VENTURA COUNTY
HEALTH CARE PLAN

Prior Authorization DRUG Guidelines

Benlysta® (Belimumab)

Effective Date: 1/31/12
Date Developed: 12/9/11 by Albert Reeves MD
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Benlysta (Belimumab) is a Monoclonal Antibody for treatment of autoantibody- positive (antinuclear antibody [ANA] and/or anti-double-stranded DNA [anti-ds- DNA]) systemic lupus erythematosus (SLE) in addition to standard therapy. Benlysta lowers the body's harmful response to diseases of the immune system.

Pre-Authorization Criteria: treatment of adult patients with active, autoantibody-positive systemic lupus erythematosus (SLE) who are receiving standard therapy.

Note: VCHCP requires that Benlysta be prescribed by a rheumatologist or PCP after consultations with rheumatologist.

Note: 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.

Note: This medication is in a class the Institute for Safe Medication Practices (ISMP) includes among its list of drug classes that have a heightened risk of causing significant patient harm when used in error.

Dosing ADULTS:

SLE: I.V.: Initial: 10 mg/kg every 2 weeks for 3 doses; Maintenance: 10 mg/kg every 4 weeks.

Dosage Forms: Injection, powder for reconstitution: 120 mg, 400 mg
Note: contains polysorbate 80

Administration

Administer intravenously over 1 hour through a dedicated I.V. line. Do not give as an I.V. push or bolus. Discontinue infusion for severe hypersensitivity reaction (eg, anaphylaxis, angioedema). The infusion may be slowed or temporarily interrupted for minor reactions. Consider premedicating for prophylaxis against infusion reactions.

WARNINGS / PRECAUTIONS

Special handling:

Hazardous agent: Use appropriate precautions for handling and disposal.

Concerns related to adverse effects:

Deaths: Deaths due to infection, cardiovascular disease, and suicide were higher in belimumab patients compared to placebo during clinical trials.

Hypersensitivity reactions: Has been associated with hypersensitivity reactions; rare anaphylaxis also reported. Immediately discontinue use if severe reaction occurs. It is unknown if premedication prevents or reduces the severity of hypersensitivity reactions.

Infections: Use is not recommended if severe active infection is present; serious and potentially fatal infections may occur during treatment. Consider discontinuing belimumab in patients who develop infections and initiate appropriate anti-infective treatment.

Infusion reactions: Infusion reactions have been associated with use; discontinue for anaphylaxis or angioedema. Most reactions occur during or within 24 hours of the infusion. The most common reactions

include: headache, nausea, rash and skin reactions. Additional reactions may include hypotension, dyspnea, bradycardia, and myalgia. The infusion may be slowed or temporarily interrupted for minor reactions.

Malignancy: May increase the risk of malignancy.

Psychiatric: The most common symptoms reported included anxiety, depression, and/or insomnia. New onset or worsening of existing depression, and suicide, has been reported; most patients had a history of a psychiatric disorder and were already receiving treatment.

DRUG Interactions

Abatacept: May enhance the adverse/toxic effect of Belimumab. *Risk X: Avoid combination*

Abciximab: May enhance the potential for allergic or hypersensitivity reactions to Monoclonal Antibodies. Also may cause thrombocytopenia or diminished therapeutic effects. *Risk C: Monitor therapy*

Alefacept: May enhance the adverse/toxic effect of Belimumab. *Risk X: Avoid combination*

BCG: Immunosuppressants may diminish the therapeutic effect of BCG. *Risk X: Avoid combination*

Belatacept: May enhance the adverse/toxic effect of Belimumab. *Risk X: Avoid combination*

Coccidioidin Skin Test: Immunosuppressants may diminish the diagnostic effect of Coccidioidin Skin Test. *Risk C: Monitor therapy*

Cyclophosphamide: Belimumab may enhance the adverse/toxic effect of Cyclophosphamide. *Risk X: Avoid combination*

Denileukin Diftitox: May enhance the adverse/toxic effect of Belimumab. *Risk X: Avoid combination*

Denosumab: May enhance the adverse/toxic effect of Immunosuppressants. Specifically, the risk for serious infections may be increased. *Risk C: Monitor Therapy*

Echinacea: May diminish the therapeutic effect of Immunosuppressants. *Risk D: Consider therapy modification*

Etanercept: May enhance the adverse/toxic effect of Belimumab. *Risk X: Avoid combination*

Leflunomide: Immunosuppressants may enhance the adverse/toxic effect of Leflunomide. Specifically, the risk for hematologic toxicity such as pancytopenia, agranulocytosis, and/or thrombocytopenia may be increased. Management: Consider not using a leflunomide loading dose in patients receiving other immunosuppressants. Patients receiving both leflunomide and another immunosuppressant should be monitored for bone marrow suppression at least monthly. *Risk D: Consider therapy modification*

Monoclonal Antibodies: May enhance the adverse/toxic effect of Belimumab. *Risk X: Avoid combination*

Natalizumab: Immunosuppressants may enhance the adverse/toxic effect of Natalizumab. Specifically, the risk of concurrent infection may be increased. *Risk X: Avoid combination*

Pimecrolimus: May enhance the adverse/toxic effect of Immunosuppressants. *Risk X: Avoid combination*

Roflumilast: May enhance the immunosuppressive effect of Immunosuppressants. *Risk D: Consider therapy modification*

Sipuleucel-T: Immunosuppressants may diminish the therapeutic effect of Sipuleucel-T. *Risk C: Monitor therapy*

Tacrolimus (Topical): May enhance the adverse/toxic effect of Immunosuppressants. *Risk X: Avoid combination*

Trastuzumab: May enhance the neutropenic effect of Immunosuppressants. *Risk C: Monitor therapy*

Vaccines (Inactivated): Belimumab may diminish the therapeutic effect of Vaccines (Inactivated). *Risk D: Consider therapy modification*

Vaccines (Inactivated): Immunosuppressants may diminish the therapeutic effect of Vaccines (Inactivated). *Risk C: Monitor therapy*

Vaccines (Live): Immunosuppressants may enhance the adverse/toxic effect of Vaccines (Live). Vaccinial infections may develop. Immunosuppressants may diminish the therapeutic effect of Vaccines (Live). Management: Avoid use of live organism vaccines with immunosuppressants; live-attenuated vaccines should not be given for at least 3 months after immunosuppressants. *Risk X: Avoid combination*

Vaccines (Live): Belimumab may enhance the adverse/toxic effect of Vaccines (Live). *Risk X: Avoid combination*

REFERENCES

1. Navarra SV, Guzmán RM, Gallacher AE, et al, "Efficacy and Safety of Belimumab in Patients With Active Systemic Lupus Erythematosus: A Randomised, Placebo-Controlled, Phase 3 Trial," *Lancet*, 2011, 26(377):721-31. [PubMed 21296403]

2. Wallace DJ, Stohl W, Furie RA, et al, "A Phase II, Randomized, Double-Blind, Placebo-Controlled, Dose-Ranging Study of Belimumab in Patients With Active Systemic Lupus Erythematosus," *Arthritis Rheum*, 2009, 61(9):1168-78. [PubMed 19714604]

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