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Section:	Prescription Drugs	**Effective Date:**	April 1, 2024
Subsection:	Miscellaneous Products	**Original Policy Date:**	December 7, 2011
Subject:	Benlysta	**Page:**	1 of 7

Last Review Date: March 8, 2024

Benlysta

Description

Benlysta (belimumab)

Background
Benlysta (belimumab) is a B-lymphocyte stimulator (BLyS)-specific inhibitor indicated for the treatment of systemic lupus erythematosus (SLE) and lupus nephritis. In many patients with SLE, higher concentrations of BLyS promote increased B-cell survival, including the survival of autoreactive B cells. Benlysta binds to soluble BLyS, inhibiting its binding to B-cell receptors. By binding to BLyS, Benlysta inhibits the survival of B cells, including autoreactive B cells, and reduces the differentiation of B cells into immunoglobulin-producing plasma cells. By reducing the autoreactive B-cell population, Benlysta decreases the production of autoantibodies and lupus disease activity (1).

Regulatory Status
FDA-approved indications: Benlysta is a B-lymphocyte stimulator (BLyS)-specific inhibitor indicated for the treatment of: (1)

1. Patients aged 5 years and older with active, autoantibody-positive, systemic lupus erythematosus who are receiving standard therapy.
2. Patients aged 5 years and older with active lupus nephritis who are receiving standard therapy.

Limitations of Use: The efficacy of Benlysta has not been evaluated in patients with severe active central nervous system lupus. Benlysta has not been studied in combination with other biologics. Use of Benlysta is not recommended in these situations (1).

Limitations of Use in Underrepresented Populations: Benlysta did not demonstrate significant clinical benefit in Black/African American subjects in the original two pivotal trials based on subgroup analysis. A subsequent large randomized, multicenter prospective trial over 52 weeks in 448 African American subjects with SLE did not achieve statistical significance for efficacy benefit compared with standard drug therapy. In the treatment of SLE and acute lupus nephritis, Benlysta has limited data in the Black/African American population and its improvement in response rates versus standard treatment has not been established (2).

Serious and sometimes fatal infections can occur in patients receiving Benlysta. It is recommended that practitioners exercise caution when using Benlysta in patients with chronic infections. Patients receiving any treatment for a chronic infection should not begin therapy with Benlysta. Consider interrupting Benlysta therapy in patients who develop a new infection while undergoing treatment with Benlysta and monitor these patients closely (1).

Acute hypersensitivity reactions, including anaphylaxis and death, have been reported in association with Benlysta. These events may occur within hours of the infusion; however they may occur later. Benlysta infusions should be administered by healthcare providers prepared to manage infusion reactions. Patients should be monitored during and for an appropriate period of time after administration of Benlysta (1).

A patient may self-inject or the patient caregiver may administer Benlysta subcutaneously after the healthcare provider determines it is appropriate (1).

Live vaccines should not be given for 30 days before or concurrently with Benlysta as clinical safety has not been established. Based upon the mechanism of action, Benlysta may interfere with the response to immunizations (1).

The safety and effectiveness of Benlysta in pediatric patients less than 5 years of age have not been established (1).

Subcutaneous dosing of Benlysta has not been evaluated and is not approved for patients younger than 18 years of age (1).

Related policies
Lupkynis, Saphnelo

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Benlysta may be considered **medically necessary** if the conditions indicated below are met.

Benlysta may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 5 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Systemic lupus erythematosus (SLE)

   AND ALL of the following:
   a. Must have active SLE
   b. Must be autoantibody-positive
   c. Must be receiving standard therapy [e.g., corticosteroids, NSAID, azathioprine, leflunomide, methotrexate, mycophenolate, tacrolimus, and antimalarials (e.g., hydroxychloroquine, chloroquine, quinine, quinidine, mefloquine)]
   d. Patients age **5-17 only**: Patient will be receiving Benlysta as an intravenous infusion
   e. Prescriber agrees to review and discuss with Black/African American patients the limited evidence of benefit of Benlysta in this population compared to standard treatment [(2)]

2. Lupus nephritis

   AND ALL of the following:
   a. Must have active lupus nephritis
   b. Must be receiving standard therapy (e.g., corticosteroids, cyclosporine,

tacrolimus, cyclophosphamide, azathioprine, mycophenolate and rituximab)

c. Patients age **5-17 only**: Patient will be receiving Benlysta as an intravenous infusion
d. Prescriber agrees to review and discuss with Black/African American patients the limited evidence of benefit of Benlysta in this population compared to standard treatment [(2)]

AND NONE of the following for **ALL** indications:

1. Chronic infection, including, but not limited to Hepatitis B, Hepatitis C, HIV, TB
2. Severe active central nervous system lupus
3. Concurrent therapy with a biologic medication
4. Given concurrently with live vaccines

Prior – Approval *Renewal* Requirements

Age 5 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Systemic lupus erythematosus (SLE)

AND ALL of the following**:**

a. Must be receiving standard therapy
b. Documented clinical benefit from therapy (e.g., improvement in functional impairment, decrease of corticosteroid dose, decrease in pain medications, decrease in the number of exacerbations since prior to the start of Benlysta)
c. Patients age **5-17 only**: Patient will be receiving Benlysta as an intravenous infusion
d. Prescriber agrees to review and discuss with Black/African American patients the limited evidence of benefit of Benlysta in this population compared to standard treatment [(2)]

2. Lupus nephritis

AND ALL of the following:

a. Must be receiving standard therapy (i.e., corticosteroids, cyclosporine, tacrolimus, cyclophosphamide, azathioprine, mycophenolate and rituximab)
b. Documented clinical benefit from therapy (i.e., decrease or stabilization of symptoms, improvement in functional impairment, decrease of corticosteroid dose, decrease in pain medications, decrease in the number of exacerbations since prior to the start of Benlysta)
c. Patients age **5-17 only**: Patient will be receiving Benlysta as an intravenous infusion
d. Prescriber agrees to review and discuss with Black/African American patients the limited evidence of benefit of Benlysta in this population compared to standard treatment [(2)]

AND NONE of the following for **ALL** indications:

1. Chronic infection, including, but not limited to Hepatitis B, Hepatitis C, HIV, TB
2. Severe active central nervous system lupus
3. Concurrent therapy with a biologic medication
4. Given concurrently with live vaccines

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Duration 6 months

Prior – Approval *Renewal* Limits

Duration 12 months

Rationale

Summary
Benlysta (belimumab) is indicated for the treatment of systemic lupus erythematosus (SLE) and lupus nephritis. Benlysta has limited data in the Black/African American population and its improvement in response rates versus standard treatment has not been established. The efficacy of Benlysta has not been evaluated in patients with severe active central nervous system lupus. Serious and sometimes fatal infections and hypersensititivy reactions can occur in patients receiving Benlysta. Benlysta infusions should be administered by healthcare providers prepared to manage infusion reactions. The safety and effectiveness of Benlysta in pediatric patients less than 5 years of age have not been established (1-2).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of Benlysta while maintaining optimal therapeutic outcomes.

References
1. Benlysta [package insert]. Research Triangle Park, NC: GlaxoSmithKline; February 2023.
2. Ginzler E, Guedes Barbosa LS, D'Cruz D, et al. Phase III/IV, Randomized, Fifty-Two-Week Study of the Efficacy and Safety of Belimumab in Patients of Black African Ancestry With Systemic Lupus Erythematosus. Arthritis Rheumatol. 2021 Jun 23. doi: 10.1002/art.41900. Epub ahead of print. PMID: 34164944

Policy History

Date	Action
December 2011	New Policy
December 2012	Annual editorial review
June 2014	Annual editorial review and reference update Addition to criteria requirements that the patient must not have severe active lupus nephritis, not have active central nervous system lupus, patient must not use Benlysta in combination with biologic medication nor intravenous cyclophosphamide
September 2015	Annual editorial review and reference update
December 2015	Annual review and reference update
December 2016	Annual editorial review and reference update Addition of age to the renewal section Policy number change from 5.11.01 to 5.99.01
June 2017	Annual editorial review and reference update
June 2018	Annual review and reference update

May 2019	Reduced age limit from 18 and older to 5 and older. Added requirement that patients age 5-17 must use Benlysta as an intravenous infusion
June 2019	Annual review
June 2020	Annual review and reference update
January 2021	Addition of indication: active lupus nephritis in adult patients. Updated Limitations of Use to remove severe active lupus nephritis and no dual therapy with IV cyclophosphamide
March 2021	Annual review
June 2021	Annual editorial review and reference update
December 2021	Annual review
February 2022	Per FEP, addition of Limitations of Use in Underrepresented Populations section, and (optional) requirement for prescriber to review and discuss with Black/African American patients the limited evidence of benefit of Benlysta in this population compared to standard treatment
March 2022	Annual review
August 2022	Active lupus nephritis indication was expanded to include pediatric patients 5-17 years old per PI update
September 2022	Annual review
March 2023	Annual review
March 2024	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 8, 2024 and is effective on April 1, 2024.