Package leaflet: Information for the patient

Xembify 200 mg/mL solution for subcutaneous injection
Human normal immunoglobulin (SCIg)

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects that you may get. See the end of section 4 for how to report side effects.

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, pharmacist or nurse.
- 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, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Xembify is and what it is used for

What Xembify is
Xembify is a solution of human immunoglobulins (antibodies, mainly immunoglobulin G) to help your body fight infections.

Xembify contains immunoglobulins that come from plasma of healthy people. Immunoglobulins help to fight infections caused by bacteria and viruses. The medicine works in exactly the same way as the immunoglobulins naturally present in human blood made by the immune system.

What Xembify is used for
You are using Xembify because you have abnormally low levels of immunoglobulins due to a medical condition called an immune deficiency. Xembify infusions increase the levels of immunoglobulin (antibodies), specifically immunoglobulin G (IgG) in your blood to normal levels.

This medicine is for adults, children and adolescents (0 - 18 years) who do not have sufficient antibodies (replacement therapy):

1. Patients with primary immunodeficiency syndromes (PID) with an inborn lack of antibodies.
2. Hypogammaglobulinaemia (a condition implying low immunoglobulin levels in your blood) and recurrent bacterial infections in patients with chronic lymphocytic leukaemia (cancer of the blood where too many white blood cells are produced), in whom prophylactic antibiotics have failed.
3. Hypogammaglobulinaemia and recurrent bacterial infections in multiple myeloma (tumour composed of cells derived from the bone marrow).
4. Hypogammaglobulinaemia in patients after stem cell transplantation (allogeneic haematopoetic stem cell transplantation, HSCT), when you are given stem cells from another person.

2. What you need to know before you use Xembify

Do not use Xembify
- if you are allergic to human normal immunoglobulin or any of the other ingredients of this medicine (listed in section 6).
- if you have had a severe allergic reaction (such as anaphylaxis) to a human immunoglobulin.
- if you have antibodies against immunoglobulin A (IgA) in your blood. This may occur if you have IgA deficiency. Since Xembify contains IgA, you might have an allergic reaction.
- by injecting it into a blood vessel (intravenously) or into a muscle (intramuscularly).

Tell your doctor, pharmacist or nurse prior to infusing Xembify if you have ever experienced any side effects from an immunoglobulin or from any of the ingredients.

Warnings and precautions
Talk to your doctor, pharmacist or nurse before using Xembify.

- Tell your doctor if you previously have a history of heart disease, blood vessel disease, a blood clot in a blood vessel (such as a stroke, heart attack, or pulmonary embolism), thick blood, diabetes mellitus, high blood pressure, a bleeding or clotting disorder, or if you have been immobile for some time. Tell your doctor if you take estrogen, typically as a contraceptive. You may have a greater risk of developing a blood clot after infusion of Xembify. Contact your doctor immediately if you experience shortness of breath; chest pains; pain and swelling of an arm or leg; or weakness or numbness on one side of your body. You may have a blood clot in a blood vessel.

- Contact your doctor if you experience severe headache, neck stiffness, drowsiness, fever, extreme sensitivity to light, nausea or vomiting. These side effects may come on hours or even within a few days after infusing Xembify. You may have aseptic meningitis syndrome.

- Xembify may cause kidney problems, including renal failure. Tell your doctor if you have reduced kidney function.

- Xembify may interfere with certain blood tests (serological tests). Always tell your doctor that you are being treated with Xembify prior to any blood test.

<u>Allergic reactions</u>

Allergic reactions are rare. However you may have an allergy to immunoglobulins without knowing it. Allergic reactions such as sudden fall in blood pressure or anaphylactic shock (a sharp fall in blood pressure with other symptoms such as swelling of the throat, breathing difficulties and skin rash) are rare but they can occasionally occur even if you had no side effects to immunoglobulins in the past. You are at increased risk of allergic reactions if you have IgA deficiency with anti-IgA antibodies. Be sure to tell your doctor if you have an IgA deficiency. Xembify contains some IgA which may increase the risk of an allergic reaction. See section 4 of this leaflet (Possible side effects) for the signs and symptoms of an allergic reaction.

<u>Risk of disease transmission</u>

Xembify is purified from human plasma obtained from healthy donors. When medicinal biological products are administered, the possibility of infectious diseases due to transmission of pathogens cannot be totally excluded. However, in the case of products prepared from human plasma, the risk of transmission of pathogens is reduced by: (1) epidemiological controls on the donor population and selection of individual donors by a medical interview; (2) screening of individual donations and plasma pools for viral infection markers; and (3) manufacturing procedures with demonstrated capacity to inactivate/remove pathogens.

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), hepatitis B virus and hepatitis C virus and for the non-enveloped hepatitis A virus. The measures taken may be of limited value against non-enveloped viruses such as parvovirus B19.

Immunoglobulins have not been associated with hepatitis A or parvovirus B19 infections, possibly because the antibodies against these infections, which are contained in the product, are protective.

It is strongly recommended that every time you receive a dose of this medicine, the name and batch number of the medicine (stated on the label and carton after lot) are recorded in order to maintain a record of the batches used.

Children and adolescents
The warnings and precautions apply to adults, children and adolescents.

Other medicines and Xembify
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

Always infuse Xembify by itself without mixing in any other medicine.

If you are going to be vaccinated, tell the doctor that you are being treated with Xembify. Xembify may interfere with some vaccines (live virus vaccines) such as measles, mumps, rubella and chicken pox. You may have to wait up to 3 months after receiving Xembify before being vaccinated. For measles vaccine, you may have to wait for up to 1 year.

These interactions apply to children, adults, and the elderly.

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 pharmacist for advice before taking this medicine.

Xembify has not been studied in pregnant women or breast-feeding women, and therefore your doctor or pharmacist will guide you. Clinical experience with immunoglobulins suggests that no harmful effects on the course of pregnancy, or on the foetus and the baby are to be expected. If you are breast-feeding, the immunoglobulins in Xembify can also be found in your breast milk. These may protect your baby from certain infections. Clinical experience with immunoglobulins suggests that no harmful effects on fertility are expected.

Driving and using machines
Your ability to drive and operate machines may be impaired by some adverse reactions, such as dizziness, associated with Xembify. If you experience adverse reactions during treatment, wait for these to resolve before driving or operating machines.

3. How to use Xembify

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

Xembify has to be infused under the skin (subcutaneous or SC administration).

Treatment with Xembify will be started by your doctor or nurse. Do not begin treatment with Xembify at home until you have received complete instructions.

Dose
The recommended dose and dosing schedule are established by your doctor. Your doctor will calculate the correct dose for you based on your body weight, any previous treatment you may have received and your response to treatment. Always use this medicine exactly as described in this leaflet or as your doctor, pharmacist or nurse has told you. Check with them if you are not sure.

Your first dose may be what is called a "loading dose" which is meant to rapidly increase the immunoglobulin levels in your blood. Your doctor will determine whether you need a "loading dose" (for adults or children) of at least 1 to 2.5 mL/kg of body weight. You may receive this loading dose divided over several days.

You will be given Xembify on a regular basis from daily to once every 2 weeks; the cumulative dose per month will be about 1.5 to 5 mL/kg of body weight. Your doctor may adjust your dose depending on your response to treatment.

Do not change this dose or the time interval to the next dose without talking to your doctor first.

If you think you should receive a different dose or you want to modify your dosing schedule, talk to your doctor first. Contact your doctor if you miss a dose.

You will need to have routine blood tests to measure the level of immunoglobulin in your blood. Discuss the schedule with your doctor.

There is no difference in the dose for adults, including the elderly (65 years of age and older), as for children and infants, since the amount of Xembify infused is based on body weight.

Method of administration
You will receive Xembify by a slow infusion under the skin into fatty tissue (a subcutaneous infusion). Xembify will be delivered using a pump or injector. Subcutaneous infusion for home treatment must be initiated and monitored by a healthcare professional experienced in guiding patients for home treatment.

You (or your caregiver) must be instructed in:
- the use of an administration device, for example syringe pump, if needed
- aseptic (germ free) infusion techniques,
- keeping a treatment diary, and
- recognition of and measures to be taken in case of severe side effects.

You must carefully follow your doctor's instructions regarding the dose, infusion speed and schedule for infusing Xembify so that your treatment works for you.

Infusion sites
Xembify is for subcutaneous infusion only. Infuse Xembify into subcutaneous tissue at sites such as
- abdomen,
- thighs,
- upper arms, and
- the side of the hip

When selecting infusion sites, avoid: bony areas, visible blood vessels, scars and any areas of inflammation (irritation) or infection. Rotate sites at every administration.

For your initial two infusions, the infusion speed will start at 10 mL per hour per infusion site. If you do not experience a side effect (see section 4), the speed may be increased every 10 minutes to a maximum of 20 mL per hour per infusion site for children and adolescents, and 25 mL per hour per infusion site for adults. After 2 infusion sessions, the dose rate may be gradually increased to up to 35 mL per hour per infusion site. Talk to your doctor before increasing the infusion rate.

You may infuse simultaneously in more than one site as long as they are at least 5 cm apart. Adults can split the dose between multiple sites, especially if the volume is greater than 30 mL. There is no limit to the number of sites you may use. You may use more than one pump to do this.

Instructions for use
Subcutaneous infusion for home treatment must be initiated and monitored by a health care professional experienced in the guidance of patients for home treatment. Infusion pumps appropriate for subcutaneous administration of immunoglobulins can be used. The patient or a caregiver must be instructed in the use of an infusion pump, the infusion techniques, the keeping of treatment diary, recognition of and measures to be taken in case of severe adverse reactions.

Follow the steps below and use aseptic technique to administer Xembify.

Prior to use, allow the solution to come to room or body temperatures (20 – 37 °C). This can take 60 minutes or longer.

Do not apply heat or place in the microwave.

Step 1: Assemble supplies

Gather the Xembify vial(s), ancillary supplies, sharps container, patient's treatment diary/logbook, and the infusion pump(s).

Step 2: Clean surface

Set up your infusion area on a clean, flat, non-porous surface, such as a kitchen counter.

Avoid using porous surfaces such as wood. Clean the surface with an alcohol wipe using a circular motion from the center outward.

Step 3: Wash hands

Wash and dry your hands thoroughly before using Xembify.

Your healthcare provider may recommend that you use antibacterial soap or that you wear gloves.

Step 4: Check vials

The liquid in the vial should be clear to slightly opalescent, and colourless or pale yellow or light brown.

Do not use the vial if:

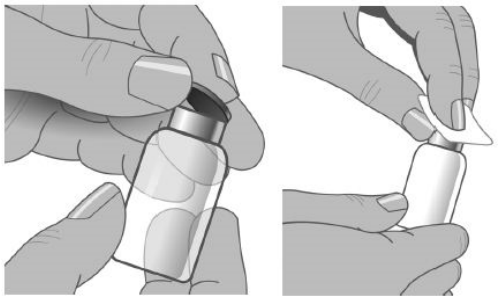
- the solution is cloudy or discoloured. The solution should be clear to slightly opalescent, and colourless or pale yellow or light brown.
- the protective cap is missing, or there is any evidence of tampering. Tell your healthcare provider immediately.

- the expiration date has passed.

Step 5: Remove the protective cap

Remove the protective cap from the vial to expose the middle of the stopper.

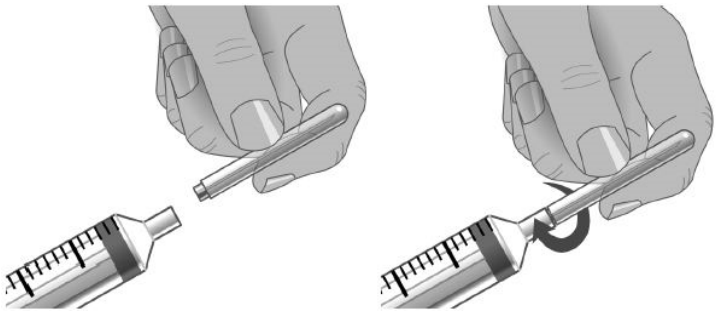
Wipe the stopper with alcohol and allow to dry.



Step 6: Transfer Xembify from vial(s) to syringe

Do not allow your fingers or other objects to touch the inner stem of the plunger, the syringe tip, or other areas that can touch the Xembify solution. Make sure needles are capped until used and that needles and syringes stay on the clean area created in Step 2. This is called “aseptic technique” to prevent germs from getting into the Xembify.

Using aseptic technique, attach each needle to the syringe tip.



Step 7: Prepare the syringe and draw Xembify solution into syringe

Remove cap from needle.

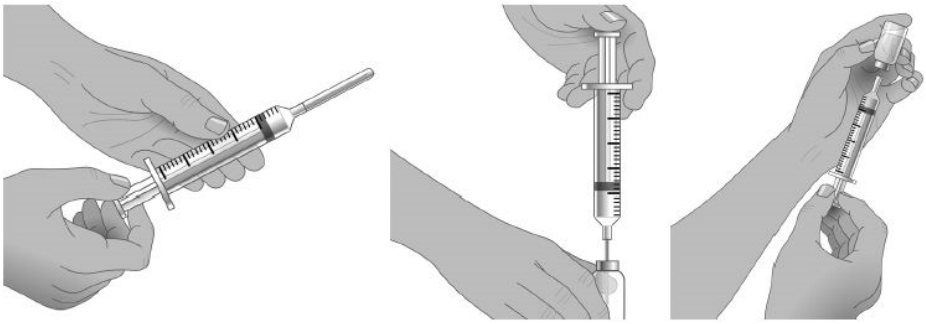
Pull the syringe plunger back to the level matching the amount of Xembify to be withdrawn from the vial.

Place the Xembify vial on a clean flat surface and insert the needle into the center of the vial stopper.

Inject air into the vial. The amount of air should match the amount of Xembify to be withdrawn.

Turn the vial upside down and withdraw the correct amount of Xembify. If multiple vials are required to get the correct dose, repeat Step 4.

Administer immediately after transferring Xembify from the vial to a syringe.



Step 8: Prepare the infusion pump

Follow the pump manufacturer's instructions for preparing the infusion pump, administration tubing and Y-site connection tubing, if needed.

Prime the administration tubing with Xembify to take out any air left in the tubing or needle. To prime, hold the syringe in one hand and the administration tubing's capped needle in the other. Gently squeeze on the plunger until you see a drop of Xembify come out of the needle.

Step 9: Select the number and location of infusion sites

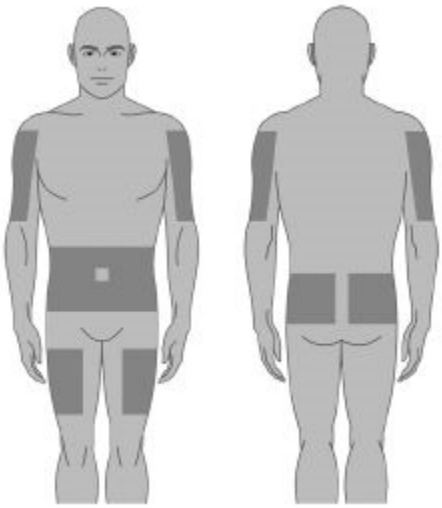
Select one or more infusion sites as directed by your healthcare provider.

The number and location of infusion sites depends on the volume of the total dose.

Suitable sites for infusion are: abdomen, thighs, upper arms and the side of the hip.

Avoid: bony areas, visible blood vessels, scars, and any areas of inflammation (irritation) or infection.

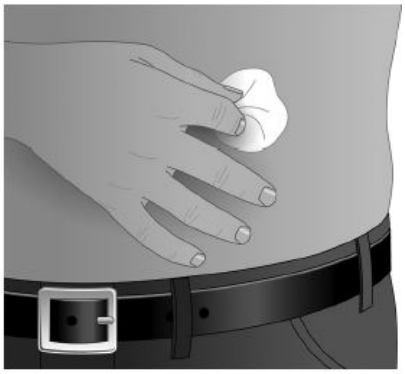
Rotate sites between future infusions.



Step 10: Prepare the infusion site

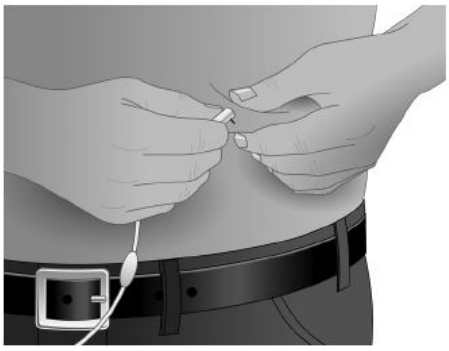
Wipe the infusion site(s) with a sterile alcohol wipe beginning at the center of each infusion site and moving outward in circular motion. Allow the infusion site(s) to dry (at least 30 seconds).

Before infusion, sites should be clean, dry, and at least 5 cm apart.



Step 11: Insert the needle

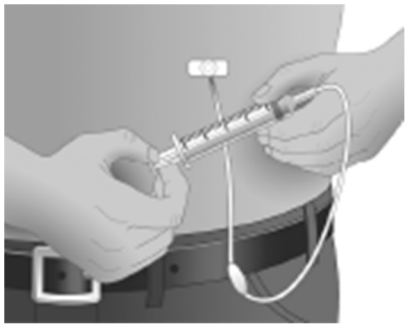
Grasp the skin between two fingers (pinch at least 2.5 cm of skin) and insert the needle at a 90-degree angle into the tissue underneath the skin or subcutaneous tissue.



Step 12: Make sure the needle is not in a blood vessel

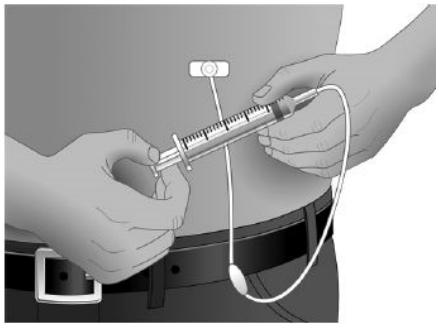
After inserting each needle into tissue (and before your infusion), make sure that a blood vessel has not been accidentally entered. To do this, attach a sterile syringe to the end of the primed administration tubing. Pull back on the syringe plunger and watch for any blood flowing back into administration tubing.

If you see any blood, remove and discard the needle and administration tubing.



Repeat priming and needle insertion steps using a new needle, administration tubing and a new infusion site.

Secure the needle in place by applying sterile gauze or transparent dressing over the site.



Step 13: Repeat for other sites, as needed

Step 14: Infuse Xembify

Infuse Xembify as soon as possible after it is prepared.

Follow the manufacturer's instructions for filling the tubing and using the infusion pump.

Step 15: After infusion

Follow manufacturer's instructions to turn off the pump.

Undo and discard any dressing or tape.

Gently remove the inserted needle(s) or catheter(s).

Discard any unused solution in an appropriate waste container as instructed.

Discard any used administration equipment in an appropriate waste container.

Store your supplies in a safe place.

Follow manufacturer's instructions to care for the syringe pump.

Step 16: Record each infusion

Remove the peel-off label with the product lot number from the Xembify vial and use this to complete the patient record. Include information about each infusion such as:

- the time and date,
- the dose,
- lot number(s),
- infusion sites, and
- any reactions.

Remember to bring your journal with you when you visit your doctor. Your doctor may ask to see your treatment diary/logbook.

Tell your doctor about any problems you have during your infusions. Call your healthcare provider for medical advice about side effects.

Use in children and adolescents
In infants and children infusion site may be changed every 5 to 15 mL.

If you use more Xembify than you should
Contact your doctor for instructions.

If you forget to use Xembify
Do not take a double dose to make up for a forgotten dose. Contact your doctor for instructions.

If you stop using Xembify
If you have any further questions on the use of this medicine, ask your doctor.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.
Rarely human normal immunoglobulins may cause a sudden fall in blood pressure and, in isolated cases, anaphylactic shock, even when the patient has shown no hypersensitivity to previous administration.

Signs or symptoms of these rare allergic reactions include:

- feeling light headed, dizzy or faint
- skin rash and itchiness, swelling in the mouth or throat, difficulty breathing, wheezing
- abnormal heart rate, chest pain, blueness of lips or fingers and toes

If you notice any signs of allergic reaction or anaphylactic-type reaction during infusion of Xembify, immediately **stop the infusion and contact your doctor or go to the nearest hospital**. Please see Section 2 of this leaflet (Warnings and precautions). If you notice any of these signs during the infusion of Xembify when it is being given by a healthcare professional, **tell your doctor or nurse immediately**. He or she will decide whether to slow down the infusion or stop the infusion completely.

Local reactions at infusion sites, such as swelling, soreness, redness, induration (hard lump), local heat, itching, bruising and rash, may occur.

Xembify may occassionally cause chills, headache, dizziness, fever, vomiting, allergic reactions, feeling sick (nausea), joint pain, low blood pressure and moderate low back pain.

The following side effect is very common with Xembify (may affect 1 or more people in 10):

- Local infusion site reaction

The following side effects are common with Xembify (may affect 1 or more people in 100):

- Headache
- Arthralgia (pain in joints)
- Back pain
- Rhinitis (runny nose, sneezing, and stuffiness)
- Diarrhoea
- Nausea
- Pyrexia (fever)
- Blood immunoglobulin G decreased
- Pruritus (itching)
- Papule (small raised area of skin)

Postmarketing side effects
The following adverse reactions have been identified and reported during the postmarketing use of Xembify (all non-serious): dyspnoea (shortness of breath), fatigue, pain, nausea, headache and local infusion site reaction such as erythema (redness) and swelling. It is not always possible to reliably estimate the frequency of these reactions.

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme, Website: 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 Xembify

Keep this medicine out of the sight and reach of children.

- Store in a refrigerator (2 ºC – 8 °C).
  - Xembify may be stored at temperatures not to exceed 25 °C for up to 6 months any time prior to the expiration date.
  - On the day product is removed from the refrigerator, write in the space provided on the carton for "Discard Date" either the date 6 months from now or the expiry date imprinted on the carton flap, whichever is sooner.
  - If stored at room temperatures, do not return the product to the refrigerator. Use the product by the "Discard Date" or discard it.
- Do not freeze.
- Keep the vial in the outer carton in order to protect from light.
- Administer as soon as possible after Xembify is transferred from the vial into a syringe.

Do not use this medicine after the expiry date which is stated on the label and carton.

Do not use this medicine if you notice it is discoloured, cloudy, has deposits, or if it has been frozen.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist 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 Xembify contains
- The active substance is human normal immunoglobulin (SCIg), one mL contains 200 mg of human normal immunoglobulin, of which at least 98% is IgG.
  The percentage of IgG subclasses is approximately 62% IgG_1, 30% IgG_2, 4.3% IgG_3 and 3.2% IgG_4. It contains some IgA (not more than 160 micrograms/mL).
- The other ingredients are glycine (E 640), polysorbate 80 (E 433), and water for injections.

What Xembify looks like and contents of the pack
Xembify is a solution for subcutaneous injection. The solution is clear to slightly opalescent and colourless or pale yellow or light brown.

Xembify is packaged in a carton containing a clear glass vial with a stopper, aluminum overseal, plastic top and shrink band that guarantee the intactness of packaging.

Xembify is supplied in pack sizes of
1 g / 5 mL
2 g / 10 mL
4 g / 20 mL
10 g / 50 mL

Each carton contains 1 vial Xembify and 1 Patient Information Leaflet.

Marketing Authorisation Holder and Manufacturer
Instituto Grifols, S.A.
Can Guasc, 2 - Parets del Vallès
08150 Barcelona - Spain

This leaflet was last revised in 10/2021.

Other sources of information

Detailed information on this medicine is available on the website of
https://www.medicines.org.uk/emc#gref