Blue Cross Blue Shield Blue Care Network of Michigan

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P&T Date: 06/05/2025

Benlysta® (belimumab)

HCPCS: J0490

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

A. Coverage of the requested drug is provided when all the following are met:
   a. FDA approved indication
   b. FDA approved age
   c. Patients have tested positive for serum antibodies at 2 independent time points
   d. Patients must have active disease
   e. If the patient has lupus nephritis ONLY and no other symptoms of system lupus erythematosus (SLE):
      i. Must have active disease of the kidney confirmed on biopsy
   f. Patient does not have active central nervous system lupus
   g. Previous treatment courses of at least 12 weeks each with 2 or more of the following have been ineffective: chloroquine, hydroxychloroquine, methotrexate, azathioprine, cyclophosphamide, OR mycophenolate mofetil, unless all are contraindicated or not tolerated
   h. Patient is currently receiving and will continue to receive a stable standard of care regimen. Standard of care treatment regimen comprised of any of the following drug classes, alone or in combination:
      i. Antimalarials
      ii. Corticosteroids
      iii. Non-biologic immunosuppressants
   i. Not to be used in combination with other biologics (ex. Humira®)
   j. Trial and failure, contraindication, or intolerance to the preferred drugs as listed in BCBSM/BCN's prior authorization and step therapy documents or BCBSM/BCN's medical utilization management drug list

B. Quantity Limitations, Authorization Period and Renewal Criteria
   a. Quantity Limits: Align with FDA recommended dosing
   b. Initial Authorization Period: 6 months
   c. Renewal Authorization Period: 1 year
   d. Renewal Criteria: Clinical documentation must be provided to confirm that current criteria are met and that the medication is providing clinical benefit

***Note: Coverage and approval duration may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at http://www.cms.hhs.gov/. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Background Information:

- Benlysta is indicated for the treatment of patients aged 5 years and older with active, autoantibody-positive, systemic lupus erythematosus (SLE) who are receiving standard therapy and adult patients with active lupus nephritis who are receiving standard therapy.

- The efficacy of Benlysta has not been evaluated in patients with severe active central nervous system lupus. Severe active central nervous system lupus was defined as seizures, psychosis, organic brain syndrome, cerebrovascular accident, cerebritis, or CNS vasculitis requiring therapeutic intervention within the previous 60 days before initiation of Benlysta in the clinical trials. Use of Benlysta in patients with this condition is not recommended.

- Use of Benlysta also has not been studied in combination with other biologics and is not recommended.

- Seropositivity was defined in the clinical trials by 2 positive ANA titers (≥ 1:80) or anti-dsDNA antibodies (≥ 30 IU/mL) on different days. The 2019 EULAR/ACR classification system for SLE allow ANA levels to be used as a qualifier for SLE, however, because ANA can elevate transiently and also be a marker for other diagnoses, a second confirmatory test must be done to confirm seropositivity. While other classification systems exist to define lupus, these systems do not ensure patients are seropositive as they only have to meet a certain number of criterion for diagnosis. Those criterion may or may not include positive tests for elevated ANA or anti-dsDNA titers.

- Both the intravenous and subcutaneous formulation of Benlysta were studied in phase III, multicenter, randomized, placebo-controlled trials of patients with active, autoantibody-positive SLE. The intravenous formulations were assessed in the BLISS-76 and BLISS-52 trials and the subcutaneous formulation in the BLISS-SC trial. All trials included seropositive patients who were stable and maintained on standard therapy throughout the study. People with severe lupus nephritis or severe CNS lupus were excluded. Subjects were required to have a SELENA-SLEDAI score greater than 6 in the intravenous trials and greater than 8 in the subcutaneous trials. All studies primary endpoints were the SLE Responder Index (SRI4) response rate at week 52. The SRI4 is a composite index requiring a 4-point reduction in the SELENA–SLEDAI score, no worsening (increase from baseline) in the physician's global assessment (on a 0 – 10-cm visual analog scale), and no new British Isles Lupus Assessment Group (BILAG) A organ domain score or 2 new BILAG B organ domain scores at week 52 compared with baseline. In all studies, the Benlysta treatment arms showed statistical significance versus placebo for the primary endpoint.

- The use of Benlysta in patients with active lupus nephritis was studied in the BLISS-LN trial, a phase III, multinational, multicenter, randomized, double-blind, placebo-controlled study of 448 patients. The trial included seropositive patients who were stable and maintained on standard therapy throughout the study. Patients had biopsy proven lupus nephritis showing active lesions prior to study entry. Patients with a GFR of less than 30 ml/min/1.73 m^2 of body surface area (BSA) were excluded. The study met its primary endpoint demonstrating that a statistically significant greater number of patients achieved primary efficacy renal response (PERR) at 104 weeks when treated with Benlysta plus standard therapy compared to placebo plus standard therapy (43% vs 32%, odds ratio (95% CI) 1.55 (1.04, 2.32), p-value = 0.0311). Statistical significance compared to placebo across all four major secondary endpoints was achieved, including complete renal response and time to renal-related event or death. The safety results are consistent with the known safety profile of Benlysta.

- The 2020 EULAR guidelines recommend kidney biopsy for SLE patients showing any sign of kidney involvement including glomerular hematuria and/or cellular casts, proteinuria greater than 0.5 g/24 hours, spot urine protein-to-creatine ratio (UPCR) greater than 500 mg/g, or unexplained decrease in glomerular filtration rate. The 2003 International Society of Nephrology/Renal Pathology Society (ISN/RPS) classification still represents the gold standard for assessment of kidney biopsy in LN. Patients with class III focal lupus nephritis, class IV diffuse lupus nephritis with or without coexisting class V membranous lupus nephritis, or pure class V lupus nephritis were included in the BLISS-LN trial.

- The 2020 EULAR guidelines recommend use of hydroxychloroquine in all patients with the use of glucocorticoids to treat flares. The goal of therapy is for patients to get into remission or a state of low disease activity. If hydroxychloroquine use is still resulting in disease flare, use of immunosuppressants should be considered. The guidelines state Benlysta should be considered in patients who have failed hydroxychloroquine in combination with glucocorticoids and immunosuppressants.

References:

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<table>
<tr><th colspan="3">Policy History</th></tr>
<tr><th>#</th><th>Date</th><th>Change Description</th></tr>
<tr><td>2.4</td><td>Effective Date: 06/05/2025</td><td>Annual review of criteria was performed, no changes were made</td></tr>
<tr><td>2.3</td><td>Effective Date: 06/06/2024</td><td>Annual review of criteria was performed, no changes were made</td></tr>
<tr><td>2.2</td><td>Effective Date: 06/08/2023</td><td>Annual review of criteria was performed, no changes were made</td></tr>
<tr><td>2.1</td><td>Effective Date: 06/09/2022</td><td>Annual review of criteria was performed, no changes were made</td></tr>
<tr><td>2.0</td><td>Effective Date: 06/10/2021</td><td>Updated to remove not to be used with cyclophosphamide</td></tr>
<tr><td>1.9</td><td>Effective Date: 02/04/2021</td><td>Updated to add new indication for use in lupus nephritis</td></tr>
<tr><td>1.8</td><td>Effective Date: 06/11/2020</td><td>Updated policy to not allow use with other biologic medications and add the trial and failure of preferred products statement</td></tr>
<tr><td>1.7</td><td>Effective Date: 06/06/2019</td><td>Updated for new FDA approved age requirements</td></tr>
<tr><td>1.6</td><td>Effective Date: 02/14/2019</td><td>Annual review of criteria was performed, no changes were made</td></tr>
<tr><td>1.5</td><td>Effective Date: 02/08/2018</td><td>Added SQ formulation</td></tr>
<tr><td>1.4</td><td>Effective Date: 07/05/2017</td><td>UM medical management system update for MAPPO and BCNA
<table>
<tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr>
<tr><td>BCBS</td><td>Yes</td></tr>
<tr><td>BCN</td><td>Yes</td></tr>
<tr><td>MAPPO</td><td>Yes</td></tr>
<tr><td>BCNA</td><td>Yes</td></tr>
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<tr><td>1.3</td><td>Effective Date: 05/04/2017</td><td>Updated Medicare disclaimer</td></tr>
<tr><td>1.2</td><td>Effective Date: 08/11/2016</td><td>Annual review of criteria was performed, no changes were made</td></tr>
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<tr><td>1.1</td><td>Effective Date: 01/22/2013</td><td>UM medical management system update for BCBSM and BCN
<table><tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr><tr><td>BCBS</td><td>Yes</td></tr><tr><td>BCN</td><td>Yes</td></tr><tr><td>MAPPO</td><td>No</td></tr><tr><td>BCNA</td><td>No</td></tr></table></td></tr>
<tr><td>1.0</td><td>Effective Date: 05/10/2012</td><td>New Policy</td></tr>
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** The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or http://dailymed.nlm.nih.gov/dailymed/index.cfm*