Xembify®
(immune globulin subcutaneous human-klhw) 20%

SUBCUTANEOUS IMMUNE GLOBULIN (SCIG) ADMINISTRATION GUIDE

Please see Important Safety Information on pages 36–39 and full Prescribing Information for XEMBIFY.

GRIFOLS

Xembify®
(immune globulin subcutaneous human-klhw) 20%

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Please see Important Safety Information on pages 36–39 and full Prescribing Information for XEMBIFY.

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WHAT IS IMMUNOGLOBULIN G (IgG)?

IgG is an antibody made by the body's immune system[1,2]

Plasma is the liquid part of blood that remains after blood cells are removed, and contains many proteins, including antibodies

The immunoglobulin G (IgG) antibody is a Y-shaped molecule with antigen binding sites at the tip of each arm of the Y

Antibodies protect against infection by coating the microbes and signaling the body to destroy them

Although there are 5 types of antibodies (IgG, IgM, IgD, IgA, and IgE), IG products predominantly contain IgG[3]

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Xembify® (immune globulin subcutaneous human-klhw) 20%

WHAT IG IS USED FOR

IG is used to treat a spectrum of immune disorders[4*]

IMMUNODEFICIENCY DISORDERS

Primary humoral immunodeficiency disease (PIDD)[4,5]

- PIDD is a group of more than 450 hereditary immunodeficiency disorders
- A common feature of these is an ineffective immune system leading to frequent infections

AUTOIMMUNE DISORDERS

Chronic inflammatory demyelinating polyneuropathy (CIDP)[6†]

In CIDP, the immune system attacks the myelin covering that is protecting the peripheral nerves of the arms and legs, causing impairment of conduction. This causes weakness in arms or legs, numbness or tingling in the fingers or toes, loss of reflexes, tiredness, and/or pain.

Idiopathic thrombocytopenic purpura (ITP)[7†]

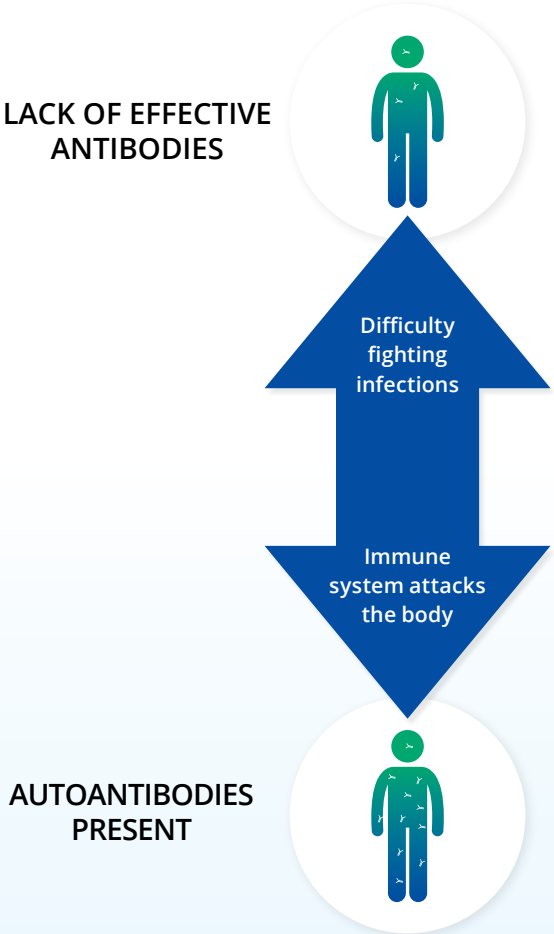
In ITP, the immune system attacks platelets, resulting in low blood platelet counts and an increased risk of bleeding.

*The disorders shown above do not include all indications for IG therapy.
†XEMBIFY is not indicated for CIDP and ITP.

Indication

XEMBIFY® (immune globulin subcutaneous human–klhw) is a 20% immune globulin indicated for treatment of primary humoral immunodeficiency disease (PIDD) in patients 2 years of age and older. XEMBIFY is for subcutaneous administration only.

Please see Important Safety Information on pages 36–39 and full Prescribing Information for XEMBIFY.



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WHERE DOES IG COME FROM?

Grifols has more than 300 plasma donation centers across the United States[2,9]

The plasma donation process at Grifols has several steps, each with rigorous safety measures built in.

STEP 1: CHECK-IN

Plasma donors check in at the donation center with their ID and proof of address. The National Donor Deferral Registry will be checked to verify donor eligibility.

STEP 2: SCREENING

Volunteer donors undergo health screening that includes a medical history, vital signs (weight, blood pressure, pulse, and temperature), and basic chemistries to ensure the health of the donor.

STEP 3: PHYSICAL EXAM

Donors go through a physical exam on their first donation and once a year thereafter.

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STEP 4: PLASMA DONATION

Plasmapheresis is a method of removing plasma from the body by withdrawing blood, separating it into plasma and red blood cells, and returning the red blood cells back into the bloodstream.

STEP 5: COMPLETION

Plasma regenerates very quickly, giving volunteers the opportunity to donate twice in a 7-day period with at least 48 hours in between donations. Donors are given instructions to take it easy and to drink lots of water.

It takes approximately 130 plasma donations to treat 1 patient with PIDD for 1 year[2]

Because XEMBIFY is made from human blood, it may carry a risk of transmitting infectious agents, eg, viruses, the variant Creutzfeldt-Jakob disease (vCJD) agent, and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent.[8]

Please see Important Safety Information on pages 36–39 and full Prescribing Information for XEMBIFY.

HOW XEMBIFY IS MADE

Grifols manufactures IG utilizing a state-of-the-art process that can take up to 12 months from donation to finished product[2]

STEP 1: PLASMA DONATION TESTING

- Plasma donations are collected from healthy donors in the US and are tested for viral markers
- Inventory hold and the inventory lookback processes enable the confirmation of donor health and give Grifols the opportunity to exclude donations not suitable for use in the manufacturing of plasma-derived biotherapeutics

Please see Important Safety Information on pages 36–39 and full Prescribing Information for XEMBIFY.

STEP 2: PLASMA POOLING

- Plasma donations from healthy donors are combined into a fractionation pool

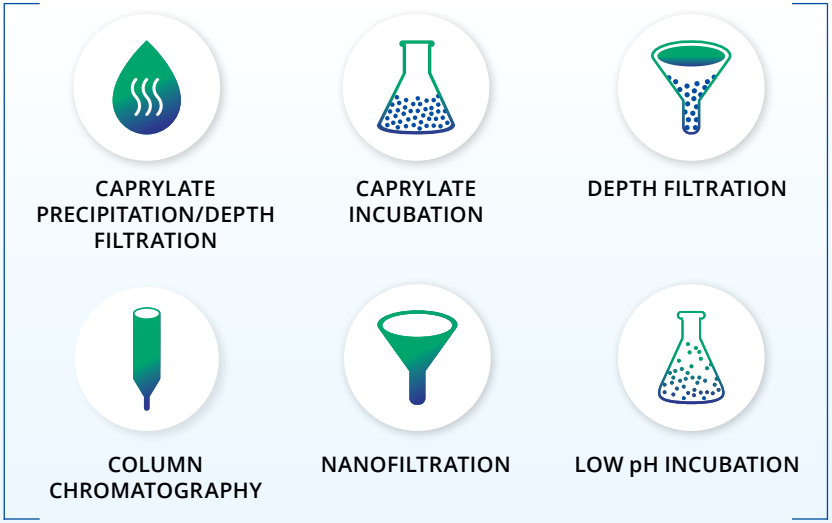
STEP 3: PLASMA FRACTIONATION

- Pooled plasma is separated into various proteins that will be used to make plasma-derived therapies
- XEMBIFY is purified from the fraction that has concentrated immune globulins
- Grifols is a global leader in fractionation capacity (20 million liters of plasma/year)[2]

Please see Important Safety Information on pages 36–39 and full Prescribing Information for XEMBIFY.

STEP 4: PROTEIN PURIFICATION

- XEMBIFY is purified using a unique caprylate/chromatography process
- During purification, the immunoglobulin proteins remain in solution, minimizing the risk of denaturing the IgG molecules[10]
- The purification process yields a final IgG product that closely reflects the IgG subclass distribution found in normal human serum
- The process includes protein purification steps with pathogen clearance capacity, including caprylate precipitation/depth filtration, depth filtration, and column chromatography[8]
- In addition, the process includes dedicated steps with pathogen clearance capacity, including caprylate incubation, nanofiltration, and low pH incubation



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STEP 5: FORMULATION

- Formulation at low pH provides a stable IgG solution
- XEMBIFY contains glycine, a natural amino acid, as a stabilizer
- The purified product is then packaged into vials. XEMBIFY is available in multiple vial sizes: 1 g, 2 g, 4 g, and 10 g
- Grifols employs PediGri®—a unique system that provides complete traceability and easy access to all information on each batch of XEMBIFY, from plasma donation to finished product

Grifols manufactures IG using a state-of-the-art process focused on safety at every step, from donation to finished product

Because XEMBIFY is made from human blood, it may carry a risk of transmitting infectious agents, eg, viruses, the variant Creutzfeldt-Jakob disease (vCJD) agent, and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent.

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Xembify® (immune globulin subcutaneous human-klhw) 20%

gamunex®-c immune globulin injection (human), 10% caprylate/chromatography purified

UNIQUE MANUFACTURING PROCESS OFFERING MAXIMUM PURITY AND MAXIMUM POTENCY[8,11]*

XEMBIFY and GAMUNEX-C are both made using the caprylate/chromatography process[8,12]

THE CAPRYLATE/CHROMATOGRAPHY PROCESS[8,10,11]:

- Yields maximum percentage of IgG
  - » ≥98% IgG
- Minimizes the risk of denaturing the IgG protein
  - » Maintains IgG in liquid phase
- Provides maximum monomeric activity

*Zero serious bacterial infections and 0 hospitalizations due to infections. One subject reported sepsis due to an animal bite, an event deemed unrelated to the treatment. This event was included in the calculations, giving an annual rate of 0.049 events per subject-year (N=49).[13]

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Xembify®
(immune globulin subcutaneous human-klhw) 20%

Maximum purity with maximum percentage of IgG

Maximum potency* of IgG without alteration of structure, function, or efficacy

Consistent fractionation and purification process allows for continuity of care from IV to SC

- XEMBIFY is concentrated into a 20% SCIG through ultrafiltration[11]

*Zero serious bacterial infections and 0 hospitalizations due to infections. One subject reported sepsis due to an animal bite, an event deemed unrelated to the treatment. This event was included in the calculations, giving an annual rate of 0.049 events per subject-year (N=49).[13]

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MAXIMUM PURITY AND PROVEN FORMULATION

Product characteristics that may meet the needs of a wide range of PIDD patients[13,14]

SUGAR-FREE

Consider for patients with:

- Pre-diabetes/diabetes
- Advanced age

TRACE AMOUNTS OF SODIUM

Consider for patients with:

- Cardiac impairment
- Advanced age

CLOSE TO PHYSIOLOGIC OSMOLALITY

Consider for patients with:

- Cardiac impairment
- Advanced age

STABILIZED & ISOTONICITY

Maintained by glycine

XEMBIFY is contraindicated in patients who have had an anaphylactic or severe systemic reaction to the administration of human immune globulin. It is contraindicated in IgA-deficient patients with antibodies against IgA and a history of hypersensitivity.[8]

Please see Important Safety Information on pages 36–39 and full Prescribing Information for XEMBIFY.

Xembify® (immune globulin subcutaneous human-klhw) 20%

PROVEN TOLERABILITY PROFILE

Adverse reactions in ≥5% of subjects[8]

Adverse Reactions[‡]	By Subject n (%)[§] (N=49 subjects)	By Infusion n (rate)[‖] (N=1053 infusions)
Local adverse reactions		
Infusion-site erythema	19 (39%)	123 (0.117)
Infusion-site pain	9 (18%)	32 (0.030)
Infusion-site swelling	8 (16%)	124 (0.118)
Infusion-site bruising	8 (16%)	26 (0.025)
Infusion-site nodule	8 (16%)	13 (0.012)
Infusion-site pruritus	5 (10%)	28 (0.027)
Infusion-site induration	4 (8%)	6 (0.006)
Infusion-site scab	3 (6%)	6 (0.006)
Infusion-site edema	3 (6%)	5 (0.005)
Systemic adverse reactions		
Cough	3 (6%)	4 (0.004)
Diarrhea	3 (6%)	3 (0.003)

[‡]Including all adverse reactions that occurred after the first dose of XEMBIFY regardless of causality, excluding infections.

[§]Number and percentage of subjects with the adverse reaction.

[‖]Rate per infusion is calculated as the total number of adverse reactions divided by the total number of infusions.

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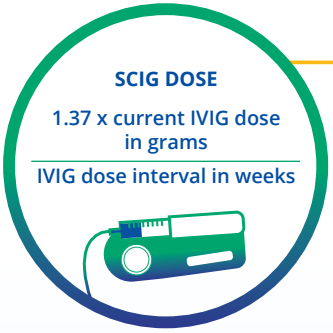
Xembify® (immune globulin subcutaneous human-klhw) 20%

DOSING RECOMMENDATIONS FOR XEMBIFY

Customizable dosing to meet your patients' needs[8]



INFUSION RATE

Infusion Rate: up to 25 mL/h/site from the start of treatment

Number of Sites: ≤6

Site Distance: ≥2 inches apart

- Children will require less total volume for a specific XEMBIFY dose (mg/kg body weight) than adults
- The healthcare provider may choose a smaller volume/site for children and/or fewer infusion sites to achieve the target total dose, depending on the needs of the child

Please see Important Safety Information on pages 36–39 and full Prescribing Information for XEMBIFY.

Weekly to more frequent dosing

WEEKLY

to more frequent dosing
(2-7 times/week)

- Tailor the dosing schedule to meet your patient's individual needs and preferred infusion schedule
- Patients choose the number of infusion sites from 1 to 6 as directed by their healthcare provider
  - » Most infusions in the study were conducted using 2 or 4 sites (30.5% or 56.2%, respectively)
- Infuse at a customizable rate up to 25 mL/h/site from the start of treatment
  - » Maximum volume to be infused is 25 mL/site

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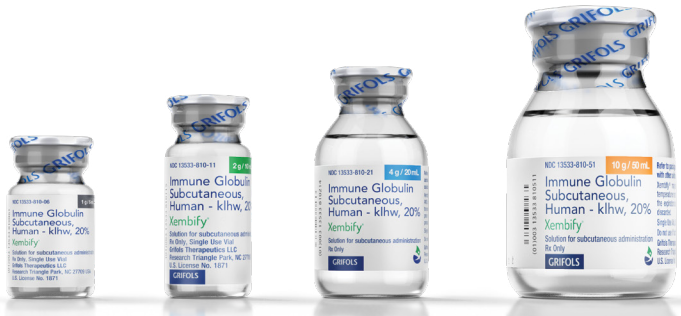
CHOICE OF VIAL SIZES

XEMBIFY is available in a wide range of vial sizes



1 g	2 g	4 g	10 g
5 mL	10 mL	20 mL	50 mL

Convenient handling and storage

- No refrigeration needed for up to 6 months¶
- Can be stored under refrigeration for up to 36 months¶

¶XEMBIFY may be stored for 36 months at 2-8°C (36-46°F) from the date of manufacture, and the product may be stored at temperatures not to exceed 25°C (77°F) for up to 6 months any time prior to the expiration date. Following 25°C (77°F) storage, use the product immediately or discard. Do not freeze.

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HELP ENSURE SUCCESSFUL SCIG SELF-INFUSIONS

Facilitating self-infusions through education[15]

- Educate patients/caregivers on how to perform SCIG infusions and answer any questions they may have
- Teach self-infusion in a systematic, stepwise manner
- Follow up with patients regarding any issues with self-infusions
- Adjust the infusion process as necessary by changing:
  - Needle gauge or length
  - Location or number of infusion sites
  - Infusion tubing

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FACTORS THAT INFLUENCE THE SUCCESS OF SCIG THERAPY

Managing the following factors can help ensure patient success[15]

Efficacy and IgG trough levels

- Dose
- Infusion interval

Tolerability

- Side effect management
- Infusion rate, sites, and volume
- Patient comorbidities
- Product characteristics
- Infusion equipment and technique

Compliance

- Site of care
- Route of administration (if indicated for PIDD)
- Patient understanding and commitment to therapy

Please see Important Safety Information on pages 36–39 and full Prescribing Information for XEMBIFY.

MONITORING PATIENTS UNDERGOING INFUSIONS FOR PIDD

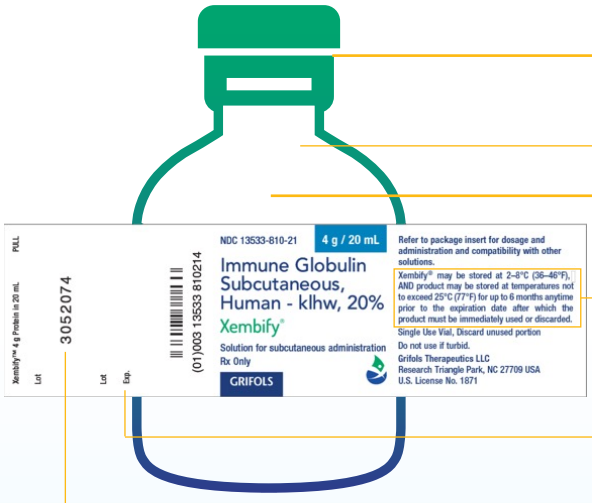
Some questions you could ask patients or caregivers[16]

- How is your IG treatment going so far?
- Have you experienced a recent cold, flu, or had any symptoms of infection (eg, fever, chills)?
- Have you missed any infusions?
- Have you been sick or missed any work/school due to illness?
- Do you experience fatigue after your infusions?
- Is there anything you want to change about your treatment plan?

Please see Important Safety Information on pages 36–39 and full Prescribing Information for XEMBIFY.

INSPECTING THE IG PRODUCT

Check the product for the following before infusion[8,16]



NEVER SHAKE IG PRODUCT

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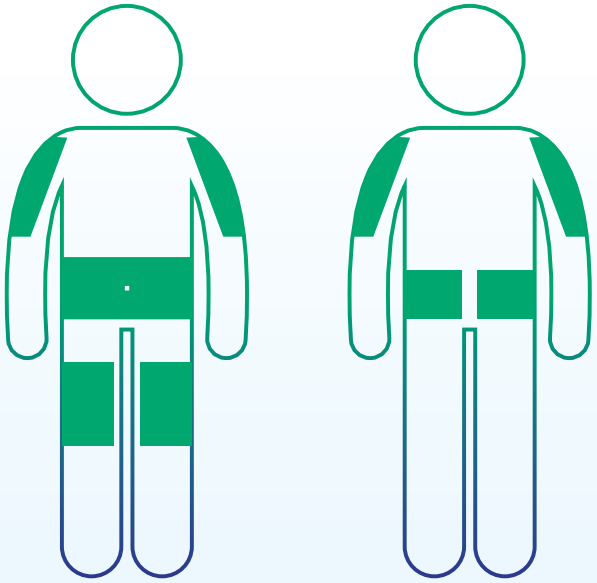
FACTORS TO CONSIDER WHEN SELECTING SITES FOR INFUSIONS

Site selection for adult and pediatric patients 2 years of age and older[8,16]

- Select areas with adequate subcutaneous tissue
- Ensure sites are at least 2 inches apart
- Rotate the sites
- Up to 6 sites can be used simultaneously



FRONT BACK

Please see Important Safety Information on pages 36–39 and full Prescribing Information for XEMBIFY.

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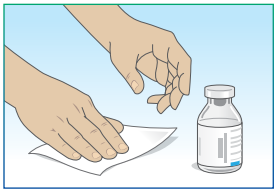
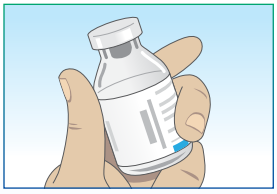
XEMBIFY SCIG INFUSION

Consider these steps for preparation of the site and administration[8,17]



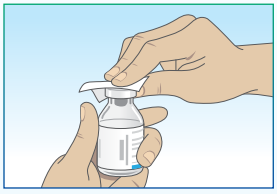
STEP 1

Disinfect surface to be used for your infusion. Allow the vial(s) of XEMBIFY to reach room temperature. Set up all of the supplies you will need. Wash and dry your hands thoroughly.



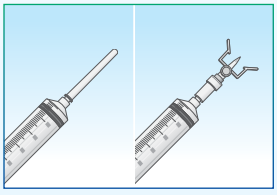
STEP 2

Check the vial of XEMBIFY. Confirm the name and expiration date. If the product is past the expiration date, if the liquid is cloudy or has particles, or if the vial shows any sign of tampering, do not use that vial. Contact your healthcare provider for guidance in that case.



STEP 3

Remove the tamper-resistant seal and protective cap from the vial of XEMBIFY. Clean the rubber stopper with an alcohol wipe and allow to air dry.

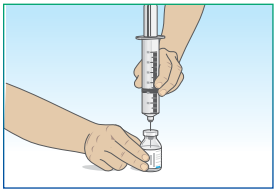


STEP 4

Draw XEMBIFY into the syringe using either a needle or a transfer device. If you are using a needle, refer to Step 5. If using a transfer device, refer to Step 6.

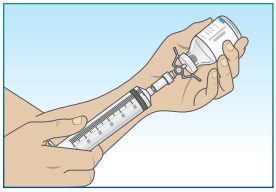
Please see Important Safety Information on pages 36–39 and full Prescribing Information for XEMBIFY.

XEMBIFY SCIG INFUSION, continued[8,16,17]



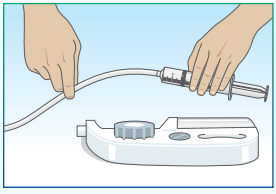
STEP 5

Attach the needle to the syringe tip and remove the cap. Pull the syringe plunger back to the level of XEMBIFY you want to withdraw. Place the vial on a flat surface, insert the needle, and inject air. Turn the vial and syringe upside down. Make sure the needle is placed below the fluid level and withdraw XEMBIFY.



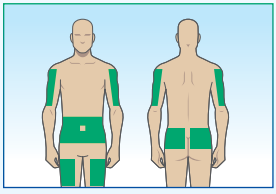
STEP 6

Uncap the transfer device and attach it to the syringe. Place the vial on a flat surface and insert the device into the top of the vial. Turn the vial and syringe upside down and withdraw the desired amount of XEMBIFY. Then, remove the syringe and transfer device.



STEP 7

Follow the pump manufacturer's instructions to attach the infusion tubing and needle set to the syringe. Be sure to prime the administration tubing by filling it with XEMBIFY. Make sure the needle remains dry while priming.

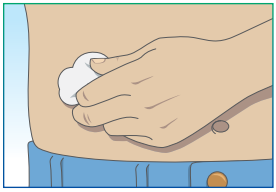


STEP 8

XEMBIFY is infused in the abdomen, thigh, upper arm, sides, back, or hip. Select one or more infusion sites as directed by your healthcare provider. Be sure to choose sites that are different from your last infusion.

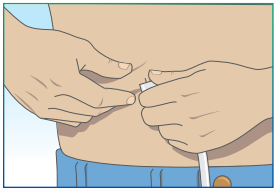
Please see Important Safety Information on pages 36–39 and full Prescribing Information for XEMBIFY.

XEMBIFY SCIG INFUSION, continued[8,16]



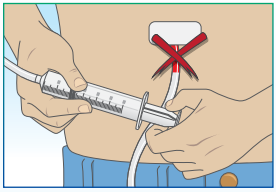
STEP 9

Prepare the infusion site(s) by cleaning with an alcohol wipe. The sites should be clean, dry, at least 2 inches apart, and 2 inches away from the belly button. Do not use more than 6 infusion sites at the same time.



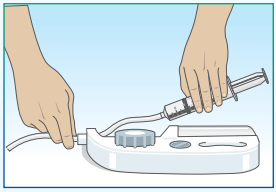
STEP 10

Grasp the skin between 2 fingers and insert the needle into the subcutaneous tissue, which is the innermost layer of the skin.



STEP 11

Make sure a blood vessel has not been entered. If you see blood when pulling back on the plunger, remove and discard the needle and tubing. Repeat steps 8-10 using a new needle, administration tubing, and a new infusion site. Secure needle with adhesive dressing. Repeat for other sites as needed.



STEP 12

Follow the pump manufacturer's instructions to load the syringe and start the infusion. The infusion is complete when the syringe is empty. Use XEMBIFY within 2 hours of drawing up in a syringe to avoid the potential formation of particles caused by siliconized syringes.

Please see Important Safety Information on pages 36–39 and full Prescribing Information for XEMBIFY.

Xembify® (immune globulin subcutaneous human-klhw) 20%

WHAT TO LOOK FOR DURING SCIG ADMINISTRATION

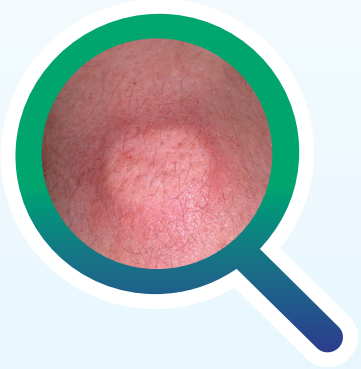
Check infusion sites for local adverse reactions such as erythema, discomfort, and swelling[8,16]

Troubleshooting infusion-site reactions[8,15-17]

- Make sure your patient is following appropriate dry needle insertion technique
- Consider changing needle length if there is pain or leakage at the infusion site[16]
- Make sure infusion sites are 2 inches apart and 2 inches from belly button
- Make sure patient is rotating sites
- Monitor the amount of fluid per site; maximum amount is 25 mL/h/site

Mild infusion-site reaction

Moderate infusion-site reaction



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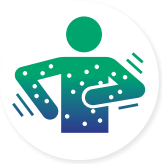
COMMON ADVERSE REACTIONS WITH SCIG INFUSIONS

Local infusion-site reactions are most common[16,18]



Local itching

POTENTIAL INTERVENTION

Apply cold compress. Do not apply directly to the skin

CONSIDERATIONS FOR FUTURE INFUSIONS

Use longer needle

Decrease volume per site and gradually increase to maximum volume

Ensure dry needle insertion

Topical steroid

Redness

POTENTIAL INTERVENTION

Apply cold compress. Do not apply directly to the skin

CONSIDERATIONS FOR FUTURE INFUSIONS

Consider changing dressing tape

Provide education to the patient that this should decrease with each subsequent infusion

Please see Important Safety Information on pages 36–39 and full Prescribing Information for XEMBIFY.

Burning

POTENTIAL INTERVENTION

Clamp catheter for 5-10 minutes

Apply cold compress. Do not apply directly to the skin

Remove needle and place in another site

Slow rate of infusion

CONSIDERATIONS FOR FUTURE INFUSIONS

Decrease infusion rate

Consider changing the infusion volume

Consider shorter needle

Consider changing antiseptic used for skin prep

Swelling

POTENTIAL INTERVENTION

Warm compress for 5-10 minutes (if using a heating pad, use low setting), gentle massage

CONSIDERATIONS FOR FUTURE INFUSIONS

Adjust volume/consider alternate site

Consider moving arm/leg with infusion site to mobilize fluid

Rash/hives

POTENTIAL INTERVENTION

Stop infusion/contact prescriber for instructions

CONSIDERATIONS FOR FUTURE INFUSIONS

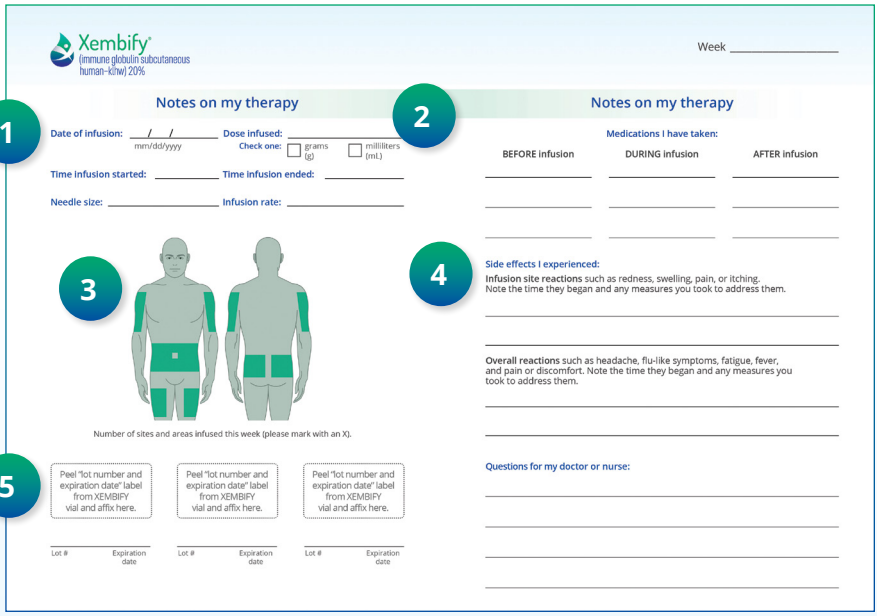
Stop infusion/contact prescriber for instructions

Please see Important Safety Information on pages 36–39 and full Prescribing Information for XEMBIFY.

Xembify®
(immune globulin subcutaneous human-klhw) 20%

DOCUMENTING PIDD SCIG INFUSIONS

Encourage your patients to use the XEMBIFY Infusion Log Book to record important information about their infusions



Xembify®
(immune globulin subcutaneous human-klhw) 20%

Week _____

1

Notes on my therapy

Date of infusion: ___/___/_____ (mm/dd/yyyy)
Dose infused: _____
Check one: ☐ grams (g) ☐ milliliters (mL)

Time infusion started: _____ Time infusion ended: _____

Needle size: _____ Infusion rate: _____

3

Number of sites and areas infused this week (please mark with an X).

5

Peel "lot number and expiration date" label from XEMBIFY vial and affix here.

Lot # Expiration date

Peel "lot number and expiration date" label from XEMBIFY vial and affix here.

Lot # Expiration date

Peel "lot number and expiration date" label from XEMBIFY vial and affix here.

Lot # Expiration date

2

Notes on my therapy

Medications I have taken:

BEFORE infusion	DURING infusion	AFTER infusion

4

Side effects I experienced:

Infusion site reactions such as redness, swelling, pain, or itching. Note the time they began and any measures you took to address them.

Overall reactions such as headache, flu-like symptoms, fatigue, fever, and pain or discomfort. Note the time they began and any measures you took to address them.

Questions for my doctor or nurse:

Please see Important Safety Information on pages 36–39 and full Prescribing Information for XEMBIFY.

REQUEST YOUR PATIENTS TO RECORD THE FOLLOWING INFORMATION[8,18]:

1. Date and time the infusion started and ended
2. The exact dose that was infused
3. The number and location of infusion sites
4. Any side effects they experienced
5. Affix the peel-off label from the vial to the allocated space in the log book

Please see Important Safety Information on pages 36–39 and full Prescribing Information for XEMBIFY.

A PARTNERSHIP WITH DEDICATED SUPPORT

Eligible XEMBIFY patients may pay as little as ZERO copay!

$ ZERO COPAY FOR XEMBIFY

Xembify connexions™

Please see Important Safety Information on pages 36–39 and full Prescribing Information for XEMBIFY.

Xembify® (immune globulin subcutaneous human-klhw) 20%

- **Copay Program** offering up to $10,000 per calendar year[#]
- **Patient Assistance Program** to help your patients in the event of loss of insurance
- **Committed case managers** provide a dedicated, single point of contact for you, your office staff, and your patients

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[#]Subject to terms and conditions.

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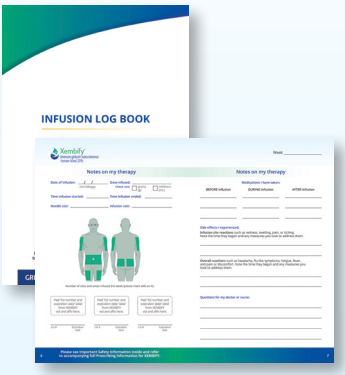
Xembify®
(immune globulin subcutaneous human-klhw) 20%

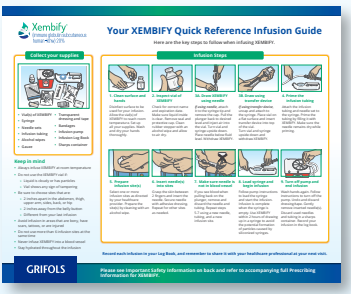
XEMBIFY PATIENT STARTER KIT

Buzzy Bee

Comfort item
(may not be available in your region)



Infusion Log Book



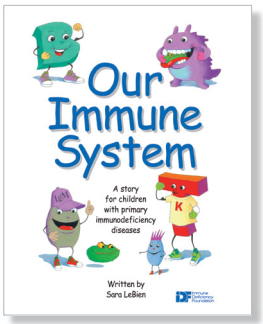
Quick Reference Guide

Please see Important Safety Information on pages 36–39 and full Prescribing Information for XEMBIFY.

Xembify®
(immune globulin subcutaneous human-klhw) 20%

Pediatric add-on kit

Comfort item
(may not be available in your region)



IDF Children's Book

Pediatric Therapy Journal

Please see Important Safety Information on pages 36–39 and full Prescribing Information for XEMBIFY.

Xembify®
(immune globulin subcutaneous human-klhw) 20%

XEMBIFY IMPORTANT SAFETY INFORMATION

Indication

XEMBIFY® (immune globulin subcutaneous human–klhw) is a 20% immune globulin indicated for treatment of primary humoral immunodeficiency disease (PIDD) in patients 2 years of age and older. XEMBIFY is for subcutaneous administration only.

Important Safety Information

WARNING: THROMBOSIS

- **Thrombosis may occur with immune globulin products, including XEMBIFY. Risk factors may include: advanced age, prolonged immobilization, estrogens, indwelling vascular catheters, hyperviscosity, and cardiovascular risk factors. Thrombosis may occur in the absence of known risk factors**
- **For patients at risk of thrombosis, administer XEMBIFY at the minimum dose and infusion rate practicable. Ensure adequate hydration in patients before administration. Monitor for signs and symptoms of thrombosis and assess blood viscosity in patients at risk of hyperviscosity**

Contraindications

XEMBIFY is contraindicated in patients who have had an anaphylactic or severe systemic reaction to the administration of human immune globulin. It is contraindicated in IgA-deficient patients with antibodies against IgA and a history of hypersensitivity.

Warnings and Precautions

Hypersensitivity. Severe hypersensitivity reactions may occur with immune globulin products, including XEMBIFY. In case of hypersensitivity, discontinue infusion immediately and institute appropriate treatment. XEMBIFY contains IgA. Patients with known antibodies to IgA may have a greater risk of developing potentially severe hypersensitivity and anaphylactic reactions.

Thrombosis. Thrombosis may occur following treatment with immune globulin products, including XEMBIFY. Thrombosis may occur in the absence of known risk factors. In patients at risk, administer at the minimum dose and infusion rate practicable. Ensure adequate hydration before administration. Monitor for signs and symptoms of thrombosis and assess blood viscosity in patients at risk of hyperviscosity.

Aseptic meningitis syndrome (AMS). AMS may occur with human immune globulin treatment, including XEMBIFY. Conduct a thorough neurological exam on patients exhibiting signs and symptoms to rule out other causes of meningitis. Discontinuation of treatment has resulted in remission within several days without sequelae.

Please see full Prescribing Information for XEMBIFY.

Renal dysfunction/failure. Acute renal dysfunction/failure, acute tubular necrosis, proximal tubular nephropathy, osmotic nephrosis, and death may occur with use of human immune globulin products, especially those containing sucrose. XEMBIFY does not contain sucrose. Ensure patients are not volume-depleted prior to starting infusion. In patients at risk due to preexisting renal insufficiency or predisposition to acute renal failure, assess renal function prior to the initial infusion of XEMBIFY and again at appropriate intervals thereafter. If renal function deteriorates, consider discontinuation.

Hemolysis. XEMBIFY may contain blood group antibodies that may cause a positive direct antiglobulin reaction and hemolysis. Monitor patients for clinical signs and symptoms of hemolysis. If signs and symptoms are present after infusion, perform confirmatory lab testing.

Transfusion-related acute lung injury (TRALI). Noncardiogenic pulmonary edema may occur in patients following treatment with immune globulin products, including XEMBIFY. Monitor patients for pulmonary adverse reactions. If TRALI is suspected, perform appropriate tests for the presence of antineutrophil and anti-HLA antibodies in both the product and patient serum. TRALI may be managed using oxygen therapy with adequate ventilatory support.

Transmissible infectious agents. Because XEMBIFY is made from human blood, it may carry a risk of transmitting infectious agents, eg, viruses, the variant Creutzfeldt-Jakob disease (vCJD) agent, and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent. No cases of transmission of viral diseases, vCJD, or CJD have ever been associated with the use of XEMBIFY.

Interference with lab tests. After infusion of XEMBIFY, passively transferred antibodies in the patient's blood may yield positive serological testing results, with the potential for misleading interpretation.

Adverse Reactions

The most common adverse reactions in ≥ 5% of subjects in the clinical trial were local adverse reactions, including infusion-site erythema (redness), infusion-site pain, infusion-site swelling (puffiness), infusion-site bruising, infusion-site nodule, infusion-site pruritus (itching), infusion-site induration (firmness), infusion-site scab, infusion-site edema, and systemic reactions including cough and diarrhea.

Drug Interactions

Passive transfer of antibodies may transiently interfere with the immune responses to live attenuated virus vaccines (eg, measles, mumps, rubella, and varicella).

Please see full Prescribing Information for XEMBIFY.

GAMUNEX-C IMPORTANT SAFETY INFORMATION

GAMUNEX®-C (immune globulin injection [human], 10% caprylate/chromatography purified) is indicated for the treatment of primary humoral immunodeficiency disease (PIDD) in patients 2 years of age and older, idiopathic thrombocytopenic purpura (ITP) in adults and children, and chronic inflammatory demyelinating polyneuropathy (CIDP) in adults.

Thrombosis may occur with immune globulin products, including GAMUNEX-C. Risk factors may include: advanced age, prolonged immobilization, hypercoagulable conditions, history of venous or arterial thrombosis, use of estrogens, indwelling central vascular catheters, hyperviscosity, and cardiovascular risk factors. Thrombosis may occur in the absence of known risk factors. For patients at risk of thrombosis, administer GAMUNEX-C at the minimum dose and infusion rate practicable. Ensure adequate hydration in patients before administration. Monitor for signs and symptoms of thrombosis and assess blood viscosity in patients at risk for hyperviscosity.

Renal dysfunction, acute renal failure, osmotic nephrosis, and death may occur with immune globulin intravenous (IVIG) products in predisposed patients. Patients predisposed to renal dysfunction include those with any degree of preexisting renal insufficiency, diabetes mellitus, age greater than 65, volume depletion, sepsis, paraproteinemia, or patients receiving known nephrotoxic drugs. Renal dysfunction and acute renal failure occur more commonly in patients receiving IVIG products containing sucrose. GAMUNEX-C does not contain sucrose. For patients at risk of renal dysfunction or failure, administer GAMUNEX-C at the minimum concentration available and the minimum infusion rate practicable.

GAMUNEX-C is contraindicated in patients who have had an anaphylactic or severe systemic reaction to the administration of human immune globulin. It is contraindicated in IgA-deficient patients with antibodies against IgA and history of hypersensitivity.

Severe hypersensitivity reactions may occur with IVIG products, including GAMUNEX-C. In case of hypersensitivity, discontinue GAMUNEX-C infusion immediately and institute appropriate treatment.

Monitor renal function, including blood urea nitrogen (BUN), serum creatinine, and urine output in patients at risk of developing acute renal failure.

Hyperproteinemia, increased serum viscosity, and hyponatremia may occur in patients receiving IVIG treatment, including GAMUNEX-C.

Please see full Prescribing Information for GAMUNEX-C.

There have been reports of aseptic meningitis, hemolytic anemia, and noncardiogenic pulmonary edema (transfusion-related acute lung injury [TRALI]) in patients administered with IVIG, including GAMUNEX-C.

The high-dose regimen (1g/kg x 1-2 days) is not recommended for individuals with expanded fluid volumes or where fluid volume may be a concern.

Because GAMUNEX-C is made from human blood, it may carry a risk of transmitting infectious agents, eg, viruses, the variant Creutzfeldt-Jakob disease (vCJD) agent, and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent.

Do not administer GAMUNEX-C subcutaneously in patients with ITP because of the risk of hematoma formation.

Periodic monitoring of renal function and urine output is particularly important in patients judged to be at increased risk of developing acute renal failure. Assess renal function, including measurement of BUN and serum creatinine, before the initial infusion of GAMUNEX-C and at appropriate intervals thereafter.

Consider baseline assessment of blood viscosity in patients at risk for hyperviscosity, including those with cryoglobulins, fasting chylomicronemia/markedly high triacylglycerols (triglycerides), or monoclonal gammopathies, because of the potentially increased risk of thrombosis.

If signs and/or symptoms of hemolysis are present after an infusion of GAMUNEX-C, perform appropriate laboratory testing for confirmation.

If TRALI is suspected, perform appropriate tests for the presence of antineutrophil antibodies and anti-HLA antibodies in both the product and patient's serum.

After infusion of IgG, the transitory rise of the various passively transferred antibodies in the patient's blood may yield positive serological testing results, with the potential for misleading interpretation.

In clinical studies, the most common adverse reactions with GAMUNEX-C were headache, pyrexia, hypertension, chills, rash, nausea, arthralgia, and asthenia (in CIDP); cough, rhinitis, pharyngitis, headache, asthma, nausea, fever, diarrhea, and sinusitis with intravenous use (in PIDD) and local infusion-site reactions, fatigue, headache, upper respiratory tract infection, arthralgia, diarrhea, nausea, sinusitis, bronchitis, depression, allergic dermatitis, migraine, myalgia, viral infection, and pyrexia with subcutaneous use (in PIDD); and headache, ecchymosis, vomiting, fever, nausea, rash, abdominal pain, back pain, and dyspepsia (in ITP).

The most serious adverse reactions in clinical studies were pulmonary embolism (PE) in 1 subject with a history of PE (in CIDP), an exacerbation of autoimmune pure red cell aplasia in 1 subject (in PIDD), and myocarditis in 1 subject that occurred 50 days post-study drug infusion and was not considered drug related (in ITP).

Please see full Prescribing Information for GAMUNEX-C.

Contact your local Nurse Educator or Grifols sales representative for more information about XEMBIFY therapy.

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References: 1. National Institute of Allergy and Infectious Diseases, National Cancer Institute. *Understanding the Immune System: How It Works.* Bethesda, MD: National Institutes of Health, US Dept of Health and Human Services; 2003. **2.** Data on file, Grifols. **3.** Siegel J. Immune globulins: therapeutic, pharmaceutical, cost, and administration considerations. *Pharmacy Practice News.* May 2023. Accessed June 5, 2024. https://www.pharmacypracticenews.com/Monographs-and-Whitepapers/Article/05-23/Immune-Globulins-Therapeutic-Pharmaceutical-Cost-and-Administration-Considerations/70243 **4.** Orange JS, Hossny EM, Weiler CR, et al. Use of intravenous immunoglobulin in human disease: a review of evidence by members of the Primary Immunodeficiency Committee of the American Academy of Allergy, Asthma and Immunology. *J Allergy Clin Immunol.* 2006;117(suppl 4):S525-S553. **5.** About primary immunodeficiencies. Immune Deficiency Foundation website. Accessed June 5, 2024. http://primaryimmune.org/about-primary-immunodeficiencies **6.** Mathey EK, Park SB, Hughes RA, et al. Chronic inflammatory demyelinating polyradiculoneuropathy: from pathology to phenotype. *J Neurol Neurosurg Psychiatry.* 2015;86(9):973-985. **7.** Platelet disorders: immune thrombocytopenia (ITP). NIH National Heart, Lung, and Blood Institute website. Accessed June 5, 2024. https://www.nhlbi.nih.gov/health/immune-thrombocytopenia **8.** XEMBIFY Prescribing Information. Grifols. August, 2020. **9.** Donate Plasma. Plasma Protein Therapeutics Association website. Accessed June 24, 2024. https://www.pptaglobal.org/donate#donation-process **10.** Lebing W, Remington KM, Schreiner C, Paul HI. Properties of a new intravenous immunoglobulin (IGIV-C, 10%) produced by virus inactivation with caprylate and column chromatography. *Vox Sang.* 2003;84(3):193-201. **11.** Alonso W, Vandeberg P, Lang J, et al. Immune globulin subcutaneous, human 20% solution (Xembify®), a new high concentration immunoglobulin product for subcutaneous administration. *Biologicals.* 2020;64:34-40. **12.** GAMUNEX-C Prescribing Information. Grifols. January, 2020. **13.** Sleasman JW, Lumry WR, Hussain I, et al. Immune globulin subcutaneous, human - klhw 20% for primary humoral immunodeficiency: an open-label, Phase III study. *Immunotherapy.* 2019;11(16):1371-1386. **14.** Gelfand EW. Differences between IGIV products: impact on clinical outcome. *Int Immunopharmacol.* 2006;6(4):592-599. **15.** Jolles S, Orange J, Gardulf A, et al. Current treatment options with immunoglobulin G for the individualization of care in patients with primary immunodeficiency disease. *Clin Exp Immunol.* 2015;179(2):146-160. **16.** IgNS Immunoglobulin National Society. *Immunoglobulin Therapy Standards of Practice*. Edition 3.1. Woodland Hills, CA: Ig National Society; 2023. **17.** Alberta Health Services. Home Infusion of Subcutaneous Immune Globulin (SCIG). Calgary, Alberta. **18.** Immune Deficiency Foundation. *IDF Guide for Nurses: Immunoglobulin Therapy for Primary Immunodeficiency Diseases.* 4th ed. Towson, MD: Immune Deficiency Foundation; 2016.

Please see Important Safety Information on pages 36–39 and full Prescribing Information for XEMBIFY.

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