Your patients with lupus want to know…

When can we start talking about how lupus **may impact my kidneys**?

Keep reading to see how **kidneys fit** into the **lupus story**

FOR MANY PATIENTS WITH SLE, KIDNEY DAMAGE MAY JUST BE A MATTER OF TIME

Up to **5 of the next 10 SLE patients a doctor sees** may develop **lupus nephritis**[1]

31-48% of patients will develop lupus nephritis at some point after their initial lupus diagnosis.[1]*

2 out of 10 of patients with **lupus nephritis** will develop **ESKD** within **10 years** of diagnosis[2]

Lupus nephritis is a major risk factor for morbidity and mortality in patients with lupus[3,4]

* Data from a pragmatic review of 26 publications involving patients with LN with or without a proven biopsy.

INDICATION FOR BENLYSTA (belimumab)

BENLYSTA is indicated for patients aged ≥5 with active systemic lupus erythematosus (SLE) or active lupus nephritis who are receiving standard therapy. BENLYSTA is not recommended in patients with severe active central nervous system lupus.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATION

Previous anaphylaxis with BENLYSTA.

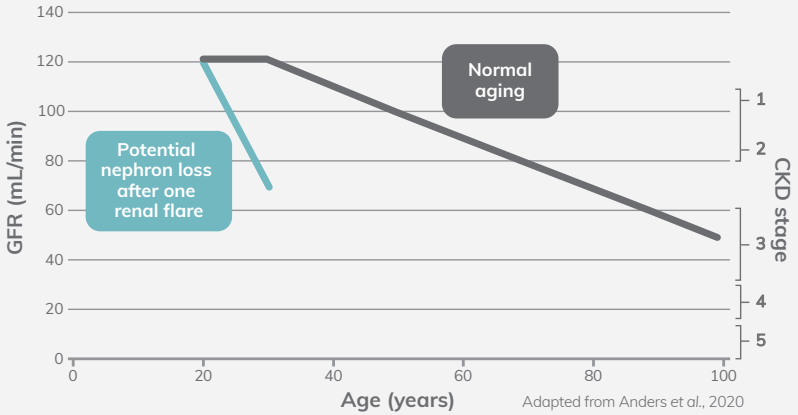
Please see additional Important Safety Information throughout and accompanying full Prescribing Information, including Medication Guide, for BENLYSTA.

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

JUST ONE RENAL FLARE COULD SHORTEN A KIDNEY'S LIFE SPAN BY DECADES[4-6]*

With each renal flare, there is irreversible nephron loss – shortening the kidney's life span and increasing the risk of ESKD[4-6]*

By the time lupus nephritis is diagnosed, kidney damage may already be severe.[4]



Adapted from Anders *et al.*, 2020

* Renal flares are defined as a rise in serum creatine level and/or proteinuria, abnormal urinary sediment, or reduction in creatine clearance.

ESKD = end stage kidney disease; SLE = systemic lupus erythematosus.

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS

Serious Infections: Serious and sometimes fatal infections have been reported and occurred more frequently with BENLYSTA. 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. If PML is confirmed, stop immunosuppressant therapy, including BENLYSTA.

Hypersensitivity Reactions (Including Anaphylaxis): Acute hypersensitivity reactions, including anaphylaxis and death, and infusion-related reactions have been reported. Generally, reactions occurred within hours of the infusion but may occur later, including in patients who have previously tolerated BENLYSTA.

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BENLYSTA (belimumab) HELPS MORE PATIENTS ACHIEVE COMPLETE RENAL RESPONSE[7,8]

74%

GREATER ODDS OF ACHIEVING CRR[7,8]*

Patients achieving CRR: BENLYSTA + ST† (30%, n=223) vs placebo + ST (20%, n=223)

(Secondary endpoint; OR=1.74; 95% CI: 1.11, 2.74; *P*=0.0167)

Primary endpoint: Renal response defined as eGFR ≥60 mL/min/1.73 m^2 or eGFR no worse than 20% below preflare value, uPCR ≥0.7, and not a treatment failure at Week 104. Significantly more BENLYSTA patients (n=223) achieved renal response vs placebo (n=223); 43% vs 32%, respectively (*P*=0.031).[7,8]

Study design: In a Phase III study, 448 adult patients with active lupus nephritis were randomized to BENLYSTA + ST or placebo + ST. BENLYSTA 10 mg/kg or placebo was administered by IV infusion on Days 0, 14, and 28, and at 4-week intervals thereafter through Week 104. Treatment failures were defined as patients who received prohibited medications.[7]

* CRR at Week 104 was defined as eGFR ≥90mL/min/1.73 m^2 or eGFR no worse than 10% below the preflare value, and uPCR <0.5, and not a treatment failure.
† ST was defined as MMF + high-dose steroids, followed by MMF + low-dose steroids; OR CYC + high-dose steroids, followed by AZA + low-dose steroids.

AZA = azathioprine; CI = confidence interval; CRR = complete renal response; CYC = cyclophosphamide; eGFR = estimated glomerular filtration rate; IV = intravenous; LN = lupus nephritis; MMF = mycophenolate mofetil; OR = odds ratio; ST = standard therapy; uPCR = urine protein:creatinine ratio.

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS (CONT'D)

Hypersensitivity Reactions (Including Anaphylaxis): (cont'd)

Non-acute hypersensitivity reactions (eg, rash, nausea, fatigue, myalgia, headache, and facial edema) typically occurred up to a week after infusion. Monitor patients during and after treatment and be prepared to manage anaphylaxis and infusion-related reactions. Be aware of the risk of hypersensitivity reactions, which may present as infusion-related reactions. Discontinue immediately in the event of a serious reaction. With intravenous administration, if an infusion reaction develops, slow or interrupt the infusion.

Depression and Suicidality: Depression and suicidality were reported in patients receiving BENLYSTA. 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/behavior, or other mood changes.

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Scan or click for more lupus nephritis data

PRESERVATION OF KIDNEY FUNCTION[9]

Patients on BENLYSTA experienced a

55%

REDUCTION IN RISK OF RENAL FLARE*

(HR=0.45; 95% CI: 0.28, 0.72)

In patients treated with BENLYSTA + ST, 14% (28/194) had ≥1 renal flare from Week 24 to 104; in patients treated with placebo + ST, 26% (51/196) had ≥1 renal flare from Week 24 to 104.

Patients on BENLYSTA experienced

63%

LESS eGFR LOSS OVER TIME WITH BENLYSTA

3.61 eGFR slope difference from Week 24 to 104 vs ST alone (95% CI: 0.15, 7.06)

In patients treated with BENLYSTA + ST (n=223), the eGFR slope (mL/min/1.73 m^2/year) was -2.12; in patients treated with ST alone (n=223), the eGFR slope was -5.72 from Week 24 to Week 104.†

Post hoc analysis. Results are descriptive.

* Renal flares were defined as impaired kidney function accompanied by proteinuria and/or cellular casts, increase in proteinuria compared with Week 24, or treatment failure due to kidney disease-related intake of prohibited medications.

† On study population: includes all available data for patients on treatment at Week 24 inclusive of those who discontinued treatment but remained enrolled.

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS (CONT'D)

Malignancy: There is an increased risk of malignancies with the use of immunosuppressants. The impact of BENLYSTA on the development of malignancies is unknown.

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: Available data do not support the safety and efficacy of concomitant use of BENLYSTA with rituximab in patients with SLE. An increased incidence of serious infections and post-injection systemic reactions in patients receiving BENLYSTA concomitantly with rituximab compared to patients receiving BENLYSTA alone has been observed. The safety and efficacy of BENLYSTA concomitantly with other biologic therapies, including B-cell-targeted therapies, have not been established. Caution should be exercised if BENLYSTA is administered in combination with other biologic therapies.

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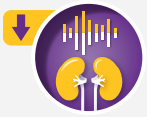
PROVEN TO REDUCE LUPUS SYMPTOMS



61%

OF PATIENTS HAD REDUCED DISEASE ACTIVITY (SRI-4) AT WEEK 52[10-13]*

Study design: In 3 Phase III double-blind multicenter studies, 2520 adult SLE patients were randomized to BENLYSTA + ST or placebo + ST. In 2 of the trials, BENLYSTA 10 mg/kg, BENLYSTA 1 mg/kg, or placebo was administered by 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 SC BENLYSTA 200 mg or placebo for 52 weeks. BENLYSTA 1 mg/kg is not an approved dose and is not included in data shown. Disease activity reduction, as assessed by SRI-4, at Week 52 was the primary endpoint in all trials.[10-13]

* SRI-4 response at Week 52. SRI-4 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 worsening from baseline in the PGA by ≥0.3 points. To be considered a responder, patients must meet all 3 components.[14]

BILAG = British Isles Lupus Assessment Group; IV = intravenous; PGA = Physician's Global Assessment; SC = subcutaneous; SELENA-SLEDAI = Safety of Estrogens in Lupus Erythematosus: National Assessment version of the Systemic Lupus Erythematosus Disease Activity Index; SRI-4 = SLE Responder Index; ST = standard therapy.

IMPORTANT SAFETY INFORMATION (CONT'D)

ADVERSE REACTIONS

The most common serious adverse reactions in adult SLE clinical trials were serious infections; some were fatal. The most common adverse reactions (≥5%) were nausea, diarrhea, pyrexia, nasopharyngitis, bronchitis, insomnia, pain in extremity, depression, migraine, pharyngitis, and injection site reactions (subcutaneous injection).

Adverse reactions reported in clinical trials with SLE pediatric patients (≥5 years) and adult patients with lupus nephritis were consistent with those observed in adult SLE trials.

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.

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IMPROVEMENT IN KIDNEYS AND MORE[8]*

In a post hoc, pooled analysis involving 5 SLE studies.† Results are descriptive.

53% **of patients on BENLYSTA + ST had improvements in kidneys, including urinary casts, hematuria, proteinuria, and pyuria**

(n=319)
vs 40% of patients on ST alone (n=223)

59% **of patients on BENLYSTA + ST had improvements in skin**

(n=1585)
vs 49% of patients on ST alone (n=1039)

60% **of patients on BENLYSTA + ST had improvements in joints**

(n=1180)
vs 50% of patients on ST alone (n=780)

* Improvement in organ domain, as defined by SELENA-SLEDAI, at Week 52 among patients with organ involvement at baseline. Measured skin improvements included rash, alopecia, and mucosal ulcers. Measured joint improvements included arthritis and myositis. Measured kidney improvements included urinary casts, hematuria, proteinuria, and pyuria. Studies were designed to evaluate efficacy in overall disease activity and were not powered to evaluate efficacy in specific organ domains.

† A pooled post hoc analysis of 5 double-blind placebo-controlled studies evaluating BENLYSTA trials (BLISS-52, BLISS-76, NE Asia, BLISS-SC, and EMBRACE). The primary endpoint (SRI-4 at Week 52) was not met in EMBRACE. Patients were treated with BENLYSTA (10 mg/kg or 200 mg SC) (n=1869) or placebo (IV or SC) (n=1217). The analysis included SRI-4 by visit and organ domain improvement from baseline (as defined by SELENA-SLEDAI).

IV = intravenous; NE = northeast; SC = subcutaneous; SELENA-SLEDAI = Safety of Estrogens in Lupus Erythematosus: National Assessment version of the Systemic Lupus Erythematosus Disease Activity Index; SRI-4 = Systemic Lupus Erythematosus; ST = standard therapy.

IMPORTANT SAFETY INFORMATION (CONT'D)

USE IN SPECIFIC POPULATIONS (CONT'D)

Pregnancy Registry: HCPs are encouraged to refer patients and pregnant women are encouraged to enroll themselves by calling 1-877-311-8972 or visiting https://mothertobaby.org/ongoing-study/benlysta-belimumab/.

To report SUSPECTED ADVERSE REACTIONS, contact GSK at 1-888-825-5249 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

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PRESCRIBED TO 85,000+ PATIENTS AND COUNTING[15]

IQVIA - APLD Longitudinal Claims Data - BENLYSTA Patient Volume; March 2011 - September 2022.

Discover why your peers keep choosing BENLYSTA >

References: 1. Mahajan A, *et al. Lupus.* 2020;29(9):1011-1020. **2.** Tektonidou MG, *et al. Arthritis Rheumatol.* 2016;68(6):1432-1441. **3.** Parikh SV, *et al. Am J Kidney Dis.* 2020;76(2):265-281. **4.** Anders HJ, *et al. Nat Rev Dis Primers.* 2020;6(1):7. **5.** Rijnink EC, *et al. Clin J Am Soc Nephrol.* 2017 May 8;12(5):734-743. **6.** Sprangers B, *et al. Nat Rev Nephrol.* 2012 Dec;8(12):709-17. **7.** Furie R, *et al. N Engl J Med.* 2020;383(12):1117-1128. **8.** Data on file, GSK. **9.** Rovin BH, *et al. Kidney Int.* 2021;S0085-2538(21)00862-0. **10.** BENLYSTA [package insert]. Durham, NC: GlaxoSmithKline; 2023. **11.** Navarra SV, *et al. Lancet.* 2011;377(9767):721-731. **12.** Furie R, *et al. Arthritis Rheum.* 2011;63(12):3918-3930. **13.** Stohl W, *et al. Arthritis Rheumatol.* 2017;69(5):1016-1027. **14.** Furie RA, *et al. Arthritis Rheum.* 2009;61(9):1143-1151. **15.** Source data.

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