Lupus Prior Authorization with Quantity Limit Program Summary

Your health benefit plan may not cover certain prescription drug products or drug categories included in this document. Please consult your benefit plan materials for details about your particular benefit. This document may include drugs that are not included on your plan's formulary. For drug coverage status, please consult your plan's formulary.

POLICY REVIEW CYCLE

Effective Date 07-01-2025

Date of Origin

FDA LABELED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Benlysta® (belimumab) Subcutaneous injection	Treatment of patients 5 years of age and older with active systemic lupus erythematosus (SLE) who are receiving standard therapy Treatment of patients 5 years of age and older with active lupus nephritis (LN) who are receiving standard therapy Limitations of use: • Efficacy has not been evaluated in patients with severe active central nervous system lupus. Use of Benlysta is not recommended in this situation		1
Lupkynis® (voclosporin) Capsule	In combination with a background immunosuppressive therapy regimen for the treatment of adult patients with active lupus nephritis Limitations of use: • Safety and efficacy of Lupkynis have not been established in combination with cyclophosphamide. Use is not recommended in this situation.		9

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Systemic Lupus Erythematosus (SLE)	Systemic lupus erythematosus (SLE) is a chronic inflammatory autoimmune disease of unknown cause.(3) It has a broad range of clinical and serological manifestations and can affect many organs. Clinical symptoms of SLE include fatigue, fever, arthralgia, myalgia, changes in weight, skin lesions, oral/nasal ulcers, and vasculitis. SLE can have multisystem involvement including musculoskeletal, skin, renal, cardiovascular, pulmonary, and/or neuropsychiatric. Due to the nonspecific symptoms and biomarkers often being negative (or normal) early in the course of the disease, the diagnosis of SLE may be difficult.(2) The American College of Rheumatology (ACR) recommends referral to a rheumatologist or other appropriate specialist when SLE is suspected to establish or confirm the diagnosis. The specialist should assess disease activity and severity, establish a treatment plan, and provide management of the disease. After referral, primary care physicians may then monitor and treat mild, stable disease.(3) The 2023 update of the EULAR recommendations for the management of SLE state the following:(5)

	• Hydroxychloroquine is recommended for all patients with SLE, unless contraindicated.
	• Glucocorticoids, if needed, are dosed based on the type and severity of organ involvement, and should be reduced to maintenance dose of less than or equal to 5mg/day (prednisone equivalent) and, when possible, withdrawn; in patients with moderate-to-severe disease, pulses of intravenous methylprednisolone (125–1000mg/day, for 1–3 days) can be considered.
	• In patients not responding to hydroxychloroquine (alone or in combination with glucocorticoids) or patients unable to reduce glucocorticoids below doses acceptable for chronic use, addition of immunomodulating/immunosuppressive agents (e.g., methotrexate, azathioprine, or mycophenolate) and/or biological agents (e.g., belimumab or anifrolumab) should be considered.
	  ○ Although both belimumab and anifrolumab seem to have better efficacy in serologically active patients at baseline, this should not limit their use to this subset of patients.
	• In patients with organ-threatening or life-threatening disease, intravenous cyclophosphamide should be considered; in refractory cases, rituximab may be considered.
	• Treatment of active skin disease should include topical agents (glucocorticoids, calcineurin inhibitors), antimalarials (hydroxychloroquine, chloroquine), and/or systemic glucocorticoids as needed, with methotrexate, mycophenolate, anifrolumab, or belimumab considered as second-line therapy.
	• In active neuropsychiatric disease (central nervous system lupus) attributed to SLE, glucocorticoids and immunosuppressive agents for inflammatory manifestations and antiplatelet agents/anticoagulants for atherothrombotic/antiphospholipid antibodies (aPL)-related manifestations should be considered.
	  ○ For patients with severe neuropsychiatric disease, anifrolumab and belimumab are not recommended.
	
	The treatment and management of SLE in pediatric patients follows a similar algorithm as adults. All pediatric patients should initially be treated with hydroxychloroquine (unless contraindicated) as first-line therapy. A conventional immunosuppressant or biologic is implemented when an intolerance or inadequate response to hydroxychloroquine is observed, or in scenarios where disease onset is more aggressive. The short term use of glucocorticoids can assist as a bridging therapy for flares or when an immunosuppressant/biologic is initiated, but glucocorticoids should be reduced in dose or withdrawn once the disease is under control. However, unacceptable doses of glucocorticoids are sometimes inappropriately continued long term. Mycophenolate mofetil is generally the immunosuppressant of choice in pediatric patients, but methotrexate and azathioprine are also used; and for severe disease, cyclophosphamide.(4)

Lupus Nephritis (LN)	Lupus nephritis (LN) is a common cause of kidney injury and failure in patients with SLE. Roughly 50% of patients with SLE will develop LN at some point in their SLE disease course and between 10% to 30% of those patients will progress to kidney failure requiring kidney transplant. Mortality in patients with LN is significantly higher than those that do not develop LN, with death occurring in 5% to 25% of patients with proliferative LN within 5 years of onset. LN typically develops early in the SLE disease course and can often be present at initial diagnosis of SLE. LN results due to an accumulation of immune complexes in the glomeruli, and intrarenal inflammation occurs leading to permanent damage to the kidney.(6) Diagnosis of LN can be challenging, especially if the patient has not been initially diagnosed with SLE. Serum creatinine levels, urine dipstick testing, and urine sediment examination are necessary tools for LN evaluation. Proteinuria in patients with SLE is suggestive of a diagnosis of LN.(6) The American College of Rheumatology (ACR) indicates that patients with SLE who have proteinuria greater than 0.5 g/g and/or impaired kidney function not otherwise explained should undergo a renal biopsy to confirm a diagnosis of LN.(13) The International Society of Nephrology/Renal

Pathology Society (ISN/RPS) classification system is used to guide treatment decisions in LN. The ISN/RPS divides LN into the following 6 classes based on kidney biopsy:(8)

- Class I: minimal mesangial lupus nephritis
- Class II: mesangial proliferative lupus nephritis
- Class III: focal lupus nephritis
- Class IV: diffuse lupus nephritis
- Class V: membranous lupus nephritis
- Class VI: advanced sclerotic lupus nephritis

Goals of treatment for LN include preserving kidney function, reducing morbidity and mortality, minimizing medication related adverse effects, and optimizing quality of life.(13)

The 2024 ACR Guideline for the Screening, Treatment, and Management of Lupus Nephritis contains the following treatment recommendations:(13)

<u>General management information (Class III, IV, or V):</u>

- Strongly recommend initiation and continuation of hydroxychloroquine to manage and prevent lupus clinical manifestations, unless contraindicated
- Conditionally recommend the following glucocorticoid treatment regimen: pulse intravenous glucocorticoids 250-1000 mg methylprednisolone daily x 1-3 days, followed by oral glucocorticoid less than or equal to 0.5 mg/kg/day (maximum dose 40 mg/day) with taper to a target dose of less than or equal to 5mg/day by 6 months
    - Note: This treatment regimen should be referred to when glucocorticoids are stated as part of a treatment regimen below
- Triple therapy is the most desirable therapy for LN (except Pure Class V in patients with proteinuria less than 1 g/g)
    - Dual therapy may be used if triple therapy is not available or tolerated
- Mycophenolic acid analog (MPAA)-based regimen conditionally recommended over a cyclophosphamide (CYC)-based regimen
    - Conditionally recommend Euro Lupus Nephritis Trial (ELNT) low-dose CYC IV regimen over a high-dose monthly pulse CYC IV regimen
        - ELNT low-dose CYC = 500 mg IV every 2 weeks for 6 doses
    - Strongly recommend ELNT low-dose CYC IV regimen over a daily oral CYC regimen
- Complete renal response is defined as meeting both of the following:
    - Reduction in proteinuria to less than or equal to 0.5 g/g within 6 to 12 months, and
    - Stabilization or improvement in kidney function (+/- 20% baseline)
- Conditionally recommend a total duration of therapy for at least 3-5 years after achieving/sustaining a complete renal response after treatment with any (triple or dual) immunosuppressive therapy

<u>Class III/IV (with or without Class V) - active/new onset/flare:</u>

- Conditionally recommend a triple immunosuppressive regimen consisting of glucocorticoids plus one of the following:
    - MPAA plus belimumab [preferred]
        - Belimumab containing regimen conditionally recommended for patients with extra-renal manifestations
    - MPAA plus calcineurin inhibitor (CNI) [preferred]
        - Conditionally recommend this regimen for patients with proteinuria greater than or equal to 3 g/g
    - ELNT low-dose CYC plus belimumab (MPAA substituted for CYC after CYC course complete) [alternative]
- Dual therapy may be used if triple therapy is not available or tolerated, consisting of glucocorticoids plus one of the following:

	○ MPAA ○ ELNT low-dose CYC (MPAA substituted for CYC after CYC course complete) <u>Pure Class V - active/new onset/flare:</u> • For patients with proteinuria greater than or equal to 1 g/g, conditionally recommend treatment with a triple immunosuppressive regimen consisting of glucocorticoids, MPAA, plus CNI [preferred] ○ Alternative regimens include the following: • Glucocorticoids, MPAA, plus belimumab • Glucocorticoids, ELNT low-dose CYC, plus belimumab • Dual therapy may be used if triple therapy is not available or tolerated, consisting of glucocorticoids plus one of the following: ○ MPAA ○ ELNT low-dose CYC (MPAA substituted for CYC after CYC course complete) • For patients with proteinuria less than 1 g/g, conditionally recommend treatment with glucocorticoids and/or immunosuppressant therapy (MPAA, AZA, or CNI) [glucocorticoid only or dual therapy] <u>Maintenance (Class III, IV, or V)*:</u> • For patients who have undergone triple immunosuppressive therapy: ○ If complete renal response achieved, conditionally recommend continuing the same immunosuppressive regimen ○ If partial renal response achieved, conditionally recommend individualizing therapy depending on clinical factors that include the trajectory of response • For patients who have undergone dual immunosuppressive therapy: ○ If complete renal response achieved, conditionally recommend continuing therapy with MPAA (over azathioprine [AZA]) ○ If partial renal response achieved, conditionally recommend escalating therapy to a triple immunosuppressive regimen (see above for triple therapy regimen examples) **Kidney Disease: Improving Global Outcomes (KDIGO) 2024 clinical practice guideline for the management of lupus nephritis states azathioprine (AZA) is an alternative to MPAA after completion of initial therapy in patients who do not tolerate MPAA, who do not have access to MPAA, or who are considering pregnancy*(10) <u>Nonresponsive or Refractory LN (Class III, IV, or V):</u> • Medication dose and patient adherence should be assessed as an important first step in evaluating inadequate response or refractory LN, as insufficient treatment is an important cause of non-response • For patients with an inadequate renal response (i.e., have not achieved at least a partial renal response by 6 to 12 months), conditionally recommend escalation of treatment to one of the following: ○ For initial dual therapy, escalate to triple therapy ○ For initial triple therapy, change to an alternative triple therapy regimen (see above for triple therapy regimen examples) or consider addition of an anti-CD20 agent (e.g., rituximab or obinutuzumab) as a second immunosuppressive • For patients with refractory disease (i.e., failed two standard therapy courses), conditionally recommend treatment escalation to a more intensive regimen, including addition of anti-CD20 agents, or combination therapy with three non-

	glucocorticoid immunosuppressives (i.e., MPAA, belimumab and CNI), or referral for investigational therapy The treatment and management of LN in pediatric patients uses immunosuppression regimens similar to those used in adults. However, issues relevant to this population should be considered when devising the therapy plan, such as dose adjustments for glucocorticoid regimens, monitoring for decreased growth or delayed puberty, fertility, and psychosocial factors.(10,13)
Efficacy	**SLE** ***Benlysta*** The safety and efficacy of Benlysta (belimumab) administered intravenously were evaluated in two randomized, double-blind, placebo-controlled, phase III studies involving patients age 18 and older with SLE (BLISS-52 study [NCT00424476] and BLISS-76 study [NCT00410384]). The design of these studies was based on the results of a phase II study (NCT00071487) which identified that patients who were autoantibody-positive at screening had a better response to belimumab. As a result, BLISS-52 and BLISS-76 limited the study population to only include patients autoantibody-positive at screening.(1) Seropositivity was defined as positive anti-nuclear antibody (ANA) or anti-double-stranded DNA (anti-dsDNA) test results (ANA titers greater than or equal to 1:80 and/or anti-dsDNA antibodies greater than or equal to 30 IU/mL).(11,12) Patients were on a standard of care SLE treatment regimen for at least 30 days before the first study dose comprising of at least one of the following: corticosteroids, antimalarials, nonsteroidal anti-inflammatory drugs (NSAIDS), and/or immunosuppressives (azathioprine, methotrexate, or mycophenolate).(1,11,12) Patients with severe active lupus nephritis and severe active central nervous system (CNS) lupus were excluded. Patients were excluded from the trial if they had ever received treatment with a B-cell-targeted agent or if they were currently receiving other biologic agents. Intravenous cyclophosphamide was not permitted within the previous 6 months or during the trial.(1) BLISS-52 (N=865) and BLISS-76 (N=819) had similar designs with the exception of duration. BLISS-52 was 52 weeks in duration and BLISS-76 was 76 weeks in length. Eligible patients had active SLE disease which was defined as a Safety of Estrogen in Lupus Erythematosus National Assessment-SLE Disease Activity Index (SELENA-SLEDAI) score greater than or equal to 6. Patients were randomly assigned to receive belimumab 1 mg/kg, 10 mg/kg, or placebo in addition to standard of care. The study medication was administered on Days 0, 14, 28, and then every 28 days for 48 weeks in BLISS-52 and 72 weeks in BLISS-76.(1) The primary efficacy endpoint, SLE Responder Index-4 (SRI-4), defined response as a greater than or equal to 4 point reduction in SELENA-SLEDAI score, no new British Isles Lupus Assessment Group (BILAG) A organ domain score or 2 new BILAG B organ domain scores, and no worsening (less than 0.30-point increase) in Physician's Global Assessment (PGA) score at week 52 compared with baseline. In both BLISS-52 and BLISS-76, the proportion of SRI-4 response was significantly higher in the belimumab 10 mg/kg group than placebo, while the effect on SRI-4 was not consistently significantly different for the belimumab 1 mg/kg group compared to placebo.(1) The safety and effectiveness of Benlysta administered subcutaneously were evaluated in a randomized, double-blind, placebo-controlled trial (NCT01484496) involving 836 adult patients with SLE. The trial (2:1 randomization) evaluated Benlysta 200 mg once weekly plus standard therapy (n = 556) compared with placebo once weekly plus standard therapy (n = 280) over 52 weeks in patients with active SLE disease. Patients had to have a SELENA-SLEDAI score of greater than or equal to 8 and positive autoantibody test (ANA and/or anti-dsDNA) results at screening. Baseline concomitant medications included corticosteroids (86%), antimalarials (69%), and immunosuppressives (46%, including azathioprine, methotrexate, and mycophenolate). Most patients (approximately 80%) were receiving 2 or more classes of SLE medications. The primary efficacy endpoint was the same as the intravenous trials. The proportion of patients achieving an SRI-4 response was significantly higher

	in patients receiving Benlysta plus standard therapy compared with placebo plus standard therapy (61% vs 48%, odds ratio 1.7 [95% CI: 1.3, 2.3], P=0.0006).(1) The safety and efficacy of Benlysta administered intravenously in pediatric patients was evaluated in an international, randomized, double-blind, placebo-controlled, 52-week study conducted in 93 patients with a clinical diagnosis of SLE according to the ACR classification criteria. Patients had a SELENA-SLEDAI score greater than or equal to 6 and positive autoantibodies at screening. Patients were on a stable SLE treatment regimen and had similar inclusion and exclusion criteria as in the adult studies. The primary endpoint was the same as the adult trials, and there was a numerically higher proportion of pediatric patients achieving a response in SRI-4 and its components in patients receiving Benlysta plus standard therapy compared with placebo plus standard therapy (53% vs 44%, odds ratio 1.49 [95% CI: 0.64, 3.46]).(1) Belimumab has a gradual mode of drug action, with responders accumulating over a period of 6 to 12 months.(16) The real-world effectiveness of belimumab in patients with SLE was evaluated in six countries in the OBSErve program. A post hoc pooled analysis of patient-level data from these six retrospective, observational cohort studies was conducted to further evaluate the real-world effectiveness in a large sample of patients (n=830). It was found that belimumab treatment for at least 6 months improved clinical manifestations of SLE in the majority of patients and resulted in corticosteroid dose reductions. After 6 months of therapy, most patients (n=791; 95.3%) showed improvement in their overall condition, 71% of patients were able to reduce their corticosteroid dose, and 8% were able to discontinue corticosteroids.(14) In a large Spanish longitudinal retrospective multicenter cohort study of SLE patients treated with belimumab (n=324), therapeutic objectives were achieved beginning at 6 months and continued to increase through 12 months. It was found that some physicians were withdrawing belimumab treatment during the period of 0 to 6 months due to reasoning of inefficacy, a strategy most likely adopted based on their experience with other rheumatic disorders. However, based on the results of the study showing response between the 6 to 12 month period, it was cautioned that belimumab may be prematurely withdrawn during the first 6 months of therapy in clinical practice. The study states this early withdrawal should be avoided since this is not an optimal time to assess response, and due to the scarce therapeutic options available for SLE.(15) Finally, a Greek multicenter observational study of 188 active SLE patients treated with belimumab showed most withdrawals occurred at 6 to 12 months after treatment initiation, implying physicians consider this time frame as appropriate to assess response and effectiveness.(16) **LN** ***Benlysta*** The safety and efficacy of Benlysta administered intravenously in patients with lupus nephritis (LN) was evaluated in a 104 week, randomized, double-blind, placebo controlled trial that included 448 patients with active proliferative and/or membranous lupus nephritis (NCT01639339).(1) Patients had to be at least 18 years of age and have autoantibody-positive SLE that fulfilled the ACR classification criteria. Patients were required to have a urine protein to creatinine ratio (UPCR) of 1 or more and biopsy-proven lupus nephritis International Society of Nephrology/Renal Pathology Society (ISN/RPS) class III, IV, or V.(7) Active renal disease requiring standard therapy was required at screening, and standard therapy had to be initiated within 60 days before randomization that included either: induction with glucocorticoids in combination with 1) mycophenolate mofetil (MMF) for induction followed by MMF for maintenance therapy, or 2) IV cyclophosphamide for induction followed by azathioprine (AZA) for maintenance therapy. Patients were randomly assigned in a 1:1 ratio to receive either Benlysta 10 mg/kg or placebo on Days 0, 14, 28, and then every 28 days plus standard therapy.(1,7) The primary efficacy endpoint was Primary Efficacy Renal Response (PERR) at week 104, defined as a response at Week 100 confirmed by a repeat measurement at week 104 of the following parameters: UPCR less than or equal to 0.7 g/g, and estimated

	glomerular filtration rate (eGFR) greater than or equal to 60 mL/min/1.73 m^2 or no decrease in eGFR of greater than 20% from pre-flare value.(1) The major secondary endpoints included Complete Renal Response (CRR) (defined as a response at week 100 confirmed by a repeat measurement at week 104 of the following parameters: UPCR less than 0.5 g/g and eGFR greater than or equal to 90 mL/min/1.73 m^2 or no decrease in eGFR of greater than 10% from pre-flare value); PERR at week 52; and time to renal-related event or death (renal-related event defined as first event of end-stage renal disease, doubling of serum creatinine, renal worsening [defined by quantified increase in proteinuria and/or impaired renal function], or receipt of renal disease-related prohibited therapy due to inadequate lupus nephritis control or renal flare management).(1) The proportion of patients achieving PERR at Week 104 was significantly higher in patients receiving Benlysta plus standard therapy compared with placebo plus standard therapy (43% vs 32%, p=0.031). The subgroup analysis of PERR and CRR by biopsy class indicated the odds ratios for patients with class 5 without combined class III or class IV favored placebo plus standard therapy over Benlysta plus standard therapy. The odds ratio for all other biopsy classes or combinations favored Benlysta plus standard therapy. Major secondary endpoints showed significant improvement with Benlysta plus standard therapy compared with placebo plus standard therapy, including: CRR at week 104 (30% vs 20%, p=0.017), PERR at week 52 (47% vs 35%, p=0.025), and time to renal-related event or death (hazard ratio 0.5 [95% CI: 0.3, 0.8], p=0.001). Patients receiving Benlysta were significantly less likely to experience a renal-related event or death compared with placebo.(1) ***Lupkynis*** The safety and efficacy of Lupkynis were investigated in a 52-week, randomized, double-blind, placebo-controlled trial (NCT03021499) in patients with a diagnosis of systemic lupus erythematosus and with ISN/RPS biopsy-proven active Class III or IV LN (alone or in combination with Class V LN) or Class V LN. Patients with Class III or IV LN (alone or in combination with Class V LN) were required to have a urine protein to creatinine ratio (UPCR) of greater than or equal to 1.5 mg/mg; patients with Class V LN were required to have a UPCR of greater than or equal to 2 mg/mg. Patients with baseline eGFR less than or equal to 45 mL/min/1.73 m^2 were not enrolled in this study.(9) A total of 357 patients with LN were randomized in a 1:1 ratio to receive either Lupkynis 23.7 mg twice daily or placebo. Patients in both arms received background treatment with MMF and corticosteroids. Throughout the study, patients were prohibited from using immunosuppressants other than MMF and hydroxychloroquine/chloroquine.(9) The primary efficacy endpoint was the proportion of patients achieving complete renal response at week 52, defined as: UPCR less than or equal to 0.5 mg/mg; and estimated glomerular filtration rate (eGFR) greater than or equal to 60 mL/min/1.73 m^2, or no confirmed decrease in eGFR of greater than 20% from baseline, or no treatment- or disease-related eGFR-associated event. In order to be considered a responder, the patient must not have received more than 10 mg prednisone for greater than or equal to 3 consecutive days or for greater than or equal to 7 days in total during Weeks 44 through 52. Patients who received rescue medication or withdrew from the study were considered non-responders. A higher proportion of patients in the Lupkynis arm than the placebo arm achieved complete renal response at week 52 (Lupkynis 40.8% vs placebo 22.5%, p less than 0.001).(9) A higher proportion of patients in the Lupkynis arm than the placebo arm achieved complete renal response at week 24 (32.4% vs. 19.7%; odds ratio: 2.2; 95% CI: 1.3, 3.7). Time to UPCR of less than or equal to 0.5 mg/mg was shorter in the Lupkynis arm than the placebo arm (median time of 169 days vs. 372 days; hazard ratio: 2.0; 95% CI: 1.5, 2.7).(9)

Safety	Benlysta is contraindicated in patients who have had anaphylaxis with belimumab.(1) Lupkynis is contraindicated in the following:(9) • Patients concomitantly using strong CYP3A4 inhibitors (e.g., ketoconazole, itraconazole, clarithromycin) because these medications can significantly increase exposure to Lupkynis which may increase the risk of acute and/or chronic nephrotoxicity • Patients who have a known serious or severe hypersensitivity reaction to Lupkynis or any of its excipients Lupkynis has a boxed warning due to the increased risk for developing malignancies and serious infections with Lupkynis or other immunosuppressants that may lead to hospitalization or death.(9)

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Number	Reference
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POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
Benlysta	belimumab subcutaneous solution auto-injector	200 MG/ML	M ; N ; O ; Y	N		
Benlysta	belimumab subcutaneous solution prefilled syringe	200 MG/ML	M ; N ; O ; Y	N		
Lupkynis	voclosporin cap	7.9 MG	M ; N ; O ; Y	N		

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
Benlysta	belimumab subcutaneous solution auto-injector	200 MG/ML	4	Pens	28	DAYS			
Benlysta	belimumab subcutaneous solution prefilled syringe	200 MG/ML	4	Syringes	28	DAYS			
Lupkynis	voclosporin cap	7.9 MG	180	Capsules	30	DAYS			

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Benlysta	belimumab subcutaneous solution auto-injector	200 MG/ML	Accord Enhanced ; Accord Standard ; Choice NetR - A Select ; Choice NetR - F Performance ; Choice NetR-HIM
Benlysta	belimumab subcutaneous solution prefilled syringe	200 MG/ML	Accord Enhanced ; Accord Standard ; Choice NetR - A Select ; Choice NetR - F Performance ; Choice NetR-HIM
Lupkynis	voclosporin cap	7.9 MG	Accord Enhanced ; Accord Standard ; Choice NetR - A Select ; Choice NetR - F Performance ; Choice NetR-HIM

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Benlysta	belimumab subcutaneous solution auto-injector	200 MG/ML	Accord Enhanced ; Accord Standard ; Choice NetR - A Select ; Choice NetR - F Performance ; Choice NetR-HIM
Benlysta	belimumab subcutaneous solution prefilled syringe	200 MG/ML	Accord Enhanced ; Accord Standard ; Choice NetR - A Select ; Choice NetR - F Performance ; Choice NetR-HIM
Lupkynis	voclosporin cap	7.9 MG	Accord Enhanced ; Accord Standard ; Choice NetR - A Select ; Choice NetR - F Performance ; Choice NetR-HIM

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
PA	**Initial Evaluation** **Target Agent(s)** will be approved when ALL of the following are met: 1. ONE of the following: A. The requested agent is eligible for continuation of therapy AND ONE of the following: **Agents Eligible for Continuation of Therapy** All target agents are eligible for continuation of therapy 1. The patient has been treated with the requested agent (starting on samples is not approvable) within the past 90 days **OR** 2. The prescriber states the patient has been treated with the requested agent (starting on samples is not approvable) within the past 90 days AND is at risk if therapy is changed **OR** B. BOTH of the following: 1. ONE of the following: A. The patient has a diagnosis of active systemic lupus erythematosus (SLE) WITHOUT active lupus nephritis (LN) AND BOTH of the following: 1. The requested agent is FDA labeled or compendia supported for SLE **AND** 2. BOTH of the following: A. ONE of the following: 1. The patient has ONE of the following: A. Has tried and had an inadequate response to hydroxychloroquine **OR** B. Has an intolerance or hypersensitivity to hydroxychloroquine **OR** 2. The patient has an FDA labeled contraindication to hydroxychloroquine **AND** B. ONE of the following: 1. The patient has ONE of the following: A. Has tried and had an inadequate response to ONE

Module	Clinical Criteria for Approval
	corticosteroid OR immunosuppressive agent (i.e., azathioprine, methotrexate, mycophenolate, cyclophosphamide) **OR** B. Has an intolerance or hypersensitivity to ONE corticosteroid OR immunosuppressive agent (i.e., azathioprine, methotrexate, mycophenolate, cyclophosphamide) **OR** 2. The patient has an FDA labeled contraindication to ALL corticosteroids AND immunosuppressive agents (i.e., azathioprine, methotrexate, mycophenolate, cyclophosphamide) **OR** B. The patient has a diagnosis of active lupus nephritis (LN) AND BOTH of the following: 1. The requested agent is FDA labeled or compendia supported for LN **AND** 2. The patient has Class III, IV, or V lupus nephritis confirmed via kidney biopsy **OR** C. The patient has another FDA labeled indication for the requested agent and route of administration **AND** 2. If the patient has an FDA labeled indication, then ONE of the following: A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR** B. There is support for using the requested agent for the patient's age for the requested indication **OR** C. The patient has another indication that is supported in compendia for the requested agent and route of administration **AND** 2. If the patient has a diagnosis of active systemic lupus erythematosus (SLE) WITHOUT active LN, then BOTH of the following: A. The patient is currently treated with standard SLE therapy (i.e., corticosteroids, hydroxychloroquine, azathioprine, methotrexate, mycophenolate, cyclophosphamide) **AND** B. The patient will continue standard SLE therapy (i.e., corticosteroids, hydroxychloroquine, azathioprine, methotrexate, mycophenolate, cyclophosphamide) in combination with the requested agent **AND** 3. If the patient has a diagnosis of active LN, the patient will be using background immunosuppressive LN therapy (e.g., Lupkynis requests: corticosteroids plus mycophenolate; Benlysta requests: corticosteroids plus mycophenolate, azathioprine, or cyclophosphamide) in combination with the requested agent **AND** 4. The prescriber is a specialist in the area of the patient's diagnosis (e.g., rheumatologist, nephrologist), or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 5. If the requested agent is Benlysta, then ALL of the following: A. The patient does NOT have severe active central nervous system (CNS) lupus **AND** B. ONE of the following: 1. The patient will NOT be using the requested agent in combination with Lupkynis **OR** 2. BOTH of the following: A. The patient has a diagnosis of active LN **AND** B. The patient has tried and had an inadequate response to TWO standard therapy courses (e.g., corticosteroids and Benlysta plus mycophenolate, azathioprine, or cyclophosphamide; corticosteroids and Lupkynis plus mycophenolate) and will be using Benlysta in combination with Lupkynis plus mycophenolate (medical records required) **AND** C. ONE of the following (Please refer to "Agents NOT to be used Concomitantly" table):

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	1. The patient will NOT be using the requested agent in combination with another immunomodulatory agent (e.g., TNF inhibitors, JAK inhibitors, IL-4 inhibitors) **OR** 2. The patient will be using the requested agent in combination with another immunomodulatory agent AND BOTH of the following: A. The prescribing information for the requested agent does NOT limit the use with another immunomodulatory agent **AND** B. There is support for the use of combination therapy (submitted copy of clinical trials, phase III studies, or guidelines required) **AND** 6. If the requested agent is Lupkynis, then BOTH of the following: A. The patient will NOT be using the requested agent in combination with cyclophosphamide OR Saphnelo **AND** B. ONE of the following: 1. The patient will NOT be using the requested agent in combination with Benlysta **OR** 2. BOTH of the following: A. The patient has a diagnosis of active LN **AND** B. The patient has tried and had an inadequate response to TWO standard therapy courses (e.g., corticosteroids and Benlysta plus mycophenolate, azathioprine, or cyclophosphamide; corticosteroids and Lupkynis plus mycophenolate) and will be using Lupkynis in combination with Benlysta plus mycophenolate (medical records required) **AND** 7. The patient does NOT have any FDA labeled contraindications to the requested agent **Compendia Allowed:** AHFS, or DrugDex 1 or 2a level of evidence **Length of Approval:** 12 months NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria. **Renewal Evaluation** **Target Agent(s)** will be approved when ALL of the following are met: 1. The patient has been previously approved for the requested agent through the plan's Prior Authorization process [Note: patients not previously approved for the requested agent will require initial evaluation review] **AND** 2. The patient has had clinical benefit with the requested agent **AND** 3. ONE of the following: A. The patient has a diagnosis of active systemic lupus erythematosus (SLE) WITHOUT active lupus nephritis (LN) AND BOTH of the following: 1. The patient is currently treated with standard SLE therapy (i.e., corticosteroids, hydroxychloroquine, azathioprine, methotrexate, mycophenolate, cyclophosphamide) **AND** 2. The patient will continue standard SLE therapy (i.e., corticosteroids, hydroxychloroquine, azathioprine, methotrexate, mycophenolate, cyclophosphamide) in combination with the requested agent **OR** B. The patient has a diagnosis of active lupus nephritis (LN) AND BOTH of the following: 1. The patient is currently treated with background immunosuppressive LN therapy (e.g., Lupkynis requests: corticosteroids plus mycophenolate; Benlysta requests: corticosteroids plus mycophenolate, azathioprine, or cyclophosphamide) **AND** 2. The patient will continue background immunosuppressive LN therapy (e.g., Lupkynis requests: corticosteroids plus mycophenolate; Benlysta

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	requests: corticosteroids plus mycophenolate, azathioprine, or cyclophosphamide) in combination with the requested agent **OR** C. The patient has a diagnosis other than active SLE OR active LN **AND** 4. The prescriber is a specialist in the area of the patient's diagnosis (e.g., rheumatologist, nephrologist), or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 5. If the requested agent is Benlysta, then ALL of the following: A. The patient does NOT have severe active central nervous system (CNS) lupus **AND** B. ONE of the following: 1. The patient will NOT be using the requested agent in combination with Lupkynis **OR** 2. BOTH of the following: A. The patient has a diagnosis of active LN **AND** B. The patient has tried and had an inadequate response to TWO standard therapy courses (e.g., corticosteroids and Benlysta plus mycophenolate, azathioprine, or cyclophosphamide; corticosteroids and Lupkynis plus mycophenolate) and will be using Benlysta in combination with Lupkynis plus mycophenolate (medical records required) **AND** C. ONE of the following (Please refer to "Agents NOT to be used Concomitantly" table): 1. The patient will NOT be using the requested agent in combination with another immunomodulatory agent (e.g., TNF inhibitors, JAK inhibitors, IL-4 inhibitors) **OR** 2. The patient will be using the requested agent in combination with another immunomodulatory agent AND BOTH of the following: A. The prescribing information for the requested agent does NOT limit the use with another immunomodulatory agent **AND** B. There is support for the use of combination therapy (submitted copy of clinical trials, phase III studies, or guidelines required) **AND** 6. If the requested agent is Lupkynis, then BOTH of the following: A. The patient will NOT be using the requested agent in combination with cyclophosphamide OR Saphnelo **AND** B. ONE of the following: 1. The patient will NOT be using the requested agent in combination with Benlysta **OR** 2. BOTH of the following: A. The patient has a diagnosis of active LN **AND** B. The patient has tried and had an inadequate response to TWO standard therapy courses (e.g., corticosteroids and Benlysta plus mycophenolate, azathioprine, or cyclophosphamide; corticosteroids and Lupkynis plus mycophenolate) and will be using Lupkynis in combination with Benlysta plus mycophenolate (medical records required) **AND** 7. The patient does NOT have any FDA labeled contraindications to the requested agent **Length of Approval:** 12 months NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria.

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

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Universal QL	**Quantity limit for the Target Agent(s)** will be approved when ONE of the following is met: 1. The requested quantity (dose) does NOT exceed the program quantity limit **OR** 2. The requested quantity (dose) exceeds the program quantity limit AND ONE of the following: A. BOTH of the following:

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	1. The requested agent does NOT have a maximum FDA labeled dose for the requested indication **AND** 2. There is support for therapy with a higher dose for the requested indication **OR** B. BOTH of the following: 1. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication **AND** 2. There is support for why the requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does NOT exceed the program quantity limit **Length of Approval**: up to 12 months **Note:** If approving initial loading dose for Benlysta, approve the loading dose per FDA labeling for 1 month, followed by maintenance dosing for the remainder of the length of approval.

CONTRAINDICATION AGENTS

Contraindicated as Concomitant Therapy
Agents NOT to be used Concomitantly Abrilada (adalimumab-afzb) Actemra (tocilizumab) Adalimumab Adbry (tralokinumab-ldrm) Amjevita (adalimumab-atto) Arcalyst (rilonacept) Avsola (infliximab-axxq) Benlysta (belimumab) Bimzelx (bimekizumab-bkzx) Cibinqo (abrocitinib) Cimzia (certolizumab) Cinqair (reslizumab) Cosentyx (secukinumab) Cyltezo (adalimumab-adbm) Dupixent (dupilumab) Ebglyss (lebrikizumab-lbkz) Enbrel (etanercept) Entyvio (vedolizumab) Fasenra (benralizumab) Hadlima (adalimumab-bwwd) Hulio (adalimumab-fkjp) Humira (adalimumab) Hyrimoz (adalimumab-adaz) Idacio (adalimumab-aacf) Ilaris (canakinumab) Ilumya (tildrakizumab-asmn) Imuldosa (ustekinumab-srlf) Inflectra (infliximab-dyyb) Infliximab Kevzara (sarilumab) Kineret (anakinra) Leqselvi (deuruxolitinib) Litfulo (ritlecitinib) Nemluvio (nemolizumab-ilto) Nucala (mepolizumab) Olumiant (baricitinib) Omvoh (mirikizumab-mrkz) Opzelura (ruxolitinib)

Contraindicated as Concomitant Therapy
Orencia (abatacept) Otezla (apremilast) Otulfi (ustekinumab-aauz) Pyzchiva (ustekinumab-ttwe) Remicade (infliximab) Renflexis (infliximab-abda) Riabni (rituximab-arrx) Rinvoq (upadacitinib) Rituxan (rituximab) Rituxan Hycela (rituximab/hyaluronidase human) Ruxience (rituximab-pvvr) Saphnelo (anifrolumab-fnia) Selarsdi (ustekinumab-aekn) Siliq (brodalumab) Simlandi (adalimumab-ryvk) Simponi (golimumab) Simponi ARIA (golimumab) Skyrizi (risankizumab-rzaa) Sotyktu (deucravacitinib) Spevigo (spesolimab-sbzo) subcutaneous injection Stelara (ustekinumab) Steqeyma (ustekinumab-stba) Taltz (ixekizumab) Tezspire (tezepelumab-ekko) Tofidence (tocilizumab-bavi) Tremfya (guselkumab) Truxima (rituximab-abbs) Tyenne (tocilizumab-aazg) Tysabri (natalizumab) Ustekinumab Velsipity (etrasimod) Wezlana (ustekinumab-auub) Xeljanz (tofacitinib) Xeljanz XR (tofacitinib extended release) Xolair (omalizumab) Yesintek (ustekinumab-kfce) Yuflyma (adalimumab-aaty) Yusimry (adalimumab-aqvh) Zeposia (ozanimod) Zymfentra (infliximab-dyyb)