Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope
Benlysta (belimumab)	MP-RX-FP-11-23	☒ MMM MA ☒ MMM Multihealth

Service Category

☐ Anesthesia
☐ Surgery
☐ Radiology Procedures
☐ Pathology and Laboratory Procedures
☐ Medicine Services and Procedures
☐ Evaluation and Management Services
☐ DME/Prosthetics or Supplies
☒ Part B Drugs

Service Description

This document addresses the use of Benlysta (belimumab) , a drug approved by the Food and Drug Administration (FDA) for the treatment of active, antibody-positive systemic lupus erythematosus (SLE) and active lupus nephritis, as add-on treatment to standard therapy, such as corticosteroids, antimalarials, and/or immunosuppressants.

Background Information

Benlysta is an IV or SC administered human monoclonal antibody drug that specifically recognizes and inhibits the biological activity of B-lymphocyte stimulator, also known as B cell activation. Only the IV formulation of Benlysta was studied and approved in the pediatric population. Dosing between the IV and SC products differs in adult patients.

The American College of Rheumatology (ACR) uses the ACR classification criteria to diagnose an individual with SLE. The ACR requires 4 of these 11 criteria simultaneously or in succession for an individual to be classified as having SLE: malar rash, discoid rash, photosensitivity, oral ulcers, arthritis, serositis, renal disorders, neurological disorder, hematological disorder, immunological disorder, and anti-nuclear antibody.

The SELENA-SLEDAI (Safety of Estrogens in Systemic Lupus Erythematosus National Assessment -- Systemic Lupus Erythematosus Disease Activity Index) is a system used to evaluate the activity of lupus in clinical studies. This system is used for quantification of lupus disease, primarily for the purpose of determining whether a new drug evaluated for the disease is effective. The SELENA-SLEDAI is a slightly modified version of the SLEDAI and was developed by the NIH. It is a weighted index in which signs and symptoms, laboratory tests, and physician's assessment for each of nine organ systems are given a weighted score and summed up if present at the time of the visit or in the preceding 10 days. The maximum theoretical score for the SELENA-SEDAI is 105 (all 24 descriptors present simultaneously) with 0 indicating inactive disease.

Lupus nephritis (LN), or kidney inflammation, is one of the most common and serious complications of systemic lupus erythematosus (SLE), an autoimmune disease which causes widespread inflammation and tissue damage. If poorly controlled, LN may lead to irreversible kidney damage and the eventual need for dialysis or kidney transplant. BLISS (Belimumab in Subjects with SLE) study groups included adult patients with a diagnosis of SLE according the ACR, active disease with SELENA-SLEDAI score greater than or equal to 6, and

Policy Name	Policy Number	Scope
Benlysta (belimumab)	MP-RX-FP-11-23	☒ MMM MA ☒ MMM Multihealth

anti-nuclear antibody (ANA) greater than or equal to 1:80 and/or anti-dsDNA greater than or equal to 30 IU/mL.

BLISS-LN study groups included adult patients with SLE and active lupus nephritis (class III, IV, or V) confirmed by renal biopsy. In both studies, Benlysta was added to standard therapy for treatment.

Approved Indications

A. Active, antibody-positive systemic lupus erythematosus (SLE)
B. Active lupus nephritis

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS	Description
J0490	Injection, belimumab, 10 mg [Benlysta]

ICD-10	Description
M32.10-M32.9	Systemic lupus erythematosus (SLE)

Medical Necessity Guidelines

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Benlysta (belimumab)

A. Criteria For Initial Approval

Initial requests for intravenous Benlysta (belimumab) may be approved if the following criteria are met:

I. Individual has a diagnosis of Systemic Lupus Erythematosus per the American College of Rheumatology (ACR); **AND**
A. Documentation is provided that disease is active and documented by a SELENA-SLEDAI score greater than or equal to 6 while on current treatment regimen for SLE; **AND**
B. Documentation is provided that individual has a positive anti-nuclear antibody (ANA) titer greater than or equal to 1:80 or anti-dsDNA greater than or equal to 30 IU/mL; **AND**
C. Individual's SLE disease remains active while on corticosteroids, antimalarials, or immunosuppressants (alone or as combination therapy) for at least the last 30 days; **AND**
D. Individual is using in combination with standard therapy (for example, corticosteroids, antimalarials, and/or immunosuppressants [but not other biologics or IV cyclophosphamide]).

OR

II. Individual has a diagnosis of active Lupus Nephritis; **AND**
A. Documentation is provided that individual has autoantibody-positive SLE (anti-nuclear antibody (ANA) titer greater than or equal to 1:80 or anti-dsDNA greater than or equal to 30 IU/mL); **AND**
B. Individual has Class III, IV, or V lupus nephritis showing active or chronic lesions, and confirmed by renal biopsy; **AND**
C. Documentation is provided that individual has a urinary protein to creatinine ratio of greater than or equal to 1; **AND**
D. Individual did not have disease progression to lupus nephritis while on Benlysta therapy for SLE without LN; **AND**
E. Individual's disease remains active while on corticosteroids, antimalarials, or immunosuppressants (alone or as combination therapy) for at least the last 30 days; **AND**
F. Individual is using in combination with standard therapy (for example, corticosteroids, antimalarials, and/or immunosuppressants [but not other biologics or IV cyclophosphamide]).

Initial requests for subcutaneous Benlysta (belimumab) may be approved if the following criteria are met:
I. Individual is 18 years of age or older, and has a diagnosis of Systemic Lupus Erythematosus per the American College of Rheumatology (ACR); AND
A. Documentation is provided that disease is active and documented by a SELENA-SLEDAI score greater than or equal to 6 while on current treatment regimen for SLE; AND

Medical Policy

Healthcare Services Department

Policy Name	Policy Number	Scope
Benlysta (belimumab)	MP-RX-FP-11-23	☒ MMM MA ☒ MMM Multihealth

Initial requests for intravenous Benlysta (belimumab) may be approved if the following criteria are met:

I. Individual has a diagnosis of Systemic Lupus Erythematosus per the American College of Rheumatology (ACR); AND
A. Documentation is provided that disease is active and documented by a SELENA-SLEDAI score greater than or equal to 6 while on current treatment regimen for SLE; AND
B. Documentation is provided that individual has a positive anti-nuclear antibody (ANA) titer greater than or equal to 1:80 or anti-dsDNA greater than or equal to 30 IU/mL; AND
C. Individual's SLE disease remains active while on corticosteroids, antimalarials, or immunosuppressants (alone or as combination therapy) for at least the last 30 days; AND
D. Individual is using in combination with standard therapy (for example, corticosteroids, antimalarials, and/or immunosuppressants [but not other biologics or IV cyclophosphamide]).

OR
II. Individual has a diagnosis of active Lupus Nephritis; AND
A. Documentation is provided that individual has autoantibody-positive SLE (anti-nuclear antibody (ANA) titer greater than or equal to 1:80 or anti-dsDNA greater than or equal to 30 IU/mL); AND
B. Individual has Class III, IV, or V lupus nephritis showing active or chronic lesions, and confirmed by renal biopsy; AND
C. Documentation is provided that individual has a urinary protein to creatinine ratio of greater than or equal to 1; AND
D. Individual did not have disease progression to lupus nephritis while on Benlysta therapy for SLE without LN; AND
E. Individual's disease remains active while on corticosteroids, antimalarials, or immunosuppressants (alone or as combination therapy) for at least the last 30 days; AND
F. Individual is using in combination with standard therapy (for example, corticosteroids, antimalarials, and/or immunosuppressants [but not other biologics or IV cyclophosphamide]).

Initial requests for subcutaneous Benlysta (belimumab) may be approved if the following criteria are met:
I. Individual is 18 years of age or older, and has a diagnosis of Systemic Lupus Erythematosus per the American College of Rheumatology (ACR); AND
A. Documentation is provided that disease is active and documented by a SELENA-SLEDAI score greater than or equal to 6 while on current treatment regimen for SLE; AND
B. Documentation is provided that individual has a positive anti-nuclear antibody (ANA) titer greater than or equal to 1:80 or anti-dsDNA greater than or equal to 30 IU/mL; AND
C. Individual's SLE disease remains active while on corticosteroids, antimalarials, or immunosuppressants (alone or as combination therapy) for at least the last 30 days; AND
D. Individual is using in combination with standard therapy (for example, corticosteroids, antimalarials, and/or immunosuppressants [but not other biologics or IV cyclophosphamide]);

OR
II. Individual is 18 years of age or older, and has a diagnosis of active Lupus Nephritis (LN); AND

Policy Name	Policy Number	Scope
Benlysta (belimumab)	MP-RX-FP-11-23	☒ MMM MA ☒ MMM Multihealth

A. Documentation is provided that individual has autoantibody-positive SLE (anti-nuclear antibody (ANA) titer greater than or equal to 1:80 or anti-dsDNA greater than or equal to 30 IU/mL); AND
B. Individual has Class III, IV, or V lupus nephritis showing active or chronic lesions, and confirmed by renal biopsy; AND
C. Documentation is provided that individual has a urinary protein to creatinine ratio of greater than or equal to 1; AND
D. Individual did not have disease progression to lupus nephritis while on Benlysta therapy for SLE without LN; AND
E. Individual's disease remains active while on corticosteroids, antimalarials, or immunosuppressants (alone or as combination therapy) for at least the last 30 days; AND
F. Individual is using in combination with standard therapy (for example, corticosteroids, antimalarials, and/or immunosuppressants [but not other biologics or IV cyclophosphamide]).

B. Criteria For Continuation of Therapy:

I. Documentation is provided for previous improvement in disease activity following treatment with Benlysta (belimumab) indicating a therapeutic response, including lack of disease progression to lupus nephritis while on Benlysta if initially only using for SLE without LN; AND
II. Individual has no evidence of active central nervous system lupus (such as psychosis or seizures); AND
III. Individual is using in combination with standard therapy (for example, corticosteroids, antimalarials, and/or immunosuppressants [but not other biologics or IV cyclophosphamide]).

Continuation of therapy with Benlysta (belimumab IV or subcutaneous) may be approved if all of the following criteria are met:

I. Documentation is provided for previous improvement in disease activity following treatment with Benlysta (belimumab) indicating a therapeutic response, including lack of disease progression to lupus nephritis while on Benlysta if initially only using for SLE without LN; **AND**
II. Individual has no evidence of active central nervous system lupus (such as psychosis or seizures); **AND**
III. Individual is using in combination with standard therapy (for example, corticosteroids, antimalarials, and/or immunosuppressants [but not other biologics or IV cyclophosphamide]).

Benlysta (belimumab IV or subcutaneous) may not be approved for the following:

I. Individual has evidence of active central nervous system lupus (such as psychosis or seizures); **OR**
II. Individual is using in combination with IV cyclophosphamide (excluding cyclophosphamide use for induction therapy), voclosporin (Lupkynis), or intravenous immunoglobulin; **OR**
III. Individual is using in combination with another biologic, including rituximab or any other B cell targeted therapy, and anifrolumab-fnia (Saphnelo); **OR**
IV. Individual has required treatment for an acute or chronic infection within the past 60 days (NCT00424476, NCT00410384); **OR**
V. Individual has human immunodeficiency virus (HIV) infection, hepatitis B virus infection, or hepatitis C virus infection (NCT00424476, NCT00410384).

Policy Name	Policy Number	Scope
Benlysta (belimumab)	MP-RX-FP-11-23	☒ MMM MA ☒ MMM Multihealth

C. Authorization Duration

i. Approval Duration:

a. Initial Approval Duration: 6 months

b. Reauthorization Approval Duration: 1 year

Limits or Restrictions

A. Quantity Limitations

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. The chart below includes dosing recommendations as per the FDA-approved prescribing information.

Drug	Limit
Benlysta (belimumab) 200 mg/ml prefilled autoinjector or syringe for subcutaneous use** Benlysta (belimumab) 120 mg, 400 mg vial for intravenous (IV) infusion*	4 injections per 28 days 10 mg/kg every 4 weeks
Exceptions	
*Initiation of therapy of Benlysta vials for IV infusion, may approve 10mg/kg dosing at 2 week intervals for the first 3 doses. ** Initiation of therapy of subcutaneous Benlysta for active lupus nephritis, for individuals not transitioning from Benlysta IV, may approve 4 additional injections for the first 4 doses (i.e., 8 injections for the first 28 days).	

Reference Information

1. American College of Rheumatology (ACR). Guidelines for referral and management of systemic lupus erythematosus in adults. Arthritis & Rheumatism. 1999; 42(9): 1785-1796.

2. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.: 2022. URL: http://www.clinicalpharmacology.com. Updated periodically.

3. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Accessed: July 13, 2022.

4. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.

5. Furie R, Petri M, Zamani O, et al. BLISS-76 Study Group. A phase III, randomized, placebo-controlled study of belimumab, a monoclonal antibody that inhibits B lymphocyte stimulator, in patients with systemic lupus erythematosus. Arthritis Rheum. 2011 Dec;63(12):3918-30. doi: 10.1002/art.30613.

6. Furie R, Rovin BH, Houssiau F, Malvar A, Teng YKO, Contreras G, Amoura Z, Yu X, Mok CC, Santiago MB, Saxena A, Green Y, Ji B, Kleoudis C, Burriss SW, Barnett C, Roth DA. Two-Year, Randomized, Controlled Trial of

Policy Name	Policy Number	Scope
Benlysta (belimumab)	MP-RX-FP-11-23	☒ MMM MA ☒ MMM Multihealth

Belimumab in Lupus Nephritis. N Engl J Med. 2020 Sep 17;383(12):1117-1128. doi: 10.1056/NEJMoa2001180.
7. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2022; Updated periodically.
8. Navarra SV, Guzman RM, Gallacher AE, et al. BLISS-52 Study Group. Efficacy and safety of belimumab in patients with active systemic lupus erythematosus: a randomized, placebo-controlled, phase 3 trial. Lancet. 2011; 377(9767):721-731.
9. NCT00410384. U.S. National Library of Medicine, ClinicalTrials.gov website. https://clinicaltrials.gov/ct2/show/NCT00410384?term=nct+00410384&rank=1.
10. NCT00424476. U.S. National Library of Medicine, ClinicalTrials.gov website. https://clinicaltrials.gov/ct2/show/NCT00424476?term=nct+00424476&rank=1.
11. NCT01649765. U.S. National Library of Medicine, ClinicalTrials.gov website. https://clinicaltrials.gov/ct2/show/NCT01649765?term=nct+01649765&rank=1.
12. Centers for Medicare and Medicaid Services (CMS). Local Coverage Article (A52571): Self-Administered Drug Exclusion List. Retrieved from Article - Self-Administered Drug Exclusion List: (A52571) (cms.gov).

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.

Policy History

Revision Type	Summary of Changes	P&T Approval Date	MPCC Approval Date
Policy Inception	Elevance Health's Medical Policy adoption.	N/A	11/30/2023