Package leaflet: Information for the user

Berinert® 3000 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

What is Berinert?
Berinert is presented as powder and solvent. The made up solution is to be given by injection under the skin.

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 prevention of recurrent hereditary angioedema (HAE) attacks in adolescent and adult patients. 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 have experienced life-threatening immediate hypersensitivity reactions, including anaphylaxis, 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:
Talk to your doctor or pharmacist before using Berinert,
- if severe allergic or anaphylactic-type reactions occur (a serious allergic reaction that causes severe difficulty in breathing or dizziness)**.Administration of Berinert should be stopped immediately (e.g. discontinue injection).**
- if you have a history of blood clotting problems. Blood clots have occurred in patients receiving intravenous Berinert. Very high doses of Berinert in diseases other than HAE, could increase the risk of blood clots. However, for subcutaneous Berinert, there is no established link with blood clots at the dose that your doctor is recommended to prescribe. Tell your doctor if you have a history of heart or blood vessel disease, stroke, blood clots or have thick blood, an indwelling catheter/access device in one of your veins, or have been immobile for some time. These things may increase your risk of having a blood clot after using Berinert. Also tell your doctor what drugs you are using, as some drugs, such a birth control pills or certain androgens, may increase your risk of developing a blood clot.

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
- Tell your doctor or pharmacist if you are taking, have recently taken or might take any other 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.

Driving and using machines
Berinert does not affect your ability to drive and use machines.

Berinert contains sodium
Berinert 2000 IU contains less than 1 mmol sodium (23mg) per vial, that is to say essentially "sodium-free".
Berinert 3000 IU contains up to 29 mg sodium (main component of cooking/table salt) in each vial. This is equivalent to 1.5 % of the recommended maximum daily dietary intake of sodium for an adult.

3. How to use Berinert

Berinert is intended for self-administration by subcutaneous injection. You or your carer has to be trained on how to administer Berinert as needed.

Dosage
The recommended dose of Berinert is 60 IU/kg body weight.

Paediatric population
The recommended dose is the same as in adults.

Overdose
No case of overdose has been reported.

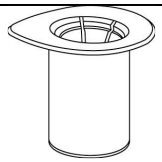
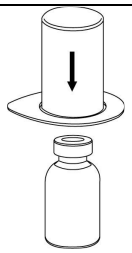
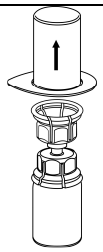
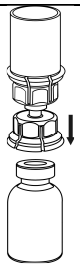
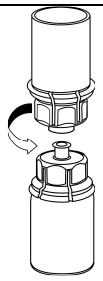
Reconstitution and method of administration
If your doctor decides that you may be suitable for home-treatment, he/she will give you detailed instructions. You will be required to keep a diary in order to document each treatment received at home and to bring it to each of your visits to the doctor. Regular review of your/your carer's injection technique will be performed to ensure continued appropriate handling.

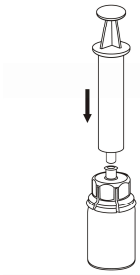
General instructions
- The powder must be dissolved and withdrawn from the vial under aseptic conditions. Use the syringe provided with the product.
- The made up solution should be colourless and clear to slightly opalescent. After filtering or withdrawal (see below) the solution should be checked by 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.

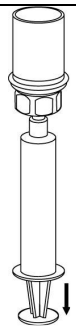
Reconstitution
Without opening either vial, warm the Berinert powder and the solvent to room temperature. This can be done either by leaving the vials at room temperature for about an hour, or by holding them in your hands for a few minutes. DO NOT expose the vials to direct heat. The vials must not 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 counterclockwise 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 by screwing clockwise. 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 by unscrewing counterclockwise.

Administration

<u>Self-administration (subcutaneous administration)</u>

Your doctor will teach you how to safely administer Berinert. Once you learn how to self-administer, follow the instructions provided below.

Berinert self-administration instructions

Step 1: Assemble supplies

Gather the Berinert syringe, the following disposable supplies and other items (sharps or other container, treatment diary or log book):

- Hypodermic needle or S.C. infusion set
- Sterile syringe (Use a silicone-free syringe)
- Alcohol wipes
- Gloves (if recommended by your healthcare provider)

Step 2: Clean surface

- Thoroughly clean a table or other flat surface using alcohol wipes.

Step 3: Wash hands

- Thoroughly wash and dry your hands.
- If you have been told to wear gloves when preparing your infusion, put the gloves on.

Step 4: Prepare injection site

- Select an area on your abdominal area (stomach) for the injection unless your doctor has told you to use another area (Figure 1).
- Use a different place from your last injection; you should rotate the places where you are injecting.
- New injection sites should be at least 2 inches (5 centimeters) away from the place where you gave yourself an injection before.
- Never give yourself an injection in areas where the skin is itchy, swollen, painful, bruised, or red.
- Avoid giving yourself injections in places where you have scars or stretch marks.
- Clean the skin at the injection site with an alcohol swab and let the skin dry (Figure 2).

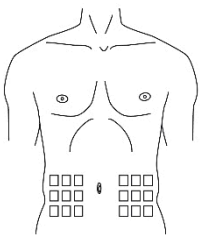


Figure 1

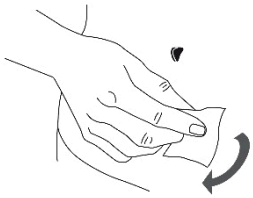


Figure 2

Step 5: Injection in the abdominal area

As instructed by your healthcare provider:

- Attach a hypodermic needle or S.C. infusion set (butterfly) to the syringe as instructed by your healthcare provider. Prime the needle or tubing as required and instructed.

Injection with Hypodermic Needle:

- Insert the needle into the fold of skin (Figure 3).

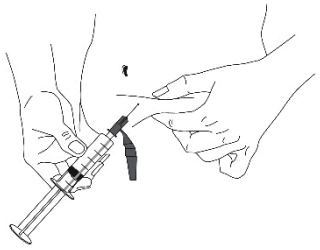


Figure 3

Injection by S.C Infusion Set:

- Insert the needle into the fold of skin (Figure 4).

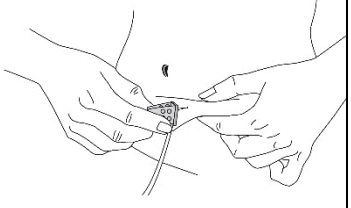


Figure 4

Step 6: Clean up • After injecting the entire amount of Berinert, remove the needle. • Discard any unused solution and all administration equipment in an appropriate manner as per local requirements.	
Step 7: Record treatment • Record the lot number from the Berinert vial label in your treatment diary or log book with the date and time of infusion every time you use Berinert**.**	

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 very commonly (may affect more than 1 in 10 people):
- Reactions at the site where the injection was given (bruising, coldness, discharge, erythema, haematoma, haemorrhage, induration, oedema, pain, pruritus, rash, scar, swelling, urticaria, warmth).
- Nasopharyngitis (runny or stuffy nose, sneezing, watery eyes).

The following side effects have been observed commonly (may affect up to 1 in 10 people):
- Hypersensitive or allergic reactions (such as hypersensitivity, pruritus, rash and urticaria).
- Dizziness

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 on the safety of this medicine.

Ireland:
HPRA Pharmacovigilance
Website: www.hpra.ie

5. How to store Berinert

- 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 after EXP.
- 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 (2000 or 3000 IU/vial; after reconstitution with 4 or 5.6 ml of water for injections respectively 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
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.

Presentations

Box containing:
1 vial with powder
1 vial with 5.6 ml water for injections
1 filter transfer device 20/20

Administration set (inner box):
1 disposable 10 ml syringe
1 hypodermic needle
1 subcutaneous injection set (butterfly)
2 alcohol swabs
1 plaster

Multipack for 5 x 3000 IU, including a box with 5 administration sets.
Multipack for 20 x 3000 IU, including 4 boxes with 5 administration sets.

Not all pack sizes may be marketed.

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:

Ireland
CSL Behring GmbH
Tel: +49 6190 75 84700

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

Berinert 3000 I.E. Pulver und Lösungsmittel zur Herstellung einer Injektionslösung	Austria
Berinert 3000 IE, poeder en oplosmiddel voor oplossing voor injectie	Belgium, Netherlands
Berinert 3000	Cyprus, Germany, Greece, Poland, Portugal
Беринерт 3000, Прах и разтворител за инжекционен разтвор С1- естеразен инхибитор, човешки	Bulgaria
Berinert 3000 IU	Czech Republic, Slovakia
Berinert 3000 IU prašak i otapalo za otopinu za injekciju	Croatia
Berinert	Denmark, Italy
Berinert SC	Estonia
Berinert 3000 IU, injektiokuiva-aine ja liuotin, liuosta varten	Finland
Berinert 3000 UI, poudre et solvant pour solution injectable	France, Luxembourg
Berinert 3000 NE por és oldószer oldatos injekcióhoz	Hungary
Berinert 3000 a.e. stungulyfsstofn og leysir, lausn	Iceland
Human C1-esterase inhibitor CSL Behring 3000 TV milteliai ir tirpiklis injekciniam tirpalui	Lithuania
Berinert 3000 IU pulver og væske til injeksjonsvæske, oppløsning	Norway
Berinert 3000 3000 UI, pulbere şi solvent pentru soluţie injectabilă	Romania
Berinert 3000 i.e. prašek in vehikel za raztopino za injiciranje	Slovenia
Berinert 3000 UI polvo y disolvente	

para solución inyectable subcutánea _____Spain
Berinert 3000 IE, pulver och vätska till
injektionsvätska, lösning _____Sweden
Berinert 3000 IU Powder and solvent
for solution for injection_____UK, Malta, Ireland

This leaflet was last revised in December 2024

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 is related to the current WHO Standard for C1-esterase inhibitor products.