LUPUS: A CHRONIC DISEASE WITH LONG-TERM CONSEQUENCES

Even for patients managed with therapy

Lupus nephritis is a major risk factor for overall morbidity and mortality[1]

of patients with lupus will develop lupus nephritis.[2,3]*

of patients with lupus nephritis will progress to ESKD in the 10 years after diagnosis.[4]

Commonly used standard therapies for lupus nephritis include[5]:

- Steroids (IV or oral)
- Mycophenolate mofetil
- Cyclophosphamide
- Azathioprine

Commonly used standard treatments for lupus nephritis have a high non-response rate and are associated with both short- and long-term toxicities[1,6]

THE GOALS OF TREATMENT SHOULD INCLUDE BOTH SYMPTOMATIC MANIFESTATIONS AND UNDERLYING DISEASE ACTIVITY.[7]

ESKD = end-stage kidney disease; IV = intravenous

* Including patients with and without biopsy-proven lupus nephritis.

INDICATION

BENLYSTA is indicated for patients aged ≥5 with active, autoantibody-positive systemic lupus erythematosus (SLE) receiving standard therapy and patients aged ≥18 with active lupus nephritis receiving standard therapy. BENLYSTA is not recommended in patients with severe active central nervous system lupus or in combination with other biologics.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATION

Previous anaphylaxis with BENLYSTA.

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, consider stopping immunosuppressant therapy, including 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

BENLYSTA: PROVEN EFFICACY FOR PATIENTS WITH LUPUS NEPHRITIS

COMPLETE RENAL RESPONSE*

BENLYSTA + ST† (30%, n=223) vs placebo + ST (20%, n=223)

>70% **greater odds of achieving response**[9,10]

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

SIGNIFICANTLY REDUCED THE RISK OF RENAL-RELATED EVENTS OR DEATH OVER 2 YEARS BY ~HALF‡§

Percentage of patients experiencing a renal-related event or death: BENLYSTA 16% vs placebo 28%

(Secondary endpoint; HR=0.51; 95% CI: 0.34, 0.77; *P*=0.0014)

Primary endpoint: Renal response defined as eGFR ≥60 mL/min/1.73m^2 or 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=233); 43% vs 32%, respectively (*P*=0.0311).

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.

* Complete renal response was defined as eGFR ≥90 mL/min/1.73m^2 or eGFR no worse than 10% below the preflare value, and uPCR <0.5, and not a treatment failure.

† Standard therapy (ST) was defined as mycophenolate mofetil + high-dose steroids, followed by mycophenolate mofetil + low-dose steroids; OR cyclophosphamide + high-dose steroids, followed by azathioprine + low-dose steroids.

‡ Time to renal-related event or death was defined as first instance of ESKD, doubling of serum creatinine, renal worsening (increased proteinuria and/or impaired renal function), renal disease–related treatment failure, or death occurring after Day 1.

§ When excluding deaths (BENLYSTA=1, ST=2), the percentage of patients with a renal–related event was 15% vs 27%, respectively (HR=0.51; 95% CI: 0.34, 0.78).

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS (CONT'D)

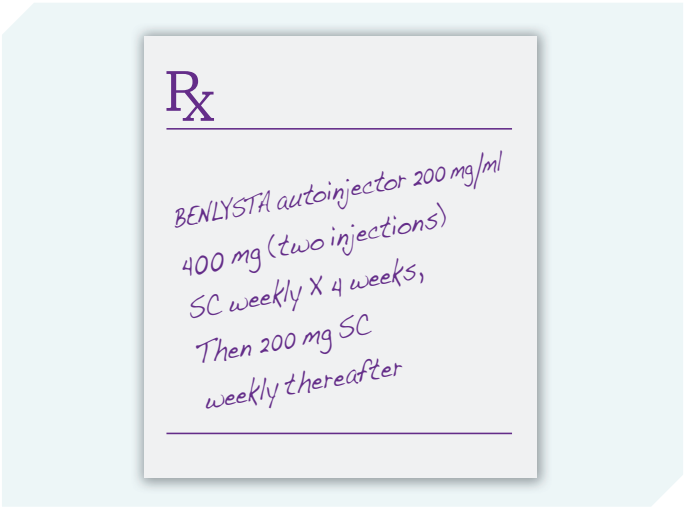
Hypersensitivity Reactions (Including Anaphylaxis): Acute hypersensitivity reactions, including anaphylaxis (eg, hypotension, angioedema, urticaria or other rash, pruritus, and dyspnea) and death, have been reported. Generally, reactions occurred within hours of the infusion but may occur later, including in patients who have previously tolerated BENLYSTA. 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; discontinue immediately in the event of a serious reaction.

Infusion Reactions: Serious infusion reactions (eg, bradycardia, myalgia, headache, rash, urticaria, and hypotension) were reported in adults. If an infusion reaction develops, slow or interrupt the infusion.

START BENLYSTA FOR YOUR PATIENTS WITH LUPUS NEPHRITIS

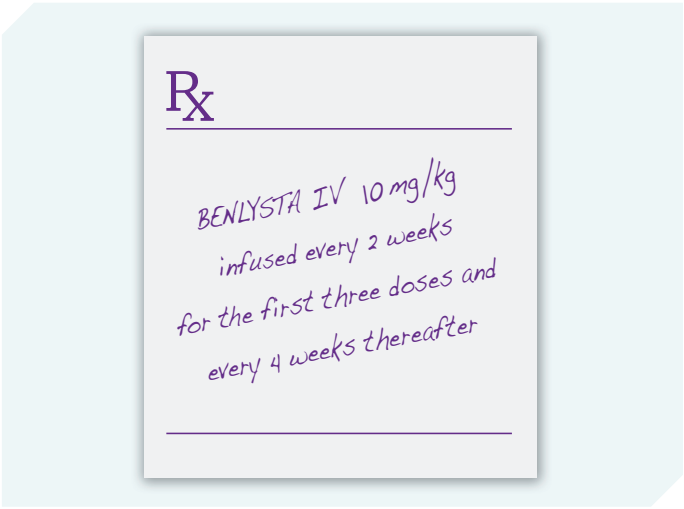
BENLYSTA Autoinjector

- A once-weekly dosing option with **at-home convenience**



BENLYSTA IV

- Scheduling the first 3 doses in advance may be helpful for patients choosing in-office administration



For full instructions, refer to the full Prescribing Information for BENLYSTA.

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS (CONT'D)

Depression and Suicidality: Psychiatric events primarily related to depression, insomnia, anxiety, and suicidality were reported more frequently with 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, 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.

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

BENLYSTA'S SAFETY PROFILE HAS BEEN ESTABLISHED IN 8 CLINICAL TRIALS*

THE SAFETY PROFILE OF BLISS-LN

IS CONSISTENT WITH THE **KNOWN SAFETY PROFILE** OF **BENLYSTA IV** IN SLE TRIALS

BENLYSTA is the only FDA-approved treatment for lupus nephritis studied with **mycophenolate mofetil and cyclophosphamide**.

* Adult Phase II, BLISS-52, BLISS-76, BLISS-SC, BLISS-LN, EMBRACE, PLUTO, and BASE.

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS (CONT'D)

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: BENLYSTA has not been studied and is not recommended in combination with other biologic therapies, including B-cell targeted therapies.

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.

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

BENLYSTA: DOSING OPTIONS FOR YOUR PATIENTS WITH LUPUS NEPHRITIS

Dosing for FDA-approved lupus nephritis medications

	DOSING					
	START	STAY				
		Week 1	Week 2	Week 3	Week 4	Week 5
BENLYSTA Autoinjector	 2 × 200 mg for first 4 doses, once per week for 4 weeks*					
BENLYSTA IV	10 mg/kg every 2 weeks for the first 3 infusions, and then every 4 weeks thereafter					
Lupkynis (voclosporin)[8]	3 capsules, twice per day[8†]					

* The 400-mg dose for active lupus nephritis requires subcutaneous administration of 2 autoinjectors or 2 prefilled syringes.
† Total number of capsules per day may vary based on dosing recommendations in Prescribing Information.

Dosage adjustment recommendations for FDA-approved lupus nephritis medications

	DOSAGE ADJUSTMENT RECOMMENDATIONS			
	Blood pressure	eGFR	Renal impairment	Hepatic impairment
BENLYSTA Autoinjector	**No dosage adjustment is recommended**			
BENLYSTA IV				
Lupkynis (voclosporin)[8]	☒	☒	☒	☒

These dosing presentations are not intended to compare the efficacy or safety of the treatments shown. Please refer to each product's Prescribing Information for more information.

IMPORTANT SAFETY INFORMATION (CONT'D)

USE IN SPECIFIC POPULATIONS (CONT'D)

Pregnancy (cont'd): 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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BENLYSTA: DELIVERING RESULTS FOR YOUR PATIENTS WITH LUPUS NEPHRITIS[9,10]

Achieved response

Significantly more patients on BENLYSTA achieved renal response

Maintained response

Increased likelihood of achieving and maintaining renal response lasting to Week 104 (results are descriptive; other pre-specified endpoint)[9,10]

Reduced disease worsening

Significantly reduced risk of renal-related events or death at any time up to Week 104

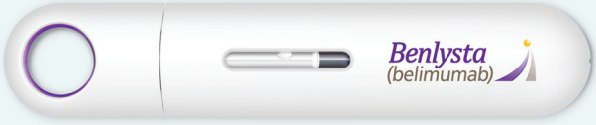
Consistent safety profile

Safety profile of BLISS-LN is consistent with the known safety profile of BENLYSTA IV in lupus trials

In patients with lupus

BENLYSTA AUTOINJECTOR: PREFERRED OVER BENLYSTA IV BY 3 OUT OF 4 PATIENTS[9,11]*

A once-weekly dosing option with at-home convenience



Learn more at **BENLYSTAHCP.com**

* A follow-up survey was conducted in patients (N=43) who completed open-label, multidose, usability, tolerability, and safety study of subcutaneous (SC) belimumab, in which patients with SLE were switched from IV or prefilled syringe belimumab to self-administered doses using the autoinjector for 8 weekly doses. Patients (n=42) were asked, "What is your preference for receiving BENLYSTA: using the autoinjector or IV?"[11]

IMPORTANT SAFETY INFORMATION

CONTRAINDICATION

Previous anaphylaxis with BENLYSTA.

References: 1. Anders H-J, Saxena R, Zhao M-h, *et al.* Lupus nephritis. *Nat Rev Dis Primers.* 2020;6(1):7. **2.** Alarcón GS, McGwin G, Metri M, *et al.* Baseline characteristics of a multiethnic lupus cohort: PROFILE. *Lupus.* 2002;11:95-101. **3.** Hanly JG, O'Keeffe AG, Su L, *et al.* The frequency and outcome of lupus nephritis: results from an international inception cohort study. *Rheumatol.* 2016;55:252-262. **4.** Tektonidou MG, Dasgupta A, Ward MM. Risk of end-stage renal disease in patients with lupus nephritis, 1971-2015: a systematic review and Bayesian meta-analysis. *Arthritis Rheumatol.* 2016;68(6):1432-1441. **5.** Hahn BH, McMahon MA, Wilkinson A, *et al.* American College of Rheumatology guidelines for screening, treatment, and management of lupus nephritis. *Arthritis Care Res.* 2012;64(6):797-808. **6.** Parikh SV, Rovin BH. Current and emerging therapies for lupus nephritis. *J Am Soc Nephrol.* 2016;27(10):2929-2939. **7.** Fanouriakis A, Kostopoulou M, Alunno A, *et al.* 2019 update of the EULAR recommendations for management of systemic lupus erythematosus. *Ann Rheum Dis.* 2019;78:736-745. **8.** Lupkynis capsules [package insert]. January 2021. Rockville, MD: Aurinia Pharmaceuticals Inc. **9.** Data on file, GSK. **10.** Furie R, Rovin BH, Houssiau F, *et al.* Two-year, randomized, controlled trial of belimumab in lupus nephritis. *N Engl J Med.* 2020;383:1117-1128. **11.** Dashiell-Aje E, Harding G, Pascoe K, DeVries J, Berry P, Ramachandran S. Patient evaluation of satisfaction and outcomes with an autoinjector for self-administration of subcutaneous belimumab in patients with systemic lupus erythematosus. *Patient.* 2018;11(1):119-129.

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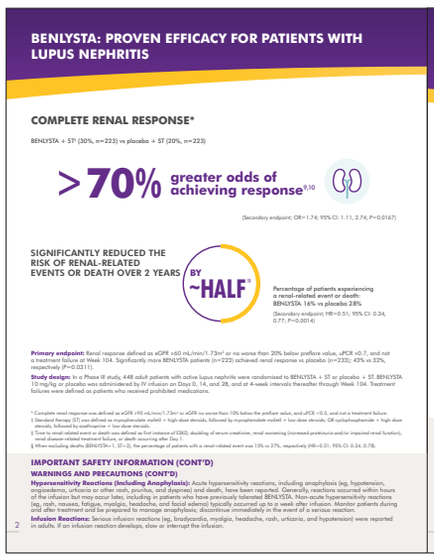
Produced in USA. 0002-0012-12

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

Schematic for 2253 submission purposes only – do not print

Cover



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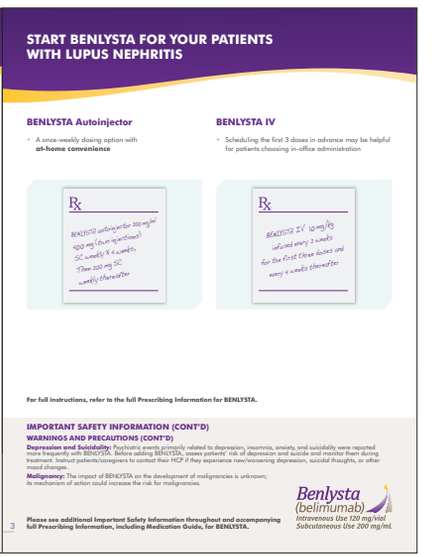

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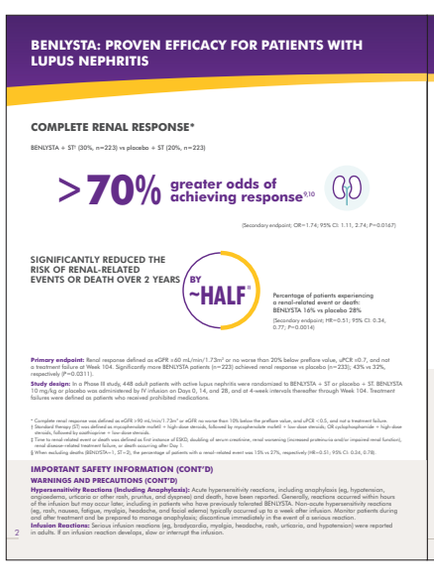

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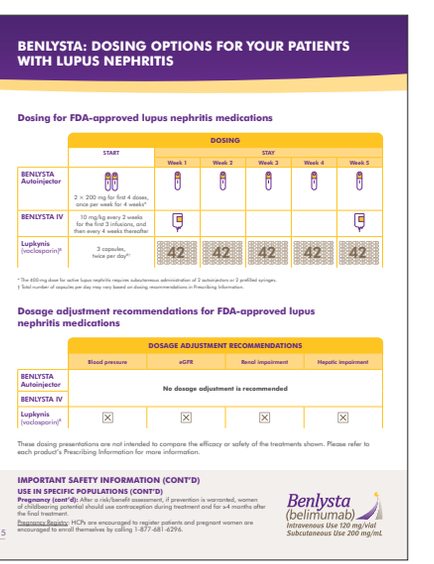

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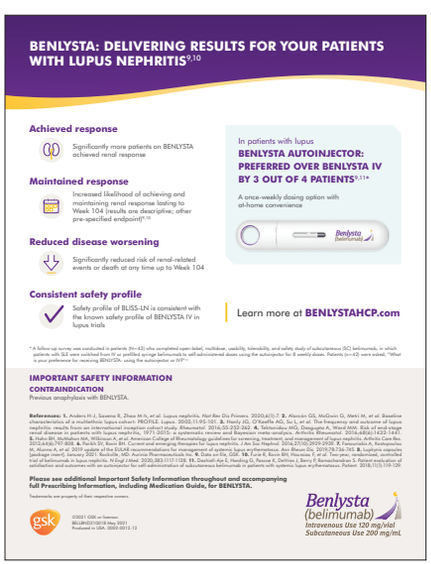

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