For the subcutaneous treatment of primary humoral immunodeficiency disease (PIDD)

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

PRODUCT HIGHLIGHTS



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 14-15 and refer to accompanying full Prescribing Information for XEMBIFY.

CHARACTERISTICS

Offers product characteristics that meet the needs of a wide range of PIDD patients



Formulated for PIDD patients ≥2 years of age, including those with risk factors

No difference observed in PK parameters or tolerability from age 2 to elderly[3]

- Prediabetes/ diabetes[4]
- Renal dysfunction[4]
- Thromboembolic risk[4]
- Cardiac impairment[4]

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.

Provides ≥98% IgG protein for maximum purity and maximum potency[5,6]



Made with a unique caprylate/chromatography process that:

- Yields maximum amounts of IgG protein*
- Maintains IgG in liquid phase
- Minimizes the risk of denaturing the IgG protein

Reliable steady-state IgG level that PIDD patients need

- Peak IgG exposure occurred at approximately 3 days
  - » The average mean IgG trough level at steady state was 1245 mg/dL with SC:IV of 1.333
- All patients maintained IgG trough level >580 mg/dL, well above the therapeutic threshold of 500 mg/dL (5 g/L)[3]

PK parameters did not significantly differ between age groups

*The average IgA content is ≤0.07 mg/mL and the average IgM content is <0.004 mg/mL.[2]

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 Important Safety Information on pages 14-15 and refer to accompanying full Prescribing Information for XEMBIFY.

TOLERABILITY

Demonstrated tolerability with mild to moderate local and systemic reactions



Overall rate of systemic adverse reactions[3]

0.007
per infusion*



Overall rate of headaches[3]

0.001
per infusion*

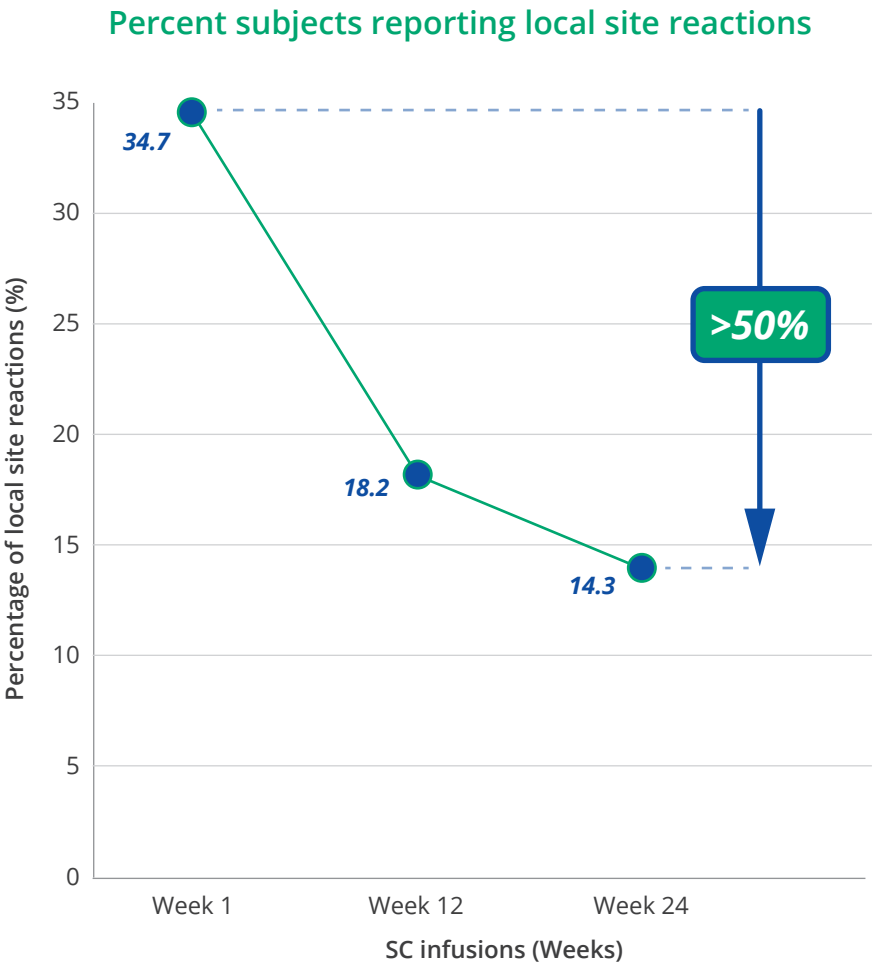
Results from an open-label, multicenter, phase 3 clinical study of patients with primary immunodeficiency (N=49).

No noticeable tolerability differences were observed between age groups[3]

- No serious or severe adverse reactions were attributed to XEMBIFY[3]
- Results per subject: overall rate of headaches (1/49); overall rate of systemic adverse reactions (7/49)[3]

*N=1053 infusions.

Local site reactions decreased by >50% over time



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

- 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]

Please see Important Safety Information on pages 14-15 and refer to accompanying full Prescribing Information for XEMBIFY.

TOLERABILITY

Proven safety and tolerability profile

Adverse reactions in ≥5% of subjects

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.

Please see Important Safety Information on pages 14-15 and refer to accompanying full Prescribing Information for XEMBIFY.



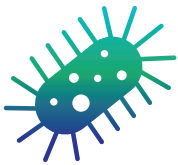
EFFICACY

Protecting a wide range of PIDD patients from infections



Serious bacterial infections[3]

Zero
per subject-year*†



Annualized rate of any infection[3]

2‡
per subject-year

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

*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).
† The threshold considered effective for preventing infections is <1 serious bacterial infection per subject-year.
‡ 2.37 (95% CI).

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.

Reducing the impact of PIDD on your patient's life



Days missed from work/school or unable to perform daily activities[3]

2* per subject-year



Hospitalizations due to infections[3]

Zero† per subject-year



Days treated with antibiotics[3]

29‡ per subject-year

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

*2.27 (95% CI).
†0.049 (95% CI).
†28.9 (95% CI).

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.

Please see Important Safety Information on pages 14-15 and refer to accompanying full Prescribing Information for XEMBIFY.

DOSING

XEMBIFY can be infused at regular intervals, from 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)[3]
- Infuse at a customizable rate up to 25 mL/h/site from the start of treatment

Convenient handling and storage

- No refrigeration needed for up to 6 months*
- Can be stored under refrigeration for up to 36 months*
- Available in 1 g, 2 g, 4 g, and 10 g single-use vials

* 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.

Customized dosing to meet your patient's needs

Example patient starting XEMBIFY treatment



Tim 40 years old | 192 lb (~87 kg)

Tim is a dad with two active kids who are on various sports teams. He was recently diagnosed with PIDD. He has a family history of cardiac disease and diabetes, and presented with risk factors for the latter. He needed an IG treatment like XEMBIFY, that fits his busy lifestyle.

Tim's customized dosing schedule*

- Dosing frequency and interval: once weekly
- Weekly XEMBIFY dose: 12 g (60 mL)†
- Number of infusion sites: 3
- Infusion rate: 20 mL/h/site
- Infusion time: 30 minutes to 1 hour, depending on regulator used

*To convert the XEMBIFY dose in grams to milliliters (mL), multiply the calculated SCIG dose in grams by 5.
†To convert IVIG dose to SCIG dose, calculate using a conversion factor of 1.37. Multiply IVIG dose (in grams) by 1.37 and divide by the number of weeks between IVIG doses.

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.

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SUPPORT

Xembify Connexions helps PIDD patients start and stay on treatment

Copay assistance

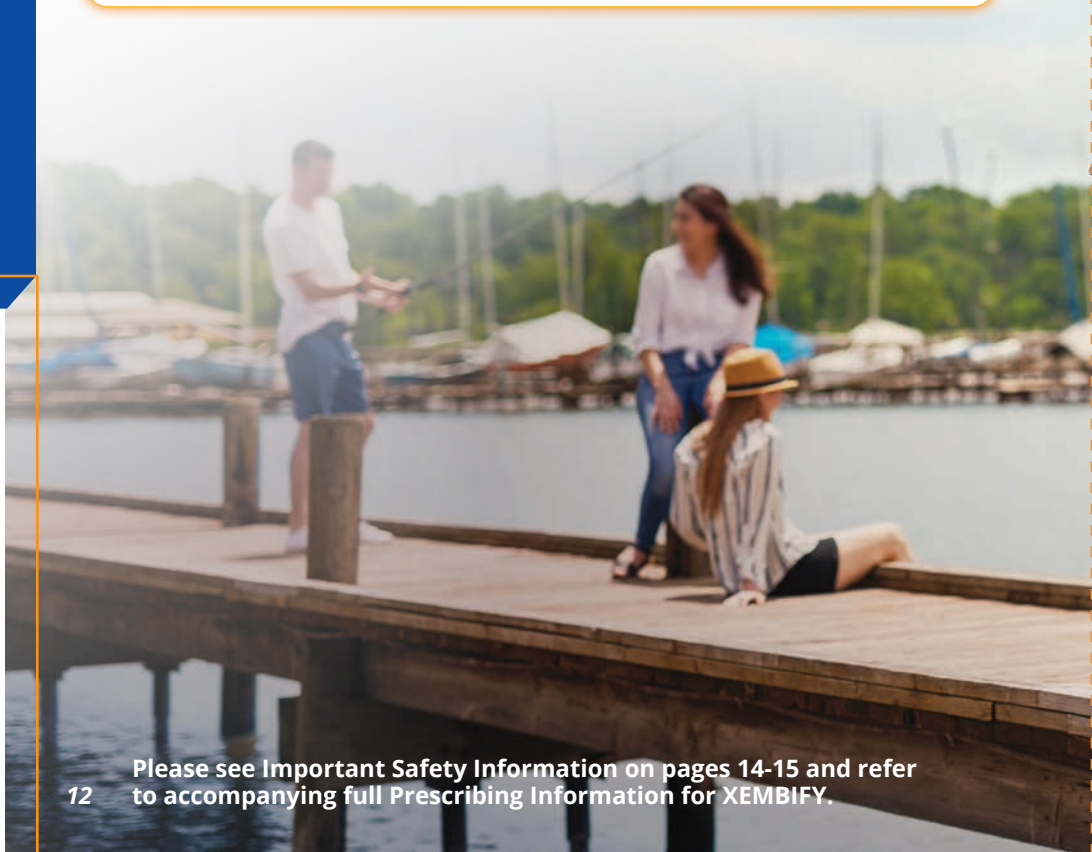
Eligible patients may save up to $5000 per calendar year, with no monthly cap, on their prescription.

Dedicated support program

Partnering with you and your PIDD patients to ensure ongoing access and continuity of care.

Access to XEMBIFY

Call Xembify Connexions at 1-844-MYXEMBIFY to access XEMBIFY through our distribution partners.



Please see Important Safety Information on pages 14-15 and refer to accompanying full Prescribing Information for XEMBIFY.

References: 1. Vandeberg P, Lang J, Alonso W. A new 20% concentration immunoglobulin for subcutaneous administration (IGSC 20%). Poster presented at: American Academy of Allergy, Asthma & Immunology; February 23, 2019; San Francisco, CA. **2.** Data on file, Grifols. **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.** Gelfand EW. Differences between IGIV products: impact on clinical outcome. *Int Immunopharmacol*. 2006;6(4):592-599. **5.** XEMBIFY® (immune globulin subcutaneous human-klhw) 20% Prescribing Information. Grifols. **6.** 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.



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.

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 accompanying full Prescribing Information for XEMBIFY.

LIFE empowered

A 20% SCIG for a wide range of PIDD patients ≥2 years of age

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

Unique caprylate/chromatography process

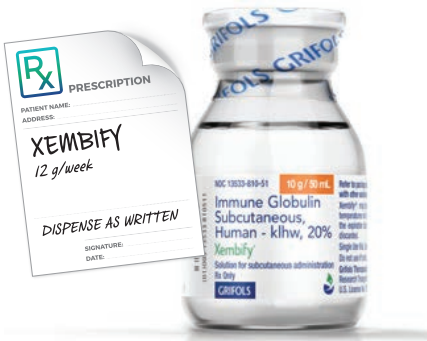
- Made with a process that minimizes the risk of denaturing the IgG protein[5,6]
- Provides ≥98% IgG protein[5,6]
- Sugar-free with trace amounts of sodium and stabilized with glycine[1,2]

Maximum purity[3]*

- All adverse events were mild or moderate with no differences between age groups
- 0.007 overall rate of systemic adverse reactions per infusion (N=1053 infusions; 7/49 subjects)
- Rate of local site reactions decreased by >50% over time

Maximum potency for infection protection[3]

- Peak IgG exposure of 1245 mg/dL achieved at ~3 days with SC:IV of 1.333
- All patients maintained IgG trough level >580 mg/dL
- No significant difference in PK parameters between age groups
- Reliable reduction in all infections, and missed days from work/school with 0 serious bacterial infections† and 0 hospitalizations‡



XEMBIFY.com

1-844-MYXEMBIFY

1-844-699-3624

*Results from an open-label, multicenter, phase 3 clinical study of patients with primary immunodeficiency (N=49).
† 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).
‡ Annualized rate of any infection, 2.37 (95% CI); annual rate of hospitalizations due to infections, 0.049 (95% CI); days missed from work/school, 2.27 (95% CI); N=49.

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.

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