Benlysta (belimumab) Prior Authorization with Quantity Limit Program Summary

This prior authorization applies to Commercial, NetResults A series, SourceRx and Health Insurance Marketplace formularies.

This policy only targets subcutaneous Benlysta.

OBJECTIVE

The intent of the Benlysta (belimumab) Prior Authorization (PA) program is to ensure appropriate selection of patients for treatment according to product labeling and/or clinical studies and/or guidelines and according to dosing recommended in product labeling (10 mg/kg). The program will consider belimumab appropriate for adult patients with active, autoantibody and/or anti-dsDNA positive, systemic lupus erythematosus (SLE) who are receiving standard of care therapy. The criteria will not approve belimumab for patients with the following: severe active lupus nephritis or severe active central nervous system lupus or current therapy with other biologic agents or intravenous cyclophosphamide. The initial criteria will also allow for a patient who has any FDA approved diagnosis that is not already addressed in the criteria set with a requested dosage that is within FDA limits. Renewal criteria will have similar requirements to initial criteria with the exception that the patient will have to have improvement or stabilization in at least one SLE diagnostic criterion. The dose of belimumab will be limited to the FDA labeled dosage.

TARGET AGENT

Benlysta® (belimumab)

Brand (generic)	GPI	Multisource Code	Quantity Limit
Benlysta (belimumab)			
200 mg/mL autoinjector	9942201500D520	M, N, O, or Y	4 prefilled autoinjectors/ 28 days
200 mg/mL prefilled syringe	9942201500E520	M, N, O, or Y	4 prefilled syringes/ 28 days

CRITERIA FOR APPROVAL

Initial Evaluation

Benlysta (belimumab) will be approved when ALL of the following are met:

1. ONE of the following:
    i. The patient has a diagnosis of active systemic lupus erythematosus (SLE) disease **AND** ALL of the following:
        a. The patient is 18 years of age or over
        AND
        b. The patient has a history of positive antinuclear antibody (ANA) and/or positive anti-dsDNA results
        AND
        c. The patient has a history of at least 4 SLE related disease manifestations (SLE related disease manifestations include, but are not limited to: malar rash, discoid rash, photosensitivity, oral ulcers, nonerosive arthritis, pleuritis/pericarditis, renal disorder [persistent proteinuria >0.5 grams/day or cellular casts], hematologic disorder

[hemolytic anemia (with reticulocytosis), leukopenia, lymphopenia], or immunologic disorder [positive finding of antiphospholipid antibodies or anti-Sm antibodies])

AND

d. ONE of the following:
    1. BOTH of the following:
        a. The patient has had inadequate response to TWO of the following: corticosteroids, antimalarials (hydroxychloroquine, chloroquine), nonsteroidal anti-inflammatory drugs (NSAIDS), aspirin, and/or immunosuppressives (azathioprine, methotrexate, cyclosporine, oral cyclophosphamide, or mycophenolate)

        AND

        b. The patient is currently on a standard of care SLE treatment regimen comprised of at least one of the following: corticosteroids, antimalarials (e.g. hydroxychloroquine, chloroquine), nonsteroidal anti-inflammatory drugs (e.g. NSAIDS), aspirin, and/or immunosuppressives (e.g. azathioprine, methotrexate, cyclosporine, oral cyclophosphamide, or mycophenolate)

    OR

    2. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to ALL the standard of care drug classes listed above

OR

ii. The patient has another FDA labeled diagnosis

AND

2. The patient does NOT have severe active lupus nephritis requiring inter-current treatment with cyclophosphamide or other biologic therapy or the initiation of other immunosuppressive therapy

AND

3. The patient does NOT have severe active central nervous system lupus complications requiring inter-current treatment with cyclophosphamide or other biologic therapy or the initiation of other immunosuppressive therapy

AND

4. The patient is NOT currently being treated with intravenous cyclophosphamide OR intravenous cyclophosphamide will be discontinued before starting therapy with Benlysta

AND

5. The patient is NOT currently using another biologic agent OR the biologic agent will be discontinued before starting therapy with Benlysta

AND

6. The patient does not have any FDA labeled contraindications to the requested agent

AND

7. ONE of the following:
    a. The requested quantity (dose) is NOT greater than the program quantity limit

    OR

    b. ALL of the following:
        i. The requested quantity (dose) is greater than the program quantity limit **AND**
        ii. The requested quantity (dose) is less than or equal to the FDA labeled dose **AND**
        iii. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the limit

    OR

    c. ALL of the following:
        i. The requested quantity (dose) is greater than the program quantity limit **AND**
        ii. The requested quantity (dose) is greater than the FDA labeled dose **AND**
        iii. The prescriber has submitted documentation in support of therapy with a higher dose for the intended diagnosis (must be reviewed by the Clinical Review pharmacist)

Length of Approval: 12 months

Renewal Evaluation

Benlysta (belimumab) will be approved when ALL of the following are met:

1. The patient has been previously approved for Benlysta through the Prime Therapeutics medical drug policy process
   AND
2. ONE of the following:
   a. The patient is currently on a standard of care SLE treatment regimen comprised of at least one of the following: corticosteroids, antimalarials (e.g. hydroxychloroquine, chloroquine), nonsteroidal anti-inflammatory drugs (e.g. NSAIDS), aspirin, and/or immunosuppressives (e.g. azathioprine, methotrexate, cyclosporine, oral cyclophosphamide, or mycophenolate)
      OR
   b. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to ALL the standard of care drug classes listed above

   AND
3. The patient has had a decrease in symptoms or stabilization in at least one SLE related disease manifestation present prior to administration of Benlysta (belimumab) (SLE related disease manifestations include, but are not limited to: malar rash, discoid rash, photosensitivity, oral ulcers, nonerosive arthritis, pleuritis/pericarditis, renal disorder [persistent proteinuria >0.5 grams/day or cellular casts], hematologic disorder [hemolytic anemia (with reticulocytosis), leukopenia, lymphopenia], or immunologic disorder [positive finding of antiphospholipid antibodies or anti-Sm antibodies])
   AND
4. The patient does NOT have severe active lupus nephritis requiring inter-current treatment with cyclophosphamide or other biologic therapy or the initiation of other immunosuppressive therapy
   AND
5. The patient does NOT have severe active central nervous system lupus complications requiring inter-current treatment with cyclophosphamide or other biologic therapy or the initiation of other immunosuppressive therapy
   AND
6. The patient is NOT currently being treated with intravenous cyclophosphamide OR intravenous cyclophospamide will be discontinued before starting therapy with Benlysta
   AND
7. The patient is NOT currently using another biologic agent OR the biologic therapy will be discontinued before starting therapy with Benlysta
   AND
8. The patient does not have any FDA labeled contraindications to the requested agent
   AND
9. ONE of the following:
   a. The requested quantity (dose) is NOT greater than the program quantity limit
      OR
   b. ALL of the following:
      i. The requested quantity (dose) is greater than the program quantity limit **AND**
      ii. The requested quantity (dose) is less than or equal to the FDA labeled dose **AND**
      iii. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the limit

      OR
   c. ALL of the following:
      i. The requested quantity (dose) is greater than the program quantity limit **AND**
      ii. The requested quantity (dose) is greater than the FDA labeled dose **AND**
      iii. The prescriber has submitted documentation in support of therapy with a higher dose for the intended diagnosis (must be reviewed by the Clinical Review pharmacist)

Length of Approval: 12 months

This pharmacy policy is not an authorization, certification, explanation of benefits or a contract. Eligibility and benefits are determined on a case-by-case basis according to the terms of the member's plan in effect as of the date services are rendered. All pharmacy policies are based on (i) information in FDA approved package inserts (and black box warning, alerts, or other information disseminated by the FDA as applicable); (ii) research of current medical and pharmacy literature; and/or (iii) review of common medical practices in the treatment and diagnosis of disease as of the date hereof. Physicians and other providers are solely responsible for all aspects of medical care and treatment, including the type, quality, and levels of care and treatment.

The purpose of Blue Cross and Blue Shield of Alabama's pharmacy policies are to provide a guide to coverage. Pharmacy policies are not intended to dictate to physicians how to practice medicine. Physicians should exercise their medical judgment in providing the care they feel is most appropriate for their patients.

Neither this policy, nor the successful adjudication of a pharmacy claim, is guarantee of payment.

FDA APPROVED INDICATIONS AND DOSAGE[1]

Agent	Indication*	Dosage
Benlysta® (belimumab)	Treatment of adult patients with active autoantibody positive, systemic lupus erythematosus who are receiving standard therapy	Intravenous administration: 10 mg/kg at 2-week intervals for the first 3 doses and at 4-week intervals thereafter Subcutaneous administration: 200 mg once weekly

* Limitation of use: efficacy has not been evaluated in patients with severe active lupus nephritis or severe active central nervous system lupus. It has not been studied in combination with other biologics or intravenous cyclophosphamide so is not recommended in these situations.

CLINICAL RATIONALE

Systemic Lupus Erythematosus (SLE)

Systemic Lupus Erythematosus (SLE) is a chronic inflammatory autoimmune disease of unknown cause.[3] It has a broad range of clinical and serological manifestations and can affect any organ. Clinical symptoms of SLE include fatigue, fever, myalgia, changes in weight, skin and mucus membrane lesions and ulcers, and vascular disease. SLE can also include cardiac, renal, pulmonary, and neurologic involvement. Due to its multisystem involvement and likelihood of changes in presentation, the diagnosis of SLE may be difficult.[3]

The American College of Rheumatology published criteria to aid in diagnosing patients with SLE. The criteria requires the patient has, at any time in his or her medical history, at least four of the following diagnostic criteria: malar rash, discoid rash, photosensitivity, oral ulcers, nonerosive arthritis, serositis (e.g. pleuritis/pericarditis), renal disorder [e.g. persistent proteinuria >0.5 grams/day or cellular casts], hematologic disorder [e.g. hemolytic anemia (with reticulocytosis), leukopenia, lymphopenia, or thrombocytopenia], and/or immunologic disorder (e.g. positive finding of antiphospholipid antibodies or anti-Sm antibodies).[3,9]

In the 2012 revised American College of Rheumatology (ACR) SLE classification criteria, a person is classified as having SLE in the presence of biopsy-proven lupus nephritis with antinuclear antibodies (ANA) or anti-dsDNA antibodies or if 4 of the ACR diagnostic criteria, including at least 1 clinical and 1 immunologic criterion have been established.[4] When SLE is suspected standard laboratory evaluations include CBC with differential, serum creatinine, and urinalysis with microscopy.[3,9]

Management of SLE depends on the organ system involved. Nonspecific symptomatic treatments such as nonsteroidal anti-inflammatory drugs (NSAIDs), salicylates, and topical therapies may be used initially in SLE patients. Additional conventional SLE therapies include antimalarial drugs, such as hydroxychloroquine and quinacrine, and many nonspecific immunosuppressive medications, such as glucocorticoids, azathioprine, methotrexate, mycophenolate mofetil, and cyclophosphamide.[3,9] The American Academy of Family Physicians (AAFP) recommends belimumab to be used after other therapies have been tried, including systemic glucocorticoids, hydroxychloroquine, azathioprine, mycophenolate, and methotrexate. AAFP recommends hydroxychloroquine as the as the cornerstone of treatment to reduce disease flares and other constitutional symptoms. Low-dose glucocorticoids can be also used to treat most manifestations.[9]

Guidelines

The American College of Rheumatology (ACR)[4] and The European League Against Rheumatism (EULAR)[5] have published guidelines for the management of adults with SLE. The guidelines are based on available evidence-based information for the diagnosis and management of SLE with the goal of improving the quality of care for patients by primary care physicians. The recommendations are based on both evidence-based

research, as well as expert consensus. Neither set of guidelines provides specific recommendations for drug selection and use.

Compendia Supported Indications
For the purposes of the criteria, indications deemed appropriate are those that are supported in AHFS, DrugDex with a level of evidence of 2a or NCCN with a level of evidence of 2a or stronger.

References

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2. Goldberg A, Katzap E. Belimumab for the Treatment of Systemic Lupus Erythematosus. *International Journal of Clinical Rheumatology*. 2010;5(4):407-413.
3. FDA Arthritis advisory committee meeting briefing document BLA 125370. October 2010. Available at: www.fda.gov/.../CommitteesMeetingMaterials/Drugs/ArthritisDrugsAdvisoryCommittee/UCM233581.pdf. Accessed April 12, 2011.
4. American College of Rheumatology and Ad Hoc Committee on Systemic Lupus Erythematosus Guidelines. Guidelines for referral and management of systemic lupus erythematosus in adults. *Arthritis Rheum.* 1999;42:1785–96.
5. Bertsias G, Ioannidis J, Boletis J, et al. EULAR recommendations for the management of systemic lupus erythematosus (SLE) report of a task force of the European Standing Committee for International Clinical Studies Including Therapeutics (ESCISIT). *Ann Rheum Dis.* 2008;67:195–205.
6. Navarra S, Guzmán R, Gallacher A, Hall S, et al. Efficacy and safety of belimumab in patients with active systemic lupus erythematosus: a randomised, placebo-controlled, phase 3 trial. *Lancet.* 377(9767):721-31.
7. Wiglesworth A, Ennis K, Kockler, D. Belimumab: A BLyS-Specific Inhibitor for Systemic Lupus Erythematosus. *Annals of Pharmacotherapy.* 2010;44:1955-1961.
8. Bartels, Christie. Systemic Lupus Erythematosus (SLE) Treatment & Management. Medscape. Available at http://emedicine.medscape.com/article/332244-treatment. Accessed 7/20/17.