Belimumab (Benlysta®)

Belimumab (Benlysta®) is a BLyS-specific inhibitor that blocks the binding of soluble BLyS, a B-cell survival factor to its receptors on B-cells. Belimumab does not bind -cells directly, but by binding BLyS, it inhibits the survival of B-cells including autoreactive B-cells, and reduces the differentiation of B cells into immunoglobulin-producing plasma cells.

Resources from Manufacturer

Benlysta Patient Medication Guide
Benlysta Prescribing Information
Benlysta Co-pay Assistance Program
GSK Patient Assistance Foundation

FDA-Approved Indications and Dosing in Rheumatology

Belimumab is indicated for:

- Patients aged 5 years and older with active systemic lupus erythematosus (SLE) who are receiving standard therapy
- Patients aged 5 years and older with active lupus nephritis who are receiving standard therapy
- Limitations of Use: The efficacy of belimumab has not been evaluated in patients with severe active central nervous system lupus. Use of belimumab is not recommended in this situation.

Dosing:

- Intravenous dosing for adults and pediatric patients with SLE or lupus nephritis:
  - 10 mg/kg every 2 weeks for the first 3 doses, then every 4 weeks thereafter
  - Consider prophylactic premedication for infusion reactions and hypersensitivity reactions.
- Subcutaneous Dosing:
  - Adults with SLE: 200 mg SC once weekly
  - Pediatric Patients with SLE
    Weighing greater than or equal to 40 kg: 200 mg once weekly
    Weighing 15 kg to less than 40 kg: 200 mg once every 2 weeks
  - Adults with lupus nephritis: 400 mg (two 200-mg injections) once weekly for 4 doses, then 200 mg once weekly thereafter.

Transitioning from Intravenous to Subcutaneous Administration:

- SLE: Administer the first subcutaneous dose 1 to 4 weeks after the last intravenous dose.
- Lupus Nephritis: A patient with lupus nephritis may transition from intravenous therapy with belimumab to subcutaneous therapy after the patient completes the first 2 intravenous doses. If transitioning, administer the first subcutaneous dose of 200 mg 1 to 2 weeks after the last intravenous dose.

Contraindications

Previous anaphylaxis to belimumab.

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Warnings and Precautions

- Serious Infections: Serious and sometimes fatal infections have occurred in patients receiving immunosuppressive agents, including belimumab. Use with caution in patients with severe or chronic infections. Consider interrupting therapy with belimumab if patients develop a new infection during treatment with belimumab.
- Progressive Multifocal Leukoencephalopathy (PML): Evaluate patients with new-onset or deteriorating neurological signs and symptoms for PML. If PML is suspected, immunosuppressant therapy, including belimumab, must be suspended until PML has been excluded. If PML is confirmed, immunosuppressant therapy, including belimumab, must be discontinued.
- Hypersensitivity reactions, including anaphylaxis–Serious and fatal reactions have been reported.
- Depression and suicidality were reported in trials with belimumab. Assess for depression and risk of suicide before treatment with belimumab and monitor during treatment. Instruct patients to contact their healthcare provider if new or worsening depression, suicidal thoughts, or other mood changes occur.
- Immunization: Live vaccines should not be given concurrently with belimumab

Adverse Reactions

Most common adverse reactions (>5%):

- Nausea
- Diarrhea
- Pyrexia
- Nasopharyngitis
- Bronchitis
- Insomnia
- Pain in extremity
- Depression
- Migraine
- Pharyngitis
- Injection site reactions (subcutaneous administration)

Medication Strength and Preparations

- Single-dose pre-filled syringe: 200 mg/mL
- Single-dose prefilled auto-injector: 200 mg/mL
- Single-dose vial (lyophilized powder for reconstitution and dilution for IV infusion):
  - ❑ 120 mg/5 mL
  - ❑ 400 mg/20 mL

Medication Administration and Storage

- Store in original carton to protect from light
- Store in refrigerator at 2°C to 8°C (36°F to 46°F)–do not freeze
- The vial stoppers, autoinjectors, and pre-filled syringes are not made with natural rubber latex

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Administration Instructions for Subcutaneous Injection

1. Remove the autoinjector or prefilled syringe from the refrigerator and allow it to sit at room temperature for 30 minutes prior to the subcutaneous injection. Do not warm belimumab in any other way.
2. Prior to administration, visually inspect the window of the autoinjector or the prefilled syringe for particulate matter or discoloration. Belimumab should be clear to opalescent and colorless to pale yellow. Do not use belimumab if the product exhibits discoloration or particulate matter. Do not use the autoinjector or prefilled syringe if dropped on a hard surface.
3. When injecting in the same body region, use a different injection site for each injection; never give injections into areas where the skin is tender, bruised, red, or hard. When a 400-mg dose is administered at the same site, it is recommended that the 2 individual 200-mg injections be administered at least 5 cm (approximately 2 inches) apart.
4. Instruct the patient or patient caregiver to administer belimumab, preferably on the same day each week or the same day of alternate weeks, as appropriate.
5. If a dose is missed, administer a dose as soon as the patient remembers. Thereafter, the patient can resume dosing on their usual day of administration or start a new schedule from the day that the missed dose was administered.

Intravenous Administration Pre-Infusion Checklist

- Ask the patient if he/she:
  - ❑ Has a current or recent infection or illness
  - ❑ Is taking antibiotics
  - ❑ Has an upcoming surgery
- If the answer is yes to any of these questions, notify the ordering provider before initiating the infusion therapy.

Intravenous Medication Preparation

Belimumab for intravenous use is provided as a lyophilized powder in a single-dose vial and should be reconstituted and diluted by a healthcare professional using aseptic technique as follows. Use of a 21- to 25-gauge needle is recommended when piercing the vial stopper for reconstitution and dilution.

Reconstitution Instructions for Intravenous Use:

1. Remove the vial of belimumab from the refrigerator and allow to stand for 10 to 15 minutes for the vial to reach room temperature.
2. Reconstitute the belimumab powder with Sterile Water for Injection, USP, as follows. The reconstituted solution will contain a concentration of 80 mg/mL belimumab.
   - Reconstitute the 120-mg vial with 1.5 mL Sterile Water for Injection, USP.
   - Reconstitute the 400-mg vial with 4.8 mL Sterile Water for Injection, USP.
3. The stream of sterile water should be directed toward the side of the vial to minimize foaming. Gently swirl the vial for 60 seconds. Allow the vial to sit at room temperature during reconstitution, gently swirling the vial for 60 seconds every 5 minutes until the powder is dissolved. Do not shake. Reconstitution is typically complete within 10 to 15 minutes after the sterile water has been added, but it may take up to 30 minutes. Protect the reconstituted solution from sunlight.
4. If a mechanical reconstitution device (swirler) is used to reconstitute belimumab, it should not exceed 500 rpm and the vial swirled for no longer than 30 minutes.
5. Once reconstitution is complete, the solution should be opalescent and colorless to pale yellow, and without particles. Small air bubbles, however, are expected and acceptable.

continued

ACR/ARP Medication Guide

American College of Rheumatology
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Association of Rheumatology Professionals
The Interprofessional Division of the American College of Rheumatology

Dilution Instructions for Intravenous Use:

1. Dextrose intravenous solutions are incompatible with belimumab. Belimumab should only be diluted in 0.9% Sodium Chloride Injection, USP (normal saline), 0.45% Sodium Chloride Injection, USP (half-normal saline), or Lactated Ringer's Injection, USP to a volume of 250 mL for intravenous infusion. To prepare the intravenous infusion solution for patients whose body weight is less than or equal to 40 kg, a 100 mL bag or bottle of normal saline, half-normal saline, or Lactated Ringer's Injection may be used such that the resulting belimumab concentration in the infusion bag does not exceed 4 mg/mL. From a 250-mL (or 100-mL) infusion bag or bottle of normal saline, half-normal saline, or Lactated Ringer's Injection, withdraw and discard a volume equal to the volume of the reconstituted solution of belimumab required for the patient's dose. Then add the required volume of the reconstituted solution of belimumab into the intravenous infusion solution in the infusion bag or bottle. Gently invert the bag or bottle to mix the intravenous infusion solution. Any unused solution in the vials must be discarded.
2. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Discard the solution if any particulate matter or discoloration is observed.
3. The reconstituted solution of belimumab, if not used immediately, should be stored protected from direct sunlight and refrigerated at 36°F to 46°F (2°C to 8°C). Solutions of belimumab diluted in normal saline, half-normal saline, or Lactated Ringer's Injection may be stored at 36°F to 46°F (2°C to 8°C) or room temperature. The total time from reconstitution of belimumab to completion of infusion should not exceed 8 hours.
4. No incompatibilities between belimumab and polyvinylchloride or polyolefin bags have been observed.

Administration Instructions for Intravenous Use:

1. The diluted solution of belimumab should be administered by intravenous infusion over a period of 1 hour.
2. Belimumab should not be infused concomitantly in the same intravenous line with other agents. No physical or biochemical compatibility studies have been conducted to evaluate the coadministration of belimumab with other agents.

Intravenous Medication Administration and Monitoring

1. Consider administering pre-medications as prophylaxis prior to intravenous dosing.
2. The diluted solution should be administered by intravenous infusion over 1 hour.
3. The infusion rate may be slowed or interrupted if the patient develops an infusion reaction.
4. The infusion must be discontinued immediately if the patient experiences a serious hypersensitivity reaction.
5. Do not infuse belimumab concomitantly in the same IV line with other agents. No physical biochemical or compatibility studies have been conducted.

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