Benlysta® (belimumab)

FDA approval: March 9, 2011
HCPCS: J0490
Benefit: Medical

Policy/Criteria:

Note: Requests must be supported by submission of chart notes and patient specific documentation.

A. Benlysta® may be considered medically necessary in patients ≥ 18 years of age when the criteria below are met:

   a. Diagnosis of systemic lupus erythematosus (SLE)

   b. Patients have tested positive for serum antibodies at 2 independent time points. Positive serum antibody tests are:
      • Anti-nuclear antibody (ANA) titer ≥ 1:80
      • Anti-double-stranded DNA ≥ 30 IU/mL

   c. Patients have active disease as indicated by a score on the safety of estrogens in Lupus Erythematosus National Assessment modification on the SLE Disease Activity Index (SELENA-SLEDAI) of at least 6.

   d. Patient does not have severe lupus nephritis, defined as either:
      • Proteinuria > 6g/24 hours, or
      • Serum creatinine > 2.5 mg/dL

   e. Patient does not have active nephritis or active central nervous system lupus, defined as:
      • A negative urinalysis for significant RBCs and WBCs
      • No evidence of active CNS inflammation, including seizures, psychosis, organic brain syndrome, cerebrovascular accident, cerebritis, or CNS vasculitis requiring therapeutic intervention within the previous 60 days before initiation of Benlysta.

   f. Previous treatment courses of at least 12 weeks each with 2 or more of the following have been ineffective: chloroquine, hydroxychloroquine, methotrexate, azathioprine, cyclophosphamide OR mycophenolate mofetil, unless all are contraindicated or not tolerated.

   g. Patient is currently receiving, and will continue to receive a stable standard of care regimen. Standard of care treatment regimen comprise of any of the following drug classes, alone or in combination;
      • Antimalarials
• Corticosteroids
• Non-biologic immunosuppressives

B. Quantity Limitations, Authorization Period and Renewal Criteria

a. 10 mg/kg infusion at 2-weeks intervals for the first 3 doses and at 4-week intervals thereafter
b. Coverage will be provided initially for 6 months. Renewal will be provided when the following criteria are met:
   • Decrease on the SELENA-SLEDAI of at least 4 points

c. Authorization will be reviewed annually thereafter to assess treatment response. If there has been deterioration in clinical status, as defined by any of the following, discontinuation of Benlysta should be considered:
   • Increase in SELENA-SLEDAI or 8 or more points, or
   • Increase in BILAG of 8 or more points

C. Benlysta is considered investigational when used for all other conditions, including but not limited to:

a. Rheumatoid arthritis
b. Sensitization before renal transplantation
c. Sjogren’s syndrome
d. Waldenstrom’s macroglobulinemia

***Note: Coverage may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at http://www.cms.hhs.gov/. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia

Therapeutic considerations:

B. FDA approved indication / Diagnosis

Treatment of adult patients with active, autoantibody-positive, systemic lupus erythematosus who are receiving standard therapy.

Limitations of use: Use is not recommended in patients with severe active lupus nephritis, severe active CNS lupus, or in combination with other biologics, including B-cell targeted therapies or intravenous (IV) cyclophosphamide.

*Please refer to most recent prescribing information.

C. Background Information

Benlysta blocks the binding of soluble B lymphocyte stimulator, BLyS, protein which reduces immunoglobulin-producing plasma cells and decreases the immune system’s attack on healthy tissue.

The clinical development program of Benlysta in SLE included one pivotal Phase II dose-escalating trial and 2 pivotal Phase III trials. The Phase II trial randomized 449 seropositive and seronegative SLE patients to one of 3 doses of Benlysta for 24 weeks. Primary clinical endpoints were improvement in the SELENA-SLEDAI and time to flare. Neither endpoint was met. However, post-hoc subgroup analysis revealed that among seropositive patients, the mean
improvement in SELENA-SLEDAI score was 29 points compared to 14 points among seronegative patients (p=0.044). For this reason, only seropositive patients were included in the phase 3 trials.

Patients with active central nervous system lupus, severe lupus nephritis, active nephritis, or requiring hemodialysis were excluded from the studies. The primary outcome measure was the SLE Responder Index, a nonvalidated index that aims to assess clinically meaningful improvement coincident with no significant worsening in overall disease activity. Clinically meaningful improvement was defined by a decrease on the SELENA-SLEDAI of at least 4 points. The American College of Rheumatology (ACR) has reported that a clinically meaningful difference is an improvement of 7 points. Worsening in overall disease activity was defined by pre-specified limits of change on the British Isles Lupus Assessment Group (BILAG) instrument and by physician global assessment (PGA). The ACR has reported that a clinically meaningful difference is a worsening of 8 points for the SELENA-SLEDAI score and BILAG score.

Other pharmacologic treatments of SLE include corticosteroids, antimalarials (such as hydroxychloroquine, chloroquine) and immunosuppressives (such as azathioprine, cyclophosphamide, methotrexate, mycophenolate).

### Cross References

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### D. Efficacy

*Please refer to most recent prescribing information.

### E. Medication Safety Considerations

Boxed Warning: No

*Please refer to most recent prescribing information.

### F. Dosing and administration

a. **Dosing:**
   i. 10 mg/kg intravenous (IV) at 2-week intervals for the first 3 doses, and at 4-week intervals thereafter

*Please refer to most recent prescribing information.

### G. How supplied

a. 120mg and 400mg vials

*Please refer to most recent prescribing information.

### References:

4. The American College of Rheumatology response criteria for systemic lupus erythematosus clinical trials:
9. Moore, Andrew R, and Derry Sheena. Systematic review and meta-analysis of randomized trials and cohort studies of mycophenolate mofetil in lupus nephritis.Arthritis Research & Therapy. 2006, 8:R182. This article is online at: http://arthritis-research.com/content/8/6/R182

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* The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or http://dailymed.nlm.nih.gov/dailymed/index.cfm

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