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

SUBCUTANEOUS IMMUNOGLOBULIN (SCIG) ADMINISTRATION GUIDE

Not actual size.

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.

PIDD, primary humoral immunodeficiency disease.

GRIFOLS

Please see Important Safety Information on pages 40-41 and refer to full Prescribing Information for XEMBIFY.

TABLE OF CONTENTS

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

Please see Important Safety Information on pages 40-41 and refer to full Prescribing Information for XEMBIFY.

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

PIDD AT A GLANCE: KNOW THE SIGNS AND SYMPTOMS

Primary immunodeficiency disease is a group of more than 550 immunodeficiency disorders caused by genetic variants that affect the immune system. People with PIDD may be more susceptible to infections, especially those caused by bacteria, viruses, and fungi[1,2]

Signs and symptoms of PIDD can vary in number and severity for each patient due to the heterogeneous nature of the disease.[2,3]

Antibody deficiencies are the most common type of PIDD, accounting for more than 50% of disorders.[4]

70% to 90% of people with PIDD worldwide remain undiagnosed[2]

Time to diagnosis often takes many years. Symptoms are heterogeneous and can complicate the diagnosis.[2,5]

Patients with undiagnosed PIDD may experience increased morbidity and mortality.[6]

Living with undiagnosed PIDD adversely affects prognosis and increases patient risk for[6,7]:

CHRONIC COMPLICATIONS

MORE FREQUENT AND LONGER HOSPITAL STAYS

PSYCHOSOCIAL BURDENS

REDUCED QUALITY OF LIFE

PIDD, primary humoral immunodeficiency disease.

Please see Important Safety Information on pages 40-41 and refer to full Prescribing Information for XEMBIFY.

WHAT IS IMMUNE GLOBULIN (IG)?

IG is an antibody made by the body's immune system[8]

Plasma is the liquid part of blood that remains after blood cells are removed, and it contains many proteins, including antibodies[8,9]

Although there are 5 types of antibodies (IgG, IgM, IgD, IgA, and IgE), IG products predominantly contain IgG[8,10]

IgA, immunoglobulin A; IgD, immunoglobulin D; IgE, immunoglobulin E; IgG, immunoglobulin G; IgM, immunoglobulin M.

Please see Important Safety Information on pages 40-41 and refer to full Prescribing Information for XEMBIFY.

WHAT IS IMMUNE GLOBULIN (IG)? (cont.)

The IgG antibody is a Y-shaped molecule with antigen-binding sites at the tip of each arm of the Y[8]

Antibodies protect against infection by coating the microbes and signaling the body to destroy them[8]

IG is used to treat a spectrum of immune disorders, including PIDD[11]

IgG, immunoglobulin G; PIDD, primary humoral immunodeficiency disease.

Please see Important Safety Information on pages 40-41 and refer to full Prescribing Information for XEMBIFY.

GRIFOLS: A LEADING SOURCE OF IG

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

The plasma donation process at Grifols has several steps, each with rigorous built-in safety measures.[9]

STEP 1: CHECK-IN

Plasma donors check in at the donation center with their identification and proof of address.[9] The National Donor Deferral Registry will be checked to verify donor eligibility.[12]

STEP 2: SCREENING

Volunteer donors undergo health screening that includes their medical history, vital signs (weight, blood pressure, pulse, and temperature), and basic chemistries to ensure the health of the donor.[9]

STEP 3: PHYSICAL EXAM

Donors go through a physical exam before their first donation and once a year thereafter.[9]

IG, immune globulin.

Please see Important Safety Information on pages 40-41 and refer to full Prescribing Information for XEMBIFY.

GRIFOLS: A LEADING SOURCE OF IG (cont.)

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.[9]

STEP 5: COMPLETION

Plasma regenerates very quickly, giving volunteers the opportunity to donate twice in a 7-day period with at least 48 hours between donations. Donors are given instructions to take it easy and to drink lots of water.[9]

It takes approximately 130 plasma donations to treat 1 patient with PIDD for 1 year[9]

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.[13]

IG, immune globulin; PIDD, primary humoral immunodeficiency disease.

Please see Important Safety Information on pages 40-41 and refer to full Prescribing Information for XEMBIFY.

THE STATE-OF-THE-ART XEMBIFY MANUFACTURING PROCESS

Grifols manufactures IG using a process that can take 9 to 12 months from donation to finished product[9]

STEP 1: PLASMA DONATION TESTING

- Plasma donations are collected from healthy donors and tested for viral markers[9]
- Inventory is frozen on-site to ensure the integrity of the proteins[9]

IG, immune globulin.

Please see Important Safety Information on pages 40-41 and refer to full Prescribing Information for XEMBIFY.

THE STATE-OF-THE-ART XEMBIFY MANUFACTURING PROCESS (cont.)

STEP 2: PLASMA POOLING

- Plasma donations from healthy donors are combined into a fractionation pool[9]

STEP 3: PLASMA FRACTIONATION

- Pooled plasma is separated into various proteins that will be used to make plasma-derived therapies[9]
- XEMBIFY is purified from the fraction that has concentrated IgG[13]
- Grifols is a global leader in fractionation capacity (20 million liters of plasma/year)[9]

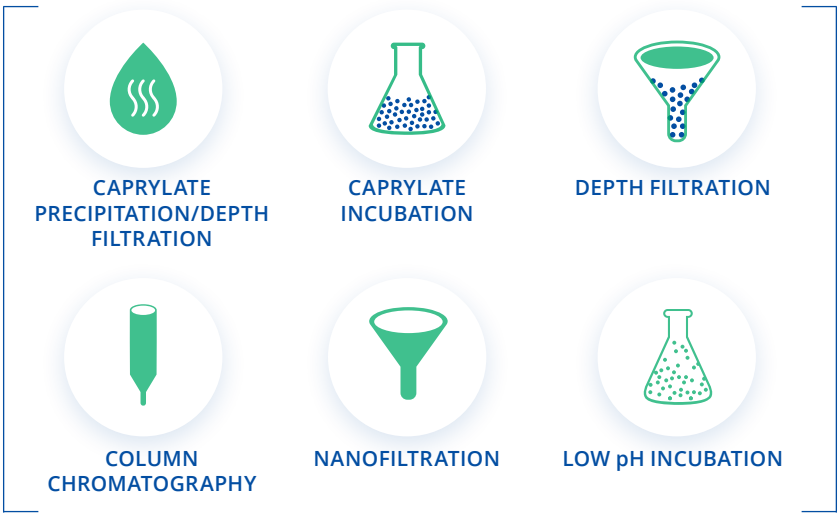
IgG, immunoglobulin G.

Please see Important Safety Information on pages 40-41 and refer to full Prescribing Information for XEMBIFY.

THE STATE-OF-THE-ART XEMBIFY MANUFACTURING PROCESS (cont.)

STEP 4: PROTEIN PURIFICATION

- XEMBIFY is purified using a unique caprylate/chromatography process[13]
- During purification, the IgG proteins remain in solution, minimizing the risk of denaturing the IgG molecules[14]
- The purification process yields a final IgG product that closely reflects the IgG subclass distribution found in normal human plasma[15]
- The process includes protein purification steps with pathogen clearance capacity, including caprylate precipitation/depth filtration, depth filtration, and column chromatography[13]
- In addition, the process includes dedicated steps with pathogen clearance capacity, including caprylate incubation, nanofiltration, and low pH incubation[13]



IgG, immunoglobulin G.

Please see Important Safety Information on pages 40-41 and refer to full Prescribing Information for XEMBIFY.

THE STATE-OF-THE-ART XEMBIFY MANUFACTURING PROCESS (cont.)

STEP 5: FORMULATION

- Formulation at low pH provides a stable IgG solution[14]
- XEMBIFY contains glycine as a stabilizer[13,15]
- The purified product is then packaged into vials. XEMBIFY is available in multiple vial sizes: 1 g, 2 g, 4 g, and 10 g[13]
- Grifols employs PediGri®—a system that provides complete traceability and easy access to all information about each batch of XEMBIFY, from plasma donation to finished product[9]

Not actual sizes.

Grifols manufactures IG using a state-of-the-art process focused on safety at every step, from donation to finished product[9]

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.[13]

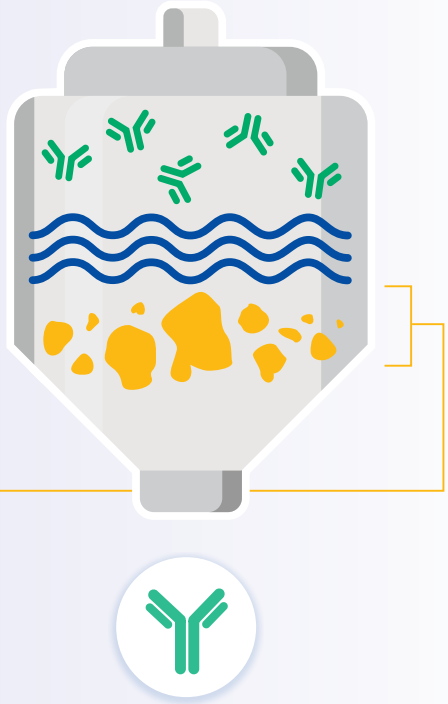
IG, immune globulin; IgG, immunoglobulin G.

Please see Important Safety Information on pages 40-41 and refer to full Prescribing Information for XEMBIFY.

THE UNIQUE MANUFACTURING PROCESS FOR XEMBIFY YIELDS ≥98% IgG PROTEIN[13,15]

CAPRYLATE PRECIPITATION AND INCUBATION

- Caprylate is added to a fractionated plasma solution
- Viruses and impurities are removed while protecting the structure and function of IgG
- **IgG is maintained in liquid phase to minimize denaturing of the protein**



ANION-EXCHANGE CHROMATOGRAPHY

- Removes non-IgG proteins
- Removes caprylate
- **Yields maximum percentage (≥98%) of IgG and maximum monomeric levels**

IgG, immunoglobulin G.

Please see Important Safety Information on pages 40-41 and refer to full Prescribing Information for XEMBIFY.

THE UNIQUE MANUFACTURING PROCESS FOR XEMBIFY YIELDS ≥98% IgG PROTEIN[13,15] (cont.)

MAXIMUM PURITY[3,13,15]

- The unique caprylate chromatography process yields a highly potent IG product with ≥ 98% purity* and proven infection protection

IG, immune globulin; IgA, immunoglobulin A; IgG, immunoglobulin G; IgM, immunoglobulin M.

*The average IgA content is ≤ 0.07 mg/mL and the average IgM content is < 0.004 mg/mL.[15]

Please see Important Safety Information on pages 40-41 and refer to full Prescribing Information for XEMBIFY.

THE UNIQUE MANUFACTURING PROCESS FOR XEMBIFY YIELDS ≥98% IgG PROTEIN[13,15] (cont.)

Grifols' consistent purification process allows a seamless transition from IVIG to SCIG[13,15]

XEMBIFY is concentrated into a 20% SCIG through ultrafiltration.

QUICK AND SUSTAINED STEADY STATE[3]

- Peak IG levels reached in an average of just 3 days
  - Reliable IgG level with an average low of 1263 mg/dL and an average high of 1358 mg/dL achieved at ~3 days with a mean IgG trough level that was 33% higher than IVIG*
- IgG concentrations consistently maintained above the commonly accepted therapeutic threshold
- No difference in pharmacokinetic profile among all age groups

IgG, immunoglobulin G; IVIG, intravenous immunoglobulin; SCIG, subcutaneous immunoglobulin.

*These levels were achieved with weekly dosing following conversion from IVIG using a dose adjustment factor of 1.37. Steady-state mean trough values for IgG were comparable for weekly and biweekly dosing.[13,16]

Please see Important Safety Information on pages 40-41 and refer to full Prescribing Information for XEMBIFY.

PRODUCT CHARACTERISTICS TO MEET A WIDE RANGE OF PATIENT NEEDS[3,10,13]

SUGAR-FREE[13]

STABILIZED WITH GLYCINE[3]

TRACE AMOUNTS OF SODIUM[10]

XEMBIFY is contraindicated in patients who have had an anaphylactic or severe systemic reaction to the administration of human IG. XEMBIFY is contraindicated in patients who are IgA deficient, have antibodies against IgA, and a history of hypersensitivity.[13]

IG, immune globulin; IgA, immunoglobulin A.

Please see Important Safety Information on pages 40-41 and refer to full Prescribing Information for XEMBIFY.

PROVEN TOLERABILITY ACROSS A WIDE RANGE OF PATIENTS[3,13]

Observed in a multicenter, open-label, phase 3 study[3]

- **0** DRUG-RELATED SERIOUS ADVERSE EVENTS
- **0** SERIOUS OR SEVERE INFUSION-SITE REACTIONS
- **<0.001** HEADACHES PER INFUSION
- **0** REPORTS OF NAUSEA OR FATIGUE

NO NOTICEABLE TOLERABILITY DIFFERENCES WERE OBSERVED ACROSS AGE GROUPS[3]

- All but one adverse event were mild or moderate*
- Results per subject: overall rate of headaches (1/49); overall rate of systemic adverse reactions (7/49)

SC, subcutaneous.

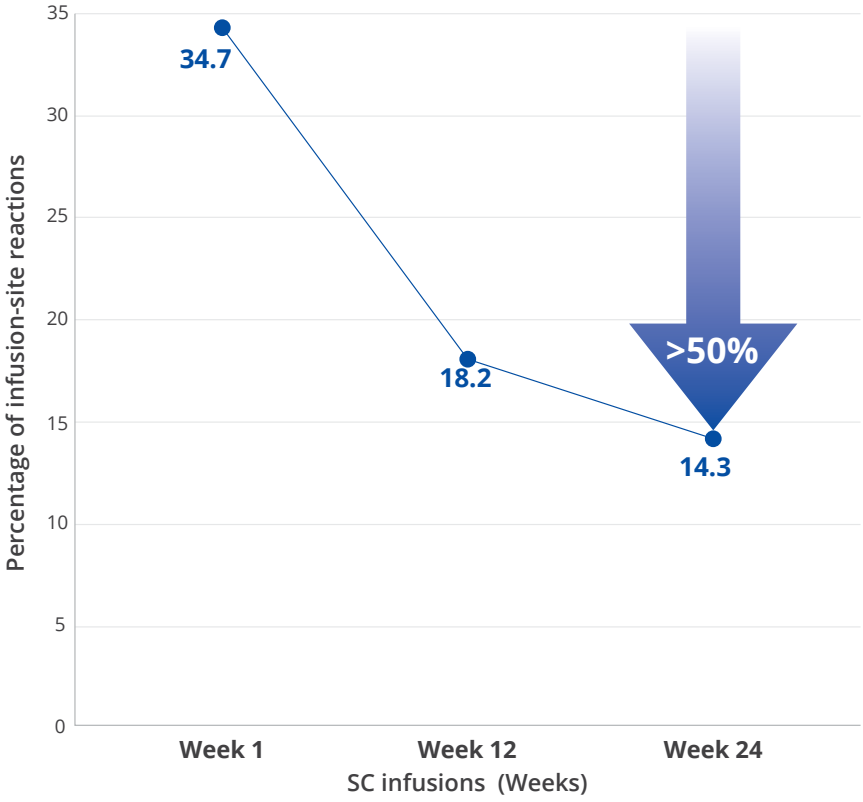
*One subject, who experienced a severe potentially related adverse event during the SC phase (on day 20), had polymyalgia rheumatica, which was considered unlikely related to study drug and resolved by day 75.[3]

Please see Important Safety Information on pages 40-41 and refer to full Prescribing Information for XEMBIFY.

MAXIMUM POTENCY AND PROVEN TOLERABILITY WITH XEMBIFY[3,13]

>50% fewer infusion-site reactions by week 24[3]

Percentage of subjects reporting infusion-site reactions



Results from an open-label, multicenter, phase 3 clinical study of patients with primary humoral immunodeficiency (N=49).[3]

Local infusion-site reactions decreased from ~34% to ~14%, from the start to the end of the 24-week SC phase, reflecting a >50% reduction.[3]

SC, subcutaneous.

Please see Important Safety Information on pages 40-41 and refer to full Prescribing Information for XEMBIFY.

MAXIMUM POTENCY AND PROVEN TOLERABILITY WITH XEMBIFY[3,13] (cont.)

Adverse reactions in ≥5% of subjects[3,13]

Adverse Reactions*	By Subject n (%) (N=49)	By Infusion n (rate)† (N=1053)
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.[13]

† Rate per infusion is calculated as the total number of adverse reactions divided by the total number of infusions.[13]

Please see Important Safety Information on pages 40-41 and refer to full Prescribing Information for XEMBIFY.

DOSING FLEXIBILITY THAT MEETS YOUR PATIENTS' NEEDS[13]

Calculating the appropriate XEMBIFY dose[13]

Treatment-Naive		Switch from IVIG		Switch from SCIG	
Loading Doses (Days 1-5)	150 mg/kg/day for 5 consecutive days	**Weekly Dosing***	Initial weekly dose of SCIG in grams = prior IVIG in grams/number of weeks between IVIG doses x 1.37	**Weekly Dosing***	Administer the same weekly dose (grams) as the weekly dose of prior SCIG treatment (grams)
Maintenance Dosing (Days 8 and beyond)	Weekly administrations of 150 mg/kg/week starting on day 8 Monitor IgG trough levels frequently every 2 weeks during first 8 weeks	**Every-2-Week Dosing**	Multiply weekly dose by 2	**Every-2-Week Dosing**	Multiply weekly dose by 2
Individualize the XEMBIFY dose based upon each patient's pharmacokinetic and clinical response					

*XEMBIFY can be administered at regular intervals from daily up to every 2 weeks.[13]

For patients switching from a weekly to every-2-weeks dose, multiply the weekly dose by 2[13]

- Children may require less total volume for a specific XEMBIFY dose (mg/kg body weight) than adults
- Children 2 to <10 years of age have a maximum infusion rate of 25 mL/hr/infusion site
- 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

IgG, immunoglobulin G; IVIG, intravenous immunoglobulin; SCIG, subcutaneous immunoglobulin.

Please see Important Safety Information on pages 40-41 and refer to full Prescribing Information for XEMBIFY.

DOSING FLEXIBILITY THAT MEETS YOUR PATIENTS' NEEDS[13] (cont.)

Customizable dosing to meet your patients' individual needs[13]

EVERY 2 WEEKS

to more frequent dosing (1 to 7 times/week)

- SCIG from the start for treatment-naive patients
- Seamless switch from IVIG or another SCIG
- Infusion rates up to 35 mL/hr/site in patients ≥10 years old
- No titration required
- Up to every-2-week dosing
- Up to 6 infusion sites

hr, hour; IVIG, intravenous immunoglobulin; SCIG, subcutaneous immunoglobulin.

Please see Important Safety Information on pages 40-41 and refer to full Prescribing Information for XEMBIFY.

CHOICE OF VIAL SIZES

XEMBIFY is available in a wide range of vial sizes[13]

Not actual sizes.

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 to 8 °C (36 to 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.[13]

Please see Important Safety Information on pages 40-41 and refer to full Prescribing Information for XEMBIFY.

FACILITATING SUCCESSFUL SCIG SELF-INFUSIONS

Facilitating self-infusions through education[17]

Educate patients and 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

SCIG, subcutaneous immunoglobulin.

Please see Important Safety Information on pages 40-41 and refer to full Prescribing Information for XEMBIFY.

FACTORS THAT INFLUENCE THE SUCCESS OF SCIG THERAPY

Managing the following factors can help ensure patient success[17]:

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

IgG, immunoglobulin G; PIDD, primary humoral immunodeficiency disease; SCIG, subcutaneous immunoglobulin.

Please see Important Safety Information on pages 40-41 and refer to full Prescribing Information for XEMBIFY.

MONITORING PATIENTS UNDERGOING INFUSIONS FOR PIDD

Some questions you could ask patients or caregivers[17]:

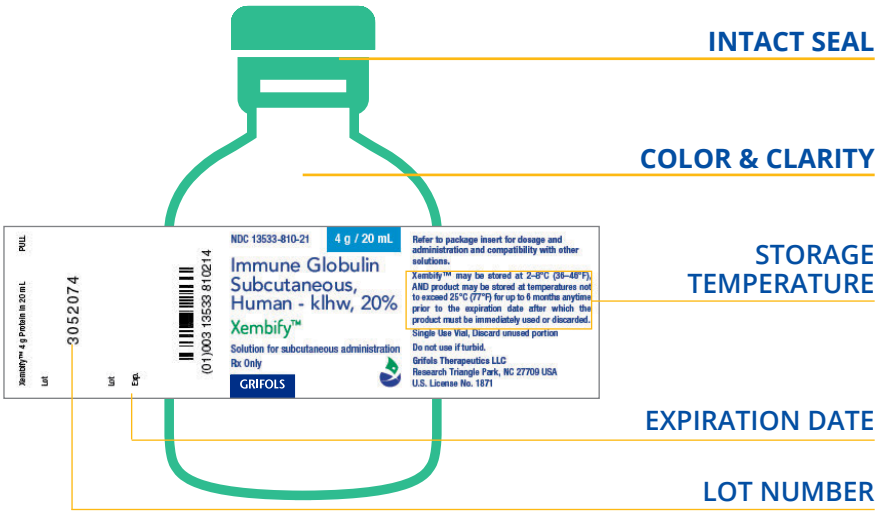
- **How is your IG treatment going so far?**
- **Have you experienced a recent cold, flu, or any symptoms of infection (eg, fever, chills)?**
- **Have you missed any infusions?**
- **Have you been sick or missed any work or school due to illness?**
- **Do you experience fatigue after your infusions?**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

IG, immune globulin; PIDD, primary humoral immunodeficiency disease.

Please see Important Safety Information on pages 40-41 and refer to full Prescribing Information for XEMBIFY.

INSPECTING XEMBIFY

Before infusion, check the product for the following[13,18]:



NEVER SHAKE IG PRODUCT

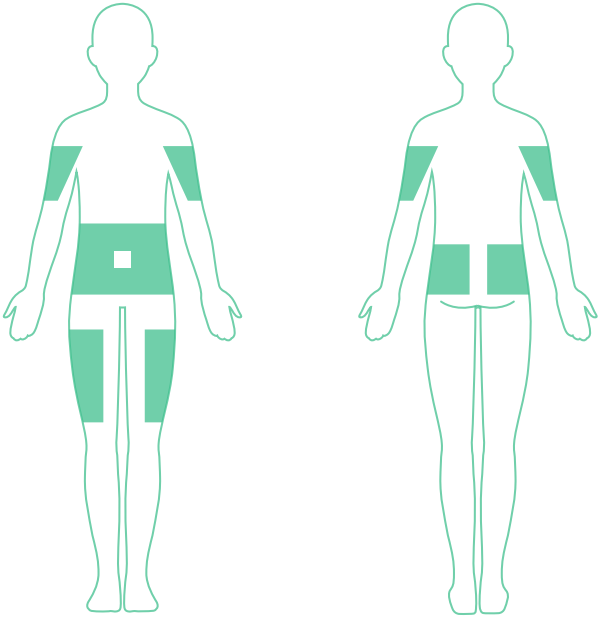
IG, immune globulin.

Please see Important Safety Information on pages 40-41 and refer to full Prescribing Information for XEMBIFY.

FACTORS TO CONSIDER WHEN SELECTING SITES FOR INFUSIONS

Site selection for adult and pediatric patients 2 years of age and older[13,18]

- Select areas with adequate subcutaneous tissue[18]
- Ensure sites are at least 2 inches apart[13]
- Rotate sites[13]
- Up to 6 sites can be used simultaneously[13]

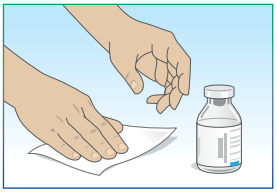


Green indicates areas for possible infusion sites.

Please see Important Safety Information on pages 40-41 and refer to full Prescribing Information for XEMBIFY.

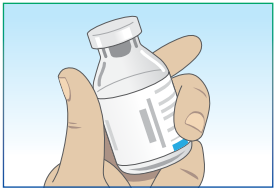
XEMBIFY SCIG INFUSION

Consider these steps for preparation of the site and administration



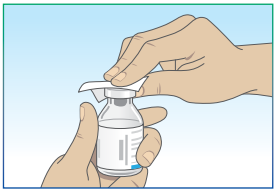
STEP 1

Disinfect surface to be used for the infusion. Allow the vial(s) of XEMBIFY to reach room temperature. Set up all the supplies you will need. Wash and dry your hands thoroughly.[13]



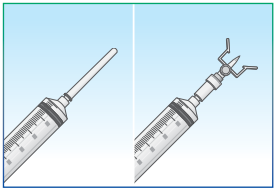
STEP 2

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. Tell your healthcare provider immediately.[13]



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.[13]



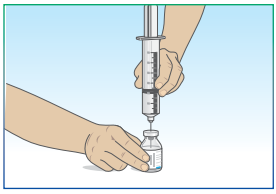
STEP 4

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.[13,19]

SCIG, subcutaneous immunoglobulin.

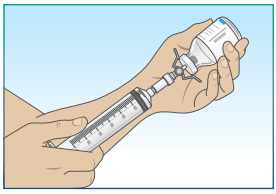
Please see Important Safety Information on pages 40-41 and refer to full Prescribing Information for XEMBIFY.

XEMBIFY SCIG INFUSION (cont.)



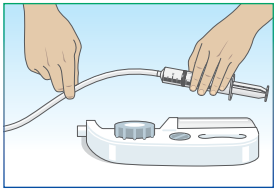
STEP 5

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. If using a needle in Step 5, skip to Step 7.[13]



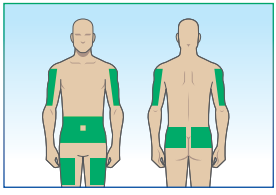
STEP 6

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.[19]



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.[13,18]

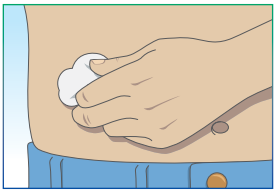


STEP 8

XEMBIFY may be 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.[13,19]

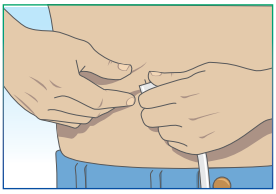
SCIG, subcutaneous immunoglobulin.

XEMBIFY SCIG INFUSION (cont.)



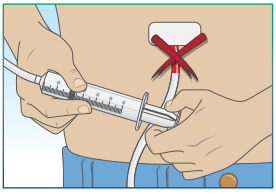
STEP 9

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.[13,18]



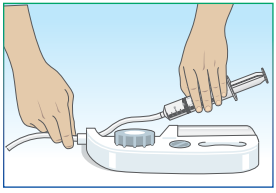
STEP 10

Grasp the skin between 2 fingers and insert the needle into the subcutaneous tissue (tissue underneath the skin).[13]



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 to 10 using a new needle, administration tubing, and infusion site. Secure needle with adhesive dressing. Repeat for other sites as needed.[13]



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.[13,18]

Scan to watch a video on how to administer XEMBIFY

xembify.com/en/hcp/dosing-administration

SCIG, subcutaneous immunoglobulin.

Please see Important Safety Information on pages 40-41 and refer to full Prescribing Information for XEMBIFY.

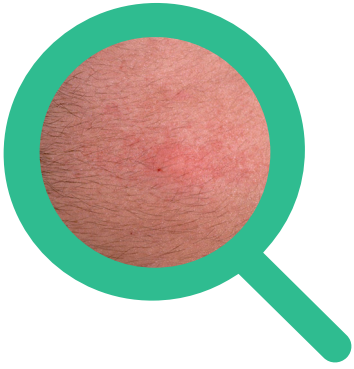
WHAT TO LOOK FOR DURING SCIG ADMINISTRATION

Check infusion sites for local adverse reactions such as erythema, discomfort, and swelling[18]

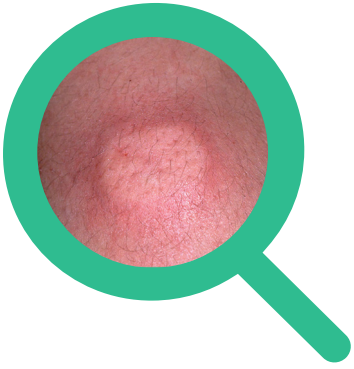
Troubleshooting infusion-site reactions

- Make sure your patient is following appropriate dry needle-insertion technique[20]
- Consider changing needle length if there is pain or leakage at the infusion site[19]
- Make sure infusion sites are 2 inches apart and 2 inches from belly button[18]
- Make sure patient is rotating sites[20]
- Monitor the amount of fluid per site[13]

Mild infusion-site reaction



Moderate infusion-site reaction

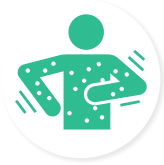


SCIG, subcutaneous immunoglobulin.

Please see Important Safety Information on pages 40-41 and refer to full Prescribing Information for XEMBIFY.

COMMON ADVERSE REACTIONS WITH SCIG INFUSIONS

Local infusion-site reactions are most common[18,20]



Local itching

POTENTIAL INTERVENTION

Apply cold compress wrapped in cloth or washcloth to site of itching. Do not apply ice directly to skin

CONSIDERATIONS FOR FUTURE INFUSIONS

Use longer needle

Decrease volume per site

Decrease volume per site and gradually increase to maximum volume

Ensure dry needle insertion

Apply topical steroid

Redness

POTENTIAL INTERVENTION

Apply cold compress. Do not apply directly to skin

CONSIDERATIONS FOR FUTURE INFUSIONS

Consider changing dressing tape

Inform patient that redness should decrease with each subsequent infusion

SCIG, subcutaneous immunoglobulin.

Please see Important Safety Information on pages 40-41 and refer to full Prescribing Information for XEMBIFY.

COMMON ADVERSE REACTIONS WITH SCIG INFUSIONS (cont.)

Local infusion-site reactions are most common[18,20]

Burning

POTENTIAL INTERVENTION

Clamp catheter for 5 to 10 minutes

Apply cold compress. Do not apply directly to skin

Remove needle and place in another site

Slow rate of infusion

CONSIDERATIONS FOR FUTURE INFUSIONS

Decrease infusion rate

Consider changing infusion volume

Consider shorter needle

Consider changing antiseptic used for skin preparation

Swelling

POTENTIAL INTERVENTION

Apply warm compress for 5 to 10 minutes (if using a heating pad, use low setting)

Try gentle massage

CONSIDERATIONS FOR FUTURE INFUSIONS

Adjust volume or consider alternate site

SCIG, subcutaneous immunoglobulin.

Please see Important Safety Information on pages 40-41 and refer to full Prescribing Information for XEMBIFY.

COMMON ADVERSE REACTIONS WITH SCIG INFUSIONS (cont.)

Local infusion-site reactions are most common[18,20]

Rash/hives

POTENTIAL INTERVENTION

Stop infusion and contact prescriber for instructions

CONSIDERATIONS FOR FUTURE INFUSIONS

Stop infusion and contact prescriber for instructions

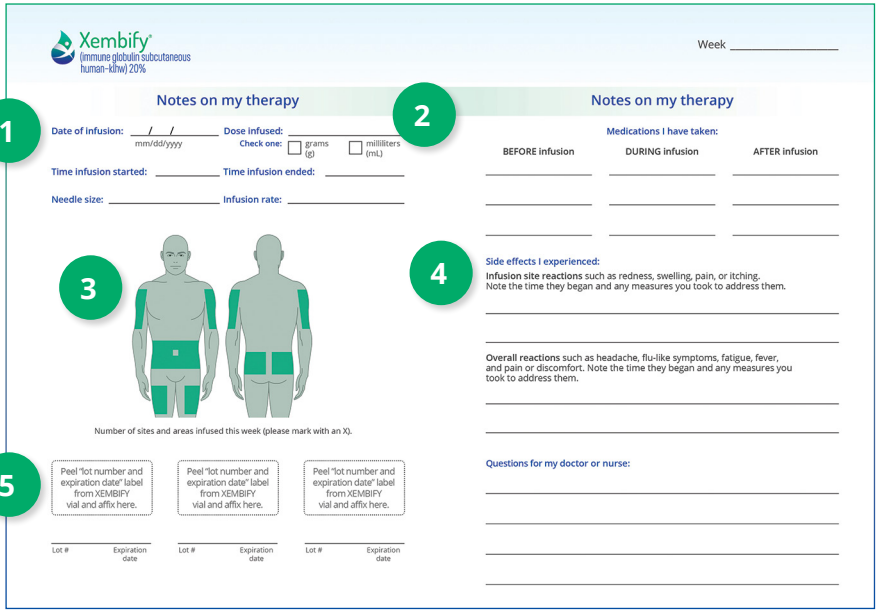
SCIG, subcutaneous immunoglobulin.

Please see Important Safety Information on pages 40-41 and refer to 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[20]



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:

Order more Infusion Log Books by calling Xembify Connexions™: 1-844-MYXEMBIFY (1-844-699-3624) Monday through Friday, 8 AM to 8 PM ET.

xembify.com/en/patients/resources-and-information

PIDD, primary humoral immunodeficiency disease; SCIG, subcutaneous immunoglobulin.

Please see Important Safety Information on pages 40-41 and refer to full Prescribing Information for XEMBIFY.

DOCUMENTING PIDD SCIG INFUSIONS (cont.)

REQUEST THAT YOUR PATIENTS RECORD THE FOLLOWING INFORMATION[13,20]:

1. Date and time the infusion started and ended
2. Exact dose that was infused
3. 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

PIDD, primary humoral immunodeficiency disease; SCIG, subcutaneous immunoglobulin.

Please see Important Safety Information on pages 40-41 and refer to full Prescribing Information for XEMBIFY.

ACCESS, SUPPORT, AND RESOURCES FOR YOUR PATIENTS

XEMBIFY CONNEXIONS™ COPAY PROGRAM*

- $0 copay for eligible patients
- Up to $10,000 copay assistance per calendar year, which covers deductibles, copayments, and coinsurance medication cost for XEMBIFY
- No monthly caps or infusion limits
- Patients should complete authorization form

ACCESS & REIMBURSEMENT SUPPORT

- Coverage criteria, coding, and billing assistance
- Prescription triage to in-network specialty pharmacy
- Copay reimbursement coordination

XEMBIFY PATIENT STARTER KIT

- A free XEMBIFY Patient Starter Kit is available for adult and pediatric patients
- Once a patient is enrolled, a Xembify Connexions case manager will coordinate with the specialty pharmacy or ship directly to the patient

*Subject to terms and conditions of the Xembify Connexions copay program. Visit **XEMBIFY.com** to read the full terms and conditions. Grifols reserves the right to rescind, revoke, or amend the program at any time without notice.

Please see Important Safety Information on pages 40-41 and refer to full Prescribing Information for XEMBIFY.

ACCESS, SUPPORT, AND RESOURCES FOR YOUR PATIENTS (cont.)

PATIENT ASSISTANCE PROGRAM (PAP)

- Financial assistance is available for eligible, uninsured patients
- Speak with a Xembify Connexions Case Manager for application support
- PAP application form required

Xembify connexions™

Xembify Connexions is a support program to provide financial and logistical assistance to ensure a smooth experience with XEMBIFY for both patients and healthcare providers

Our case managers are available Monday through Friday, 8 AM to 8 PM ET

Call 1-844-MYXEMBIFY (1-844-699-3624) or fax 1-877-375-0758

Scan to sign up your patient for XEMBIFY Connexions and receive a free Patient Starter Kit

xembify.ehipaa.com

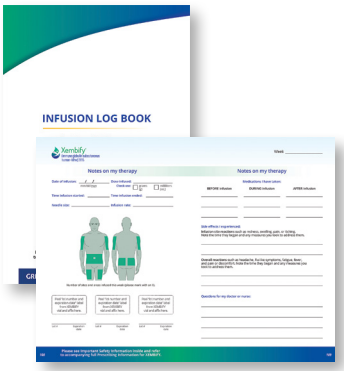
Please see Important Safety Information on pages 40-41 and refer to full Prescribing Information for XEMBIFY.

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

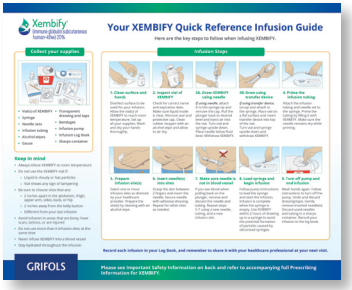
XEMBIFY PATIENT STARTER KIT

Buzzy Bee

Comfort item



Infusion Log Book

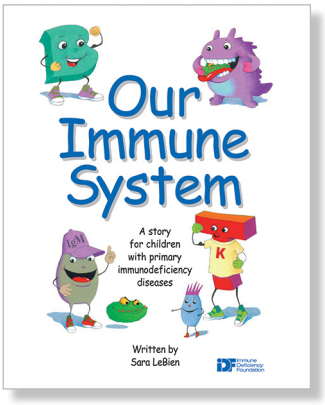


Quick Reference Guide

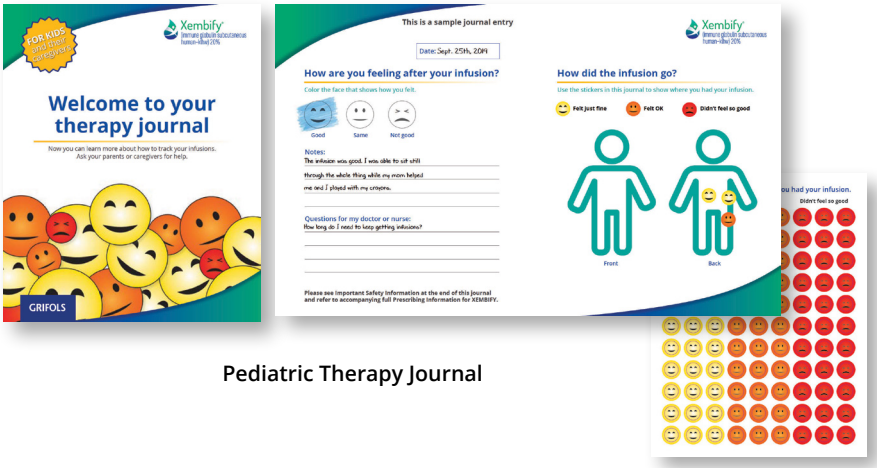
Please see Important Safety Information on pages 40-41 and refer to full Prescribing Information for XEMBIFY.

PEDIATRIC ADD-ON KIT

Comfort item



IDF Children's Book



Pediatric Therapy Journal

Please see Important Safety Information on pages 40-41 and refer to full Prescribing Information for XEMBIFY.

XEMBIFY IMPORTANT SAFETY INFORMATION

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

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, hypercoagulable conditions, history of venous or arterial thrombosis, use of 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

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.

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.

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.

Please see full Prescribing Information for XEMBIFY.

IMPORTANT SAFETY INFORMATION (cont.)

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

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.

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

Contact your local IG Nurse Educator for training on XEMBIFY administration or your Grifols sales representative for more about XEMBIFY therapy

1-844-MYXEMBIFY
(1-844-699-3624)

XEMBIFY.com

IG, immune globulin.

References: 1. Immune Deficiency Foundation. Understanding primary immunodeficiency. Immune Deficiency Foundation website. Accessed February 11, 2025. https://primaryimmune.org/understanding-primary-immunodeficiency/what-is-pi **2.** Meyts I, Bousfiha A, Duff C, et al. Primary immunodeficiencies: a decade of progress and a promising future. *Front Immunol.* 2021;11:625753. **3.** 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. **4.** Ballow M, Epland K, Heimall J, et al. *Immune Deficiency Foundation Patient & Family Handbook for Primary Immunodeficiency Diseases*. 6th ed. Immune Deficiency Foundation; 2019. **5.** Immune Deficiency Foundation. *IDF 2023 National Patient Survey*. 6th ed. Immune Deficiency Foundation; 2023. **6.** Anderson JT, Cowan J, Condino-Neto A, Levy D, Prusty S. Health-related quality of life in primary immunodeficiencies: impact of delayed diagnosis and treatment burden. *Clin Immunol.* 2022;236:108931. **7.** Rider NL, Kutac C, Hajjar J, et al. Health-related quality of life in adult patients with common variable immunodeficiency disorders and impact of treatment. *J Clin Immunol.* 2017;37(5):461-475. **8.** National Institute of Allergy and Infectious Diseases, National Cancer Institute. Understanding the immune system: how it works. US Department of Health and Human Services, National Institutes of Health; 2003. **9.** Data on file, Grifols. **10.** Siegel J. Immune globulins: therapeutic, pharmaceutical, cost, and administration considerations. *Pharmacy Practice News*. May 2023. Accessed September 16, 2024. https://www.pharmacypracticenews.com/Monographs-and-Whitepapers/Article/05-23/Immune-Globulins-Therapeutic-Pharmaceutical-Cost-and-Administration-Considerations/70243 **11.** Perez EE, Orange JS, Bonilla F, et al. Update on the use of immunoglobulin in human disease: a review of evidence. *J Allergy Clin Immunol*. 2017;139(suppl 3):S1-S46. **12.** Plasma Protein Therapeutics Association. Donate plasma. Plasma Protein Therapeutics Association website. Accessed September 16, 2024. https://www.pptaglobal.org/donate#donation-process **13.** XEMBIFY Prescribing Information. Grifols. July, 2024. **14.** 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. **15.** 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. **16.** Lumry W, Palumbo M, Hsu C, et al. Pharmacokinetics, efficacy, and safety of weekly/biweekly dosing of Xembify® in treatment-experienced patients, and loading/maintenance dosing in treatment-naive patients with primary immunodeficiency. Poster presented at: CIS 2024 Annual Meeting; May 1-4, 2024; Minneapolis, MN. **17.** 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. **18.** Immunoglobulin National Society. *Immunoglobulin Therapy: Standards of Practice*. 3.2 ed. Ig Society, Inc.; 2024. **19.** Alberta Health Services. *Home Infusion of Subcutaneous Immune Globulin (SCIG).* **20.** Immune Deficiency Foundation. *IDF Guide for Nurses: Immunoglobulin Therapy for Primary Immunodeficiency Diseases.* 4th ed. Immune Deficiency Foundation; 2016.

Please see Important Safety Information on pages 40-41 and refer to full Prescribing Information for XEMBIFY.

GRIFOLS