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Drug Class Update with New Drug Evaluation: Monoclonal Antibodies for Lupus

Date of Review: August 2026

Date of Last Review: February 2022
Dates of Literature Search:
01/01/2021 – 05/29/2026 belimumab and Anifrolumab-fnia
01/01/1946 – 05/29/2026 obinutuzumab

Generic Name: Obinutuzumab

Brand Name (Manufacturer): Gazyva (Genentech)
Dossier Received: no

Current Status of PDL Class:
See **Appendix 1**.

Purpose for Class Update:

Evaluate new comparative evidence for efficacy and safety of monoclonal antibodies indicated for the treatment of systemic lupus erythematosus (SLE) or lupus nephritis (LN), and evaluate place in therapy for belimumab, anifrolumab-fnia, and obinutuzumab. Obinutuzumab has been used for various oncology indications since initial Food and Drug Administration (FDA) approval in November 2013. In October 2025, it gained an expanded FDA indication for treatment of adult patients with active LN who are receiving standard therapy.

Plain Language Summary:

- Systemic lupus erythematosus is an autoimmune disorder which affects connective tissue in the body. An autoimmune disorder is a condition where a person's immune system attacks the body itself, instead of an outside invader, such as a virus. Symptoms of SLE include severe fatigue, joint pain, fever, hair loss and a rash across the cheeks and nose.
- Many people with SLE develop kidney disease which is a complication of the disease called lupus nephritis.
- A person with SLE or LN will often take more than one oral medicine to treat the condition and prevent flares.
- Some people may also need medicines that are infused into the veins (intravenously) or injected through the skin (subcutaneously).
- Guidelines recommend multiple combinations of medicines when first treating LN for most patients. These may include mycophenolate mofetil, steroids, cyclosporine, cyclophosphamide, injectable medications like obinutuzumab or belimumab, or others. Different patients may need different combinations of medicines. In addition, hydroxychloroquine is recommended to treat SLE.
- One medicine, called obinutuzumab, was recently approved by the FDA to treat LN. It has been approved for many years to treat certain types of cancers. It is infused through the vein every few weeks at first, then once every 6 months thereafter. Compared to a placebo (saline infusion), obinutuzumab increased the chances of having a remission or improvement in kidney function in people with LN. For one person to have this response, eight people would need to be treated.

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- Obinutuzumab can increase a person's risk of having an infection. This is a side effect that is associated with most medicines used to treat SLE or LN.
- We recommend that providers send in additional information before the Oregon Health Authority pays for obinutuzumab. This process is called prior authorization (PA).

Research Questions:

1. Is there new comparative evidence that monoclonal antibodies indicated for SLE differ in efficacy or effectiveness?
2. Is there new comparative evidence that monoclonal antibodies indicated for SLE differ in safety?
3. What is the evidence for obinutuzumab in LN?
4. Are there specific subpopulations (age, race, ethnicity, gender, diagnosis, disease severity, and comorbidity) for which some monoclonal antibodies indicated for SLE have different effectiveness or safety than other immunosuppressants?

Conclusions:

This evidence review includes 2 high-quality international guidelines, one new published pivotal randomized controlled trial (RCT) for a lupus related indication, one new formulation, and 2 medications with expanded indications. Current FDA approved biologic agents for SLE, LN, or both SLE and LN are listed in **Appendix 1.**

- There is no head-to-head comparative evidence of monoclonal antibodies approved for SLE or LN.
- The European Alliance of Associates of Rheumatology (EULAR) updated guidelines in 2025 for management of SLE with kidney involvement.[1] For patients with active LN, especially those with poor prognostic factors, recommended options include:
    - For initial treatment, mycophenolate or low-dose intravenous cyclophosphamide with belimumab (Level of Evidence [LoE] 1b/Recommendation grade A), mycophenolate with a calcineurin inhibitor (voclosporin or tacrolimus) (LoE 1b/Grade A), or mycophenolate with obinutuzumab (LoE 1b/Grade A)[1]
    - After renal response, defined here as a reduction of urine protein-to-creatinine ratio (UPCR) of < 500 mg/g, treatment should continue for at least 3 years (LoE 2b/Grade B)
        - Patients initially treated with mycophenolate alone (LoE 1a/ Grade A) or in combination with (1) belimumab (LoE 1b/Grade A), (2) a calcineurin inhibitor (LoE 1b/Grade A), or (3) obinutuzumab should remain on these drugs (noting courses beyond 12 months for obinutuzumab await further research evaluation);
        - Patients initially treated with cyclophosphamide, alone or in combination with belimumab, should replace cyclophosphamide with mycophenolate (LoE 1a/Grade A) or azathioprine (LoE 1a/Grade A).[1]
- Kidney Disease Improving Global Outcomes (KDIGO) 2024 Clinical Practice Guidelines for the Management of Lupus Nephritis include recommendations that patients with active Class III or IV LN, with or without a membranous component, be treated initially with glucocorticoids plus any one of the following:
    - mycophenolic acid analogs (1B); or
    - low-dose intravenous cyclophosphamide (1B); or
    - belimumab and either mycophenolic acid analogs or low-dose intravenous cyclophosphamide (1B); or
    - mycophenolic acid analog and a calcineurin inhibitor when kidney function is not severely impaired (i.e., estimated glomerular filtration rate [eGFR] </=45 ml/min per 1.73 m^2)(1B).[2]
    - a triple immunosuppressive regimen of belimumab, glucocorticoids, and either mycophenolic acid analogs or reduced-dose cyclophosphamide may be preferred in patients with repeated kidney flares or patients at high-risk for progression to kidney failure due to severe chronic kidney disease. This triple immunosuppressive regimen can be continued as maintenance therapy.[2]

- In adults with lupus nephritis (LN), there is moderate-quality evidence from one high-quality, phase 3, double-blind, placebo-controlled, multinational, trial (n=271) that obinutuzumab improves the number of people who achieve complete renal response (CRR) at week 76 compared to placebo (obinutuzumab 46.4% vs. placebo 33.1%; adjusted difference 13.4%, 95% confidence interval [CI] 2.0 to 24.8; p=0.02; number needed to treat [NNT] 8).[3] A CRR was considered to be urine protein-to-creatinine ratio (UPCR) less than 0.5 mg/mg based on a timed 24-hour urine collection, an estimated glomerular filtration rate (eGFR) of at least 85% of the baseline value (calculated with the use of the 2009 Chronic Kidney Disease Epidemiology Collaboration equation), and no occurrence of an intercurrent event (i.e., rescue therapy, treatment failure, death, or early trial withdrawal).[3]
- There were more serious adverse events (SAEs) reported in the obinutuzumab group (32.4%) compared to placebo (18.2%), with a low rate of discontinuations due to adverse events in both groups (7 patients [5.1%] discontinuations due to adverse events compared to 2 patients [1.5%) in the placebo treated group.[3] The most frequent SAEs observed among the obinutuzumab-treated patients were infections, including coronavirus disease 2019 (Covid-19)–related events, urinary tract infection, pneumonia, and gastroenteritis.[3]
- There is insufficient evidence to evaluate differences in efficacy or safety for specific populations based on race and ethnicity. Men are underrepresented in the study. While men develop SLE at lower rates than women, those with SLE have a higher propensity to develop LN. Safety in pregnancy and pediatric patients is unclear.
- SAPHNELO (anifrolumab-fnia) was FDA-approved in April 2026 for a weekly 120 mg/0.8 mL dose via subcutaneous self-administration with use of an autoinjector pen or prefilled syringe for adults with moderate to severe SLE.[4]
- BENLYSTA (belimumab) has received expanded indications including children age 5 years and older with active LN or active SLE who are receiving standard therapy.[5] Belimumab is available as a prefilled syringe and autoinjector for subcutaneous use for adults and pediatrics age 5 years and older.[5]

Recommendations:

- Move obinutuzumab (GAZYVA) to "Monoclonal Antibodies for Lupus" Class and apply PA with clear pathway to the oncology policy for oncology indications.
- Update anifrolumab-fnia and belimumab to allow longer approval duration.
- Evaluate costs in executive session.

Summary of Prior Reviews and Current Policy

- BENLYSTA (belimumab) was initially reviewed in May 2018 for treatment of patients aged 5 years and older with active, autoantibody-positive SLE and again in August 2021 when it was approved by the FDA for adults with active LN.
- In February 2022, the newly approved medications, LUKYNIS (voclosporin) and SAPHNELO (anifrolumab-fnia), were reviewed with BENLYSTA (belimumab). Voclosporin is non-preferred and PA is required in the immunosuppressants class. Anifrolumab-fnia and belimumab are both non-preferred and PA is required with drug specific PAs **(Appendix 7)**. They are included in the "Monoclonal Antibodies for Lupus" class. Literature was reviewed through Sept 2021 for that class update.
    a. There was low-quality evidence that *low dose* voclosporin 23.7 mg twice daily is superior to placebo at achieving CRR at 24 to 52 weeks based on 2 RCTs with background therapy of mycophenolate mofetil (MMF) (corticosteroid use varied by protocol) in patients with Class III, certain Class IV or Class V alone or in combination with Class III or IV LN.[6]
    b. There was insufficient evidence from 3 RCTs (one phase 2b, two phase 3) that anifrolumab-fnia 300 mg intravenously (IV) reduces SLE disease activity at 24 to 52 weeks in patients with moderate to severe SLE.[7-9] Evidence was downgraded due to risk of bias, imprecision, and indirectness.
    c. There was low-quality evidence that belimumab is more likely to achieve CRR or primary efficacy renal response (PERR) than placebo at week 104 in patients with Class III, Class IV, or Class V (in combination with Class III or IV) LN based on 2 randomized controlled trials (RCTs)[6]

Background:

Systemic lupus erythematosus is a chronic multisystem autoimmune disorder of the connective tissue which causes significant morbidity and mortality in the United States (U.S.) and worldwide. Estimates on prevalence vary based on changing detection methods and case definitions over time. Estimates may also vary based on genetic and environmental differences between countries.[10] Research studies conducted within the past 2 decades have described prevalence estimates of 9 to 241 per 100,000 person-years and an incidence of 0.3 to 23.2 per 100,000 person-years.[10] Data from studies conducted within the U.S. population with better designs involving strict case definitions, broad case-finding methodology, and correcting for possible case under-ascertainment show an SLE incidence of 4.6 to 6.4 per 100,000 person years and prevalence of 62.2 to 84.8 per 100,000 person years.[10] The Centers for Disease Control and Prevention estimates a U.S. prevalence of 322,000 probable or definite SLE cases.[11] Rates are generally higher among non-Whites, including both Hispanic and Arab ethnicities and those with American Indian, Alaska native, South/East Asian, and African descent.[10] Hispanic and South/East Asian individuals may have more severe disease and organ damage.[6,10] People of African descent are three times more likely to be afflicted with SLE, and have higher rates of renal involvement and mortality than Whites.[10,11] European ancestry is associated with a lower risk of LN.[10] While some of these differences may have genetic components, it has been shown that lower socioeconomic status, educational level, and poverty are associated with the health disparities of higher disease activity, organ damage, and mortality.[10]

Females in their reproductive years are most commonly afflicted with SLE.[6,10] The female-to-male ratio is estimated at 7 to 15:1 in adults and 3 to 5:1 in children. Disease onset in women is usually the 3rd to 5th decade of life; it generally presents later in men in the 5th to 7th decade. While representing about 1 in 10 SLE diagnoses, men tend to develop more severe disease and are 66% more likely to be diagnosed with LN than women based on U.S. Medicaid data.[6]

Smoking, endometriosis, alcohol consumption, and inhalational silica exposure have been strongly associated with SLE.[10] Additionally, psychological stress and environmental triggers such as ultraviolent light, certain drugs (echinacea, trimethoprim/sulfamethoxazole), infections, and mercury have been implicated.[11] The possible role of the gut microbiome is also under investigation.[10]

Systemic lupus erythematosus results from disruption of both the innate and adaptive arms of the immune system.[11] SLE patients have variable presentation, prognosis, and experience remissions and flares over the course of disease.[12] Many different organs are attacked by autoantibodies produced by the body, and this results in variety of complications.[6] Cutaneous lupus presents in nearly 90% of patients, and may manifest in an acute, subacute, or chronic fashion.[11] Non-lupus specific manifestations such as alopecia, vasculitis, (net-like pattern of skin discoloration), periungual telangiectasias, and Raynaud's phenomenon may be present.[11] Musculoskeletal involvement is very common, and arthralgia and true synovitis occur for almost 90% of patients. Renal disease and central nervous system disease are both associated with significant complications.[11] Renal disease, present in 50% of patients, is a major cause of morbidity and mortality. The delayed diagnosis of LN is a major risk factor for end-stage-renal disease (ESRD).[11] Prevalence of LN varies within US; among Medicaid beneficiaries LN is two times more common in the South.[6] Childhood-onset of SLE is associated with higher incidence and more severe LN than adult-onset disease.[13] Cognitive impairment is present is nearly 80% of SLE patients.[11] Seizures, psychosis, mononeuritis multiplex, myelitis, peripheral or cranial neuropathy, and acute confusional state are associated with SLE and may assist with diagnosis once other causes are excluded.[11] Patients with SLE are at higher risk of cardiovascular disease, and 10-15% of SLE cases are complicated by antiphospholipid syndrome. Pregnancy in patients with SLE is associated with higher rates of preterm birth, pre-eclampsia, and caesarean section. Prenatal planning and antenatal care are necessary to reduce the risk of complications to both parent and child.[11] Malignant disorders are more common in SLE patients.[10,13] Hospitalization rates due to infection, most commonly pneumonia, are twelve times higher in patient with SLE than those without, though the specific drug classes used for treatment of SLE are further risk factors for infectious complications.[10] Long-term use of steroids can also increase bone loss and fractures in patients with SLE.[13]

Diagnosis of SLE is made using clinical manifestations and positive serologies.[11,12,14] The EULAR/American College of Rheumatology (ACR) 2019 and Systemic Lupus International Collaborating Clinics (SLICC) 2012 both have classification criteria for SLE.[12,14] The more recent EULAR/ACR criteria are frequently used in practice (**Table 1**). Patients who meet the entry criterion of a positive antinuclear antibody (ANA) proceed to assessment of additive criteria. Patients with at least one clinical criterion without a more likely explanation, and a score of ≥ 10 points meet criteria for SLE diagnosis.[14]

Table 1. European League Against Rheumatism (EULAR)/American College of Rheumatology (ACR) 2019 Diagnostic Criteria[14]

Entry criterion Antinuclear antibodies at a titer of ≥ 1:80 on HEp-2 cells or an equivalent positive test ever in lifetime			
↓			
If absent, do not classify as systemic lupus erythematosus If present, apply additive criteria			
↓			
Additive criteria Do not count a criterion if there is a more likely explanation than systemic lupus erythematosus Occurrence of a criterion on a least one occasion is sufficient SLE classification requires at least one clinical criterion and ≥ 10 points Criteria need not occur simultaneously Within each domain, only the highest weighted criterion is counted toward the total scores.*			
Clinical domains and criteria	**Weight**	**Immunology domains and criteria**	**Weight**
Constitutional • Fever	2	***Antiphospholipid antibodies*** • Anti-cardiolipin antibodies OR • Anti-beta2GP1 antibodies OR • Lupus anticoagulant	2
Hematologic • Leukopenia • Thrombocytopenia • Autoimmune hemolysis	3 4 4	***Complement proteins*** • Low C3 OR low C4 • Low C3 AND low C4	3 4
Neuropsychiatric • Delirium • Psychosis • Seizure	2 3 5	***SLE-specific antibodies*** • Anti-dsDNA antibody† OR • Anti-Smith antibody	6
Mucocutaneous • Non-scarring alopecia • Oral ulcers	2 2		

• Subacute cutaneous OR discoid lupus • Acute cutaneous lupus	4 6	
Serosal • Pleural or pericardial effusion • Acute Pericarditis	 5 6	
Musculoskeletal • Joint involvement	 6	
Renal • Proteinuria >0.5g/24 h • Renal biopsy Class II or V lupus nephritis • Renal biopsy Class III or IV lupus nephritis	 4 8 10	
Total Score: If entry criterion fulfilled and score of 10 or greater should be classified as systemic lupus erythematosus		
* Additional criteria within the same domain will not be counted † Using assay with 90% specificity against relevant disease controls		

Diagnois of LN is generally confirmed through kidney biopsy. Serum creatine, urinalysis, spot protein-creatinine ratio, and serology (including anti-dsDNA and complement) are recommended in patients at SLE presentation and times of suspected SLE flare.[13] Evidence of abnormal protein/urine sediment or decreased/decreasing glomerular filtration rate (GFR) should be further evaluated to quantify proteinuria or accuracy of GFR results. Patients with 24-hour proteinuria ≥ 0.5 g/24h or abnormal eGFR with no attributable cause other than SLE should be considered for kidney biopsy.[13]

The International Society of Nephrology/Renal Pathology Society (ISN/RPS) classification system is most commonly used for LN (**Table 2**).[15] Disease classes are based on glomerular pathology ranging from class I, demonstrating minimal mesangial LN, to Class VI, demonstrating advanced sclerosis LN with ≥ 90% of glomeruli globally sclerosed without residual activity. Class III focal lupus nephritis and class IV diffuse lupus nephritis include additional subcategories for the presence of lesions which are active, active and chronic, or inactive and chronic. Additionally, classifications can differentiate segmental versus global lesions. Tubular atrophy, interstitial inflammation and fibrosis, and severity of arteriosclerosis or other vascular lesions should also be graded as mild, moderate, or severe.[12]

Table 2. ISN/RPS Lupus Nephritis Classifications[15]

Status	Description
Class I	Minimal mesangial lupus nephritis: earliest and mildest form of glomerular involvement
Class II	Mesangial proliferative lupus nephritis: excellent prognosis and no specific therapy is indicated
Class III	Focal lupus nephritis: patients present with hematuria and proteinuria, possibly to also have hypertension, decreased renal function and/or nephrotic syndrome. Light microscopy reveals less than 50 percent of glomeruli are affected.
Class IV	Diffuse lupus nephritis: patients present with hematuria and proteinuria and frequently seen with hypertension, decreased renal function and nephrotic syndrome. Light microscopy reveals more than 50 percent of glomeruli are affected.
Class V	Lupus membranous nephropathy: patients present with signs of nephrotic syndrome
Class VI	Advanced sclerosing lupus nephritis: patients present with slowly progressive kidney dysfunction associated with proteinuria

The goal of SLE treatment is to achieve remission or low disease activity.[16] Treatment of SLE for most patients involves use of hydroxychloroquine (HCQ), unless contraindicated, with the addition of GC at the lowest dose needed to enable remission or prevention of flares. Remission is characterized by a Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) score of 0 (range 0 to 105, higher scores indicate more active disease)[10] on HCQ and without need for glucocorticoid (GC).[16] Administration of GC ranges from chronic therapy to high dose pulses for severe flares, and GC should be withdrawn whenever possible for stable disease. Immunosuppressive agents such as methotrexate, azathioprine, and MMF can be added in patients unresponsive to other therapies and those unable to achieve low daily GC doses (e.g. ≤ 7.5 mg/day). Intravenous cyclophosphamide can be considered as a rescue treatment in severe or life-threatening situations when disease is unresponsive to other therapies.[17] The biologic agent rituximab has been considered in certain situations; use of rituximab for SLE is off-label, and there have been negative results in certain SLE RCTs.[16,17] Treatment for specific organ complications is dependent on the organ system involved.[16] Treatment goals for LN usually rely on a renal response, which may have varied definitions of improvement of eGFR and UPCR from baseline.

Methods:
A Medline literature search for new systematic reviews and RCTs assessing clinically relevant outcomes to active controls, or placebo if needed, was conducted. The Medline search strategy used for this review is available in **Appendix 3**, which includes dates, search terms and limits used. The OHSU Drug Effectiveness Review Project, Agency for Healthcare Research and Quality (AHRQ), National Institute for Health and Clinical Excellence (NICE), Department of Veterans Affairs, Canada's Drug Agency (CDA-AMA), the Oregon Mental Health Clinical Advisory Group (MHCAG), and the Scottish Intercollegiate Guidelines Network (SIGN) resources were manually searched for high quality and relevant systematic reviews. When necessary, systematic reviews are critically appraised for quality using the AMSTAR tool and clinical practice guidelines using the AGREE tool. The FDA website was searched for new drug approvals, indications, and pertinent safety alerts.

The primary focus of the evidence is on high quality systematic reviews and evidence-based guidelines. Randomized controlled trials will be emphasized if evidence is lacking or insufficient from those preferred sources.

Systematic Reviews:
After review, 16 systematic reviews were excluded due to poor quality (e.g., indirect network-meta-analyses), wrong study design of included trials (e.g., observational), comparator (e.g., no control or placebo-controlled), or outcome studied (e.g., non-clinical). Several reviews were duplicated amongst the different literature searches.

New Guidelines:
High Quality Guidelines:
<u>European Alliance of Associates of Rheumatology (EULAR)/European Renal Association/European Dialysis Transplantation Association (ERA-EDTA) Recommendations for the Management of Systemic Lupus Erythematosus with Kidney Involvement: 2025 update[1]</u>

EULAR updated the previous 2019 guidelines in 2025. The task force included experts outside of Europe, including the Americas and Asia, and generally followed the same standard methodology as the previous guideline iteration.[1] A new EULAR standard operating procedure suggested a maximum of 15 bullet pointed statements, resulting in a streamlining of existing recommendations.

The systematic literature search was updated to include January 2019 through March 2024, with final recommendations delayed until publication and evaluation of the phase 3 obinutuzumab RCT for inclusion in recommendations.[1] Level of evidence ratings ranged from 1 (highest) to 5 (lowest, expert opinion) using the

Oxford Centre for Evidence-based Medicine definitions, while grading of recommendation strength ranged from A (highest) to D (lowest).[1] Recommendations including monoclonal antibodies for SLE are shaded for emphasis in **Table 3**.

Overarching principles of management include:

- In patients with SLE, regular monitoring for signs and symptoms of kidney involvement, input from experts, and timely biopsy are essential to ensure optimal outcomes.[1]
- The management of patients with SLE with kidney involvement should align with the general recommendations for SLE, including treatment with hydroxychloroquine.[1]
- Kidney involvement in SLE carries the risk of progressive chronic kidney disease and is best managed with shared, informed patient-physician decisions by rheumatology-nephrology interdisciplinary care teams, with regular assessment of risk factors for chronic kidney disease progression.[1]
- Management aims to prevent progression of chronic kidney disease and flares, address comorbidities, and improve health-related quality of life; both immunosuppressive therapy and nonimmune therapy, including kidney protection, are essential.[1]

Table 3. Recommendations for management of patients with SLE and kidney involvement (Level of Evidence/GRADE)[1]

Recommendation
1. Kidney biopsy is recommended in every patient with evidence of kidney involvement, especially in those with persistent proteinuria (≥0.5 g/24 h or urine protein-creatinine ratio [UPCR] ≥500 mg/g) **(2b/B)**, glomerular hematuria **(2b/C)**, and/or unexplained decrease in glomerular filtration rate **(2b/C)**.
2. Treatment should aim for optimization (preservation or improvement) of kidney function within 3 months, accompanied by a reduction in proteinuria of at least 25% by 3 months **(2b/C)**, 50% by 6 months **(2a/B)**, and a UPCR target <700 mg/g by 12 months **(1b/B)**, and as low as possible afterwards.
3. For patients with active lupus nephritis, intravenous pulse methylprednisolone is recommended **(2b/C)**, followed by oral glucocorticoids gradually tapered to ≤5 mg/d prednisone-equivalent by 4-6 months **(2b/C)**, and slowly withdrawn in patients with sustained complete renal response.
4. For patients with active lupus nephritis, especially those with poor prognostic factors, we recommend combination therapy of (a) mycophenolate or low-dose intravenous cyclophosphamide with belimumab **(1b/A)**, (b) mycophenolate with a calcineurin inhibitor (voclosporin or tacrolimus) **(1b/A)**, or (c) mycophenolate with obinutuzumab **(1b/A)**. Alternative regimens include single-agent therapy with either mycophenolate **(1a/A)** or low-dose intravenous cyclophosphamide **(1a/A)**.
5. In patients with rapidly progressive glomerulonephritis, a short course (6-7 monthly pulses) of high-dose intravenous cyclophosphamide can also be considered **(1a/A)**.
6. Following renal response, treatment should continue for at least 3 years **(2b/B)**; patients initially treated with mycophenolate alone **(1a/A)** or in combination with (1) belimumab **(1b/A)**, (2) a calcineurin inhibitor **(1b/A)**, or (3) obinutuzumab should remain on these drugs; mycophenolate **(1a/A)** or azathioprine **(1a/A)** should replace cyclophosphamide for those initially treated with cyclophosphamide, alone or in combination with belimumab. *Note: Obinutuzumab was used for a maximum of 1 year (52 weeks) in the REGENCY trial; longer courses await further evaluation.*

7. In patients with sustained complete renal response, gradual withdrawal of immunosuppressive and/or biologic therapy should be considered after 3 years of therapy following response, taking into consideration the risk for flare **(2a/B)**.
8. For patients with persistently active or relapsing disease, switching among the aforementioned immunosuppressive **(2b/B)** and/or biologic drugs **(2b/B)** and referral to experts is recommended.
9. Repeat kidney biopsy should be considered, especially in cases of clinical uncertainty, to evaluate (1) response to treatment, (2) worsening of kidney-specific laboratory tests, or (3) contemplated withdrawal of immunosuppressive treatment **(2b/B)**.
10. Recommended nonimmune treatment includes renin-angiotensin-aldosterone blockade (for patients with persistent proteinuria or arterial hypertension) **(5/D)**, sodium glucose transporter 2 inhibitors (for stable patients with persistent proteinuria or estimated glomerular filtration rate <60 ml/min/m2, or other risk factors for progressive chronic kidney disease) **(5/D)**, statins (based on cardiovascular risk levels) **(5/D)**, and/or bone protective agents **(5/D)**.
11. In patients with features of thrombotic microangiopathy (antiphospholipid syndrome nephropathy, thrombotic thrombocytopenic purpura-like, or complement-mediated hemolytic uremic syndrome), glucocorticoids (IV pulse methylprednisolone) **(4/C)**, complement inhibitors **(4/C)**, B-cell depleting agents **(4/C)**, caplacizumab **(4/C)**, plasma exchange **(4/C)**, and/or anticoagulation **(2b/C)** should be considered.
12. In patients with inactive nephritis and adequately controlled extrarenal manifestations, pregnancy may be planned after preconception counselling, initiation of pregnancy-compatible medications, and regular multidisciplinary assessments **(1b/A)**.
13. All methods of kidney replacement therapy can be used in patients with SLE; in those with clinically inactive extrarenal disease for at least 6 months, transplantation (including living donor and pre-emptive transplantation) should be considered **(2b/C)**.

Belimumab and obinutuzumab are both recommended for use with other immunosuppressants for the treatment of active LN, particularly in patients with poor prognostic factors.[1] The authors noted that the phase 3 REGENCY trial of obinutuzumab did not include patients with pure class V LN, however they felt it was still a potential option given its efficacy in mixed proliferative and membranous nephritis.[1]

Complete renal response was defined in this document as a UPCR of less than 500 mg/g at any time point.[1] Factors leading to higher risk of suboptimal response and development of chronic kidney disease include reduced baseline GFR (<60 mL/min/m^2), previous flare, nephrotic range proteinuria at baseline, hypertension at baseline, male sex, increased chronicity index (>3, in the presence of activity), histological evidence of crescents, or severe tubulointerstitial inflammation.[1] Prognostic factors leading to increased risk of kidney flares include nonadherence to treatment, shorter duration of treatment (e.g., less than 3 years), incomplete response following initial therapy, ongoing extrarenal and serologic activity, no use of hydroxychloroquine, young age (e.g., less than 30 years), male sex, and residual histologic activity at repeat biopsy (National Institutes of Health Activity Index of 2 or greater).[1]

<u>Kidney Disease Improving Global Outcomes (KDIGO) 2024 Clinical Practice Guidelines for the Management of Lupus Nephritis[2]</u>

KDIGO updated LN guidelines in 2024 based on a literature search conducted in July 2022 and updated in April 2023.[2] Previous guidelines on the Management of Glomerular Diseases was published in 2021. This update focuses on guidance for patients with SLE and kidney involvement. Strength of recommendations were given grades of Level 1 (Strong, “we recommend”) and Level 2 (Weak, “we suggest”). Quality of supporting evidence is shown as Grade A (High), Grade B (Moderate), Grade C (Low), and Grade D (Very Low).[2] A summary of recommendations related to monoclonal antibodies for lupus is included in **Table 4**.

Table 4. KDIGO recommendation for monoclonal antibody use for LN[2]

For initial therapy for active Class III/IV lupus nephritis	We recommend that patients with active Class III or IV LN, with or without a membranous component, be treated initially with glucocorticoids plus any one of the following: i. mycophenolic acid analogs (MPAA) (1B); or ii. low-dose intravenous cyclophosphamide **(1B)**; or iii. belimumab and either MPAA or low-dose intravenous cyclophosphamide **(1B)**; or iv. MPAA and a calcineurin inhibitor (CNI) when kidney function is not severely impaired (i.e., estimated glomerular filtration rate [eGFR] </=45 ml/min per 1.73 m^2)**(1B)**.
	A triple immunosuppressive regimen of belimumab, glucocorticoids, and either MPAA or reduced-dose cyclophosphamide may be preferred in patients with repeated kidney flares or patients at high-risk for progression to kidney failure due to severe chronic kidney disease.
	Newer biologic and non-biologic therapies are under development and may offer future options for the treatment of active lupus nephritis. Rituximab may be considered for patients with persistent disease activity or inadequate response to initial standard-of-care therapy.
Maintenance therapy for Class III and Class IV lupus nephritis	Patients treated with triple immunosuppressive regimens that include belimumab or a CNI in addition to standard immunosuppressive therapy can continue with a triple immunosuppressive regimen as maintenance therapy.
Class V lupus nephritis Management of unsatisfactory response to treatment	Consider the following in patients refractory: Addition of rituximab or other biologic therapies, extended course of intravenous pulse cyclophosphamide, and enrollment in clinical trials if eligible

New Formulations or Indications:

SAPHNELO (anifrolumab-fnia) was FDA-approved in April 2026 for a weekly 120 mg/0.8 mL dose via subcutaneous self-administration with use of an autoinjector pen or prefilled syringe for adults with moderate to severe SLE.[18] The drug was previously available as a monthly 300 mg/2mL intravenous infusion in a healthcare setting. Approval was based on results of the TULIP-SC trial, evaluating safety and efficacy of subcutaneous anifrolumab in adults with moderate to severe SLE compared to placebo with those on standard therapy.[4] A 52-week interim analysis has been published, showing a statistically significant BICLA (British Isles Lupus Assessment Groups Index [BILAG]-based Combined Lupus Assessment) response for anifrolumab compared to placebo (anifrolumab vs. placebo: 59.4% vs. 43.9%; difference 15.5%, 95% CI 2.3–28.6; p = 0.0211).[4] Partial improvement in multiple affected systems may achieve BICLA response.

BENLYSTA (belimumab) has received expanded indications since previous review.

- July 2022-Expanded indication for children age 5 years to 17 years with active LN who are receiving standard therapy[5]
- May 2024-Approval of subcutaneous administration for pediatrics age 5 years and older with SLE[5]
- June 2025-Approval of use of autoinjector use for pediatric patients age 5 years and older with LN[5]

New FDA Safety Alerts:

Table 5. Description of New FDA Safety Alerts

Generic Name	Brand Name	Month / Year of Change	Location of Change (Boxed Warning, Warnings, CI)	Addition or Change and Mitigation Principles (if applicable)
Belimumab[5]	BENLYSTA	Feb 2023	Warnings and Precautions	Addition of new section for "concomitant use with other 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."*

Randomized Controlled Trials:
A total of 5 citations were manually reviewed from the initial literature search. After further review and exclusion of duplicates, all 4 remaining citations were excluded because of wrong study design (e.g., observational), comparator (e.g., no control or placebo-controlled), or outcome studied (e.g., non-clinical).

NEW DRUG EVALUATION:

See **Appendix 4** for **Highlights of Prescribing Information** from the manufacturer, including Boxed Warnings and Risk Evaluation Mitigation Strategies (if applicable), indications, dosage and administration, formulations, contraindications, warnings and precautions, adverse reactions, drug interactions and use in specific populations. Pharmacology and pharmacokinetic properties are listed in **Appendix 5**.

Clinical Efficacy:
Obinutuzumab is a humanized type II anti-CD20 monoclonal antibody. B-cell lysis is mediated through several pathways after binding with pre-B and mature B lymphocytes.[19] It has been approved for use on the U.S. market for more than a decade with indications related to chronic lymphocytic leukemia and follicular lymphoma. It was FDA approved in October 2025 for the treatment of adult patients with active LN who are receiving standard therapy.[19] Dosing for active LN is 1000 mg on day 0 then repeated on week 2, 24, 26, and every 6 months thereafter.[19] Approval for use in active LN was based on the results of the phase 3 REGENCY trial (**Table 6**).

This double-blind, placebo-controlled, multicenter, multinational, RCT included adults age 18 to 75 years who met the American College of Rheumatology (ACR) criteria for SLE with International Society of Nephrology and the Renal Pathology Society active class III or IV LN, with or without concomitant class V disease.[3] Those with an eGFR of less than 30 ml/min/1.73m^2 were excluded.[3] Additional inclusion/exclusion criteria are listed in **Table 6**. Patients were randomized 1:1 to placebo (n=136) or one of two treatment groups.[3] The active drug treatment groups were pooled (n=135) for outcome assessment and differed only with the inclusion or exclusion of a dose at Week 50 which was intended to evaluate pharmacokinetic and pharmacodynamic data and exploring dose-related efficacy for long-term treatment beyond 76 weeks.[3] Treatment groups were similar in demographics and baseline disease severity.[3]

The primary endpoint was CRR at Week 76.[3] This was defined as UPCR less than 0.5 mg/mg based on a timed 24-hour urine collection, an eGFR of at least 85% of the baseline value (calculated with the use of the 2009 Chronic Kidney Disease Epidemiology Collaboration equation), and no occurrence of an intercurrent event (i.e., rescue therapy, treatment failure, death, or early trial withdrawal).[3] Treatment failure was considered ESRD or the use of long-term dialysis or renal transplantation, receipt of rescue therapy (except for glucocorticoid-only rescue), or clinically significant and sustained worsening of the UPCR or eGFR beyond week 24 that led the center investigator to conclude that the assigned regimen had failed. The obinutuzumab group achieved CRR at week 76 (46.4%) at a statistically significantly higher rate than placebo treated patients (33.1%)(adjusted difference 13.4%, 95% CI 2.0 to 24.8, p=0.02).

Multiple secondary endpoints were also assessed. These include CRR at week 76 with a prednisone dose of 7.5 mg per day or lower between weeks 64 and 76 (obinutuzumab 42.7% versus placebo 30.9%; adjusted difference 11.9, 95% CI 0.6 to 23.2; p=0.04); a UPCR less than 0.8 at week 76 with no intercurrent event (obinutuzumab 55.5% versus placebo 41.9%; adjusted difference 13.7, 95% CI 2.0 to 25.4; p=0.02); a change in the eGFR from baseline to week 76 (no significant difference); death or a renal-related event through week 76 (obinutuzumab 18.9% versus placebo 35.6%; adjusted difference -16.8%, 95% CI -27.4 to -6.2; p not reported); an overall renal response at week 50, which was defined as a complete renal response or a partial renal response (no significant difference); and a change in score on the Functional Assessment of Chronic Illness Therapy–Fatigue (FACIT-F) from baseline to week 76 (no significant difference). [3] The lack of statistical significance at week 50, compared to achieving the primary endpoint at week 76, may indicate clinical response to treatment is not rapid.

Clinical Safety:
The safety population included all the patients who received any infusion of obinutuzumab or placebo in a blinded manner.[3] The patients in the safety population were grouped according to the infusion that was actually administered, regardless of the randomly assigned trial group.

Serious adverse events occurred more frequently in the obinutuzumab group (32.4%) compared to placebo (18.2%), with 7 discontinuations due to adverse event compared to 2 in the placebo treated group. The most frequent SAEs observed among the obinutuzumab-treated patients were infections, including Covid-19–related events, urinary tract infection, pneumonia, and gastroenteritis.

FDA labeling includes warnings and precautions related to both lupus and oncology indications. It has a black box warning for hepatitis B reactivation and all patients should be screened prior to treatment.[19] Labeling carries a second black box warning for potential for progressive multifocal leukoencephalopathy (PML), which can be fatal.[19] Patients require premedication with glucocorticoids, acetaminophen, and antihistamines to prevent and mitigate infusion-related reactions.[19] Hypersensitivity reactions, including serum sickness, can also occur.[19] Live vaccines should be administered prior to start of therapy or held until b-cell recovery, and females of childbearing potential must use effective contraception due to embryo-fetal toxicity.[19] Given the similar mechanism of action to rituximab, the medications should not be used concomitantly.

Look-alike / Sound-alike Error Risk Potential: none

Comparative Endpoints:

Clinically Meaningful Endpoints:
1) Reduction in disease activity
2) Clinical response or remission
3) Quality of Life

Primary Study Endpoint:
1) Complete renal response at week 76

4) Serious adverse events
5) Study withdrawal due to an adverse event

Table 6. Comparative Evidence Table.[3]

Ref./ Study Design	Drug Regimens/ Duration	Patient Population	N	Efficacy Endpoints	ARR/ NNT	Safety Outcomes	ARR/ NNH	Risk of Bias/ Applicability
1. REGENCY trial[3] Phase 3, DB, PC, RCT	1. Obinutuzumab IV 1000 mg day 1, weeks 2, 24, 26, 50, 52 + standard therapy 2. Obinutuzumab IV 1000 mg day 1, weeks 2, 24, 26, 52 + standard therapy 3. Placebo + standard therapy 1:1 randomization Standard therapy beginning at screening if not already receiving: mycophenolate mofetil and glucocorticoids (goal prednisone 7.5 mg daily by week 12 and 5 mg daily by week 24).	Demographics: -Mean Age ~33 years -Female 84.5% -White 47.6% -Black 14.8% -American Indian/Alaska Native 18.9% -Asian 5.9% -Hispanic or Latino 57.6% -Median eGFR ~108 ml/min/1.73m^2 -Median UPCR 2.13-2.73 mg/mg -Previously diagnosed Lupus Nephritis 57.9% Key Inclusion Criteria: -18-75 years old -ACR criteria for SLE with active class III or IV Lupus Nephritis -Biopsy-proven active Lupus Nephritis (w/ or w/o class V disease) -UPCR ratio of at least 1 using 24 hr urine collection -ANA positive Key Exclusion Criteria:	ITT: 1+2: 135 3: 136 Safety: 1+2: 136 3: 132 Completed week 76: 1+2: 13 (9.6%) 3: 16 (11.8%) Discontinued treatment: 1+2: 29 (21.3%) 3: 38 (28.8%)	Primary Endpoint: Complete Renal Response at week 76 1+2: 46.4% 3: 33.1% Adjusted Difference: 13.4% (95% CI, 2.0 to 24.8) P=0.02 Secondary Endpoints: Complete Renal response at week 76 with a prednisone dose of 7.5 mg/day or lower between weeks 64 and 76 1+2: 42.7% 3: 30.9% Adjusted Difference: 11.9% (95% CI, 0.6 to 23.2) P=0.04 Death or renal related event through week 76 1+2: 18.9% 3: 35.6% Adjusted Difference: -16.8% (95% CI, -27.4 to -6.2)	13.4/ 8 11.9/ 9 16.8/ 6	Total AE: 1+2: 748 3: 665 Any AE: 1+2: 126 (92.6%) 3: 117 (88.6%) SAE: 1+2: 44 (32.4%) 3: 24 (18.2%) AE with fatal outcome: 1+2: 3 (2.2%) 3: 2 (1.5%) Discontinuation due to AE: 1+2: 7 (5.1%) 3: 2 (1.5%)	NA	**Risk of Bias (low/high/unclear)**: Selection Bias: (low) Randomization using central interactive voice- and web-based response system with permuted block design. Stratified by geographic region (US or Canada, Latin America or Caribbean, or other) and race (Black or other). Baseline characteristics balanced. Performance Bias: (low) Blinding maintained until all patients completed week 76 assessment. For investigators and patients with adequate response, blinding was maintained 1 year beyond week 76 and data analysis through that point completed. Detection Bias: (low) Slightly higher rate of discontinuation due to inadequate response in placebo group (22 placebo vs. 6 obinutuzumab), but overall low. Objective outcomes decrease risk of bias. Attrition Bias: (unclear) More than 20% of patients discontinued treatment. Missing data imputed using a multiple-imputation method that used fully conditional specification with predicted mean matching (100 imputed data sets) with the use of data for patients who did not have intercurrent events. Patients who had intercurrent events were imputed as no response. Reporting Bias: (Low) Protocol published with prespecified outcomes. Other Bias: (unclear) Sponsor (F.Hoffmann-La Roche) designed and participated in data collection, analysis, interpretation, manuscript preparation and submission. **Applicability**: Patient: Applicable primarily to those with Class III or IV LN, with or without class V. Excluded medications (cyclophosphamide, tacrolimus,

		-eGFR < 30mL/min/1.73 m^2 or ESKD on dialysis or s/p transplantation -Evidence of infection -Anti-CD20 medication within 9 months -Cyclophosphamide, tacrolimus, cyclosporine, voclosporin within 2 months						cyclosporin, etc.) more likely to select for less refractory patients on first-line treatment and those with less risk for additional drug induced renal toxicity. Intervention: Appropriate based on phase 2 study, more appropriate to dose intervention the same for all patients or assess separately rather than pooled. Comparator: Placebo comparison appropriate for initial approval, comparative data vs. belimumab or a calcineurin inhibitor would be helpful for place in therapy. Outcomes: Appropriate, though complete renal response defined slightly differently than belimumab pivotal study and optimization goals in EULAR guidelines, further reinforcing need for direct comparative evidence. Setting: 15 countries
Abbreviations: ACR = American College of Rheumatology; AE = adverse event; ANA = antinuclear antibody; ARR = absolute risk reduction; CI = confidence interval; DB = double blind; eGFR = estimated glomerular filtration rate; ESKD = end-stage kidney disease; ITT = intention to treat; hr = hour; ITT = modified intention to treat; IV = intravenous; LN = lupus nephritis; N = number of subjects; NA = not applicable; NNH = number needed to harm; NNT = number needed to treat; PC = placebo controlled; PP = per protocol; RCT = randomized controlled trial; SAE = serious adverse event; SLE = systemic lupus erythematosus; s/p = status post; UPCR = urinary protein-to-creatinine ratio (in mg/mg); US = United States; w/o = without; w/ = with.								

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Appendix 1: Current Preferred Drug List

Generic	Brand	Route	Form	PDL
anifrolumab-fnia	SAPHNELO	INTRAVEN	VIAL	N
anifrolumab-fnia	SAPHNELO PEN	SUBCUT	AUTO INJCT	
belimumab	BENLYSTA	INTRAVEN	VIAL	N
belimumab	BENLYSTA	SUBCUT	AUTO INJCT	N
belimumab	BENLYSTA	SUBCUT	SYRINGE	N
obinutuzumab*	GAZYVA	INTRAVEN	VIAL	

*Currently in the “Antineoplastics, newer” drug class

Appendix 2: Abstracts of Comparative Clinical Trials

None

Appendix 3: Medline Search Strategy

Ovid medline 1946 to 5/29/26 and 2021 to 5/29/26

☐	1	obinutuzumab.mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms, population supplementary concept word, anatomy supplementary concept word]	1379
☐	2	Lupus Erythematosus, Systemic/ or Lupus Nephritis/	72287
☐	3	1 and 2	50
☐	4	limit 3 to (english language and humans and (clinical trial, all or clinical trial, phase iii or clinical trial, phase iv or comparative study or controlled clinical trial or equivalence trial or guideline or meta analysis or multicenter study or network meta-analysis or practice guideline or randomized controlled trial or "systematic review"))	16
☐	5	anifrolumab.mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms, population supplementary concept word, anatomy supplementary concept word]	439
☐	6	4 and 5	3
☐	7	belimumab.mp. [mp=title, book title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms, population supplementary concept word, anatomy supplementary concept word]	1488
☐	8	4 and 7	7

Appendix 4: Prescribing Information Highlights

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use GAZYVA safely and effectively. See full prescribing information for GAZYVA.

GAZYVA® (obinutuzumab) injection, for intravenous use
Initial U.S. Approval: 2013

WARNING: HEPATITIS B VIRUS REACTIVATION and PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY
See full prescribing information for complete boxed warning.

- **Hepatitis B Virus (HBV) reactivation, in some cases resulting in fulminant hepatitis, hepatic failure, and death. (5.1)**
- **Progressive Multifocal Leukoencephalopathy (PML) resulting in death. (5.2)**

----------RECENT MAJOR CHANGES----------

Indication and Usage, Lupus Nephritis (1.3) ----------10/2025
Dosage and Administration (2.4)----------10/2025
Warnings and Precautions (5)---------- ----------10/2025

---------- INDICATIONS AND USAGE----------

GAZYVA is a CD20-directed cytolytic antibody indicated:

- in combination with chlorambucil, for the treatment of patients with previously untreated chronic lymphocytic leukemia (CLL). (1.1, 14)
- in combination with bendamustine followed by GAZYVA monotherapy, for the treatment of patients with follicular lymphoma (FL)who relapsed after, or are refractory to, a rituximab-containing regimen. (1.2, 14)
- in combination with chemotherapy followed by GAZYVA monotherapy in patients achieving at least a partial remission, for the treatment of adult patients with previously untreated stage II bulky, III or IV follicular lymphoma. (1.2, 14)
- for the treatment of adult patients with active lupus nephritis (LN) who are receiving standard therapy (1.3, 14)

----------DOSAGE AND ADMINISTRATION----------

- Premedicate for infusion-related reactions and tumor lysis syndrome. (2.1, 5.3, 5.4)
- Administer only as intravenous infusion. Do not administer as an intravenous push or bolus. (2.1)
- The recommended dosage for chronic lymphocytic leukemia is 100 mg on day 1 and 900 mg on day 2 of Cycle 1, 1,000 mg on day 8 and 15 of Cycle 1, and 1,000 mg on day 1 of Cycles 2–6. (2.2)
- The recommended dosage for follicular lymphoma is 1,000 mg on day 1, 8 and 15 of Cycle 1, 1,000 mg on day 1 of Cycles 2-6 or Cycles 2-8, and then 1,000 mg every 2 months for up to 2 years. (2.3)
- The recommended dosage for active lupus nephritis is 1,000 mg at the initial infusion, on Week 2, 24, 26, and every 6 months thereafter. (2.4)

---------- DOSAGE FORMS AND STRENGTHS----------

Injection: 1,000 mg/40 mL (25 mg/mL) single-dose vial. (3)

---------- CONTRAINDICATIONS ----------

GAZYVA is contraindicated in patients with known hypersensitivity reactions (e.g., anaphylaxis) to obinutuzumab or any of the excipients, including serum sickness with prior obinutuzumab use. (4)

---------- WARNINGS AND PRECAUTIONS ----------

- Infusion-Related Reactions: Premedicate patients with glucocorticoid, acetaminophen, and anti-histamine. Monitor patients closely during infusions. Interrupt, reduce rate, or discontinue for infusion-related reactions based on severity. (2.1, 5.3)
- Hypersensitivity Reactions Including Serum Sickness: Discontinue GAZYVA permanently. (5.4)
- Tumor Lysis Syndrome: In CLL and FL, premedicate with anti-hyperuricemics and adequate hydration, especially for patients with high tumor burden, high circulating lymphocyte count or renal impairment. Correct electrolyte abnormalities, provide supportive care, and monitor renal function and fluid balance. (5.5)
- Serious, Including Fatal, Infections: Do not administer GAZYVA to patients with an active infection. Patients with a history of recurring or chronic infections may be at increased risk of infection. (5.6)
- Neutropenia: In patients with Grade 3 to 4 neutropenia, monitor laboratory tests until resolution and for infection. Consider dose delays and infection prophylaxis, as appropriate. (5.7)
- Thrombocytopenia: Monitor for decreased platelet counts and bleeding. Transfusion may be necessary. (5.8)
- Disseminated Intravascular Coagulation: Evaluate cause and monitor for bleeding, thrombosis, and need for supportive care. (5.9)
- Immunization: Avoid administration of live virus vaccines during GAZYVA treatment and until B-cell recovery. (5.10)
- Embryo-Fetal Toxicity: Can cause fetal harm. Advise females of reproductive potential of the potential risk to a fetus and use effective contraception. (5.11)

---------- ADVERSE REACTIONS ----------

The most common adverse reactions (incidence ≥ 20% and ≥ 2% greater in the GAZYVA treated arm in CLL and NHL, and incidence ≥ 5% in the GAZYVA treated arm in LN) were:

- Previously untreated CLL: infusion-related reactions and neutropenia. (6)
- Relapsed or refractory non-Hodgkin lymphoma (NHL): infusion-related reactions, fatigue, neutropenia, cough, upper respiratory tract infections, and musculoskeletal pain. (6)
- Previously untreated NHL: infusion-related reactions, neutropenia, upper respiratory tract infections, cough, constipation, and diarrhea. (6)
- Lupus Nephritis: upper respiratory tract infection, COVID-19, urinary tract infection, bronchitis, pneumonia, infusion-related reactions, and neutropenia. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Genentech at 1-888-835-2555 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------USE IN SPECIFIC POPULATIONS----------

- Lactation: Advise not to breastfeed. (8.1)

See 17 for PATIENT COUNSELING INFORMATION.

Revised: 10/2025

Author: Fletcher

Date: August 2026

Appendix 5. Pharmacology and Pharmacokinetic Properties[19]

Parameter	
Mechanism of Action	-Monoclonal antibody that targets the CD20 antigen expressed on the surface of pre-B and mature B lymphocytes. -Upon binding to CD20, obinutuzumab mediates B-cell lysis through (1) engagement of immune effector cells, (2) by directly activating intracellular death signaling pathways (direct cell death), and/or (3) activation of the complement cascade. The immune effector cell mechanisms include antibody-dependent cellular cytotoxicity (ADCC) and antibody-dependent cellular phagocytosis.
Oral Bioavailability	n/a
Distribution and Protein Binding	Not reported
Elimination	Clearance of 0.13 L/day via two parallel pathways, a linear clearance pathway and a non-linear clearance pathway, which changes as a function of time. The time-varying clearance decreases with time with an exponential decay coefficient, likely related to CD20 target reduction and proteinuria improvement over time, and a time-independent clearance related to the endogenous catabolic processes of IgG.
Half-Life	22.4 days
Metabolism	Not reported

Abbreviations: IgG = immune globulin G; L = liter; n/a = not applicable

Appendix 6: Key Inclusion Criteria

Population	Patients with SLE and/or LN
Intervention	Appendix 1
Comparator	Appendix 1, standard therapy (e.g., corticosteroids, cyclophosphamide, mycophenolate products, cyclosporin, voclosporin, etc.)
Outcomes	Renal response, disease activity scores, hospitalizations, need for dialysis, quality of life, adverse events
Timing	Not applicable
Setting	Outpatient

Anifrolumab-fnia

Goal(s):
- Promote use that is consistent with medical evidence.

Length of Authorization:
- Up to 12~~6~~ months

Requires PA:
- Anifrolumab-fnia provider administered and pharmacy claims

Covered Alternatives:
- Current PMPDP preferred drug list per OAR 410-121-0030 at www.orpdl.org
- Searchable site for Oregon FFS Drug Class listed at www.orpdl.org/drugs/

Approval Criteria		
1. What diagnosis is being treated?	Record ICD-10 code.	
2. Is this an FDA approved indication?	**Yes:** Go to #3	**No:** Pass to RPh. Deny; medical appropriateness
3. Does the patient have severe active central nervous system lupus or severe, active lupus nephritis?	**Yes:** Pass to RPh. Deny; medical appropriateness	**No:** Go to #4
4. Is this a request for continuation of therapy previously approved by fee-for-service (FFS)?	**Yes**: Go to **Renewal Criteria**	**No:** Go to #5
5. Is the patient currently on other biologic therapy?	**Yes:** Pass to RPh. Deny; medical appropriateness.	**No:** Go to #6

Approval Criteria		
6. Is the drug being prescribed by or in consultation with a rheumatologist, nephrologist, or a provider with experience treating SLE?	**Yes:** Go to #7	**No:** Pass to RPh. Deny; medical appropriateness
7. Does the patient have a baseline assessment of SLE disease activity available using one of the following functional assessment tools: • SLE Index Score (SIS) • British Isles Lupus Assessment Group (BILAG) • Systemic Lupus Activity Measure (SLAM) • Systemic Lupus Erythematosus Disease Activity Score (SLEDAI or modified versions, e.g. SLEDAI-2K, SELENA-SLEDAI) • Physicians Global Assessment (PGA) • Systemic Lupus International Collaborating Clinic (SLICC) Damage Index	**Yes:** Go to #8 Document baseline assessment _____.	**No:** Pass to RPh. Deny; medical appropriateness
8. Is the patient currently taking ALL of the following or have a documented contraindication: • Hydroxychloroquine • Glucocorticoids (e.g. prednisone) • Methotrexate OR Azathioprine OR Mycophenolate	**Yes:** Approve for 12~~6~~ months.	**No:** Pass to RPh. Deny; medical appropriateness.

Renewal Criteria		
1. Is the patient currently on other biologic therapy?	**Yes:** Pass to RPh. Deny; medical appropriateness.	**No:** Go to #2

Renewal Criteria		
2. Has the patient's SLE disease activity improved or stabilized as assessed by one of the following functional assessment tools: • SLE Index Score (SIS) • British Isles Lupus Assessment Group (BILAG) • Systemic Lupus Activity Measure (SLAM) • Systemic Lupus Erythematous Disease Activity Score (SLEDAI or modified versions, e.g. SLEDAI-2K, SELENA-SLEDAI) • Physicians Global Assessment (PGA) • Systemic Lupus International Collaborating Clinic (SLICC) Damage Index	**Yes:** Approve for ~~6~~ 12 months.	**No:** Pass to RPh; Deny; medical appropriateness.

P&T/DUR Review: 8/26 (SF); 2/22 (SF)
Implementation: TBD; 4/1/22

Belimumab (Benlysta®)

Goal(s):
- Promote use that is consistent with national clinical practice guidelines and medical evidence.

Length of Authorization:
- Up to 24 ~~6~~ months

Requires PA:
- Benlysta® (belimumab) pharmacy or provider administered claims.

Covered Alternatives:

- Current PMPDP preferred drug list per OAR 410-121-0030 at www.orpdl.org
- Searchable site for Oregon FFS Drug Class listed at www.orpdl.org/drugs/

Table 1: FDA approved ages

Indication	Approved formulation	
	Intravenous (IV) powder for solution	Subcutaneous (SC) Injection
Systemic Lupus Erythematosus (SLE)	5 years and older	5 years and older
Lupus Nephritis	5 years and older	5 years and older
IV (usual adult dosage): **SLE or Lupus Nephritis:** 10 mg/kg IV infusion over 1 hour every 2 weeks for the first 3 doses, then every 4 weeks thereafter SC (usual adult dosage): **SLE**: 200 mg SC once weekly **Lupus Nephritis**:400 mg (two 200-mg injections) SC once weekly into abdomen or thigh for 4 doses, then 200 mg SC once weekly thereafter		

Approval Criteria		
1. What diagnosis is being treated?	Record ICD-10 code.	
2. Does the patient have severe active central nervous system lupus?	**Yes:** Pass to RPh. Deny; medical appropriateness	**No:** Go to #3
3. Is this a request for continuation of therapy previously approved by fee-for-service (FFS)?	**Yes**: Go to **Renewal Criteria**	**No:** Go to #4
4. Is the patient diagnosed with lupus nephritis or systemic lupus erythematosus (SLE)?	**Yes:** Go to #5	**No:** Pass to RPh. Deny; medical appropriateness
5. Is belimumab dosed according to FDA label for age and formulation? appropriately and with an approved formulation for patient's age as outlined in Table 1?	**Yes:** Go to #6	**No:** Pass to RPh. Deny; medical appropriateness

Approval Criteria		
6. Is the patient currently on other targeted immune modulators?	**Yes:** Pass to RPh. Deny; medical appropriateness. Belimumab has not been studied in combination with other targeted immune modulators	**No:** Go to #7
7. Is the drug being prescribed by or in consultation with a rheumatologist, nephrologist, or a provider with experience treating SLE or lupus nephritis?	**Yes:** Go to #8	**No:** Pass to RPh. Deny; medical appropriateness
8. Does the patient have active autoantibody-positive SLE or lupus nephritis and is a baseline assessment of SLE disease activity available using one of the following functional assessment tools: • SLE Index Score (SIS) • British Isles Lupus Assessment Group (BILAG) • Systemic Lupus Activity Measure (SLAM) • Systemic Lupus Erythematosus Disease Activity Score (SLEDAI or modified versions, e.g. SLEDAI-2K, SELENA-SLEDAI) • Physicians Global Assessment (PGA) • Systemic Lupus International Collaborating Clinic (SLICC) Damage Index • Urinary protein to creatinine ratio • Most recent estimated Glomerular Filtration Rate (eGFR)	**Yes:** Go to #9 Document baseline assessment _____.	**No:** Pass to RPh. Deny; medical appropriateness

Approval Criteria		
9. Is the patient currently taking or have a contraindication to BOTH of the following: • Hydroxychloroquine • Glucocorticoids (e.g. prednisone) PLUS one of the follow if treating lupus nephritis: mycophenolate acid analog OR azathioprine OR cyclophosphamide	**Yes:** Go to #10	**No:** Pass to RPh. Deny; medical appropriateness. ~~Belimumab has not been studied as monotherapy in patients with SLE.~~
10. Does the patient have lupus nephritis AND a urine protein: creatinine ratio of >500 mg/g?	**Yes:** Go to #11	**No:** Approve for 12~~6~~ months
11. Is the patient currently taking, or have a contraindication to, either an angiotensin-converting enzyme inhibitor (ACEI) OR an angiotensin II receptor blocker (ARB)?	**Yes:** Approve for 12~~6~~ months	**No:** Pass to RPh. Deny; medical appropriateness.

Renewal Criteria		
1. Is the patient currently on another ~~therapeutic immune modulator~~biologic agent? Note: Belimumab has not been studied in combination with other ~~therapeutic immune modulators~~biologic agents.	**Yes:** Pass to RPh. Deny; medical appropriateness.	**No:** Go to #2

Renewal Criteria		
2. Has the patient's SLE disease activity improved or stabilized as assessed by one of the following functional assessment tools: • SLE Index Score (SIS) • British Isles Lupus Assessment Group (BILAG) • Systemic Lupus Activity Measure (SLAM) • Systemic Lupus Erythematous Disease Activity Score (SLEDAI or modified versions, e.g. SLEDAI-2K, SELENA-SLEDAI) • Physicians Global Assessment (PGA) • Systemic Lupus International Collaborating Clinic (SLICC) Damage Index • Urinary protein to creatinine ratio • eGFR	**Yes:** Approve for ~~6~~24 months.	**No:** Pass to RPh; Deny; medical appropriateness.

P&T/DUR Review: *08/26 (SF); 02/22 (SF); 8/21 (DM) 2/20, 5/18*
Implementation: *TBD; 4/1/22; 3/1/2020; 7/1/18*

Obinutuzumab (GAZYVA®)

Goal(s):
- Promote use that is consistent with national clinical practice guidelines and medical evidence.

Length of Authorization:
- 12 months

Requires PA:
- Gazyva® (obinutuzumab) pharmacy or provider administered claims.

Covered Alternatives:

- Current PMPDP preferred drug list per OAR 410-121-0030 at www.orpdl.org
- Searchable site for Oregon FFS Drug Class listed at www.orpdl.org/drugs/

Approval Criteria		
1. What diagnosis is being treated?	Record ICD-10 code.	
2. Is the ICD-10 for an oncology indication?	**Yes:** Use "Oncology Agents" prior authorization document to adjudicate request.	**No:** Go to #3
3. Does the patient have severe active central nervous system lupus?	**Yes:** Pass to RPh. Deny; medical appropriateness	**No:** Go to #4
4. Is this a request for continuation of therapy previously approved by fee-for-service (FFS)?	**Yes**: Go to **Renewal Criteria**	**No:** Go to #5
5. Is the patient an adult diagnosed with active lupus nephritis class III, IV, or V?	**Yes:** Go to #6	**No:** Pass to RPh. Deny; medical appropriateness
6. Is the patient currently on another biologic agent without a documented plan to switch therapy?	**Yes:** Pass to RPh. Deny; medical appropriateness.	**No:** Go to #7
7. Is the drug being prescribed by or in consultation with a rheumatologist, nephrologist, or a provider with experience treating lupus nephritis?	**Yes:** Go to #8	**No:** Pass to RPh. Deny; medical appropriateness
8. Does the patient have a baseline assessment of renal function with both of the following tools within 6 months: • Urinary protein-to-creatinine ratio (UPCR) • estimated Glomerular Filtration Rate (eGFR)	**Yes:** Go to #9 Document baseline assessment _____.	**No:** Pass to RPh. Deny; medical appropriateness

Approval Criteria		
9. Is the patient currently taking or have a contraindication to all of the following: • Hydroxychloroquine • Mycophenolate • Glucocorticoids (e.g. prednisone)	**Yes:** Go to #10	**No:** Pass to RPh. Deny; medical appropriateness.
10. Does the patient have a urine protein-to-creatinine ratio of >/= 1 mg/mg?	**Yes:** Go to #11	**No:** Pass to RPh. Deny; medical appropriateness.
11. Is the patient currently taking, or have a contraindication to, either an angiotensin-converting enzyme inhibitor (ACEI) OR an angiotensin II receptor blocker (ARB)?	**Yes:** Go to #12	**No:** Pass to RPh. Deny; medical appropriateness.
12. Is the patient of childbearing potential?	**Yes:** Go to #13	**No:** Approve for 12 months
13. Is the patient pregnant or actively trying to conceive?	**Yes:** Pass to RPh. Deny; medical appropriateness.	**No:** Go to #14
14. Is there documentation that the provider and patient have discussed the teratogenic risks of the drug if the patient were to become pregnant?	**Yes:** Approve for 12 months	**No:** Pass to RPh. Deny; medical appropriateness.

Renewal Criteria		
1. Is the patient currently on another biologic agent?	**Yes:** Pass to RPh. Deny; medical appropriateness.	**No:** Go to #2

Renewal Criteria		
2. Has the patient's renal function improved or stabilized as assessed by one of the following: • UPCR • eGFR	**Yes:** Approve for 12 months.	**No:** Pass to RPh; Deny; medical appropriateness.

P&T/DUR Review: *08/26 (SF)*
Implementation: *TBD*