Medical Drug Clinical Criteria

Subject:	Benlysta (belimumab)		
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Overview

This document addresses the use of Benlysta (belimumab) 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. 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.

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 anti-nuclear antibody (ANA) greater than or equal to 1:80 and/or anti-dsDNA greater than or equal to 30 IU/mL. Benlysta for SLE was also studied in pediatrics (5 to 17 years of age) in the PLUTO trial. Individuals had active disease with SELENA-SLEDAI score greater than or equal to 6, and positive ANA results. 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. Use of IV Benlysta for lupus nephritis in the pediatric population is based on extrapolation of efficacy from the adult study and supported by pharmacokinetic data. Safety and efficacy of subcutaneous Benlysta for lupus nephritis in the pediatric population has not been established. Additionally, of the subcutaneous devices for SLE, only the autoinjector has been studied in pediatrics, and not the prefilled syringe.

Clinical Criteria

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.

Benlysta (belimumab)

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

I. Individual is 5 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 as shown 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's diagnosis has been verified by history of 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 5 years of age of older, and has a diagnosis of active Lupus Nephritis; **AND**
A. Individual has Class III, IV, or V lupus nephritis showing active or chronic lesions, and confirmed by renal biopsy; **AND**
B. Documentation is provided that individual has a urinary protein to creatinine ratio of greater than or equal to 1; **AND**
C. Individual did not have disease progression to lupus nephritis while on Benlysta therapy for SLE without LN; **AND**
D. Individual's disease remains active while on corticosteroids, antimalarials, or immunosuppressants (alone or as combination therapy) for at least the last 30 days; **AND**
E. 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 as shown 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's diagnosis has been verified by history of 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**

A. Individual has Class III, IV, or V lupus nephritis showing active or chronic lesions, and confirmed by renal biopsy; **AND**
B. Documentation is provided that individual has a urinary protein to creatinine ratio of greater than or equal to 1; **AND**
C. Individual did not have disease progression to lupus nephritis while on Benlysta therapy for SLE without LN; **AND**
D. Individual's disease remains active while on corticosteroids, antimalarials, or immunosuppressants (alone or as combination therapy) for at least the last 30 days; **AND**
E. 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).

Approval Duration:
Initial requests: 6 months
Continuation requests: 1 year

Quantity Limits

Benlysta (belimumab) Quantity Limits

Drug	Body Weight	Limit	Program
Benlysta (belimumab) 120 mg, 400 mg vial for intravenous (IV) infusion*	N/A	10 mg/kg every 4 weeks	Dosing Limit
Benlysta (belimumab) 200 mg/ml prefilled syringe or autoinjector for subcutaneous use	15 kg to less than 40 kg	2 injections per 28 days	Dosing Limit
	40 kg and above	4 injections per 28 days**	Quantity Limit
Override Criteria			
*Initiation of therapy of Benlysta vials for IV infusion, may approve 10 mg/kg dosing at 2 week intervals for the first 3 doses. **Initiation of therapy of subcutaneous Benlysta for active lupus nephritis for adults not transitioning from Benlysta IV, may approve 4 additional injections for the first 4 doses (i.e., 8 injections for the first 28 days).			

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS

J0490	Injection, belimumab, 10 mg [Benlysta]

ICD-10 Diagnosis

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

Document History

Revised: 08/16/2024
Document History:

- 08/16/2024 – Annual Review: Update criteria to expand minimum age for subcutaneous agent for SLE to allow for pediatric use per label. Update quantity limits. Clarify diagnosis requirements for SLE. Wording and formatting changes. Coding Reviewed: No changes.
- 08/18/2023 – Annual Review: Update criteria for lupus nephritis to remove ANA/anti-dsDNA requirement. Wording and formatting updates. Coding Reviewed: No changes.
- 08/19/2022 – Annual Review: Update non-approvable to clarify concomitant use with immunoglobulins and rituximab. Update non-approvable criteria to restrict use with Saphnelo for consistency with Saphnelo criteria. Wording and formatting updates. Coding reviewed: No changes.
- 09/13/2021 – Annual Review: Update criteria for LN to clarify use and administration of SC formulation. Update quantity limit override to clarify use in LN when transitioning from IV formulation. Coding reviewed: No changes.
- 08/01/2021 – Administrative update to add documentation.
- 02/19/2021 – Select Review: Update criteria to add indication for active lupus nephritis per label, and remove previous restriction. Update and reformat criteria to separate out use of subcutaneous agent. Update non-approvable criteria to remove restriction with high-dose steroids and clarify use with cyclophosphamide. Update SLE criteria to require use with standard therapy per label. Update continuation criteria to restrict use with disease progression for previous Benlysta users. Update non-approvable criteria to restrict use with biologics. Update quantity limits to allow override for subcutaneous agent during initiation period for lupus nephritis. Wording and formatting changes. Coding Reviewed: Added M32.10, removed M32.0.
- 09/14/2020 – Annual Review: Clarify use in severe lupus nephritis (i.e., severe renal disease caused by SLE). Coding reviewed: No changes.
- 09/23/2019 – Administrative update to add drug specific quantity limit.
- 08/16/2019 – Annual Review: Add new FDA approved indication for use in pediatrics. Wording and formatting changes to include references.
- 08/17/2018 – Annual Review: Initial review of CG-DRUG-84. No changes.

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13. NCT01649765. U.S. National Library of Medicine, ClinicalTrials.gov website. https://clinicaltrials.gov/ct2/show/NCT01649765?term=nct+01649765&rank=1.

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.