Clinical Policy: Belimumab (Benlysta)

Reference Number: CP.PHAR.88
Effective Date: 10.01.11
Last Review Date: 05.22
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Belimumab (Benlysta®) is B-lymphocyte stimulator specific inhibitor.

FDA Approved Indication(s)

Benlysta is indicated for the treatment of:

- Patients aged 5 years and older with active, autoantibody-positive, systemic lupus erythematosus (SLE) who are receiving standard therapy.
- Patients aged 5 years and older with active lupus nephritis (LN) who are receiving standard therapy.

Limitation(s) of use: The efficacy of Benlysta has not been evaluated in patients with severe active central nervous system lupus. Use of Benlysta is not recommended in this situation.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Benlysta is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Systemic Lupus Erythematosus (must meet all)**:**

1. Diagnosis of SLE;
2. Prescribed by or in consultation with a rheumatologist;
3. Age ≥ 5 years;
4. Documentation confirms that member is positive for an SLE autoantibody (e.g., anti-nuclear antibody (ANA), anti-double-stranded DNA (anti-dsDNA), anti-Smith (anti-Sm), anti-ribonucleoprotein (anti-RNP), anti-Ro/SSA, anti-La/SSB, antiphospholipid antibody);
5. Prescribed in combination with standard therapy for SLE that includes one or more of the following agents, unless all agents are contraindicated: glucocorticoids (e.g., prednisone), antimalarial (e.g., hydroxychloroquine or chloroquine), non-biologic immunosuppressants (e.g., azathioprine, methotrexate, mycophenolate);
6. Request meets one of the following (a or b):
   a. Adults (≥ 18 years of age):
      i. IV: Dose does not exceed 10 mg/kg per dose at 2-week intervals for the first 3 doses and at 4-week intervals thereafter;
      ii. SC: 200 mg per week;

b. Pediatrics (≥ 5 years of age): Dose does not exceed 10 mg/kg per dose IV at 2-week intervals for the first 3 doses and at 4-week intervals thereafter.

Approval duration:
Medicaid/HIM – 6 months
Commercial – 6 months or to member's renewal date, whichever is longer

B. Lupus Nephritis (must meet all)**:**
1. Diagnosis of LN with kidney biopsy that confirms one of the following (a, b, or c):
   a. LN Class III (focal);
   b. LN Class IV (diffuse segmental or global);
   c. LN Class V (membranous);
2. Prescribed by or in consultation with a nephrologist or rheumatologist;
3. Age ≥ 5 years;
4. Member has a confirmed diagnosis of systemic lupus erythematosus;
5. Prescribed in combination with standard therapy for SLE that includes one or more of the following agents, unless all agents are contraindicated: glucocorticoids (e.g., prednisone), antimalarial (e.g., hydroxychloroquine or chloroquine), non-biologic immunosuppressants (e.g., azathioprine, cyclophosphamide, methotrexate, mycophenolate);
6. Request meets one of the following (a or b):
   a. IV: Dose does not exceed 10 mg/kg per dose at 2-week intervals for the first 3 doses and at 4-week intervals thereafter;
   b. SC in adults (≥ 18 years of age): Dose does not exceed 400 mg per week SC for the first 4 doses*, then 200 mg/week SC;

   **Loading doses not permitted if previously receiving Benlysta for treatment of SLE*

Approval duration:
Medicaid/HIM – 6 months
Commercial – 6 months or to member's renewal date, whichever is longer

C. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Member meets one of the following (a or b):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
2. Member meets one of the following (a or b):
   a. For SLE: Member is responding positively to therapy;
   b. For LN: Member is responding positively to therapy as evidenced by one of the following (i, ii, or iii):
      i. Reduced level of proteinuria measured by UPCR ≤ 0.5 mg/mg from baseline with low dose steroids (e.g., prednisone);
      ii. No reduction from baseline in eGFR of greater than 20% with low dose steroids (e.g., prednisone);
      iii. eGFR ≥ 60 mL/min/1.73 m^2 with low dose steroids (e.g., prednisone);
3. Prescribed in in combination with standard therapy for SLE that includes one or more of the following agents, unless all agents are contraindicated: glucocorticoids (e.g., prednisone), antimalarial (e.g., hydroxychloroquine or chloroquine), non-biologic immunosuppressants (e.g., azathioprine, methotrexate, mycophenolate);
4. If request is for a dose increase, request meets one of the following (a or b):
   a. Adults (≥ 18 years of age):
      i. IV: Dose does not exceed 10 mg/kg per dose at 2-week intervals for the first 3 doses and at 4-week intervals thereafter;
      ii. SC: 200 mg per week;
   b. Pediatrics (≥ 5 years of age): Dose does not exceed 10 mg/kg per dose IV at 2-week intervals for the first 3 doses and at 4-week intervals thereafter.

Approval duration:
Medicaid/HIM – 12 months
Commercial – 6 months or to member's renewal date, whichever is longer

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

B. Autoantibody negative SLE.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ANA: anti-nuclear antibody
Anti-dsDNA: anti-double-stranded DNA
Anti-Sm: anti-Smith
DNA: deoxyribonucleic acid
FDA: Food and Drug Administration
LN: lupus nephritis
SLE: systemic lupus erythematosus

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
glucocorticoids (e.g., prednisone)	Varies	Varies
antimalarial agents (e.g., hydroxychloroquine, chloroquine)	Varies	Varies
non-biologic immunosuppressants (e.g., azathioprine, methotrexate, mycophenolate)*	Varies	Varies

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.
** For LN, cyclophosphamide is also an acceptable immunosuppressant.*

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): previous anaphylaxis to belimumab
- Boxed warning(s): none reported

Appendix D: Autoantibody Positive Versus Negative SLE

Only one of the five Benlysta pivotal trials included patients with autoantibody negative SLE; no significant differences between any of the Benlysta groups and the placebo group were observed. However, on further analysis Benlysta appeared to offer benefit to a subgroup of autoantibody positive patients. Benlysta's efficacy was confirmed in the remaining four trials which included only autoantibody positive patients. Because of the apparent lack of efficacy in autoantibody negative patients and because the FDA has approved Benlysta in

only autoantibody positive patients, Benlysta coverage will not be authorized for patients with autoantibody negative SLE.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose

SLE, LN	• IV (pediatrics and adults)
	  ○ 10 mg/kg at 2 week intervals for the first 3 doses and at 4 week intervals thereafter
	• SC (adults only)
	  ○ For SLE, 200 mg once weekly
	  ○ For LN, 400 mg once weekly for 4 doses, then 200 mg once weekly
	• Transition from IV to SC therapy (adults)
	  ○ May transition from IV to SC therapy any time after the first 2 IV doses; administer first SC dose 1 to 2 weeks after the last IV dose
		IV: 10 mg/kg/dose
		SC: 200 mg/week

VI. Product Availability

- Single-dose vial: 120 mg and 400 mg lyophilized powder for reconstitution
- Single-dose prefilled autoinjector/syringe: 200 mg/mL

VII. References

1. Benlysta Prescribing Information. Research Triangle Park, NC: GlaxoSmithKline; July 2022. Available at http://www.benlysta.com. Accessed August 22, 2022.
2. Kidney Disease: Improving Global Outcomes (KDIGO) Glomerular Diseases Work Group. KDIGO 2021 Clinical Practice Guideline for the Management of Glomerular Diseases. Kidney Int. 2021 Oct; 100(4S):S1-S276.
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;0:1–10. doi:10.1136/annrheumdis-2019-215089.
4. Petri M, Orbai AM, Alarcón GS, et al. Derivation and validation of the Systemic Lupus International Collaborating Clinics classification criteria for systemic lupus erythematosus. *Arthritis Rheum.* 2012; 64:2677.
5. Weening J, Vivette D, Schwartz M, et al. The Classification of Glomerulonephritis in Systemic Lupus Erythematosus Revisited. JASN February 2004, 15(2)241-250.
6. Gordon C, Amissah-Arthur MB, Gayed M, et al. The British Society for Rheumatology guideline for the management of systemic lupus erythematosus in adults. *Rheumatology.* 2018;57:e1-e45. doi:10.1093/rheumatology/kex286.
7. Furie R, Rovin B, Houssiau F, et al. Two-year randomized, controlled trial of belimumab in lupus nephritis. *N Engl J Med*. 2020;3838(12):1117-1128. doi: 10.1056/NEJMoa2001180.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J0490	Injection, belimumab, 10 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
3Q 2018 annual review: Policies combined for Commercial and Medicaid lines of business; HIM-Medical added; no significant changes from previously approved corporate policy; Medicaid: added prescriber requirement, removed requirement to confirm lack of chronic infection treatment, expanded list of accepted autoantibodies consistent with existing Commercial approach; references reviewed and updated.	05.09.18	08.18
3Q 2019 annual review: labeled age updated from adults down to age 5 and older; antiphospholipid antibody added to examples of SLE antibodies; added separate approval duration for commercial line of business to the continued therapy section; added that concurrent standard therapy be continued in the continued approval section; references reviewed and updated.	05.14.19	08.19
3Q 2020 annual review: no significant changes; revised from HIM-Medical Benefit to HIM line of business; references reviewed and updated.	05.12.20	08.20
RT4: added criteria to reflect new indication for lupus nephritis in adults and aligned with Lupkynis (voclosporin); updated reference for HIM off-label use to HIM.PA.154 (replaces HIM.PHAR.21).	02.16.21	05.21
Added IV dosing option for LN per FDA labeling.	06.08.21	
Added cyclosphosphamide as allowed standard of care treatment for LN; clarified dosing for transitioning from IV to SC.	07.22.21	
2Q 2022 annual review: no significant changes; references reviewed and updated.	02.04.22	05.22
RT4: updated FDA approved indications to expand age down to 5 years of age for LN; updated LN dosing for SC to apply only in adults; revised limitations of use to align with prescribing information. Template changes applied to other diagnoses/indications and continued therapy section.	08.22.22	

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical

practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.