I. POLICY

Preauthorization required:

Note: The maximum initial authorization will be twelve weeks.

Note: Safety and effectiveness of Benlysta have not been established in children.

Note: Benlysta should not be given via home infusion due to potential anaphylactic reaction.

Note: 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 pregnant or nursing mothers.

Note: The use of Benlysta is not recommended in combination with biologic therapies or intravenous cyclophosphamide. Live vaccines should not be given concurrently with Benlysta.

Initial Therapy

Belimumab (Benlysta®) may be considered medically necessary for the treatment of adult patients with active autoantibody-positive systemic lupus who are receiving standard therapy, and when the following criteria are met:

- Consulting rheumatologist recommends treatment with Belimumab (Benlysta)
- The patient has an inadequate response to standard treatments (e.g. prednisone, Plaquenil, aspirin).

Maintenance Therapy

Belimumab (Benlysta®) maintenance therapy may be considered medically necessary when therapy has demonstrated improvement in disease activity at 12 weeks and maintenance of that improvement at each six-month re-evaluation.

Belimumab (Benlysta®) for all other indications than those listed above is considered investigational. There is insufficient evidence to support a conclusion concerning the health outcomes or benefits associated with treatment of this drug for other indications.
Cross-reference

MP-2.103 Off-Label Use of Prescription Drug and Medical Devices

II. PRODUCT VARIATIONS

[N] = No product variation, policy applies as stated
[Y] = Standard product coverage varies from application of this policy, see below

[N] Capital Cares 4 Kids  [N] Indemnity
[N] PPO  [N] SpecialCare
[N] HMO  [N] POS
[Y] SeniorBlue HMO*  [Y] FEP PPO**
[Y] SeniorBlue PPO*

* “FDA approved drugs used for indications other than what is indicated on the official label may be covered under Medicare if determined that the use is medically accepted, taking into consideration the major drug compendia, authoritative medical literature and/or accepted standards of medical practice.” Refer to Medicare Benefit Policy Manual (100-2, Chapter 15, Section 50.4.2- Unlabeled Use of Drug).”

** Refer to FEP Medical Policy Manual MP-10.07.30 Benlysta. The FEP Medical Policy manual can be found at:


III. DESCRIPTION/BACKGROUND

Systemic lupus erythematosus (SLE) is the most common type of lupus which can lead to symptoms of fever, swollen joints, anemia, and kidney failure. Symptoms of lupus vary widely depending on the individual case and the form of lupus present. There are generally four recognized forms or types of lupus: Cutaneous (skin) Lupus Erythematosus, Systemic Lupus Erythematosus, Drug-induced Erythematosus and Neonatal Lupus. According to the Lupus Foundation of America, SLE affects 1.5 million Americans, mostly women.

There is no single test to diagnose lupus. However, there are many laboratory tests which can assist the physician in making a lupus diagnosis. Commonly used blood tests in the diagnosis of SLE include the following:

- Anti-nuclear antibody test (ANA) to determine if autoantibodies to cell nuclei are present in the blood
- Anti-DNA antibody test to determine if there are antibodies to the genetic material in the cell
- Anti-Sm antibody test to determine if there are antibodies to Sm, which is a ribonucleoprotein found in the cell nucleus
- Serum (blood) complement test to examine the total level of a group of proteins which can be consumed in immune reactions
- Complement proteins C3 and C4 test to examine specific levels
- Antiphospholipid antibody

However, a positive ANA test, by itself, is not proof of lupus since the test may also be positive in many other autoimmune diseases. Because the ANA is positive in so many conditions, the results of the ANA test should be interpreted in light of the person's medical history, and his or her clinical symptoms.

Principal Therapeutic Options

Until the development of belimumab (Benlysta®), there were only 3 drugs that were FDA-approved for the treatment of systemic lupus erythematosus (SLE): prednisone, aspirin, and hydroxychloroquine. Other drugs commonly used in the treatment of SLE include nonsteroidal anti-inflammatory drugs (NSAIDs) and immunosuppressive agents, such as cyclophosphamide, methotrexate, azathioprine, and mycophenolate.

Belimumab is a human monoclonal antibody drug that specifically recognizes and inhibits the biological activity of B-lymphocyte stimulator, or BLyS. BLyS is a naturally occurring protein that is required for the development of B-lymphocyte cells into mature plasma B cells. Plasma B cells produce antibodies, the body's first line of defense against infection.

In lupus and certain other autoimmune diseases, elevated levels of BLyS are believed to contribute to the production of autoantibodies - antibodies that attack and destroy the body's own healthy tissues. The presence of autoantibodies appears to correlate with disease severity. Preclinical and clinical studies suggest that belimumab can reduce autoantibody levels in SLE as well as lower the frequency of the flare-ups that plague lupus patients.

Belimumab is administered intravenously 10 mg/kg over one hour at 2-week intervals for the first 3 doses and then at 4-week intervals thereafter. Hypersensitivity reactions including serious anaphylactic reactions have been reported. Benlysta should be administered by healthcare providers prepared to manage anaphylaxis.

Serious and sometimes fatal infections have also been reported in patients receiving immunosuppressive agents, including Benlysta. Belimumab (Benlysta®) has not been studied in combination with other biologic therapies, including B-cell target therapies, or intravenous cyclophosphamide. Therefore, use of Benlysta is not recommended in
Belimumab (Benlysta®) combination with biologic therapies or intravenous cyclophosphamide. It is not known if Benlysta is safe and effective in people with severe active lupus nephritis, or severe active central nervous system lupus. Benlysta has not been studied in pregnant or nursing mothers.

Belimumab (Benlysta®) is also being studied for patients with rheumatoid arthritis who have failed prior therapy.

IV. DEFINITIONS

MONOCLONAL ANTIBODY is a type of antibody, specific to a certain antigen, created in the laboratory from hybridoma cells.

V. BENEFIT VARIATIONS

The existence of this medical policy does not mean that this service is a covered benefit under the member's contract. Benefit determinations should be based in all cases on the applicable contract language. Medical policies do not constitute a description of benefits. A member's individual or group customer benefits govern which services are covered, which are excluded, and which are subject to benefit limits and which require preauthorization. Members and providers should consult the member's benefit information or contact Capital for benefit information.

VI. DISCLAIMER

Capital's medical policies are developed to assist in administering a member's benefits, do not constitute medical advice and are subject to change. Treating providers are solely responsible for medical advice and treatment of members. Members should discuss any medical policy related to their coverage or condition with their provider and consult their benefit information to determine if the service is covered. If there is a discrepancy between this medical policy and a member's benefit information, the benefit information will govern. Capital considers the information contained in this medical policy to be proprietary and it may only be disseminated as permitted by law.

VII. REFERENCES


Centers for Medicare and Medicaid Services (CMS) Medicare Benefit Policy Manual. Publication 100-02. Chapter 15. Sections 50, 50.4.1, 50.4.3. Drugs and Biologicals. Effective 10/01/03.
MEDICAL POLICY

<table>
<thead>
<tr>
<th>POLICY TITLE</th>
<th>BELIMUMAB (BENLYSTA®)</th>
</tr>
</thead>
<tbody>
<tr>
<td>POLICY NUMBER</td>
<td>MP-2.155</td>
</tr>
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</table>


ClinicalTrials.gov. Benlysta completed clinical trial. [Website]:

Lupus Foundation of America, Inc. Understanding Lupus. [Website]:


Taber’s Cyclopedic Medical Dictionary 19th edition

VIII. CODING INFORMATION

Note: This list of codes may not be all-inclusive, and codes are subject to change at any time. The identification of a code in this section does not denote coverage as coverage is determined by the terms of member benefit information. In addition, not all covered services are eligible for separate reimbursement.

Covered when medically necessary:

<table>
<thead>
<tr>
<th>HCPCS Code</th>
<th>Description</th>
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<tbody>
<tr>
<td>J0490</td>
<td>INJECTION, BELIMUMAB, 10 MG</td>
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</table>

<table>
<thead>
<tr>
<th>ICD-9-CM Diagnosis Code*</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>710.0</td>
<td>Systemic lupus erythematosus</td>
</tr>
</tbody>
</table>

*If applicable, please see Medicare LCD or NCD for additional covered diagnoses.
The following ICD-10 diagnosis codes will be effective October 1, 2014:

<table>
<thead>
<tr>
<th>ICD-10-CM Diagnosis Code*</th>
<th>Description</th>
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<tbody>
<tr>
<td>M32.0</td>
<td>Drug-induced systemic lupus erythematosus</td>
</tr>
<tr>
<td>M32.10</td>
<td>Systemic lupus erythematosus, organ or system involvement unspecified</td>
</tr>
<tr>
<td>M32.11</td>
<td>Endocarditis in systemic lupus erythematosus</td>
</tr>
<tr>
<td>M32.12</td>
<td>Pericarditis in systemic lupus erythematosus</td>
</tr>
<tr>
<td>M32.13</td>
<td>Lung involvement in systemic lupus erythematosus</td>
</tr>
<tr>
<td>M32.14</td>
<td>Glomerular disease in systemic lupus erythematosus</td>
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<tr>
<td>M32.15</td>
<td>Tubulo-interstitial nephropathy in systemic lupus erythematosus</td>
</tr>
<tr>
<td>M32.19</td>
<td>Other organ or system involvement in systemic lupus erythematosus</td>
</tr>
<tr>
<td>M32.8</td>
<td>Other forms of systemic lupus erythematosus</td>
</tr>
<tr>
<td>M32.9</td>
<td>Systemic lupus erythematosus, unspecified</td>
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</tbody>
</table>

*If applicable, please see Medicare LCD or NCD for additional covered diagnoses.

IX. POLICY HISTORY

<p>| MP-2.155                  | CAC 7/26/11 New policy.                                                   |
|                           | CAC 1/29/13 Consensus review. No change to policy statements. References updated |</p>
<table>
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