CSL Behring

PACKAGE LEAFLET: INFORMATION FOR THE USER

Hizentra 200 mg/ml solution for subcutaneous injection

Human normal immunoglobulin
(SCIg = **S**ub**c**utaneous **I**mmuno**g**lobulin)

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 healthcare professional. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. WHAT HIZENTRA IS AND WHAT IT IS USED FOR

What Hizentra is
Hizentra belongs to the class of medicines called human normal immunoglobulins. Immunoglobulins are also known as antibodies and are blood proteins that help your body to fight infections.

How Hizentra works
Hizentra contains immunoglobulins that have been prepared from the blood of healthy people. Immunoglobulins are produced by human body's immune system. They help your body to fight infections caused by bacteria and viruses and maintain the balance in your immune system (referred to as immunomodulation). The medicine works in exactly the same way as the immunoglobulins naturally present in your blood.

What Hizentra is used for
Replacement therapy
Hizentra is used to raise abnormally low immunoglobulin levels in your blood to normal levels (replacement therapy). The medicine is used in adults and children (0–18 years) in the following situations:

1. Treatment of patients who are born with a reduced ability or inability to produce immunoglobulins (primary immunodeficiencies). This includes conditions such as:
   - low immunoglobulin levels (hypogammaglobulinaemia) or absence of immunoglobulins (agammaglobulinaemia) in the blood
   - combination of low immunoglobulin levels, frequent infections and inability to produce adequate amounts of antibodies after vaccination (common variable immunodeficiency)
   - combination of low level or absence of immunoglobulins and absence or non-functional immune cells (severe combined immunodeficiency)
   - lack of certain immunoglobulin G subclasses causing recurrent infections.

2. Treatment of patients with low or dysfunctional immunoglobulin levels in acquired conditions (secondary immunodeficiency) who experience severe or recurrent infections due to a weakened immune system resulting from other conditions or treatments.

Immunomodulatory therapy in CIDP patients
Hizentra is also used in patients with chronic inflammatory demyelinating polyneuropathy (CIDP), a form of autoimmune disease. CIDP is characterised by chronic inflammation of the peripheral nerves that causes muscle weakness and/or numbness mainly in the legs and arms. It is believed that the body's defence attack underlines such inflammation, and the immunoglobulins present in Hizentra help to protect the nerves from being attacked (immunomodulatory therapy).

2. WHAT YOU NEED TO KNOW BEFORE YOU USE HIZENTRA

Do **NOT** infuse Hizentra:
- ▶ if you are allergic to human immunoglobulins, polysorbate 80 or L-proline.
  - ☛ Tell your doctor or healthcare professional prior to treatment if you have experienced an intolerance against one of these components earlier.
- ▶ if you suffer from hyperprolinaemia (a genetic disorder causing high levels of the amino acid proline in the blood).
- ▶ into a blood vessel.

Warnings and precautions
☛ Talk to your doctor or healthcare professional before using Hizentra.

You may be allergic (hypersensitive) to immunoglobulins without knowing it. However, true allergic reactions are rare. They may occur even if you received human immunoglobulins previously and tolerated them well. It may happen particularly if you do not have enough of the immunoglobulin type A (IgA) in your blood (IgA deficiency).
☛ Tell your doctor or healthcare professional prior to treatment if you have an immunoglobulin type A (IgA) deficiency. Hizentra contains residual amounts of IgA which might cause an allergic reaction.
In these rare cases allergic reactions such as a sudden fall in blood pressure or shock may occur (see also section 4 "Possible side effects").
☛ If you notice such signs during the infusion of Hizentra, stop the infusion and contact your doctor or go to the nearest hospital immediately.
☛ Tell your doctor if you have a history of heart or blood vessel disease or blood clots, have thick blood, or have been immobile for some time. These things may increase your risk of having a blood clot after using Hizentra. Also tell your doctor what drugs you are using, as some drugs, such as those that contain the hormone oestrogen (for example, birth control pills), may increase your risk of developing a blood clot. Contact your doctor immediately if you experience signs and symptoms such as shortness of breath, chest pain, pain and swelling of a limb, weakness or numbness on one side of the body after receiving Hizentra.
☛ Contact your doctor if you experience the following signs and symptoms: severe headache, neck stiffness, drowsiness, fever, photophobia, nausea, and vomiting after receiving Hizentra. Your doctor will decide if further tests are necessary and whether Hizentra should be continued.

Your healthcare professional will avoid potential complications by ensuring:
- ▶ that you are not sensitive to human normal immunoglobulin. The medicine must be infused slowly at first. The recommended infusion rate given under section 3 "How to use Hizentra" must be closely followed.
- ▶ that you are carefully monitored for any symptoms throughout the infusion period, especially if:
  - you receive human normal immunoglobulin for the first time
  - you have switched from a different medicine
  - there has been a long interval (more than eight weeks) since the previous infusion.

  In these cases, it is recommended that you are monitored during the first infusion and for an hour afterwards. If the points above do not apply for you it is recommended that you are observed for at least 20 minutes after administration.

Other medicines and Hizentra
☛ Tell your doctor or healthcare professional if you are using, have recently used or might use any other medicines.
☛ You must not mix other medicines with Hizentra.
☛ Tell your vaccinating doctor prior to a vaccination about your treatment with Hizentra.
Hizentra may impair the effect of some live virus vaccines such as measles, rubella, mumps and chicken pox. Therefore, after receiving this medicine you may have to wait up to 3 months before receiving your live-attenuated vaccine. In the case of measles vaccinations the impairment may persist for up to 1 year.

Pregnancy, breast-feeding and fertility
☛ Tell your doctor or healthcare professional if you are pregnant, plan to become pregnant or are breast-feeding. Your doctor will decide whether you can receive Hizentra during your pregnancy or while you are breast-feeding.

No clinical studies have been performed with Hizentra in pregnant women. However, medicines that contain immunoglobulins have been used in pregnant or breast-feeding women for years, and no harmful effects on the course of pregnancy or on the baby have been observed.

If you are breast-feeding and receive Hizentra, the immunoglobulins of the medicine can also be found in the breast milk. Therefore, your baby may be protected from certain infections.

Driving and using machines
Patients may experience effects, such as dizziness or nausea, during treatment with Hizentra that might affect the ability to drive and use machines. If this happens, you should not drive or use machines until these effects have disappeared.

Hizentra contains proline
You must not take it if you suffer from hyperprolinaemia (see also section 2 "What you need to know before you use Hizentra"). Please tell your doctor prior to treatment.

Other important information about Hizentra
Blood tests
After receiving Hizentra, the results of certain blood tests (serological tests) may be impaired for a certain time.
☛ Tell your doctor about your treatment with Hizentra prior to any blood test.

Information on what Hizentra is made of
Hizentra is made from human blood plasma (this is the liquid part of the blood). 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 medicines 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 (liver inflammation), and for the non-enveloped hepatitis A virus and parvovirus B19.

☛ It is strongly recommended that every time you receive a dose of Hizentra the name and batch number of the product are recorded in order to maintain a record of the batches used (see section 3 "How to use Hizentra").

Hizentra contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per vial/syringe, that is to say essentially 'sodium-free'.

3. HOW TO USE HIZENTRA

Always use this medicine exactly as your doctor has told you. Check with your doctor if you are not sure.

Dosage
Your doctor will calculate the correct dose for you taking into account your weight and response to treatment.
The dose or dosing interval should not be changed without consulting your doctor.
If you think you should receive Hizentra more or less frequently, please speak to your doctor.
If you think you have missed a dose, speak to your doctor as soon as possible.

Replacement therapy
Your doctor will determine whether you need a loading dose (for adults and children) of at least 1 to 2.5 ml/kg of body weight divided over several days. Following this, maintenance doses may be given at repeated intervals, from daily to once every two weeks, to reach a cumulative monthly dose of about 2 to 4 ml/kg of body weight. Your healthcare professional may adjust the dose based on your response to the treatment.

Immunomodulatory therapy
Your doctor will initiate therapy with Hizentra 1 week after your last intravenous immunoglobulin infusion by administrating under the skin (subcutaneously) with a weekly dose of 1.0 to 2.0 ml/kg of body weight. Your doctor will determine your weekly Hizentra dose. The weekly maintenance doses may be divided into smaller doses and administered as often as required during the week. For dosing every two weeks, your doctor will double the weekly Hizentra dose. Your healthcare professional may adjust the dose based on your response to the treatment.

Method and route of administration
In case of home treatment, this will be initiated by a healthcare professional experienced in the treatment of immunodeficiency/CIDP with SCIg and in the guidance of patients for home treatment.

You will be instructed and trained in:
- aseptic infusion techniques
- the keeping of a treatment diary, and
- measures to be taken in case of severe side effects.

Infusion site(s)
- Administer Hizentra under the skin only.
- You may infuse Hizentra into sites such as abdomen, thigh, upper arm, and lateral hip. If large doses are given (>50 ml), try to administer them at multiple sites.
- You may use an unlimited number of sites simultaneously. Infusion sites should be at least 5 cm apart.
- In the case, you will use a device-assisted infusion technique (e.g. pump-assisted infusion), more than one infusion device can be used simultaneously.
- In the case, you will use the manual push infusion technique with a syringe, you may use only one infusion site per syringe. If you need to administer an additional Hizentra syringe, you must use a new sterile injection needle and change the infusion site.
- The volume of product infused into a particular site may vary.

Infusion rate(s)
Your doctor will determine the appropriate infusion technique and the infusion rate for you taking into account your individual dose, dosing frequency and product tolerability.

Device-assisted infusion:
The recommended initial infusion rate is up to 20 ml/hour/site. If well-tolerated, you may gradually increase the infusion rate to 35 ml/hour/site for the subsequent two infusions. Thereafter, the infusion rate can be increased further as per your tolerability.

Manual push infusion:
The recommended initial infusion rate is up to 0.5 ml/min/site (30 ml/hour/site). If well-tolerated, you may increase the infusion rate up to 2.0 ml/min/site (120 ml/hour/site) for subsequent infusions. Thereafter, the infusion rate can be increased further as per your tolerability.

Instructions for use
Follow the steps below and use aseptic technique to administer Hizentra.

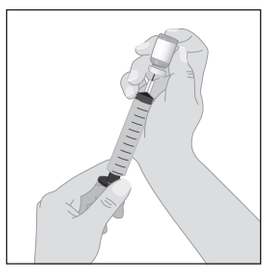
1 Clean surface
Thoroughly clean a table or other flat surface using an antiseptic wipe.

2 Assemble supplies
Place Hizentra and other supplies and equipment needed for the infusion on a clean, flat surface.

3 Thoroughly wash and dry hands

4 Check the vials
Visually inspect Hizentra for particles in the solution or discoloration as well as the expiry date before administering Hizentra. Do not use solutions that are cloudy or contain particles. Do not use solutions that have been frozen. Administer solution which is at room or body temperature. Once a vial has been opened, use the solution immediately.

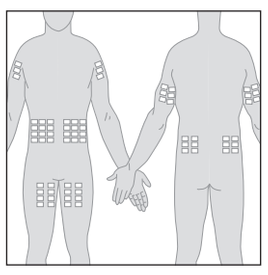
5 Preparation of Hizentra for infusion
Clean the vial stopper – Remove the protective cap from the vial to expose the central portion of the rubber stopper. Clean the stopper with an alcohol wipe or antiseptic preparation and allow it to dry.



Transfer Hizentra to syringe for infusion – Attach a transfer device or needle to a sterile syringe, using aseptic technique. If using a transfer device (vented spike), follow the instructions provided by the device manufacturer. If using a needle, pull back on the plunger to draw air into the syringe that is comparable to the amount of Hizentra to be withdrawn. Then, insert the needle into the centre of the vial stopper and, to avoid foaming, inject air into headspace of the vial (not into the liquid). Finally, withdraw the desired volume of Hizentra. When using multiple vials to achieve the desired dose, repeat this step.

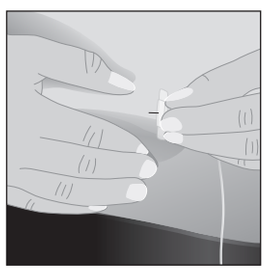
6 Prepare the tubing
Attach the administration tubing or needle set to the syringe. Prime the tubing to eliminate all remaining air.

7 Prepare infusion site(s)
Select the infusion site(s) – The number and location of infusion sites depends on the volume of the total dose. Each infusion site should be at least 5 cm apart.
You may use an unlimited number of sites simultaneously.



Clean the infusion site(s) using an antiseptic skin preparation. Allow each site to dry before proceeding.

8 Insert the needle
Grasp the skin between two fingers and insert the needle into the subcutaneous tissue.



Secure the needle to the skin – If necessary, use gauze and tape or transparent dressing to hold the needle in place.

9 Infuse Hizentra
Start infusion.
If using an infusion pump, follow the manufacturer's instructions.

10 Record the infusion
Record the following data in your treatment diary:
- the date of administration,
- the batch number of the medicine, and
- the infused volume, flow rate, the number and location of infusion sites.

11 Clean up
Discard any unused product and all used administration supplies after administration in accordance with local requirements.

If you have any further questions on the use of this medicine, please ask your doctor or healthcare professional.

If you use more Hizentra than you should
If you think you have had too much Hizentra, speak to your doctor as soon as possible.

If you forget to use Hizentra
If you think you have missed a dose, speak to your doctor as soon as possible.

4. POSSIBLE SIDE EFFECTS

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

- ▶ In isolated cases, you may be allergic (hypersensitive) to immunoglobulins and allergic reactions such as a sudden fall in blood pressure or shock may occur (e.g. you may feel light-headed, dizzy, faint on standing, cold in the hands and feet, sense an abnormal heart beat or chest pain, or have blurred vision).
- ▶ In isolated cases, you may experience pain and/or swelling of an arm or leg with warmth over the affected area, discoloration of an arm or leg, unexplained shortness of breath, chest pain or discomfort that worsens on deep breathing, unexplained rapid pulse, numbness or weakness on one side of the body, sudden confusion, or trouble speaking or understanding could be signs of a blood clot.
- ▶ In isolated cases, you may get a bad headache with nausea, vomiting, stiff neck, fever, and sensitivity to light, which could be signs of AMS (aseptic meningitis syndrome), which is a temporary reversible non-infectious inflammation of the membranes surrounding the brain and the spinal cord.

  ☛ If you notice such signs during the infusion of Hizentra, stop the infusion and go to the nearest hospital immediately.

Please see also section 2 of this leaflet about the risk of allergic reactions, blood clots and AMS.

Side effects observed in controlled clinical studies are presented in order of decreasing frequency. Side effects observed in post-marketing are of unknown frequency:

The following side effects are **very common**
(affects more than 1 patient in 10):
- Headache
- Rash
- Reactions at the infusion site

The following side effects are **common**
(affects 1 to 10 patients in 100):
- Dizziness
- Migraine
- Increased blood pressure (hypertension)

Material Number | Component Description:
REG-9534-03 LFT Hizentra 20% UK
Artwork Author: Martina Schweyer
Specification Number: n/a
Additional comments: TD-4965-01_LFT_270x600mm_35x68mm
Colours:
Black
Technical Colours (indication only – not to be printed):

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- Diarrhoea
- Abdominal pain
- Feeling sick (nausea)
- Vomiting
- Itching (pruritus)
- Hives (urticaria)
- Pain related to the musculature and bones (musculoskeletal pain)
- Joint pain (arthralgia)
- Fever
- Tiredness (fatigue), including generally feeling unwell (malaise)
- Chest pain
- Flu-like symptoms
- Pain

The following side effects are **uncommon**
(affects 1 to 10 patients in 1,000):
- Hypersensitivity
- Involuntary shaking movements in one or more parts of the body (tremor, including psychomotor hyperactivity)
- Fast heartbeat (tachycardia)
- Flushing
- Muscle spasm
- Muscular weakness
- Chills, including low body temperature
- Abnormal result of a blood test that may indicate impaired liver and kidney function

In isolated cases, infusion site ulcer or burning sensation may occur.

You may reduce possible side effects if you infuse Hizentra slowly.

Side effects such as these may occur even when you have previously received human immunoglobulins and tolerated them well.

Please also refer to section 2 "What you need to know before you use Hizentra" for additional details on circumstances which increase the risk of side effect.

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 HIZENTRA

- 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 label after EXP.
- You must use/infuse this medicine as soon as possible after opening the vial. Do not use Hizentra if the vial is open or defective.
- Do not store above 25 °C.
- Do not freeze.
- Keep the vial in the outer carton in order to protect from light.
- Do not throw away any medicines via wastewater or household waste. Ask your healthcare professional how to throw away medicines you no longer use. These measures will help protect the environment.

6. CONTENTS OF THE PACK AND OTHER INFORMATION

What Hizentra contains
- The **active substance** is human normal immunoglobulin. One ml contains 200 mg of human normal immunoglobulin, of which at least 98 % is immunoglobulin type G (IgG).
  The approximate percentage of IgG subclasses is as follows:
  IgG_1 69 %
  IgG_2 26 %
  IgG_3 3 %
  IgG_4 2 %
  This medicine contains trace amounts of IgA (not more than 50 micrograms/ml).

- The **other ingredients** (excipients) are L-proline, polysorbate 80 and water for injections.

What Hizentra looks like and contents of the pack
Hizentra is a solution for subcutaneous injection (200 mg/ml). The colour can vary from pale-yellow to light-brown.
Hizentra is available in vials of 5, 10, 20 or 50 ml.
Hizentra is also available in pre-filled syringes of 5, 10, 20 and 50 ml.

Pack sizes
Packs of 1, 10 or 20 vials
Hizentra is also available in packs of 1, 10 or 20 pre-filled syringes.

Please note that alcohol swabs, needles and other supplies or equipment are not contained in the pack.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer
CSL Behring GmbH
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For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

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This leaflet was last revised in 07/2024.