XEMBIFY COVERAGE AUTHORIZATION LETTERS

This resource is designed to help you and your staff draft coverage authorization letters for XEMBIFY when a health plan does not include XEMBIFY as part of its plan formulary or when you receive a denial for a XEMBIFY prescription for PIDD. A checklist is included below that may be helpful when creating each letter on behalf of your patient based on his/her medical needs. In addition, sample letters (in template format) are attached to this document and include information that plans often require when considering coverage.

Some third-party payers may require that the prescriber document a patient's medical necessity for treatment to obtain insurance coverage for XEMBIFY. The following information and template letters are provided for informational purposes only and do not guarantee coverage or reimbursement. Healthcare providers make the ultimate determination as to when to use a specific product based on clinical appropriateness for a patient. The prescriber should refer to the Important Safety Information in the full Prescribing Information when determining whether the product is medically appropriate for a patient. Third-party payment for medical products and services is affected by numerous factors, and Grifols cannot make any representation or guarantee concerning reimbursement or coverage for any service or product.

Health plan requirements may vary, so prescribers should refer to the prior authorization or coverage information specific to their patient's health plan before completing a coverage authorization letter when requesting coverage for XEMBIFY.

Providers are encouraged to contact third-party payers for specific information on their coverage policies.*
For additional support, please contact Xembify Connexions™ at 1-855-XEMBIFY.

- ☐ Include the full name of the patient, plan identification number, and date of birth
- ☐ Prescriber name, NPI number, specialty, address, phone/fax number, email, and submission date
- ☐ Provide XEMBIFY® (immune globulin subcutaneous human–klhw) characteristics including indication, IgA content, pH (after reconstitution), and half-life
- ☐ Disclose that you are familiar with the plan's policy. Clearly document the basis for the plan's denial within the letter, along with case identification number from the initial denial letter
- ☐ Provide a copy of the patient's records with the following details:
  - Severity of condition at baseline and during follow-up visits
  - The patient's history, diagnosis, and ICD-10 code(s)
  - The patient's recent history of other therapies including Ig dose and frequency (if applicable), list of any allergies, and existing comorbidities
  - The patient's current condition and symptoms including quality of life, and list of other key events such as hospitalizations, unplanned physician visits, required medications, side effects, etc
- ☐ Document prior treatments, duration, and rationale for why each treatment was discontinued
- ☐ Provide the clinical rationale for treatment with XEMBIFY; information may be found in the Prescribing Information and/or clinical peer-reviewed literature
- ☐ Include a Letter of Medical Necessity and explain options for therapy if XEMBIFY is not approved (see additional resources for examples)

*The Centers for Medicare & Medicaid Services (CMS) provides specific information of particular importance to beneficiaries receiving Part D drug benefits through a Part D plan and/or benefits through Medicare Part B Durable Medical Equipment (DME). Please visit the following link to download forms and instructions concerning Part D grievances, coverage determinations (including exceptions), and appeals processes. https://www.cms.gov/medicare/appeals-and-grievances/medprescriptdrugapplgriev/coveragedeterminationsandexceptions.html. For Medicare Part B please consult the appropriate regional DME Medicare Administrative Contractor or Medicare Advantage plan.

Sample Coverage Authorization Appeal Letter

[Date]

[Payer Name]

ATTN: [Medical Director]
[Payer Contact Name, if available]
[Payer Address]

Re: Appeal for Denial of XEMBIFY® (immune globulin subcutaneous human–klhw) 20%

Patient: [Patient First and Last Name]
Date of Birth: [MM/DD/YYYY]
Weight: [kg]
Subscriber Identification Number: [Insurance ID Number]
Subscriber Group Number: [Insurance Group Number]
Case Identification Number: [Case ID Number]
Dates of Service: [Dates]

Dear [Contact Name/Medical Director]:

I reviewed and recognize your guidelines for the responsible management of medications within the immunoglobulin drug class. I am writing to request that you reassess your recent denial of coverage for XEMBIFY® (immune globulin subcutaneous human–klhw) 20%. I understand that the reason for your denial is [insert reason verbatim from the plan's denial letter]. However, I believe that XEMBIFY [dose, frequency] is a necessary treatment for my patient. In further support of my recommendation for treatment with XEMBIFY, I have provided an overview of my patient's relevant clinical history on the following page.

Sample Coverage Authorization Appeal Letter (continued)

[In this section, list other key events such as hospitalizations, unplanned HCP visits, required medications, other treatments, and possible side effects that your patient is experiencing.]

Other Therapies	
Start date:	
Complications:	
Side effects:	
Reason(s) for discontinuation:	

Clinical Information and Recommendation
[In this section, provide a summary of your recommendation, including peer-to-peer discussions and your professional opinion of your patient's likely prognosis or disease progression without XEMBIFY treatment.]

Sincerely,

[Prescriber name and signature]
[Prescriber medical specialty]
[National Provider Identifier]
[Practice Name, address, phone/fax and email]

[Patient name and signature]

Enclosure(s)
[List enclosures which may include Prescribing Information, clinical notes/medical records, diagnostic test results, relevant peer-reviewed articles.

Sample Letter of Formulary Exception Request

[Date]

[Payer Name]

ATTN: [Medical Director]
[Payer Contact Name, if available]
[Payer Address]

Re: Formulary Exception Request Letter for XEMBIFY® (immune globulin subcutaneous human–klhw) 20%

Patient: [Patient First and Last Name]
Date of Birth: [MM/DD/YYYY]
Weight: [kg]
Subscriber Identification Number: [Insurance ID Number]
Subscriber Group Number: [Insurance Group Number]
Case Identification Number: [Case ID Number]
Dates of Service: [Dates]

Dear [Contact Name/Medical Director]:

My name is [Name], and I am [board certification and/or relationship to patient]. I am writing to request a formulary exception on behalf of [Patient's name], who is currently a member of [Name of health plan]. The request is for XEMBIFY® (immune globulin subcutaneous human–klhw) 20%. Treatment with XEMBIFY [dose and frequency] is medically appropriate and necessary for this patient who has been diagnosed with primary humoral immunodeficiency disease, [ICD-10 code]. However, XEMBIFY is not included on your plan's formulary list. I am requesting that the plan allow a formulary exception and remove any relevant NDC* blocks so that XEMBIFY can be made available to my patient as a preferred treatment.

Previous Treatments
[In this section, explain why the plan's preferred formulary agents are not appropriate for this patient. Include any previous treatments, start/stop dates, and reasons for discontinuation where applicable including any unplanned physician, urgent care, emergency department visits, or inpatient hospitalizations.]

Clinical Rationale for XEMBIFY
[In this section, provide clinical rationale for XEMBIFY including patient's medical history and diagnosis, condition, and the full Prescribing Information supporting the use of XEMBIFY, and a statement summarizing the recommended treatment plan.]

*XEMBIFY NDCs include: 13533-0810-05; 13533-0810-10; 13533-0810-20; 13533-0810-50.

Sample Letter of Formulary Exception Request (continued)

XEMBIFY® (immune globulin subcutaneous human-klhw) 20% Characteristics

Indication	Primary humoral immunodeficiency disease in patients 2 years of age and older
IgA and IgM content	IgA is 68+19 µg/mL and the average IgM content is <4 µg/mL[*]
pH (after reconstitution)	4.1 to 4.8[†]
Plasma source	US source IQPP-certified plasma from FDA-registered sites
Formulation	No sugar, trace amounts of sodium, stabilized with glycine, close to physiologic osmolality
Pathogen inactivation/removal	Caprylate precipitation/depth filtration, caprylate incubation, depth filtration, column chromatography, low pH incubation, TSE removal

[*]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.

[†]Average sample lots.

Tolerability considerations:
Comorbidities considerations:
Allergies:
Other:
Why continuation is required (if applicable):

Clinical Information and Recommendation

[In this section, provide a summary of clinical information and your recommendation, including peer-to-peer discussions and your professional opinion of the patient's likely prognosis or disease progression without treatment with XEMBIFY. Request peer-to-peer discussion if initial rejection occurs.]

Attach letter of medical necessity.

If it would be helpful, please contact me, [HCP's name], at [HCP's telephone number, email, and/or fax] for a peer-to-peer review. I would be pleased to speak to why a formulary exception for XEMBIFY is necessary for [Patient's name] treatment of primary humoral immunodeficiency disease.

Sincerely,

[Prescriber name and signature]
[Prescriber medical specialty]
[National Provider Identifier]
[Practice Name, address, phone/fax and email]

[Patient name and signature]

Enclosure(s)

[List enclosures which may include Prescribing Information, clinical notes/medical records, diagnostic test results, relevant peer-reviewed articles.]

Sample Letter of Medical Necessity

[Date]

[Payer Name]

ATTN: [Medical Director]
[Payer Contact Name, if available]
[Payer Address]

Re: Letter of Medical Necessity for XEMBIFY® (immune globulin subcutaneous human–klhw) 20%

Patient: [Patient First and Last Name]
Date of Birth: [MM/DD/YYYY]
Weight: [kg]
Subscriber Identification Number: [Insurance ID Number]
Subscriber Group Number: [Insurance Group Number]
Case Identification Number: [Case ID Number]
Dates of Service: [Dates]

Dear [Contact Name/Medical Director]:

I am writing on behalf of my patient, [Patient name], to [request prior authorization of/document medical necessity for] treatment with XEMBIFY® (immune globulin subcutaneous human–klhw) 20%. This letter provides information about my patient's medical history and diagnosis and treatment plan. On behalf of my patient, I am requesting approval for use and payment for treatment.

Patient's Clinical History
[Patient's name] is a [age]-year-old [male/female] who was diagnosed on [date] with a primary humoral immunodeficiency disease. [Patient's name] underwent [describe treatments to date to include other immune globulin replacement therapies and prophylactic antibiotics].

- [Include diagnosis along with relevant ICD-10 code and dates]
- [Past treatments] and failure of past treatments (eg, number of recurrent infections/year)
- [Unplanned physician visit(s), urgent/emergency department visit(s), or inpatient hospitalization(s) in the previous 2 years]
- [If applicable, test results that support patient diagnosis. For patients with PIDD, test results may include:]
    - ✓ Quantitative serum IgM, IgG, and IgA levels, Complement (CH50, C3, C4), CBC differential, and ESR
    - ✓ B-cell functional evaluation, quantitative IgG subclasses, natural or commonly acquired antibodies (eg, isohemagglutinins, rubella, rubeola, tetanus), T-cell–dependent antigens (tetanus), T-cell independent antigens (eg, unconjugated pneumococcal vaccine, unconjugated Haemophilus influenzae type B vaccine)

Sample Letter of Medical Necessity (continued)

- ✓ Quantification of blood T- and B-cell subpopulations by immunofluorescence assays using monoclonal Ab markers
  - » T cells: CD3, CD4, CD8, TCR alpha/beta, TCR gamma/delta
  - » B cells: CD19, CD20, CD21, Ig (mu, delta, gamma, alpha, kappa, lambda), Ig-associated molecules (alpha, beta)
- ✓ Disease-specific analysis, MHC haplotype analysis, CD40, CD40 ligand expression, genetic analyses]

- [Extenuating circumstances that would preclude alternatives to XEMBIFY]
- [Social and family information]

[**NOTE**: If the payer has a published medical policy and/or if state statue exists, include here]

Treatment Plan
XEMBIFY® (immune globulin subcutaneous human–klhw) 20% is indicated for the treatment of primary humoral immunodeficiency disease in patients 2 years of age and older. The recommended dose for [identify disease state treated, dose and frequency prescribed, and recommended duration of treatment.]

Clinical Information and Recommendation
In summary, please consider coverage of XEMBIFY on behalf of [Patient name], and approve use and subsequent payment for XEMBIFY.

If you have any further questions regarding this matter, please do not hesitate to call me, [Prescriber name] at [phone number, email, and/or fax]. Thank you for your prompt attention to this matter.

Sincerely,

[Prescriber name and signature]
[Prescriber medical specialty]
[National Provider Identifier]
[Practice Name, address, phone/fax and email]

Enclosure(s)
[List enclosures which may include Prescribing Information, clinical notes/medical records, diagnostic test results, relevant peer-reviewed articles.]

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.

GRIFOLS

 March 2024 US-XEM-2300152