Clinical Policy: Belimumab (Benlysta)
Reference Number: CP.PHAR.88
Effective Date: 10.01.11
Last Review Date: 08.19
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 patients aged 5 years and older 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 ≥ 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. 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. Request meets one of the following (a or b):
         a. Adults (≥ 18 years of age):
            i. IV: Dose does not exceed 10 mg/kg/dose at 2-week intervals for the first 3 doses and at 4-week intervals thereafter;
            ii. SC: 200 mg/week;
b. Pediatrics (≥ 5 years of age): Dose does not exceed 10 mg/kg/dose IV at 2-week intervals for the first 3 doses and at 4-week intervals thereafter.

Approval duration:
Medicaid/HIM-Medical Benefit – 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, and CP.PMN.53 for Medicaid and HIM-Medical Benefit.

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. 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);
   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/dose at 2-week intervals for the first 3 doses and at 4-week intervals thereafter;
         ii. SC: 200 mg/week;
      b. Pediatrics (≥ 5 years of age): Dose does not exceed 10 mg/kg/dose IV at 2-week intervals for the first 3 doses and at 4-week intervals thereafter.

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

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, and CP.PMN.53 for Medicaid and HIM-Medical Benefit.
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, and CP.PMN.53 for Medicaid and HIM-Medical Benefit 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
   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.

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>glucocorticoids (e.g., prednisone)</td>
<td>Varies</td>
<td>Varies</td>
</tr>
<tr>
<td>antimalarial agents (e.g., hydroxychloroquine, chloroquine)</td>
<td>Varies</td>
<td>Varies</td>
</tr>
<tr>
<td>non-biologic immunosuppressants (e.g., azathioprine, methotrexate, mycophenolate)</td>
<td>Varies</td>
<td>Varies</td>
</tr>
</tbody>
</table>

   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.

   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
<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>SLE</td>
<td>• IV (pediatrics and adults)</td>
<td>IV: 10 mg/kg/dose</td>
</tr>
<tr>
<td></td>
<td>○ 10 mg/kg at 2 week intervals for the first 3</td>
<td>SC: 200 mg/week</td>
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<tr>
<td></td>
<td>doses and at 4 week intervals thereafter</td>
<td></td>
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<tr>
<td></td>
<td>• SC (adults only)</td>
<td></td>
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</table>
Belimumab

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
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<tbody>
<tr>
<td></td>
<td>200 mg once weekly</td>
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<tr>
<td></td>
<td>Transition from IV to SC therapy (adults)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Administer first SC dose 1 to 4 weeks after the last IV dose</td>
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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

Coding Implications
Coders 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.

<table>
<thead>
<tr>
<th>HCPCS Codes</th>
<th>Description</th>
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<tbody>
<tr>
<td>J0490</td>
<td>Injection, belimumab, 10 mg</td>
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Reviews, Revisions, and Approvals

 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.
Shortened narrative; limited appendices to abbreviation key, safety appendix, appendix of disease activity instruments.
Limited references to package insert (updated), guidelines, and a review of validated disease activity instruments.

 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.

<table>
<thead>
<tr>
<th>Date</th>
<th>P&amp;T Approval Date</th>
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<tr>
<td>11.15</td>
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<td>09.16</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.

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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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