**Approved Revision: Do Not Implement until 8/31/21**

# Belimumab (Benlysta®)

**NDC CODE(S)** 49401-0101-XX BENLYSTA 120MG Solution Reconstituted (GLAXO SMITH KLINE)
49401-0102-XX BENLYSTA 400MG Solution Reconstituted (GLAXO SMITH KLINE)

## DESCRIPTION

Belimumab is a human IgG1 monoclonal antibody specific for soluble human B lymphocyte stimulator protein (BLyS), a B cell survival factor. It is produced by recombinant DNA technology in a mammalian cell expression system. Belimumab does not bind to B cells directly but blocks access of soluble BLyS to its receptors on B cells. This inhibits the survival of B cells and reduces the differentiation of B cells into immunoglobulin-producing plasma cells. Treatment with belimumab leads to reductions in circulating CD19+, CD20+, naïve and activated B cells along with plasmacytoid cells and the systemic lupus erythematosus (SLE) B-cell subset.

## POLICY

- Belimumab for the treatment of the following is considered ***medically necessary*** if the medical appropriateness criteria are met. **(See Medical Appropriateness below.)**
  - Systemic Lupus Erythematosus (SLE)
  - Lupus Nephritis
- Belimumab or the treatment of other conditions/diseases, including, but not limited to, Active Central Nervous System Lupus is considered ***investigational.***

## MEDICAL APPROPRIATENESS

### INITIAL APPROVAL CRITERIA

- Patient is at least 18 years of age (unless otherwise specified); **AND**

### Universal Criteria

- Patient must not have an active infection; **AND**
- Patient has not received a live vaccine within 30 days before starting or concurrently with Benlysta; **AND**
- Will not be used in combination with voclosporin; **AND**
- Will be used in combination with standard therapy (e.g., anti-malarials, corticosteroids, non-steroidal anti-inflammatory drugs, immunosuppressives); **AND**
- Patient does not have any of the following exclusion criteria:
  - Severe active central nervous system lupus
  - Individuals who are on other biologics or IV cyclophosphamide; **AND**

### Systemic Lupus Erythematosus (SLE)

- Patient is at least 5 years of age ~~or older~~; **AND**
- Patient has a confirmed diagnosis of SLE with at least 4 diagnostic features (see list of diagnostic SLE criteria below)* one of which must include a positive autoantibody test (e.g., anti-nuclear antibody [ANA] greater than laboratory reference range and/or anti-double-stranded DNA [anti-dsDNA] greater than 2 fold the laboratory reference range if tested by ELISA); **AND**
- Patient has failed to respond adequately to at least two (2) standard therapies such as anti-malarials, corticosteroids, non-steroidal anti-inflammatory drugs, immunosuppressives (excluding intravenous cyclophosphamide); **AND**

- Patient has one of the following:
  - Safety of Estrogen in Lupus National Assessment – Systemic Lupus Erythematosus Disease Activity Index (SELENA-SLEDAI) score of 6-12
  - ≥2 British Isles Lupus Assessment Group (BILAG) B organ domain scores

**Lupus Nephritis**

- Patient has active lupus nephritis Class III, IV, or V as confirmed by renal biopsy; **AND**
- Patient has a confirmed diagnosis of SLE with at least 4 diagnostic features (see list of diagnostic SLE criteria below)* one of which must include a positive autoantibody test (e.g., anti-nuclear antibody [ANA] greater than laboratory reference range and/or anti-double-stranded DNA [anti-dsDNA] greater than 2 fold the laboratory reference range if tested by ELISA); **AND**
- Patient has failed to respond adequately to standard therapies including corticosteroids AND either cyclophosphamide or mycophenolate mofetil; **AND**
- Baseline measurement of one or more of the following: urine protein::creatinine ratio (uPCR), estimated glomerular filtration rate (eGFR), or urine protein

***Systemic Lupus Erythematosus Diagnostic Criteria**

**Patient must have at least 4 out of 11 diagnostic SLE features:**

1. Malar rash
2. Discoid rash
3. Photosensitivity
4. Oral ulcers
5. Nonerosive arthritis (involving 2 or more peripheral joints)
6. Pleuritis/Pericarditis
   - Pleuritis - history of pleuritic pain or rubbing heard by a physician or evidence of pleural effusion
   - Pericarditis - documented by electrocardiogram or rubbing heard by a physician or evidence of pericardial effusion
7. Renal disorder
   - Persistent proteinuria > 0.5 grams/day or > 3+ on urine dipstick
   - Cellular casts (red cell, hemoglobin, granular, tubular, or mixed)
8. Seizures/psychosis
9. Hematologic disorder
   - Hemolytic anemia with reticulocytosis
   - Leukopenia < 4,000/mm3 on ≥ 2 occasions
   - Lymphopenia < 1,500/mm3 on ≥ 2 occasions
   - Thrombocytopenia < 100,000/mm3 in the absence of offending drugs
10. Immunologic disorder
    - Presence of anti-Sm or antiphospholipid antibodies
    - Presence of anti-double-stranded DNA [anti-dsDNA] greater than 2 fold the laboratory reference range if tested by ELISA
11. Positive anti-nuclear antibody [ANA] greater than laboratory reference range

**RENEWAL CRITERIA**

- Patient continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in the Initial Approval Criteria**; AND**

- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: depression, suicidal thoughts, serious infections, signs or symptoms of progressive multifocal leukoencephalopathy (PML), malignancy, severe hypersensitivity reactions/anaphylaxis, serious infusion reactions, etc.; **AND**

**Systemic Lupus Erythematosus (SLE)**

- Adequate documentation of disease stability and/or improvement as indicated by one or more of the following when compared to pre-treatment baseline:
  - Improvement in the SELENA-SLEDAI score of ≥4 points; **OR**
  - No new BILAG-A organ domain score or 2 new BILAG-B organ domain scores; OR
  - No worsening (<0.30-point increase) in Physician's Global Assessment (PGA) score; OR
  - Seroconverted (negative);

**Lupus Nephritis**

- Adequate documentation of disease stability and/or improvement as indicated by one or more of the following when compared to pre-treatment baseline:
  - Urine protein:creatinine ratio (uPCR); OR
  - Estimated glomerular filtration rate (eGFR); OR
  - Urine protein

**DOSAGE/ADMINISTRATION**

| INDICATION | DOSE |
|---|---|
| Systemic Lupus Erythematosus (SLE) or Lupus Nephritis | • Loading Dose: 10 mg/kg intravenously (by a healthcare provider) every 2 weeks x 3 doses (days 1, 15 and 29)<br>• Maintenance Dose: 10 mg/kg intravenously (by a healthcare provider) every 4 weeks |

**LENGTH OF AUTHORIZATION**

Coverage will be provided for 12 months and may be renewed.

**DOSAGE LIMITS**

**Max Units (per dose and over time) [HCPCS Unit]:**

- Loading Dose (doses administered on days 1, 15 and 29):
  - 360 billable units per 29 days
- Maintenance Dose:
  - 120 billable units per 28 days

**APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS**

BlueCross BlueShield of Tennessee's Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

## IMPORTANT REMINDER

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the Medical Policy and a health plan, the express terms of the health plan will govern.

## ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

## SOURCES

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**EFFECTIVE DATE** 8/31/2021

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