Package leaflet: Information for the user

Respreeza® 1,000 mg powder and solvent for solution for infusion
Respreeza® 4,000 mg powder and solvent for solution for infusion
Respreeza® 5,000 mg powder and solvent for solution for infusion

Human alpha$_1$-proteinase 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 healthcare professional.
- 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 healthcare professional. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Respreeza is and what it is used for

What Respreeza is

This medicine contains the active substance human alpha$_1$-proteinase inhibitor, which is a normal component of the blood and is found in the lung. There, its main function is to protect the lung tissue by limiting the action of a certain enzyme, called neutrophil elastase. Neutrophil elastase can cause damage if its action is not controlled (for example, in case you have an alpha$_1$-proteinase inhibitor deficiency).

What Respreeza is used for

This medicine is used in adults with known severe alpha$_1$-proteinase inhibitor deficiency (an inherited condition also called alpha$_1$ antitrypsin deficiency) who have developed a lung condition called emphysema.

Emphysema develops when the lack of alpha$_1$-proteinase inhibitor results in a condition in which neutrophil elastase is not being properly controlled, damaging the tiny air sacs in the lungs through which oxygen passes into the body. Because of this damage, the lungs do not work properly.

Using this medicine regularly increases the blood and lung levels of alpha$_1$-proteinase inhibitor thus slowing the progression of emphysema.

2. What you need to know before you use Respreeza

Do NOT take Respreeza

- if you are allergic to human alpha$_1$-proteinase inhibitor or any of the other ingredients of this medicine (listed in section 6).
- if you have been found to have a deficiency of certain blood proteins called immunoglobulin type A (IgA) and have developed antibodies against them.

Warnings and precautions

➔ Talk to your doctor or healthcare professional before using Respreeza.

Information on allergic reactions: when slowing or stopping the infusion may be required?
You may be allergic to human alpha$_1$-proteinase inhibitor even if you have previously received human alpha$_1$-proteinase inhibitors and had tolerated them well. In some cases, severe allergic reactions may occur. Your doctor will inform you about signs of allergic reactions (for example chills, flushing, faster heartbeat, fall in blood pressure, light-headedness, rash, hives, itching, difficulty in breathing or swallowing as well as swelling of your hands, face, or mouth) (see also section 4).

➔ Tell your doctor or healthcare professional **immediately** if you notice such reactions during the infusion of this medicine. Depending on the nature and severity of the reaction, your doctor may decide whether to slow or stop the infusion completely and start the appropriate treatment.

➔ In case of self-administration / home-treatment, stop the infusion **immediately** and contact your doctor or healthcare professional.

Information on safety with respect to infections
Respreeza is made from human blood plasma (this is the liquid part of the blood with the blood cells removed).
Because blood can carry infections, when medicines are made from human blood or plasma certain measures are put in place to prevent these from being present in the medicine and passed on to patients. These include:

- careful selection of blood and plasma donors to make sure those at risk of carrying infections are excluded,
- the testing of samples of donated blood and plasma to try to avoid use of material with signs of virus/infections,
- the inclusion of steps in the processing of the blood or plasma that can inactivate or remove viruses.

The measures taken are considered effective for viruses such as human immunodeficiency virus (HIV), hepatitis A virus, hepatitis B virus, hepatitis C virus, and parvovirus B19 virus.

However, 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.

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

➔ It is strongly recommended that every time you receive a dose of Respreeza the name and batch number of the product are recorded in order to maintain a record of the batches used.

Smoking
Since tobacco smoke is an important risk factor for the development and progression of emphysema, you are strongly advised to stop smoking and avoid passive smoking.

Children and adolescents

This medicine is not for use in children or adolescents below 18 years of age.

Other medicines and Respreeza

➔ Tell your doctor or healthcare professional if you are taking, have recently taken or might take any other medicines.

Pregnancy, breast-feeding and fertility

➔ If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or healthcare professional for advice before taking this medicine.

Since alpha$_1$-proteinase inhibitor is a normal component of human blood, the recommended dose of this medicine is not expected to cause harm to the developing foetus. However, as there is no information available regarding the safety of Respreeza use during pregnancy, if you are pregnant, this medicine should only be given to you with caution.
It is unknown whether Respreeza passes into human milk. If you are breast-feeding, your doctor will discuss with you the risks and benefits of taking this medicine.
There are no data concerning the effect on fertility but as alpha$_1$-proteinase inhibitor is a normal component of human blood, no adverse effects on fertility are expected if you use Respreeza at the recommended dose.

Driving and using machines

Dizziness may occur after the administration of this medicine. If you experience dizziness, you should not drive or use machines until the dizziness has passed (see section 4).

Respreeza contains sodium

This medicinal product contains approximately 37 mg sodium per 1,000 mg Respreeza vial, 149 mg sodium per 4,000 mg Respreeza vial and 186 mg sodium per 5,000 mg Respreeza vial, equivalent to 1.9%, 7.4% and 9.3% respectively, of the WHO recommended maximum daily intake of 2 g sodium for an adult. Your doctor or healthcare professional will take that into consideration if you are on a controlled sodium diet.

3. How to use Respreeza

After reconstitution, Respreeza is given by infusion into a vein. A healthcare professional experienced in the treatment of alpha$_1$-proteinase inhibitor deficiency will supervise the first infusions.

Home treatment / Self-administration

After the first infusions, you or your caregiver might also administer Respreeza, but only after receiving adequate training. If your doctor decides that you are suitable for such home-treatment / self-administration, he or she will instruct you in:

- how to prepare and give this medicine (see the illustrated instructions at the end of this leaflet in "Information for health-care professionals and for patients suitable for home-treatment / self-administration"),
- how to keep the product sterile (aseptic infusion techniques),
- how to keep a treatment diary,
- how to identify side effects, including signs of allergic reactions, and measures to be taken in case such effects occur (see also section 2 and section 4).

Your doctor or your healthcare professional will regularly review your / your caregiver's infusion technique to ensure continued appropriate handling.

Dose

The amount of Respreeza you are given is based on your body weight. The recommended dose is 60 mg per kg of body weight and should be administered once per week. The infusion solution is normally given over about 15 minutes (about 0.08 ml of solution per kg body weight each min). Your doctor will determine the appropriate infusion rate for you by taking into account your weight and your tolerability to infusion.

If you use more Respreeza than you should

Consequences of an overdose are unknown.

➔ Tell your doctor or healthcare professional if you think you have used more Respreeza as you should. He or she will take the appropriate measures.

If you forget to use Respreeza

➔ Proceed with your next dose immediately and continue at regular intervals as advised by your doctor or healthcare professional.

➔ Do not take a double dose to make up for a forgotten dose.

If you stop using Respreeza

➔ Do no stop using this medicine without consulting your doctor or healthcare professional. If treatment with Respreeza is stopped, your condition may worsen.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. Such side effects may occur even if you previously received human alpha$_1$-proteinase inhibitors and had tolerated them well.

Some side effects may be serious:

Uncommonly (may affect up to 1 in 100 people), allergic reactions have been observed. They may progress in some very rare cases (may affect up to 1 in 10,000 people) to severe allergic reactions even when you have shown no signs of allergy on previous infusions.

➔ Tell your doctor or healthcare professional **immediately** if you notice any sign of allergic reactions (for example chills, flushing, faster heartbeat, fall in blood pressure, light-headedness, rash, hives, itching, difficulty in breathing or swallowing as well as swelling of your hands, face, or mouth) during the administration of Respreeza. Depending on the nature and severity of the reaction, your doctor or healthcare professional may decide whether to slow or stop the administration completely and give appropriate treatment for the reaction.

In case of self-administration / home-treatment, stop the infusion **immediately** and contact your doctor or healthcare professional.

The other side effects may include:

Commonly (may affect up to 1 in 10 people)
Dizziness, headache, shortness of breath (dyspnoea), nausea.

Uncommonly (may affect up to 1 in 100 people)
Altered sense of touch like burning, tingling or feeling of numbness in your hands, arms, legs, or feet (paraesthesia), flushing, hives (urticaria), scaly rash and rash all over the body, physical weakness (asthenia), infusion-site reactions (such as burning, stinging, pain, swelling or redness at the infusion site (haematoma)).

Very rarely (may affect up to 1 in 10,000 people)
Decreased sense of touch like burning, tingling or feeling of numbness in your hands, arms, legs, or feet (hypoaesthesia), excessive sweating (hyperhidrosis), itching, chest pain, chills, fever (pyrexia).

Frequency not known (frequency cannot be estimated from the available data)
Pain to the lymph glands (oval-shaped masses of tissue that are distributed throughout the body and which may be palpable for example in the armpit, groin or neck), swollen face, swollen eyes and lips.

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

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

5. How to store Respreeza

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 outer carton and the vial labels after EXP. The expiry date refers to the last day of that month.
Do not store above 25 °C. Do not freeze.
After reconstitution, the solution should be used immediately. If this is not possible, solutions can be stored up to 3 hours at room temperature (up to 25°C). Do not freeze the reconstituted solution.

6. Contents of the pack and other information

What Respreeza contains

The **active substance** is human alpha$_1$-proteinase inhibitor. One vial contains approximately 1,000 mg, 4,000 mg or 5,000 mg of human alpha$_1$-proteinase inhibitor.

The **other ingredients** are sodium chloride, sodium dihydrogen phosphate monohydrate and mannitol (see section 2).
Solvent: Water for injections.

What Respreeza looks like and contents of the pack

This medicine is a white to off-white powder.
After it has been reconstituted with water for injections, the solution should be clear, colourless to slightly yellow and free from visible particles.

Presentations

One pack contains:

Respreeza 1,000 mg powder and solvent for solution for infusion:
- 1 single-use powder vial
- 1 solvent vial of 20 ml water for injections
- 1 transfer set 20/20 (Mix2Vial set) for reconstitution

Respreeza 4,000 mg powder and solvent for solution for infusion:
- 1 single-use powder vial
- 1 solvent vial of 76 ml water for injections
- 1 transfer set 20/20 (Mix2Vial set) for reconstitution

Administration set (inner box):
- 1 IV infusion set
- 1 butterfly set
- 3 alcohol swabs

Respreeza 5,000 mg powder and solvent for solution for infusion:
- 1 single-use powder vial
- 1 solvent vial of 95 ml water for injections
- 1 transfer set 20/20 (Mix2Vial set) for reconstitution

Administration set (inner box):
- 1 IV infusion set
- 1 butterfly set
- 3 alcohol swabs

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

CSL Behring GmbH
Emil-von-Behring-Strasse 76
D-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 1444 447405

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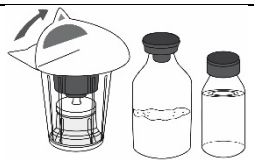
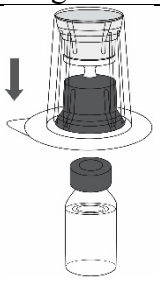
The following information is intended for healthcare professionals and for patients suitable for home-treatment / self-administration

General instructions

- The reconstitution should be performed according to the instructions provided below.
- The product must be reconstituted, administered and handled with caution using aseptic technique to maintain product sterility.
- Do not use provided sterile ancillaries for reconstitution and administration if their package is opened or if they are damaged.
- The powder must be reconstituted with solvent (water for injections).
- Total reconstitution of the powder should be obtained within 5 minutes (1,000 mg presentation) or 10 minutes (4,000 mg and 5,000 mg presentation).
- Inspect the reconstituted solution for particulate matter and discoloration prior to administration.
- The reconstituted solution should be clear, colourless to slightly yellow, and free from visible particles.

Follow the steps provided below for the preparation and reconstitution of Respreeza:

1. Ensure that the Respreeza vial and water for injections vial are at room temperature (up to 25°C).	
2. Remove the plastic flip-off cap from the water for injections vial.	
3. Wipe the rubber stopper of the **water for injections** vial with an antiseptic like an alcohol swab and allow it to dry.	
4. Open the Mix2Vial® set by peeling off the lid (Figure 1). Do not remove the Mix2Vial set from the blister package.	 Figure 1
5. Place the **water for injections** vial on an even, clean surface and hold the vial tight. Take the Mix2Vial set together with the blister package and vertically pierce the **water for injections** vial with the **blue** tip of the Mix2Vial set (Figure 2).	 Figure 2

6. 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 (Figure 3).

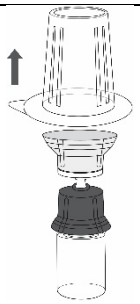


Figure 3

7. Remove the plastic flip-off cap from the **Respreeza** vial.

8. Wipe the rubber stopper of the **Respreeza** vial with an antiseptic like an alcohol swab and allow it to dry.

9. Place the **Respreeza** vial on an even and firm surface.
Invert the water for injections vial with the Mix2Vial set attached and vertically pierce the **Respreeza** vial with the **clear** tip of the Mix2Vial set (Figure 4).
The water for injections will automatically flow into the Respreeza vial.

NOTE: Ensure all water has transferred into the Respreeza vial.

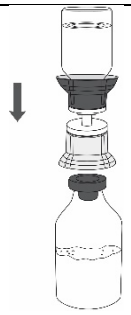


Figure 4

10. Follow steps below to remove entire Mix2Vial set from Respreeza vial:

- With one hand tightly grasp the Respreeza vial as shown in Figure 5.
- With the other hand tightly grasp the water for injections vial and the blue part of the Mix2Vial set.
- Bend **the entire Mix2Vial set** to the side until it disconnects from the Respreeza vial (Figure 5).

Discard the water for injections vial with the entire Mix2Vial set.

Figure 5

11. Gently swirl the Respreeza vial until the powder is completely dissolved (Figure 6).
DO NOT SHAKE.
Take care not to touch the rubber vial stopper.

Figure 6

12. Inspect visually the reconstituted solution. The solution should be clear, colourless to slightly yellow, and free from visible particles. Do not use solutions that are discoloured, cloudy or have particles.

13. If more than 1 vial of Respreeza is needed to achieve the required dose, repeat instructions 1 to 12 above using an additional package containing an unused Mix2Vial set. **Use a separate, unused Mix2Vial set and a water for injections vial for each Respreeza vial.**
14. The reconstituted solutions can be sequentially administered directly from the vial, or the reconstituted solutions can alternatively be transferred into an infusion container (e.g. empty intravenous bag or glass bottle (not supplied)) via a commercially available intravenous fluid tubing transfer set (not supplied) prior to administration. Use aseptic technique to transfer the reconstituted solution into an infusion container.

Administration

The reconstituted solution must be administered using an IV infusion set (supplied with the 4,000 and 5,000 package).

1. Make sure that the air vent and the roller clamp of the IV infusion set are closed. VERTICALLY pierce the Respreeza vial with the IV infusion set spike while twisting the IV infusion set spike gently or connect it to an infusion container.
2. Elevate the Respreeza vial/infusion container or hang on an infusion stand.
3. Prime the drip chamber by squeezing it until the Respreeza solution has filled the chamber roughly half-way.
4. Open the air vent cap of the IV infusion set.
5. Slowly open the roller clamp of the IV infusion set and let the Respreeza solution flow until it reaches the end of the tubing with no air bubbles.
6. Close the roller clamp.
7. Disinfect the injection site with an antiseptic like an alcohol swab before carefully inserting the needle into the vein. Make sure that there is no air in the butterfly tube left.
8. Connect the end of the IV infusion set to the butterfly set and open the roller clamp again.
9. Infuse the reconstituted solution into the vein. The solution should be infused at an infusion rate of about 0.08 ml per kg body weight each min, as determined by your response and your comfort. The recommended dose of 60 mg per kg of body weight will take approximately 15 minutes to infuse.

One vial of Respreeza is for single use only.

Any unused medicinal product or waste material should be disposed as instructed by your doctor or healthcare professional.