THE LONGER TO DIAGNOSIS, THE MORE SEVERE THE PROGNOSIS

PIDD is a group of more than 450 hereditary immunodeficiency disorders caused by genetic defects that affect the immune system.[1,2]

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

20 YEARS
is the average number of years a person goes undiagnosed[3]

67%
of patients were not diagnosed with PIDD until ≥35 years of age[3]

44%
of patients experienced permanent functional impairment while waiting for diagnosis[4]

54%
of patients reported that the most common functional decline is lung function[4]

MOST COMMON SYMPTOMS TO CONSIDER WHEN IDENTIFYING A PATIENT WITH PIDD[5,6]:

- Recurrent, unusual, or difficult-to-treat ear infections
- Multiple courses of antibiotics or IV antibiotics to clear infections
- 2 or more new sinus infections within 1 year, in the absence of allergy
- Recurrent, deep abscesses of the skin or internal organs
- Recurrent pneumonia, ear infections, or sinusitis
- Persistent thrush or fungal infection on skin or elsewhere
- Chronic diarrhea with weight loss
- Infection with normally harmless tuberculosis-like bacteria
- Recurrent viral infections (colds, herpes, warts, condyloma)
- Swollen lymph glands or an enlarged spleen
- Autoimmune disease
- Family history of PIDD

EARLY INTERVENTION CAN ALLEVIATE THE EFFECTS OF PIDD[7]

Tests to confirm a PIDD diagnosis include blood tests to identify specific immune system abnormalities[8]:

- **Complete blood count with differential white blood cell count**
- **Quantitative serum immunoglobulin (IgG, IgA, and IgM) levels**
- **Antibody titers to protein and polysaccharide vaccines**

If these tests are inconclusive and clinical suspicion of an antibody deficiency remains, it may be appropriate to conduct further testing and/or seek a second opinion.[8]

IgA, immunoglobulin A; IgG, immunoglobulin G; IgM, immunoglobulin M.
*In patients 2 years of age and older.

PIDD AT A GLANCE: KNOW THE SIGNS AND SYMPTOMS

PIDD can affect organs throughout the body, necessitating multidisciplinary care led by an immunologist.[8-11]*

Lungs

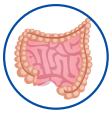
- **Lymphadenopathy**
- **Bronchiectasis**
- GLILD
- Nodules
- Interstitial lung disease
- Pulmonary granulomatous infiltrations
- X-ray-documented LIP focal pneumonias
- Recurrent bronchitis
- Chronic pneumonia

Stomach

- Helicobacter pylori

Liver/Spleen

- **Splenomegaly**
- Nodular regenerative hyperplasia
- Granulomatous hepatitis



Intestines

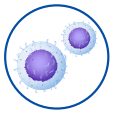
- Diarrhea
- Malabsorption
- Inflammatory bowel disease
- Nodular lymphoid hyperplasia
- Idiopathic enteropathy
- Giardia enteritis
- Salmonella
- Campylobacter jejuni

Urinary Tract

- Ureaplasma
- Mycoplasma

Ear, Nose, and Throat

- Chronic recurrent rhinosinusitis
- Sinusitis after ear tube placement
- Recurrent sinus infections
- New onset, recurrent otitis media in teens and adults
- Thrush outside of infancy
- Repeated ear tube placement



Autoimmune

- Immune thrombocytopenic purpura
- Autoimmune hemolytic anemia
- Rheumatoid arthritis
- Alopecia

*Items in **BOLD** represent signs and symptoms that may be more commonly seen.[8]

If a patient is presenting signs detailed above or total IG levels <400 mg/dL, there may be a presence of underlying PIDD[12]

GLILD, granulomatous and lymphocytic interstitial lung diseases; IG, immune globulin; LIP, lymphocytic interstitial pneumonia.

Please see Important Safety Information and full Prescribing Information for XEMBIFY.

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, 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).

References: 1. Immune Deficiency Foundation. About primary immunodeficiencies. Immune Deficiency Foundation website. https://primaryimmune.org/understanding-primary-immunodeficiency/what-is-pi. Accessed January 3, 2024. **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.** Immune Deficiency Foundation. IDF 2017 National Patient Survey: 2017. The Fourth National Survey of Patients. March 19, 2018. **4.** Orange JS, Akhter J, Seeborg FO, Boyle M, Scalchunes C, Hernandez-Trujillo V. Pulmonologist perspectives regarding diagnosis and management of primary immunodeficiency diseases. *Allergy Asthma Proc.* 2016;37(6):e162-e168. **5.** Jeffrey Modell Foundation Medical Advisory Board. 10 warning signs of primary immunodeficiency. Jeffrey Modell Foundation website. https://info4pi.org/library/educational-materials. Accessed February 27, 2024. **6.** American Academy of Allergy, Asthma & Immunology (AAAAI). AAAAI website. https://www.aaaai.org/conditions-treatments/primary-immunodeficiency-disease/primary-immunodeficiency-disease-overview. Accessed February 15, 2024. **7.** 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. **8.** Costa-Carvalho BT, Grumach AS, Franco JL, et al. Attending to warning signs of primary immunodeficiency diseases across the range of clinical practice. *J Clin Immunol*. 2014;34(1):10-22. **9.** Jeevarathnum AC, van Niekerk A, Kriel J, Green RJ. Common variable immunodeficiency disorders: What generalists should know. *Afr J Thoracic Crit Care Med*. 2021;27(3):112-116. **10.** Chapel H, Cunningham-Rundles C. Update in understanding common variable immunodeficiency disorders (CVIDs) and the management of patients with these conditions. *Br J Haematol*. 2009;145(6):709-727. **11.** McCusker C, Upton J, Warrington R. Primary immunodeficiency. *Allergy Asthma Clin Immunol*. 2018;14(Suppl 2):61. **12.** Agarwal S, Cunningham-Rundles C. Assessment and clinical interpretation of reduced IgG values. *Ann Allergy Asthma Immunol*. 2007;99(3):281-283.

Please see accompanying full Prescribing Information for XEMBIFY.

GRIFOLS

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