**PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) - 1986**

This medicine can be sold with a physician's prescription only

**Berinert is usually injected into a vein (intravenously) by the physician or nurse. You or your carer might also administer Berinert as an injection but only after receiving adequate training. If your physician decides that you are suitable for home-treatment, detailed instructions will be given to you. 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 physician. Regular review of your or your carer's injection technique will be performed to ensure continued appropriate handling.**

# Berinert®

## Powder and Solvent for Solution for Injection / Infusion

## 500 IU

The active ingredient and its quantity:
The vial with the powder contains:
C1 - Esterase Inhibitor Human 500 IU

For list of excipients, please see section 6.

**Read this entire leaflet carefully before you use this medicine.** This leaflet contains concise information about the medicine. If you have any further questions, ask your physician or pharmacist.
This medicine has been prescribed for the treatment of your illness. Do not pass it on to others. It may harm them, even if you think that their illness is the same as yours.

## 1. What is the medicine used for?

- Hereditary angioedema type I and II (HAE)
- Treatment and pre-procedure (prior to oral, dental, and upper respiratory tract procedures) prevention of acute episodes.

Hereditary Angioedema is a congenital, non-allergic disease of the vascular system.
Hereditary Angioedema is caused by deficiency, absence or defective synthesis of C1-esterase inhibitor which is an important protein.
The illness is characterized 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 breathing difficulties
- tongue swelling
- colic pain in abdominal region.

Generally, all parts of the body can be affected.

**Therapeutic group:** C1 enzyme inhibitor, medicines used in Hereditary Angioedema.

## 2. Before using the medicine

| **X Do not use the medicine if:** |
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| You are hypersensitive (allergic) to the active ingredient (Human C1 - Esterase Inhibitor) or to any of the other ingredients this medicine contains (listed in section 6). |

### ! Special warnings regarding the use of this medicine

➢ **Before taking Berinert tell your physician:**

- If you have experienced allergic reactions to Berinert in the past. Antihistamines and corticosteroids should be prophylactically taken if advised by your physician.
- If allergic or anaphylactic-type reactions occur (a serious allergic reaction that causes severe breathing difficulty 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 if required.
- Caution should be taken during unlicensed use beyond the approved indications and dosages (e.g. Capillary Leak Syndrome). See section 4 “Side Effects”.

Your physician 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.
- testing of each blood and plasma donation for signs of virus/infection.

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 viruses such as human immunodeficiency virus (HIV), hepatitis B virus, hepatitis C virus, hepatitis A virus and parvovirus B19.

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

It is strongly recommended to record the following details every time that Berinert is given: the date of administration, batch number and the injected volume.

### Tell your physician or pharmacist if you are taking or have recently taken any other medicines, including non-prescription drugs and nutrition supplements.

- Berinert should not be mixed with other medicines or diluents in the syringe.

### Pregnancy and Breastfeeding

Berinert will be used during pregnancy and breast-feeding only if it is clearly needed.
If you are pregnant, think you may be pregnant, planning to become pregnant or breast-feeding, consult your physician or pharmacist before taking this medicine.

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

### Important information about some of the ingredients of this medicine
Berinert contains up to 486 mg of sodium (approximately 21 mmol) per 100 ml solution. Please take this into account if you are on a low sodium diet.

## 3. How to use this medicine

- Always use according to your physician's instructions. Check with your physician or pharmacist if you are not sure. Treatment should be initiated and supervised only by a physician who is experienced in the treatment of C1-esterase inhibitor deficiency.

**The dosage and administration will be determined by the physician only.**
**Do not exceed the recommended dose.**

**Reconstitution and Method of Administration**
Berinert is usually injected into a vein (intravenously) by the physician or nurse. You or your carer might also administer Berinert as an injection but only after receiving adequate training. If your physician decides that you are suitable for home-treatment, detailed instructions will be given to you. 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 physician. Regular review of your or 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 prepared solution should be colorless and clear. After filtering or withdrawal (see below) and prior to administration, the solution should be checked by eye for small particles or discoloration.
- Do not use the solution if it is visibly cloudy or if it contains particles.
- Any unused product or waste material should be disposed of as instructed by your physician or nurse.

**Reconstitution**
Without opening the vials, 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 the vials 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 using the administration set (Mix2Vial) attached. Please follow the instructions given below.

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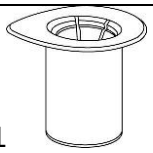
|  1 | 1. Open the Mix2Vial package by peeling off the lid**. Do not** remove the Mix2Vial from the blister package! |

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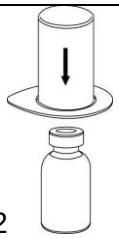
|---|---|
|  2 | 2. Place the solvent vial on an even, clean surface and hold the vial tightly. Take the Mix2Vial together with the blister package and push the spike of the blue adapter end **straight down** through the solvent vial stopper. |
|  3 | 3. Carefully remove the blister package from the 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 carefully, counter clockwise, unscrew the set 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. |

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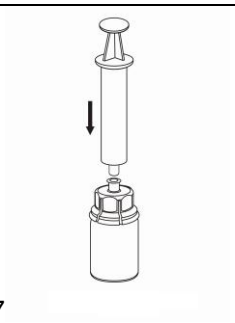
|  7 | 7. Draw air into an empty, sterile syringe. Use the syringe provided with the product. While the product vial is upright, connect the syringe to the Mix2Vial's Luer Lock fitting by screwing clockwise. Inject air into the product vial. |

**Withdrawal and application**

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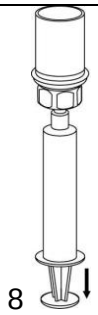
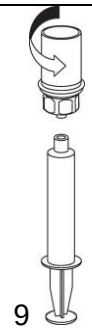
|  8 | 8. While keeping the syringe plunger pressed, turn the system upside down and draw the solution into the syringe by pulling the plunger back slowly. |
|  9 | 9. Now that the solution has been transferred into the syringe, firmly hold on to the barrel of the syringe (keeping the syringe plunger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

**Administration**
Berinert is to be administered by slow intravenous injection or infusion (4 ml/minute).

## If you have accidentally taken a higher dosage

If you have taken an overdose or if a child has accidentally swallowed the medicine, proceed immediately to a physician or a hospital emergency room and bring the package of the medicine with you.

Continue with the treatment as recommended by your physician.
Even if there is an improvement in your health, do not stop taking this medicine without consulting your physician.

- Do not take medicines in the dark! Check the label and the dose each time you take your medicine. Wear glasses if you need them.

If you have any further questions regarding the use of this medicine, consult your physician or pharmacist.

## 4. Side Effects

Like all medicines, Berinert may cause side effects in some users, although not everybody gets them. Do not be alarmed while reading the list of side effects, you may not suffer from any of them.

**Undesired reactions with Berinert are rare.**

**Rare side effects:** (effects that appear in up to 1 in 1,000 users)

- 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 surgery under extra-corporal circulation. See section 2 "Special warnings regarding the use of this medicine".
- Increase in body temperature as well as burning and stinging where the injection was given.
- Hypersensitive or allergic reactions (such as irregular heartbeat, fast heartbeat, fall or rise in blood pressure, reddening of the skin, rash, breathing difficulty, headache, dizziness, nausea).

**Very rare side effects:** (effects that appear in up to 1 in 10,000 users)

- hypersensitive reactions might progress as far as shock.

**Refer to your physician immediately if any of the side effects appears or if you experience side effects not mentioned in this leaflet.**

**Reporting of side effects**

Side effects can be reported to the Ministry of Health by clicking on the link "Reporting Side Effects Of Drug Treatment" that appears on the homepage of the Ministry of Health's website (www.health.gov.il) which links to an online form for reporting side effects, or by the following link:
https://sideeffects.health.gov.il
In addition, you can report by emailing the Registration Holder's Patient Safety Unit at:
drugsafety@neopharmgroup.com

## 5. How to Store the Medicine

- Avoid poisoning! This medicine and all other medicines must be stored in a safe place out of the reach and sight of children and/or infants to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by your physician.
- Do not use the medicine after the expiry date (exp. date) stated on the package. The expiry date refers to the last day of that month.
- Do not store at temperature above 30°C.
- Do not freeze.
- Store the product vial in the outer packaging to protect from light.

- This medicine does not contain a preservative and therefore the prepared solution should preferably be used immediately.
- If the prepared solution is not administered immediately, it must be stored only in the **vial** at a temperature below +30°C and used within 8 hours.
- Medicines should not be disposed of via household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

## 6. Additional Information

**In addition to the active ingredient, this medicine also contains:**
*Powder vial:* Glycine, Sodium chloride, Sodium citrate
*Solvent vial:* Water for injections

**What the medicine looks like and content of the package**
Berinert is presented as a white powder and is supplied with water for injections as solvent.
The made up Berinert 500 solution should be colourless and clear.

**Presentation**

Box with 500 IU contains:
1 vial with powder (500 IU)
1 vial with 10 ml water for injections
1 filter transfer device 20/20 (Mix2Vial)

Administration set (inner box):
1 disposable 10 ml syringe
1 venipuncture set
2 alcohol swabs
1 plaster

**Registration Holder and address:**
Genmedix, 12 Beit HaRishonim St., Emek–Hefer 3877701.

**Manufacturer and address:**
CSL Behring GmbH
Emil-von-Behring-Strasse 76
35041 Marburg
Germany.

**Drug registration number at the national medicines registry of the Ministry of Health:** 145 06 33056

This leaflet was checked and approved by the Ministry of Health in 04/2016.