CAREPATHrx™
Specialty Pharmacy & Infusion Solutions

CLINICAL GUIDELINES FOR BELIMUMAB (BENLYSTA) INJECTION

Section: Nursing
Compliance: ACHC Infusion Pharmacy
ACHC Standards: N/A
URAC Standards: N/A
TJC Standards: N/A
Policy ID: NUR231
Effective: 3/1/22
Reviewed: 5/1/22
Revised:
Approved by: Kathleen Patrick, President, 3/1/22

I. POLICY

Belimumab (Benlysta) is an IgG1-lambda monoclonal antibody that prevents the survival of B lymphocytes by blocking the binding of soluble human B lymphocyte stimulator protein (BLyS to receptors on B lymphocytes. This reduces the activity of B-cell mediated immunity and the autoimmune response. Belimumab is indicated for lupus nephritis and systemic lupus erythematosus (SLE). The following outlines the procedures and protocol for coordination of servicing patients in need of outpatient intravenous (IV) belimumab. Dosing and administration guidance for subcutaneous (SC) use is noted.

Patient Acceptance Criteria

A. All candidates for home care service must be evaluated by the clinician(s) and deemed appropriate to receive home care based upon admission criteria.

B. The decision to administer a first dose (intravenous) in the home by a field nurse will be determined on a case-by-case basis and reviewed by nursing and pharmacy management. The following criteria will be evaluated:

1. Prescriber preference
2. Allergy profile
3. Patient age (first dosing may be considered for adult patients)
4. Ability to secure contracted nursing for subsequent infusions
5. Other relevant social and/or medical history

C. CarepathRx treatment protocol for anaphylaxis will be instituted unless a more comprehensive patient specific order is provided by the physician. See policy NUR012 (Appendix A).

II. PHARMACOLOGY OVERVIEW

A. Indications:

1. Treatment of patients five years or older with autoantibody-positive systemic lupus erythematosus receiving standard therapy

2. Adult patients with active lupus nephritis who are receiving standard therapy

B. Intravenous Dosage

1. Lupus nephritis [≥ 18yrs]:
   IV: 10 mg/kg every 2 weeks for 3 doses followed by 10mg/kg every 4 weeks

2. Systemic lupus erythematosus (SLE) [≥ 5yrs]:
   IV: 10 mg/kg every 2 weeks for 3 doses followed by 10 mg/kg every 4 weeks

C. Subcutaneous Drugs

1. Lupus Nephritis [≥ 18yrs]:
   SC: 400mg (two, 200mg injections) once weekly for 4 doses followed by 200mg once weekly

   - Patients with lupus nephritis may transition from IV therapy to SC any time after completing the first 2 intravenous doses. If transitioning, administer the first SC dose of 200mg 1-2 weeks after the last IV dose.

2. Systemic lupus erythematosus (SLE) [≥ 18 yrs]:
   SC: 200mg once weekly

   - Patients with SLE transitioning from IV to SC administration may administer the first SC dose of 200mg 1-4 weeks after the last IV dose.

D. Contraindications: Anaphylaxis to belimumab or any component of the formulation

E. Precautions

1. 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 cyclophosphamide.

2. Hypersensitivity Reactions

   a. Acute hypersensitivity reactions including anaphylaxis and death, have been associated with treatment. Events can occur within hours of infusion or in patients who have previously tolerated infusions requiring discontinuation and appropriate medical treatment. Limited data suggest patients with a history of multiple drug allergies or significant hypersensitivity may be at increased risk.
   b. Non-acute hypersensitivity reactions including facial edema, fatigue, headache, myalgia, nausea, and rash, which may occur up to a week after infusion.
   c. Delayed hypersensitivity reactions have been reported following exposure to pharmaceutical products containing polysorbate 80 in certain individuals.

3. Infusion reactions

a. Similar to hypersensitivity reactions, with symptoms including angioedema, bradycardia, dyspnea, headache, hypotension, myalgia, pruritus, rash, and urticaria. Monitor following administration and slow or temporarily interrupt infusion for infusion reactions. May consider premedication prior to infusion.

4. Infections

    a. Serious and potentially fatal infections may occur during treatment. Monitor closely and consider interrupting belimumab in patients who develop new infections while appropriate anti-infective therapy is administered.

5. Malignancy

    a. Immunosuppressants may increase risk of malignancy

6. Progressing multifocal leukoencephalopathy (PML)

    a. Cases of progressive multifocal encephalopathy have been reported in patients with systemic lupus erythematosus receiving immunosuppressants. Consult a neurologist for patients presenting with new-onset or deteriorating neurological signs or symptoms.

7. Psychiatric Disorders

    a. Depression, suicidal ideation or behavior have been reported. Initial and ongoing assessment of risk of depression and suicide should be completed. Patients and caregivers should be advised to seek medical attention for suicidal ideation, new or worsening depression, anxiety, or other mood changes.

8. Pregnancy/Lactation

    a. Available data on use of belimumab in pregnant women is insufficient. If patient decided to prevent pregnancy, females of reproductive potential should use effective contraception during treatment and for at least 4 months after the final treatment. If pregnancy occurs while receiving belimumab, discontinue therapy and enroll in belimumab pregnancy registry for monitoring

    b. It is not known if belimumab passes into human milk, the effects of the rug on breastfed infants, or the effects of the drug on milk production.

9. Live Vaccinations

    a. Live vaccines should not be given for 30 days before or concurrently with belimumab as clinical safety has not been established. Belimumab's mechanism of action may interfere with the response to immunizations.

F. Pharmacokinetics

1. Onset of action:
    a. N cells: 8 weeks
    b. Clinical improvement: 16 weeks

2. Volume of distribution: 5L

3. Half-life elimination: 19.4 days

G. Adverse Reactions
1. Gastrointestinal: Diarrhea 12%; Nausea 15%; Viral Gastroenteritis 3%
2. Hypersensitivity reaction 13%
3. Infection: 71% to 82%; Serious infection 6%; Influenza 5%
4. Nervous system: Psychiatric disturbance 16%; Serious <1%; Anxiety 4%; Depression 5% to 6%; Headache ≥3%; Insomnia 6% to 7%; Migraine 5%; Suicidal ideation ≤1%; Suicidal tendencies ≤1%
5. Infusion related reaction 17%; injection site reaction 6%; Limb pain 6%
6. Dermatologic: Dermatologic reaction ≥3%
7. Genitourinary: Cystitis 4%; UTI > 5%
8. Hematologic: Leukopenia 4%
9. Respiratory: Bronchitis 9%; Nasopharyngitis 9%; Pharyngitis 5%; Sinusitis >5%; URTI >5%
10. Miscellaneous: Fever 10%

H. Drug Interactions

1. Avoid concomitant Use- Live vaccines, biologic anti-psoriasis agents, biologic disease modifying antirheumatic drugs, cladribine, natalizumab, pimecrolimus, talimogene laherparepvec, upadacitinib

a. Increased Effect/Toxicity
- Belimumab may increase the levels/effects of: Live vaccines, biologic anti-psoriasis agents, biologic disease-modifying antirheumatic drugs, fingolimod, leflunomide, natalizumab, ozanimod, polymethylmethacrylate, ponesimod, siponimod, talimogene laherparepvec, upadactinib

b. Decreased Effect
- Belimumab may decrease the levels/effects of: BCG vaccine, COVID-19 vaccine, inactivated vaccines, brincidofovir, coccidioides immitis skin test, pidotimod, sipuleucel-T, tertomotide
- The levels/effects of belimumab may be decreased by echninacea

III. ADMINISTRATIVE GUIDELINES

A. Intravenous Administration

1. Site: IV infusion should begin within 1 hour of reconstitution and dilution. Do not infuse with other agents. **Use in-line 0.2micron low protein binding filter.**

B. Intravenous Dosage

1. Lupus nephritis [≥ 18yrs]:
IV: 10 mg/kg every 2 weeks for 3 doses followed by 10mg/kg every 4 weeks

2. Systemic lupus erythematosus (SLE) [≥ 5yrs]:
IV: 10 mg/kg every 2 weeks for 3 doses followed by 10 mg/kg every 4 weeks

C. Subcutaneous Administration

1. It is recommended that the first SC injection be under the supervision of a healthcare professional with proper training and education provided. A patient or caregiver may administer after the provider determines it is appropriate.
2. Patients must remove the auto-injector or prefilled syringe from the refrigerator and allow it to sit at room temperature for 30 minutes prior to injection.
3. Advise patients to rotate injection sites for each injection. Do not administer on areas of skin that are bruised, red, tender, or hard. Refer to package insert for specific subcutaneous administration guidelines.

D. Subcutaneous Dosage

1. Lupus Nephritis [≥ 18yrs]
   SC: 400mg (two, 200mg injections) once weekly for 4 doses followed by 200mg once weekly
2. Systemic lupus erythematosus (SLE) [≥ 18 yrs]:
   SC: 200mg once weekly

E. Duration

1. Duration of therapy should be dependent on patient response and adverse reaction. No specific duration is noted in package insert.

F. Dose Adjustment

1. No dosage adjustment is recommended in patient with renal or hepatic impairment

G. Patient Monitoring

1. Monitor for improvements in objective measures of disease activity
2. Monitor for signs and symptoms of hypersensitivity reactions (during and after) IV Infusion

   a. Infusion reactions may occur. Premedication may be helpful as prophylaxis.
      - Premedication with Benadryl 25mg oral, 30 minutes prior to belimumab infusion is recommended. Oral medication NOT supplied by pharmacy.
      - Consider pre-medicating with an antihistamine and antipyretic for prophylaxis against hypersensitivity / infusion reactions
      - Discontinue infusion for severe hypersensitivity reaction
      - The infusion may be slowed or temporarily interrupted for minor reactions

   b. Treatment for hypersensitivity reactions should be available via anaphylaxis kit

3. SC Injection

   a. Never inject into areas where the skin is tender, bruised, red, or hard

   b. Injection site reactions such as pain, erythema, hematoma, pruritus, and induration can occur. In clinical trials, 94% did not necessitate discontinuation of treatment.

IV. NURSING PROCEDURE FOR INTRAVENOUS INFUSION

A. Supplies

1. Alcohol swabs
2. Gloves
3. Vials of Belimumab (120mg/400mg)
4. SWFI for reconstitution (1.5mL/4.8mL)
5. Bag of sodium chloride 0.9% for dilution (250 mL)
6. IV Pole
7. Infusion pump and batteries
8. IV Start Kit
9. Peripheral IV catheter (22g x 1 in. and 24g x ¾ in.)
10. Port access needle (22g x ¾ to 1 in. safe step)
11. Tape
12. Extension set 8 inches
13. IV Injection cap
14. IV administration set with 0.2-micron filter
15. Dial-a-flow tubing with extension set 0.2-micron filter
16. Syringes (5mL and 10mL for reconstitution, and various sizes depending on dose) and Needles (20g x 1 in.)
17. Sharps container

Patients may receive infusion via pole-mounted infusion pump (pediatrics) or dial-a-flow tubing

B. How supplied

1. IV: Belimumab for injection is provided as lyophilized 120mg and 400mg drug for reconstitution with 1.5 mL and 4.8 mL sterile water, respectively. Each when reconstituted has a concentration of 80ml/mL. Refer to specific product packing and prescribing information for NDC, storage, stability, and excursion information.

2. Dosing Calculator: Vial Calculator | BENLYSTA for Rheumatologists (benlystahcp.com)

C. Storage and Handling

1. Store vials at 36 degrees F to 46 degrees F (2 degrees C to 8 degrees C) in original carton protected from light. Do not freeze.
2. Reconstituted product must be infused within 1 hour of preparation
3. Refer to specific product packing and prescribing information for storage, stability, and excursion information

D. Compatibility

1. Stable in NS, ½ NS. LR
2. Do not infuse with other agents
3. Do not dilute with D5W

E. Procedures

1. Explain the reasoning for visit and use of belimumab
2. Don gloves
3. Establish venous access prior to preparation of drug
4. Counsel patient on warnings, precautions, and potential side effects including but not limited

to: infusion site reactions, nausea, diarrhea, fever, nasopharyngitis, bronchitis, insomnia, leg or arm pain, depression, headache (migraine)

5. Prepare product:

    a. Remove belimumab vials from refrigerator and allow to stand for 10-15 minutes for the vial to reach room temperature
    b. Withdraw and discard a volume of normal saline from the 250 mL stock bag equal to the volume of the reconstituted solution of belimumab required for the patient's dose. Total volume will be 250 mL.
    c. Reconstitute powder with sterile water for injection, USP as follows: 120mg vial with 1.5 mL sterile water for injection OR 400mg vial with 4.8 mL sterile water for injection. Ensure the stream of diluent is not directed onto the lyophilized powder.
    d. Swirl vial for 60 seconds, allow to stand for 5 minutes. Repeat until powder is dissolved. **DO NOT SHAKE.** May take 10 to 30 minutes to fully reconstitute.
    e. After reconstitution, each vial has volume of 1.5 mL (120 mg) or 5 mL (400 mg). Visually inspect vials for any particulate matter and that the solution is opalesce and colorless to pale yellow in color.
    f. Total dose of reconstituted product should be further diluted in 0.9%sodium chloride bag. Total volume will be 250 mL.
    g. Reconstituted belimumab must be infused within 1 hour of preparation.

6. Infusion Rates:

    a. Infusion should be administered continuously over a period of 1 hour through a dedicated IV line or per ordered titration unless previous infusion history dictates a slower rate. **Use in-line 0.2-micron low protein binding filter.**
    b. Do not infuse other agents concomitantly with belimumab in the same IV line.
    c. If a minor reaction is observed, the infusion may be slowed or temporarily interrupted.
    d. Follow CarepathRx treatment protocol for anaphylaxis. See policy NUR012 (Appendix A).
    e. Patients with a history of severe infusion reactions should only be considered for home infusion after a thorough discussion of safety for the patient and risk vs. benefit with physician. If home infusion continues, a slower rate will be utilized.

V. CLINICAL MONITORING

A. Monitor for signs and symptoms of infection. Therapy may need interrupted during an active infection.

B. Monitor for signs and symptoms of depression and suicide before and during treatment. Contact the patient's provider if they experience new or worsening depression, suicidal thoughts or behavior, or other mood changes.

C. There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to belimumab during pregnancy. Healthcare professionals are encouraged to register patients by calling 1-877-681-6296.

D. Monitor disease severity including:

1. Malar or discoid rash
2. Photosensitivity

3. Oral ulcers
4. Serositis
5. Arthritis
6. Renal disorders
7. Neurological disorders – Seizures
8. Hemolytic anemia
9. Anti-nuclear antibodies
10. Laboratory assessment – CBC, ESR, BUN/Creatinine, and LFTs
11. Disease specific assessment questions to monitor response to treatment and progression

REFERENCES:

Benlysta [package insert]. Philadelphia, PA: GlaxoSmithKline, LLC; 2011.

Fernando, MMA and Isenberg DA. Clinical presentation and monitoring of lupus nephritis. *Annals of the Rheumatic Diseases* 2005; 64**:**524-527.