Clinical Policy: Belimumab (Benlysta)
Reference Number: CP.PHAR.88
Effective Date: 10.01.11
Last Review Date: 08.18
Line of Business: Commercial, Medicaid, HIM-Medical Benefit

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 adult patients with active, autoantibody-positive, systemic lupus erythematosus (SLE) who are receiving standard therapy.

Limitation(s) of use: The efficacy of Benlysta has not been evaluated in patients with severe active lupus nephritis or severe active central nervous system lupus. Benlysta has not been studied in combination with other biologics or intravenous cyclophosphamide. Use of Benlysta is not recommended in these situations.

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 ≥ 18 years;
      4. Documentation confirms that member is positive for autoantibody (e.g., anti-nuclear antibody (ANA), anti-double-stranded DNA (anti-ds-DNA), anti-Smith antigen (anti-Sm), anti-ribonucleoprotein (anti-RNP), anti-Ro/SSA, anti-La/SSB);
      5. Currently receiving 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. Dose does not exceed 10 mg/kg/dose IV or 200 mg/week SC.

   Approval duration:
   Medicaid/HIM – 6 months
   Commercial – 6 months or to member’s renewal date, whichever is longer
B. Other diagnoses/indications
   1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace and CP.PMN.53 for Medicaid.

II. Continued Therapy
   A. Systemic Lupus Erythematosus (must meet all):
      1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
      2. Member is responding positively to therapy;
      3. If request is for a dose increase, new dose does not exceed 10 mg/kg/dose IV or 200 mg/week SC.
      Approval duration: 12 months

B. Other diagnoses/indications (1 or 2):
   1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
      Approval duration: Duration of request or 6 months (whichever is less); or
   2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 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.PHAR.21 for health insurance marketplace and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information
   Appendix A: Abbreviation/Acronym Key
   ANA: anti-nuclear antibody
   Anti-ds-DNA: anti-double-strandedDNA
   Anti-Sm: anti-Smith
   DNA: deoxyribonucleic acid
   FDA: Food and Drug Administration
   RNP: ribonucleoprotein
   SLE: Systemic lupus erythematosus

   Appendix B: Therapeutic Alternatives
   Not applicable

   Appendix C: Contraindications
   Not applicable

   Appendix D: General Information
   • In a study that enrolled both autoantibody negative as well as autoantibody positive patients with SLE, no significant differences between any of the Benlysta groups and the
placebo group were observed. Further analysis revealed that Benlysta offered benefit to autoantibody positive patients. Because of this lack of efficacy of Benlysta in autoantibody negative patients and since the FDA has approved Benlysta in autoantibody positive patients, coverage will not be authorized for patients who are autoantibody negative.

- Autoantibodies may include: ANA (antinuclear antibodies), ds-DNA (double stranded DNA), Sm (Smith antigen), RNP (ribonucleoprotein), Ro/SSA, La/SSB.

V. Dosage and Administration

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
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<tbody>
<tr>
<td>SLE</td>
<td>IV: 10 mg/kg at 2 week intervals for the first 3 doses and at 4 week intervals thereafter; SC: 200 mg once weekly</td>
<td>IV: 10 mg/kg/dose; SC: 200 mg/week</td>
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</tbody>
</table>

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

### Reviews, Revisions, and Approvals

<table>
<thead>
<tr>
<th>Description</th>
<th>Date</th>
<th>P&amp;T Approval Date</th>
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<tbody>
<tr>
<td>Updated background information</td>
<td>12.13</td>
<td>12.13</td>
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<tr>
<td>Updated safety information. Appendix B: Cyclophosphamide added</td>
<td></td>
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<tr>
<td>Algorithm modified to include current prescribing recommendations for lab testing, and question regarding chronic infection</td>
<td>12.14</td>
<td>12.14</td>
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<tr>
<td>Converted policy to new format. In criteria, broadened question around disease activity in initial and re-auth; included live vaccine limitation in the safety appendix.</td>
<td>11.15</td>
<td>11.15</td>
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<tr>
<td>Shortened narrative; limited appendices to abbreviation key, safety appendix, appendix of disease activity instruments.</td>
<td></td>
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<tr>
<td>Limited references to package insert (updated), guidelines, and a review of validated disease activity instruments.</td>
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<tr>
<td>Converted policy to new template; modified approval criteria to 6 month and 12 months for initial and renewal criteria respectively. Added anaphylaxis with prior Benlysta administration as contraindication in initial and continuation criteria.</td>
<td>09.16</td>
<td>11.16</td>
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<tr>
<td>Converted to new template. Safety criteria applied according to the safety guidance discussed at CPAC and endorsed by Centene Medical Affairs.</td>
<td>09.17</td>
<td>11.17</td>
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<tr>
<td>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.</td>
<td>05.09.18</td>
<td>08.18</td>
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### 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.

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