carefully remove the protective caps from the solvent vial and the product vial. Clean the exposed rubber stoppers of both vials with one alcohol swab each and allow them to dry. The solvent can now be transferred to the powder with the administration set (Mix2Vial) attached. Please follow the instructions given below.

 1	1. Open the Mix2Vial package by peeling off the lid. Do **not** remove the Mix2Vial from the blister package!
 2	2. Place the solvent vial on an even, clean surface and hold the vial tight. Take the Mix2Vial together with the blister package and push the spike of the blue adapter end **straight down** through the solvent vial stopper.
 3	3. Carefully remove the blister package from the Mix2Vial set by holding at the rim, and pulling **vertically** upwards. Make sure that you only pull away the blister package and not the Mix2Vial set.
 4	4. Place the product vial on an even and firm surface. Invert the solvent vial with the Mix2Vial set attached and push the spike of the transparent adapter end **straight down** through the product vial stopper. The solvent will automatically flow into the product vial.
 5	5. With one hand grasp the product-side of the Mix2Vial set and with the other hand grasp the solvent-side and unscrew the set carefully into two pieces. Discard the solvent vial with the blue Mix2Vial adapter attached.
 6	6. Gently swirl the product vial with the transparent adapter attached until the substance is fully dissolved. Do not shake.

 7	7. Draw air into an empty, sterile syringe. Use the syringe provided with the product. While the product vial is upright, connect the syringe to the Mix2Vial's Luer Lock fitting. Inject air into the product vial.

Withdrawal and application

 8	8. While keeping the syringe plunger pressed, invert the system upside down and draw the solution into the syringe by pulling the plunger back slowly.
 9	9. Now that the solution has been transferred into the syringe, firmly hold on to the barrel of the syringe (keeping the syringe plunger facing down) and disconnect the transparent Mix2Vial adapter from the syringe.

Administration
The solution is to be administered by slow intravenous (i.v.) injection.

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, or**
- **if you notice any side effects not listed in this leaflet.**

Undesired reactions with Berinert are rare.

The following side effects have been observed rarely (may affect up to 1 in 1,000 people):

- There is a risk of increased formation of blood clots in treatment attempts for prophylaxis or therapy of Capillary Leak Syndrome (outflow of fluid from the small blood vessels into the tissue) e. g. during or after cardiac surgery under extracorporal circulation. See section *2. "Warning and precautions"*.
- Increase in body temperature as well as burning and stinging where the injection was given.
- Hypersensitive or allergic reactions (such as irregular heart beat, faster heart beat, fall in blood pressure, reddening of the skin, rash, difficulty in breathing, headache, dizziness, sickness).

In very rare cases (may affect up to 1 in 10,000 people) hypersensitive reactions might progress as far as shock.

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. 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 of the safety of this medicine.

Ireland:
HPRA Pharmacovigilance
Earlsfort Terrace
IRL - Dublin 2
Tel: +353 1 6764971
Fax: +353 1 6762517
Website: www.hpra.ie
e-mail: medsafety@hpra.ie

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

5. How to store Berinert

- **Keep this medicine out of the sight and reach of children.**
- Do not use Berinert after the expiry date, which is stated on the label and carton.
- Do not store above 30°C.
- Do not freeze.
- Keep the vial in the outer carton, in order to protect from light.
- Berinert does not contain a preservative so the made-up solution should preferably be used immediately.
- If the made-up solution is not administered immediately it must be used within 8 hours and should only be stored in the **vial**.

6. Contents of the pack and other information

What Berinert contains

The active substance is:
Human C1-esterase inhibitor (1500 IU/vial; after reconstitution with 3 ml of water for injcetions 500 IU/ml)
See section *"The following information is intended for healthcare professionals only"* for further information.

The other ingredients are:
Glycine, sodium chloride, sodium citrate
See last paragraph of section 2. **"***Important information about some of the ingredients of Berinert*".
Solvent: Water for injections

What Berinert looks like and contents of the pack
Berinert is presented as a white powder and is supplied with water for injections as solvent.
The made-up solution should be colourless and clear to slightly opalescent.

Presentation
Box with 1500 IU contains:
1 vial with powder (1500 IU)
1 vial with 3 ml water for injections
1 filter transfer device 20/20
Administration set (inner box):
1 disposable 5 ml syringe
1 venipuncture set
2 alcohol swabs
1 plaster

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

This medicinal product is authorised in the Member States of the EEA under the following names:

Berinert 1500 IE Pulver und Lösungsmittel zur Herstellung einer Injektionslösung	Austria
Berinert 1500	Belgium, Cyprus, Germany, Greece, Luxembourg, Poland
Berinert 1500, 500 IU Powder and solvent for solution for injection	Bulgaria
Berinert 1500 IU	Czech Republic, Slovakia
Berinert	Denmark, Italy, Portugal

Berinert 1500 IU, injektiokuiva-aine ja liuotin, liuosta varten	Finland
Berinert 1500 UI, poudre et solvant pour solution injectable	France
Berinert 1500 NE por és oldószer oldatos injekcióhoz	Hungary
Berinert 1500 IU pulver og væske til injeksjonsvæske, oppløsning	Norway
Berinert 1500 UI, pulbere şi solvent pentru soluţie injectabilă	Romania
Berinert 1500 i.e. prašek in vehikel za raztopino za injiciranje	Slovenia
Berinert 1500 UI Polvo para solución inyectable	Spain
Berinert 1500 IE, pulver och vätska till injektionsvätska, lösning	Sweden
Berinert 1500 IU powder and solvent for solution for injection	UK

This leaflet was last revised in September 2021

The following information is intended for healthcare professionals only

QUALITATIVE AND QUANTITATIVE COMPOSITION

The potency of human C1-esterase inhibitor is expressed in International Units (IU), which are related to the current WHO Standard for C1-esterase inhibitor products.