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Clinical Guideline

Guideline Number: PG014, Ver. 3

# Benlysta (belimumab)

## Disclaimer

*Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.*

*Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.*

## Summary

Benlysta [belimumab] is an FDA-approved human monoclonal antibody used in the treatment of systemic lupus erythematosus (SLE). SLE is an autoimmune disorder in which the immune system attacks its own healthy tissues, affecting multiple organs and causing joint pain, inflammation, and sometimes a rash. Benlysta works by inhibiting B lymphocyte stimulator protein (BLyS), which causes a reduction in the B cells that attack the body's own tissues. Benlysta [belimumab] is also FDA-approved in the treatment of active lupus nephritis who are receiving standard therapy.

Generally, lupus patients can be treated with antimalarials (such as hydroxychloroquine), corticosteroids (such as prednisone, methylprednisolone, dexamethasone), and immunosuppressives (such as methotrexate, azathioprine, mycophenolate, or cyclophosphamide).

Benlysta [belimumab] has a place in therapy for lupus patients who are not responsive to the conventional agents outlined above and who have active disease. However, Benlysta [belimumab] is not used in patients with severe active central nervous system lupus. Benlysta [belimumab] is available as an intravenous (IV) and subcutaneous (SC) injection and is dosed every 4 weeks (IV) or every week (SC). The IV and SC formulations should not be used simultaneously.

Table 1: Dosage Information

| Indication | Initial dose | Subsequent dose | Additional Considerations |
|---|---|---|---|
| Systemic lupus erythematosus (SLE) - IV infusion | 10 mg/kg IV every 2 weeks for the first 3 doses | 10 mg/kg IV every 4 weeks thereafter | |
| Systemic lupus erythematosus (SLE) - SC injection | 200 mg SC once weekly ongoing | | Transition from IV to SC dosing: administer first SC dose 1 to 4 weeks after the last IV dose |
| Lupus nephritis (LN) - IV infusion | 10 mg/kg IV every 2 weeks for the first 3 doses | 10 mg/kg IV every 4 weeks thereafter | Patient should receive first 2 IV doses before transitioning to SC dosing |
| Lupus nephritis (LN) - SC injection | 400 mg SC once weekly for first 4 doses | 200 mg subQ once weekly thereafter | Transition from IV to SC dosing: administer first SC dose 1 to 2 weeks after the last IV dose |

## Definitions

"Antimalarial" is a drug class that is used to treat malaria but also is used in autoimmune diseases such as lupus and rheumatoid arthritis.

"Autoantibody" is an antibody produced by one's own immune system that attacks the body's normal cells, rather than foreign antigens (such as viruses and bacteria).

"B cells" are cells in the body that help activate an immune response.

"B lymphocyte stimulator protein (BLyS)" is a molecule in the body that aids in the development of B cells.

"Central nervous system lupus" is a complication that can be seen in lupus patients and can involve conditions such as seizures, cerebrovascular accidents (strokes), delirium, and nerve pain.

"Corticosteroid" is a drug class that reduces inflammation and suppresses the immune system.

"Human monoclonal antibody" is a protein made from human cells that is designed to bind to a specific molecule in the body and can be used to treat a variety of diseases including lupus, rheumatoid arthritis, and cancers.

"Immunosuppressives" are medications that prevent the actions of the immune system, used in diseases such as lupus, rheumatoid arthritis, psoriasis, and Crohn's disease.

"JCV" or "John Cunningham virus" refers to a virus associated with the development of progressive multifocal leukoencephalopathy (PML), a side effect of certain immunosuppressive medications. Patients who use Benlysta should be tested for JCV before starting treatment and while on treatment to help identify if they are at a higher risk for PML.

"Lupus nephritis" is inflammation of the kidney in patients with lupus.

## Medical Necessity Criteria for Initial Authorization

The Plan considers Benlysta [belimumab] medically necessary when the ALL the following criteria are met for the applicable indication listed below:

<u>For active systemic lupus erythematosus</u>

1. The member is 5 years of age or older; ***and***
2. The medication is being prescribed by a rheumatologist; ***and***
3. The member has a diagnosis of active systemic lupus erythematosus and ALL of the following:
    a. autoantibody-positive (positive for antinuclear antibody [ANA] and/or anti-double-stranded DNA [anti-dsDNA]); *and*
    b. receiving standard therapy including at least ONE of the following, alone or in combination:
        i. corticosteroids (such as prednisone, methylprednisolone, dexamethasone); ***or***
        ii. antimalarials (such as hydroxychloroquine); ***or***
        iii. immunosuppressives (such as azathioprine, methotrexate, mycophenolate)
4. The member does not have severe active central nervous system lupus (such as altered mental function or confusion, vision problems, or seizures); ***and***
5. The member is not using Benlysta in combination with another biologic or intravenous cyclophosphamide; ***and***
6. The member must have no evidence of infection [specifically tuberculosis (TB), Hepatitis B (HBV) or Hepatitis C (HCV)]; ***and***
7. The member has been tested for anti-JCV (John Cunningham virus) antibodies; ***and***
8. Chart documentation and supporting labwork are provided for review to substantiate the above listed requirements.

For active lupus nephritis

1. The member is 18 years of age or older; ***and***
2. The medication is being prescribed by a rheumatologist or nephrologist; ***and***
3. The member has a diagnosis of active lupus nephritis and ALL of the following:
    a. autoantibody-positive (positive for antinuclear antibody [ANA] and/or anti-double-stranded DNA [anti-dsDNA]); *and*
    b. receiving standard therapy including at least ONE of the following, alone or in combination:
        i. corticosteroids (such as prednisone, methylprednisolone, dexamethasone); ***or***
        ii. immunosuppressives (such as azathioprine, mycophenolate)
4. The member does not have severe active central nervous system lupus (such as altered mental function or confusion, vision problems, or seizures); ***and***
5. The member is not using Benlysta in combination with another biologic or intravenous cyclophosphamide; ***and***
6. The member must have no evidence of infection [specifically tuberculosis (TB), Hepatitis B (HBV) or Hepatitis C (HCV)]; ***and***
7. The member has been tested for anti-JCV (John Cunningham virus) antibodies; ***and***
8. Chart documentation and supporting labwork are provided for review to substantiate the above listed requirements.

If the above prior authorization criteria are met, Benlysta [belimumab] will be approved for 12 months.

## Medical Necessity Criteria for Reauthorization

Reauthorization for 12 months will be granted if the member still meets the applicable initial criteria and has chart documentation demonstrating ONE of the following:

a. The member has shown a clinical improvement in symptoms since starting the requested medication.
b. The member has experienced disease stability since starting the requested medication.

## Experimental or Investigational / Not Medically Necessary

Benlysta [belimumab] for any other indication is considered not medically necessary by the Plan, as it is deemed to be experimental, investigational, or unproven.

## Applicable Billing Codes (HCPCS/CPT Codes)

| CPT/HCPCS Codes for Applicable Medications | |
|---|---|
| *Code* | *Description* |
| J0490 | Injection, belimumab, 10 mg |
| ICD-10 Codes for Clinical Indications | |
| *Code* | *Description* |
| M32 | Systemic lupus erythematosus (SLE) |
| M32.14 | Glomerular disease in systemic lupus erythematosus, Lupus renal disease |

## References


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2. Benlysta. Available from Micromedex® (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at: https://www.micromedexsolutions.com. Accessed May 4, 2021.
3. Fanouriakis A, Kostopoulou M, Alunno A, et al. 2019 Update of the EULAR Recommendations for the Management of Systemic Lupus Erythematosus. *Ann Rheum Dis*. 2019;78:736-745.
4. Rovin BH, Parikh SV, Hebert LA, et al. Lupus nephritis: induction therapy in severe lupus nephritis – should MMF be considered the drug of choice? *Clin J Am Soc Nephrol.* 2013;8(1):147-153.
5. Hahn BH, McMahon MA, Wilkinson A, et al. American College of Rheumatology guidelines for screening, treatment, and management of lupus nephritis. *Arthritis Care & Research*. 2012;64(6):797-808.
6. Furie R, Rovin BH, Houssiau F, et al. Two-Year, Randomized, Controlled Trial of Belimumab in Lupus Nephritis. N Engl J Med. 2020;383(12):1117-1128.


## Clinical Guideline Revision / History Information

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