Pharmacy Policy Bulletin: J-0612 Benlysta (belimumab) – Commercial and Healthcare Reform	
Number: J-0612	**Category:** Prior Authorization
Line(s) of Business: ☒ Commercial ☒ Healthcare Reform ☐ Medicare	**Benefit(s):** **Commercial:** **Prior Authorization (1.):** **1.** Miscellaneous Specialty Injectable = Yes w/ Prior Authorization **Quantity Limits (1., 2., 3., or 4.):** **1.** Rx Mgmt Quantity Limits = Safety/Specialty **2.** Rx Mgmt Quantity Limits = Safety/Specialty + Dose Opt **3.** Rx Mgmt Quantity Limits = Safety/Specialty + Dose Opt + Watchful **4.** Rx Mgmt Performance = MRxC = Yes **Healthcare Reform**: Not Applicable
Region(s): ☒ All ☐ Delaware ☐ New York ☐ Pennsylvania ☐ West Virginia	**Additional Restriction(s):** None
Version: J-0612-015	**Original Date:** 08/09/2017
Effective Date: 04/24/2025	**Review Date:** 01/29/2025

Drugs Product(s):	• Benlysta (belimumab) subcutaneous
FDA-Approved Indication(s):	• Treatment of patients 5 years of age and older with active systemic lupus erythematosus (SLE) who are receiving standard therapy • Treatment of adult patients with active lupus nephritis (LN) who are receiving standard therapy

Background:	• Benlysta is a human monoclonal antibody that recognizes and blocks the biological activity of B-lymphocyte stimulator (BLyS). Elevated levels of BLyS prolong the survival of B lymphocytes (B cells), which can contribute to the production of autoantibodies. Studies have shown that Benlysta can reduce autoantibody levels and help control autoimmune disease activity. • Intravenous (IV) Benlysta is approved for use in patients 5 years of age and older for the treatment of SLE and LN. Subcutaneous (SC) Benlysta is approved for use in SLE for patients 5 years of age and older. Safety and effectiveness for Benlysta SC in LN has not been established in the pediatric population. Benlysta prefilled syringe has not be studied in children less than 18 years of age for both SLE and LN.

	• SLE is a systemic autoimmune connective tissue disease with a variety of manifestations, some of which may lead to life-threatening complications. Diagnosis is typically made by identifying organ involvement and elevated biomarkers such as anti-nuclear antibody (ANA) ≥ 1:80, anti-double stranded DNA antibody (anti-dsDNA) ≥ 30 IU/mL, antiphospholipid antibodies, C3 and C4 complement levels, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP).
	• LN, which occurs in 20 to 60% of patients with SLE, is the most common severe manifestation of SLE and a major cause of illness and death. In 10 to 30% of patients with LN, this condition progresses to end stage renal disease (ESRD).
	• LN is a subset of SLE and can occur in approximately 50% of SLE patients. LN is the most common severe manifestation of SLE and a major cause of illness and death. Approximately 10 to 30% of patients with LN will progress to end stage renal disease (ESRD). The diagnosis and classification of LN is determined by a kidney biopsy which generally guides the patient's treatment. LN can be suspected in patients with SLE with increased or persistent proteinuria (specifically > 0.5 g per day), presence of cellular casts in urine, or decrease in estimated glomerular filtration rate (eGFR).
	• The European League Against Rheumatism (EULAR) recommends for SLE hydroxychloroquine (HCQ) in all patients. Glucocorticoids (GC) can be used at doses and routes of administration that depend on type and severity of organ involvement. In patients not responding to HCQ or unable to reduce GC doses for chronic use, addition of immunosuppressive agents (for example, azathioprine, methotrexate, mycophenolic acid analogue [MPAA], biologics) should be considered.
	• Kidney Disease Improving Global Outcomes (KDIGO) recommends that patients with SLE, including those with LN, be treated with HCQ or an equivalent antimalarial unless contraindicated. For Class I or II LN, immunosuppressive treatment is recommended for low-level proteinuria, and low-dose GC may be added for nephrotic syndrome. For Class III or IV LN, treat initially with GC with one of the following: MPAA, IV cyclophosphamide (CP), belimumab + MPAA or CP, or MPAA + calcineurin inhibitor. For maintenance therapy, patients should be placed on MPAA or azathioprine. GC should be tapered to the lowest possible dose during maintenance; discontinuation of GC can be considered after patients have maintained a complete clinical renal response.
	• When ANA levels are reported, the result is based upon the lowest ratio at which the ANA can still be detected after serial dilution. First, 1 part blood is mixed with 40 parts saline to create a 1:40 dilution. The dilution is then further reduced to strengths of 1:80, 1:160, 1:320, and 1:640.
	• anti-dsDNA is an ANA that targets DNA. The anti-dsDNA test identifies the presence of these autoantibodies in the blood. In the evaluation of a member with lupus nephritis, a high anti-dsDNA titer is generally associated with ongoing inflammation and damage to the kidneys.
	• Prescribing Considerations:
	  ○ The efficacy of Benlysta has not been evaluated in patients with severe active central nervous system lupus.
	  ○ Benlysta carries warnings for serious infections, progressive multifocal leukoencephalopathy (PML), hypersensitivity reactions (including anaphylaxis), and depression/suicidality.
	  ○ Live vaccines should not be given concurrently with Benlysta.
	  ○ It is recommended that the first SC injection of Benlysta should be under the supervision of a healthcare professional. For patients less than 10 years of age, Benlysta SC must be administered by a healthcare professional or trained caregiver.

	○ For SLE, if transitioning from IV to SC therapy with Benlysta, administer the first SC dose 1 to 4 weeks after the last IV dose. ○ For LN, the 400-mg dose requires administration of 2 auto-injectors or 2 prefilled syringes. A member may transition from IV to SC therapy with Benlysta any time after the patient completes the first 2 IV doses. If transitioning, administer the first SC dose of 200 mg 1 to 2 weeks after the last IV dose.

Approval Criteria

I. Systemic Lupus Erythematosus (SLE)

A. Initial Authorization

When a benefit, coverage of Benlysta SC may be approved for SLE when all of the following criteria are met **(1. through 4.):**

1. The member is 5 years of age or older.
2. The member has a diagnosis of SLE (ICD10: M32), classified as active disease.
3. The prescriber submits documentation the member has one (1) of the following **(a. or b.)**:
   - **a.** Positive ANA titer (≥ 1:80)
   - **b.** Anti-dsDNA ≥ 30 IU/mL
4. The member will continue to receive concomitant standard of care for treatment of SLE which includes at least one (1) of the following **(a., b., or c.):**
   - **a.** Corticosteroid (for example, prednisone)
   - **b.** Antimalarial (for example, hydroxychloroquine)
   - **c.** Immunosuppressant (for example, azathioprine, mycophenolate, methotrexate)

B. Reauthorization

When a benefit, reauthorization of Benlysta SC may be approved for SLE when all of the following criteria are met **(1. and 2.)**:

1. The member is tolerating therapy and has a therapeutic response defined as one (1) of the following **(a. or b.):**
   - **a.** Disease stability
   - **b.** Disease improvement
2. The member will continue to receive concomitant standard of care for treatment of SLE which includes at least one (1) of the following (alone or in combination) **(a., b., or c.):**
   - **a.** Corticosteroid (for example, prednisone)
   - **b.** Antimalarial (for example, hydroxychloroquine)
   - **c.** Immunosuppressant (for example, azathioprine, mycophenolate, methotrexate)

II. Active LN

A. Initial Authorization

When a benefit, coverage of Benlysta SC may be approved for active lupus nephritis when all of the following criteria are met **(1. through 4.):**

1. The member is 18 years of age or older.
2. The member has a diagnosis of LN (ICD10: M32.14), classified as active disease.
3. The member meets one (1) of the following criteria **(a. or b.)**:
   - **a.** The diagnosis is confirmed by a renal biopsy.
   - **b.** The member has a contraindication to renal biopsy and meets the following criterion **(i.)**:
     - **i.** The member has laboratory findings specific to LN (for example, elevated serum creatinine, abnormal urine analysis (proteinuria ≥ 500 mg/day, hypoalbuminemia, hematuria, casts), decreased estimated glomerular filtration rate [eGFR]).
4. The member will continue to receive concomitant standard of care for LN which includes corticosteroids with one (1) of the following **(a. or b.):**

a. mycophenolate for induction followed by mycophenolate for maintenance
b. cyclophosphamide for induction followed by azathioprine for maintenance

B. Reauthorization
When a benefit, reauthorization of Benlysta SC may be approved for active lupus nephritis when all of the following criteria are met **(1. and 2.)**:
1. The member is tolerating therapy and has a therapeutic response defined as one (1) of the following **(a. or b.):**
a. Disease stability
b. Disease improvement
2. The member will continue to receive concomitant standard of care for maintenance treatment of LN with one (1) of the following **(a. or b.):**
a. mycophenolate
b. azathioprine

III. Quantity Limits
When a benefit, Benlysta SC may be authorized in quantities as follows**:**

Diagnosis	Induction Therapy	Maintenance Therapy
SLE (≥ 18 years)	N/A	Four (4) autoinjectors/prefilled syringes every four (4) weeks
SLE (5 to < 18 years) + ≥ 40 kg	N/A	Four (4) autoinjectors every four (4) weeks
SLE (5 to < 18 years) + 15 to < 40 kg	N/A	Two (2) autoinjectors every four (4) weeks
LN	Eight (8) autoinjectors/prefilled syringes within the first 4 weeks of therapy	Four (4) autoinjectors/prefilled syringes every four (4) weeks

IV. An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

Limitations of Coverage

I. Coverage of drug(s) addressed in this policy for disease states outside of the FDA-approved indications should be denied based on the lack of clinical data to support effectiveness and safety in other conditions unless otherwise noted in the approval criteria.
II. For Commercial or HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

Authorization Duration

- Commercial and HCR Plans: If approved, up to a 12 month authorization may be granted.

Automatic Approval Criteria

None

References:

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15. Lab Tests Online. Anti-dsDNA. Available at: https://labtestsonline.org/tests/anti-dsdna. Accessed August 19, 2024.
16. Rovin BH, Adler SG, Barratt J, et al. Executive summary of the KDIGO 2021 guideline for the management of glomerular diseases. *Kidney Int*. 2021;100(4):753-779.
17. Fanouriakis A, Kostopoulou M, Andersen J, et all. EULAR recommendations for the management of systemic lupus erythematosus: 2023 update. *Ann Rheum Dis*. 2024;83(1):15-29.
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