BENLYSTA Is Designed For Lupus

The first and only approved treatment designed for lupus

Over 58,000 adult patients have been prescribed BENLYSTA since 2011[1]

BENLYSTA is indicated for patients aged ≥5 years with active, autoantibody-positive systemic lupus erythematosus (SLE) who receive standard therapy. The subcutaneous (SC) formulation is approved for patients aged ≥18 years. BENLYSTA is not indicated or recommended in patients with severe active lupus nephritis, or severe active central nervous system lupus, or in combination with other biologics or intravenous cyclophosphamide.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATION

Previous anaphylaxis with BENLYSTA.

WARNINGS AND PRECAUTIONS

Serious Infections: Serious and sometimes fatal infections have been reported in patients receiving immunosuppressive agents, including BENLYSTA. The incidence of serious infections was similar in patients receiving BENLYSTA versus placebo, whereas fatal infections occurred more frequently with BENLYSTA.

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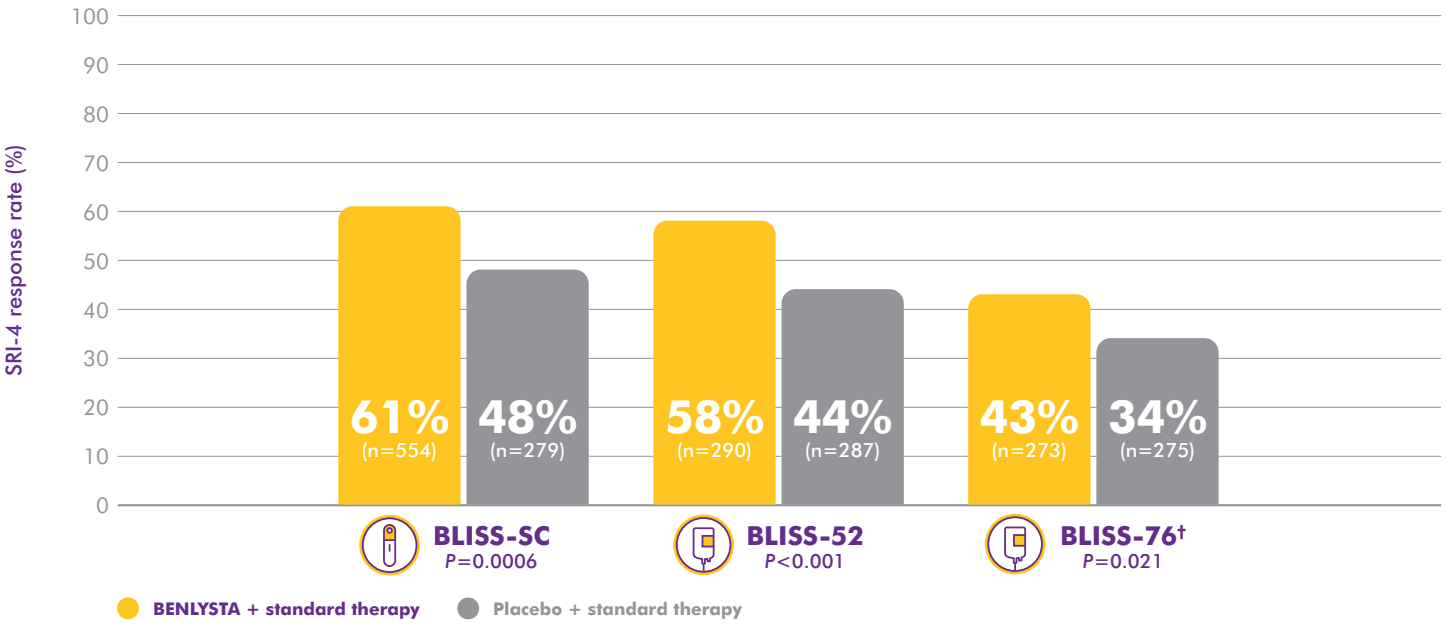
Benlysta (belimumab)
Intravenous Use 120 mg/vial
Subcutaneous Use 200 mg/mL

BENLYSTA: SUPERIOR DISEASE ACTIVITY REDUCTION (SRI-4*) VS. STANDARD THERAPY ALONE AT WEEK 52[2-4]



In 3 Phase III double-blind multicenter studies, 2,520 adult SLE patients were randomized to BENLYSTA + standard therapy or placebo + standard therapy. In 2 of the trials, BENLYSTA 10 mg/kg or placebo was administered by intravenous (IV) infusion over 1 hour on Days 0, 14, and 28, and at 4-week intervals thereafter through Week 52 (BLISS-52) or Week 76 (BLISS-76). In BLISS-SC, patients received weekly doses of subcutaneous (SC) BENLYSTA 200 mg or placebo for 52 weeks. Response rate, as assessed by SRI-4, at Week 52 was the primary endpoint in all trials.[2-4]

* The SLE responder index (SRI-4) is defined as: 1) ≥4-point reduction in SELENA-SLEDAI score; 2) no new BILAG A or no more than 1 new BILAG B domain score; and 3) no deterioration from baseline in the Physician's Global Assessment (PGA) by ≥0.3 points.[5] To be considered a responder, patients must meet all 3 components.

† In BLISS-76, the difference in SRI-4 response rates was not significantly different at Week 76 (secondary endpoint).

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS (CONT'D)

Serious Infections (CONT'D): The most frequent serious infections in adults treated with BENLYSTA IV included pneumonia, urinary tract infection, cellulitis, and bronchitis. Use caution in patients with severe or chronic infections, and consider interrupting therapy in patients with a new infection.

Progressive Multifocal Leukoencephalopathy (PML): Cases of JC virus-associated PML resulting in neurological deficits, including fatal cases, have been reported in patients with SLE receiving immunosuppressants, including BENLYSTA. If PML is confirmed, consider stopping immunosuppressant therapy, including BENLYSTA.

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IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS (CONT'D)

Hypersensitivity Reactions (Including Anaphylaxis): Acute hypersensitivity reactions, including anaphylaxis (eg, hypotension, angioedema, urticaria or other rash, pruritus, and dyspnea) and death, have been reported, including in patients who have previously tolerated BENLYSTA. Generally, reactions occurred within hours of the infusion but may occur later. Non-acute hypersensitivity reactions (eg, rash, nausea, fatigue, myalgia, headache, and facial edema) typically occurred up to a week after infusion. Patients with a history of multiple drug allergies or significant hypersensitivity may be at increased risk. With BENLYSTA SC, systemic hypersensitivity reactions were similar to those in IV trials.

Healthcare providers (HCPs) should monitor patients during and after IV administration and be prepared to manage anaphylaxis; discontinue immediately in the event of a serious reaction. Premedication may mitigate or mask a hypersensitivity response. Advise patients about hypersensitivity symptoms and instruct them to seek immediate medical care if a reaction occurs.

Infusion Reactions: Serious infusion reactions (eg, bradycardia, myalgia, headache, rash, urticaria, and hypotension) were reported in adults. HCPs should monitor patients and manage reactions if they occur. Premedication may mitigate or mask a reaction. If an infusion reaction develops, slow or interrupt the infusion.

Depression and Suicidality: In adult trials, psychiatric events reported more frequently with BENLYSTA IV related primarily to depression-related events, insomnia, and anxiety; serious psychiatric events included serious depression and suicidality, including 2 completed suicides. No serious depression-related events or suicides were reported in the BENLYSTA SC trial. Before adding BENLYSTA, assess patients' risk of depression and suicide and monitor them during treatment. Instruct patients/caregivers to contact their HCP if they experience new/worsening depression, suicidal thoughts, or other mood changes.

Malignancy: The impact of BENLYSTA on the development of malignancies is unknown; its mechanism of action could increase the risk for malignancies.

Immunization: Live vaccines should not be given for 30 days before or concurrently with BENLYSTA as clinical safety has not been established.

Use With Biologic Therapies or IV Cyclophosphamide: BENLYSTA has not been studied and is not recommended in combination with other biologic therapies, including B-cell targeted therapies, or IV cyclophosphamide.

ADVERSE REACTIONS

The most common serious adverse reactions in adults were serious infections: BENLYSTA IV 6.0% (placebo 5.2%). Fatal infections occurred in 0.3% of patients receiving BENLYSTA and in 0.1% of patients receiving placebo. Adverse reactions occurring in ≥3% of adults and ≥1% more than placebo: nausea 15% (12%); diarrhea 12% (9%); pyrexia 10% (8%); nasopharyngitis 9% (7%); bronchitis 9% (5%); insomnia 7% (5%); pain in extremity 6% (4%); depression 5% (4%); migraine 5% (4%); pharyngitis 5% (3%); cystitis 4% (3%); leukopenia 4% (2%); viral gastroenteritis 3% (1%).

Adverse reactions in pediatric patients aged ≥5 years receiving BENLYSTA IV were consistent with those observed in adults.

The safety profile observed for BENLYSTA SC in adults was consistent with the known safety profile of BENLYSTA IV with the exception of local injection site reactions.

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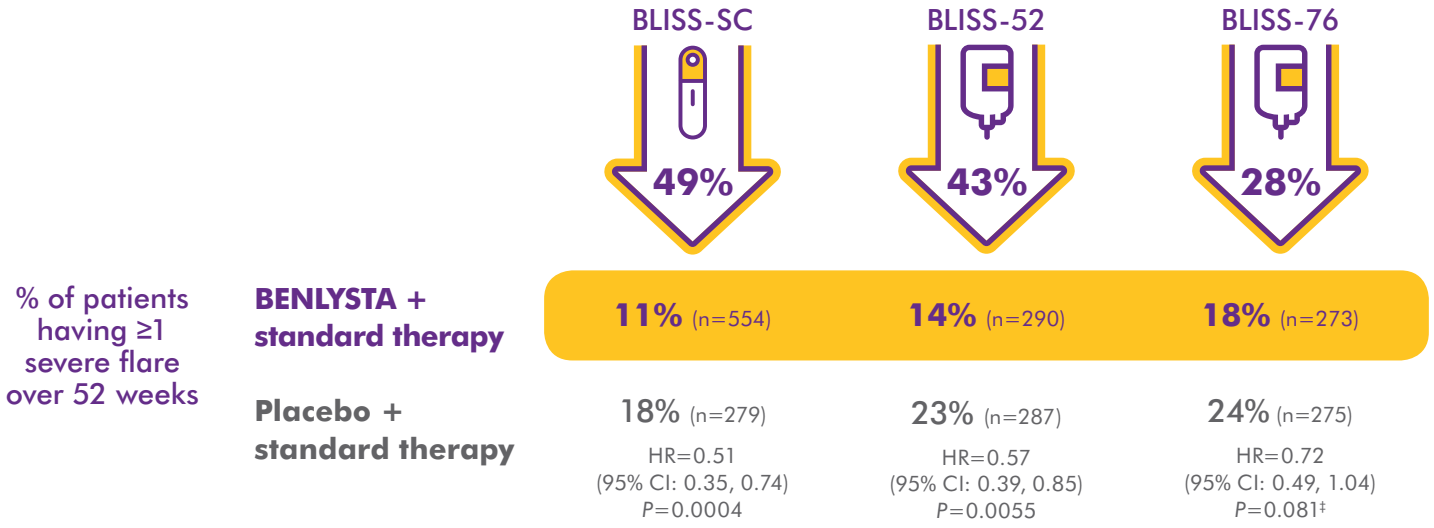
REDUCED THE RISK OF SEVERE FLARE[2-4*†]



‡ Reduction of severe flare was not statistically significant in BLISS-76.

* As measured by the SELENA-SLEDAI SLE Flare Index, modified to exclude the single criterion of increased SELENA-SLEDAI score to >12.
† The incidence of severe flare over 52 weeks was a secondary endpoint.

A severe flare was defined as at least one of the following:[6§]

- Hospitalization for SLE activity
- New/worse (requiring doubling of prednisone, or prednisone increase to >0.5 mg/kg/day, or hospitalization) for: CNS SLE, vasculitis, nephritis, myositis, platelets <60,000, or hemolytic anemia (Hb <7 g/dL or decrease in Hb of >3 g/dL)
- Increase in prednisone dose to >0.5 mg/kg/day, or
- New immunosuppressant, or
- Increase in PGA score to >2.5, or
- Change in SELENA-SLEDAI to >12[¶] accompanied by at least one of the items above

§ As defined by a modified SELENA-SLEDAI SLE Flare Index.
¶ The modified SELENA-SLEDAI excludes severe flares triggered only by an increase of the SELENA-SLEDAI score to >12.
CI = confidence interval; CNS = central nervous system; Hb = hemoglobin; HR = hazard ratio; PGA = Physician's Global Assessment; SELENA-SLEDAI = Safety of Estrogens in Lupus Erythematosus: National Assessment version of the Systemic Lupus Erythematosus Disease Activity Index

IMPORTANT SAFETY INFORMATION (CONT'D)

USE IN SPECIFIC POPULATIONS

Pregnancy: There are insufficient data in pregnant women to establish whether there is drug-associated risk for major birth defects or miscarriage. After a risk/benefit assessment, if prevention is warranted, women of childbearing potential should use contraception during treatment and for ≥4 months after the final treatment.

Pregnancy Registry: HCPs are encouraged to register patients and pregnant women are encouraged to enroll themselves by calling 1-877-681-6296.

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PATIENTS ON BENLYSTA REDUCED THEIR STEROID DOSE OVER TIME (40-52 WEEKS)[2-4]*

% of patients with a ≥**25% reduction** in steroid dose to ≤7.5 mg/day at Week 52†

	BLISS-SC	BLISS-52	BLISS-76
BENLYSTA + standard therapy	**18%** (n=335)	**19%** (n=204)	**18%** (n=120)
Placebo + standard therapy	12% (n=168)	12% (n=192)	13% (n=126)

There were no statistically significant differences between treatment groups in any trial.

* In patients who were receiving >7.5 mg/day at baseline. Overall, 60%, 69%, and 46% of patients were receiving doses >7.5 mg/day at baseline in BLISS-SC, BLISS-52, and BLISS-76, respectively.

† In BLISS-SC, BLISS-52, and BLISS-76, this was a secondary endpoint.

IMPORTANT SAFETY INFORMATION (CONT'D)

USE IN SPECIFIC POPULATIONS (CONT'D)

Lactation: No information is available on the presence of belimumab in human milk, the effects on the breastfed infant, or the effects on milk production. Consider developmental and health benefits of breastfeeding with the mother's clinical need for BENLYSTA and any potential adverse effects on the breastfed child or from the underlying maternal condition.

Pediatric Use: The safety and effectiveness have not been established for BENLYSTA IV in patients <5 years of age and for BENLYSTA SC in patients <18 years of age.

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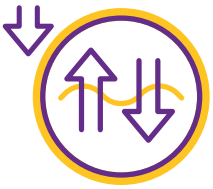
BENLYSTA: DESIGNED FOR LUPUS

When it's time for a treatment change, consider adding BENLYSTA

EFFICACY IN 3 PHASE III ADULT PIVOTAL CLINICAL TRIALS



Superior **Reduction** in disease activity (SRI-4) at Week 52

Reduced risk of severe flares over 52 weeks

Numerical **Reduction** of steroid dose over time (40-52 weeks)

Study design: In 3 Phase III double-blind multicenter studies, 2,520 adult SLE patients were randomized to BENLYSTA + standard therapy or placebo + standard therapy. In 2 of the trials, BENLYSTA 10 mg/kg or placebo was administered by intravenous (IV) infusion over 1 hour on Days 0, 14, and 28, and at 4-week intervals thereafter through Week 52 (BLISS-52) or Week 76 (BLISS-76). In BLISS-SC, patients received weekly doses of subcutaneous (SC) BENLYSTA 200 mg or placebo for 52 weeks. Response rate, as assessed by SRI-4, at Week 52 was the primary endpoint in all trials.[2-4]

References: 1. March 2011 to December 2018 data sourced from Symphony Health Solutions. Claims data based upon total unique number of patients that have had at least one claim for BENLYSTA. Not all patients remain on therapy with BENLYSTA. **2.** Navarra SV, Guzman 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;377(9767):721-731. **3.** Furie R, Petri M, Zamani O, *et al*. A phase III, randomized, placebo-controlled study of belimumab, a monoclonal antibody that inhibits B lymphocyte stimulator, in patients with systemic lupus erythematosus. *Arthritis Rheum*. 2011;63(12):3918-3930. **4.** Stohl W, Schwarting A, Okada M, *et al*. Efficacy and safety of subcutaneous belimumab in systemic lupus erythematosus: a fifty-two-week randomized, double-blind, placebo-controlled study. *Arthritis Rheumatol*. 2017;69(5):1016-1027. **5.** Furie RA, Petri MA, Wallace DJ, *et al*. Novel evidence-based systemic lupus erythematosus responder index. *Arthritis Rheum*. 2009;61(9):1143-1151. **6.** Petri M, Kim M, Kalunian K, *et al*. Combined oral contraceptives in women with systemic lupus erythematosus. *N Engl J Med*. 2005;353(24):2550-2558.

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