Policy Number	RX501.187
Policy Effective Date	07/15/2026

Obinutuzumab

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Disclaimer

Medical policies are a set of written guidelines that support current standards of practice. They are based on current generally accepted standards of care developed by: nonprofit professional association(s) for the relevant clinical specialty, third-party entities that develop treatment criteria, or other federal or state governmental agencies. A requested therapy must be proven effective for the relevant diagnosis or procedure. For drug therapy, the proposed dose, frequency and duration of therapy must be consistent with recommendations in at least one authoritative source. This medical policy is supported by FDA-approved labeling and/or nationally recognized authoritative references to major drug compendia, peer reviewed scientific literature and generally accepted standards of medical care. These references include, but are not limited to: MCG care guidelines, DrugDex (IIa level of evidence or higher), NCCN Guidelines (IIb level of evidence or higher), NCCN Compendia (IIb level of evidence or higher), professional society guidelines, and CMS coverage policy.

Carefully check state regulations and/or the member contract.

Each benefit plan, summary plan description or contract defines which services are covered, which services are excluded, and which services are subject to dollar caps or other limitations, conditions or exclusions. Members and their providers have the responsibility for consulting the member's benefit plan, summary plan description or contract to determine if there are any exclusions or other benefit limitations applicable to this service or supply. **If there is a discrepancy between a Medical Policy and a member's benefit plan, summary plan description or contract, the benefit plan, summary plan description or contract will govern.**

Coverage

NOTE 1: This medical policy does **NOT** address oncologic indications. This medical policy **IS NOT TO BE USED** for oncologic indications. Refer to RX502.061 Oncology Medications for oncologic indications.

Obinutuzumab (Gazyva®) **may be considered medically necessary** for the treatment of adults with active lupus nephritis when **ALL** of the following criteria are met:

- The individual has a diagnosis of systemic lupus erythematosus (SLE) as confirmed by laboratory testing documenting the presence of autoantibodies (e.g., antinuclear antibodies

[ANA], anti-double-stranded DNA [anti-dsDNA] antibodies, and/or anti-Smith [anti-Sm] antibodies); and
- The individual is currently receiving standard therapy (e.g., mycophenolate mofetil (MMF), azathioprine, cyclophosphamide, leflunomide, and/or hydroxychloroquine); and
- The individual has been diagnosed with Class III-V lupus nephritis.

Obinutuzumab (Gazyva®) **is considered experimental, investigational and/or unproven** for all other non-Food and Drug Administration approved indications.

Policy Guidelines

None.

Description

Lupus Nephritis
Systemic lupus erythematosus (SLE), an autoimmune disease in which the immune system attacks its own tissue, is the most common type of lupus. It causes widespread inflammation and tissue damage in affected organs, including the joints, skin, brain, lungs, kidneys, and blood vessels. Although causes of SLE are unknown, it's believed to be linked to environmental, genetic, and hormonal factors, with seriousness ranging from mild to life-threatening. (2)

Lupus nephritis is a common and severe manifestation of SLE, often developing early on. Around 40% of individuals who are diagnosed with SLE will later develop lupus nephritis. Approximately 10% to 30% of individuals who suffer from lupus nephritis experience damage that leads to end-stage renal disease (kidney failure). Women in their 30s to 40s are most likely to be affected by SLE. Accordingly, lupus nephritis is more commonly seen in women. (3)

Those with lupus nephritis usually present with clinical manifestations of SLE, including rashes, fatigue, fever, photosensitivity, serositis, oral ulcers, painful or swollen joints, seizures, psychosis, or hematologic disorders. In the early stages of lupus nephritis, individuals often have no symptoms of kidney involvement. Some may develop symptoms such as polyuria (frequent urination), nocturia (waking at night to urinate), foamy urine, elevated blood pressure, and swelling. Early indications of protein in the urine, reflecting damage to and disfunction of the functional cells of the kidney (nephrons) include foamy urine or nocturia. When protein loss in the urine worsens, peripheral edema may occur due to low levels of protein in the blood. Microscopic amounts of blood in the urine may also be present. (3)

In 2025, the European Alliance of Associations for Rheumatology (EULAR) issued updated recommendations for the management of SLE with kidney involvement. The first overarching principle set forth was the need for regular monitoring for the signs and symptoms of kidney involvement, input from experts and timely biopsy. These were considered essential components to support kidney health. A kidney biopsy was recommended for every individual

with evidence of kidney involvement, such as persistent protein or blood in the urine, or for any decrease in kidney function that was otherwise unexplained. (4)

The EULAR also addressed treatment of SLE with kidney involvement. They indicated that kidney involvement is not a separate disease process and should be managed according to general recommendations for SLE. Due to the risk of kidney damage that could lead to chronic kidney disease, specialty providers (e.g., rheumatologists and nephrologists) should be involved in care management. The overall goal of treatment is to stabilize or improve kidney function, avoiding disease flares. Comorbidities must also be addressed to in order to improve the health-related quality of life. Individuals may be prescribed medications that suppress the immune system to stop the inflammatory process that leads to kidney damage. Kidney protective medications and lifestyle measures, such as smoking cessation, are emphasized as well. (4)

Obinutuzumab (Gazyva®)
Obinutuzumab is a glycoengineered, humanized type II anti-CD20 IgG1 monoclonal antibody. It targets a specific area on CD20, which is a protein found on the membrane of a type of immune cell called a B cell, or lymphocyte. These B cells play a central role in the development of SLE. Obinutuzumab directs the destruction of B cells, leading to lower levels of circulating B cells in the body. (5)

Regulatory Status (1)
In October 2025, the U.S. Food and Drug Administration (FDA) approved obinutuzumab (Gazyva®) for the treatment of adult patients with active lupus nephritis who are receiving standard therapy. The safety and effectiveness of Gazyva® in pediatric patients have not been established.

Oncologic indications are for obinutuzumab (Gazyva®) are addressed on Medical Policy RX502.061 Oncology Medications.

Rationale

This policy is based on the U.S. Food and Drug Administration (FDA) labeled indications for obinutuzumab (Gazyva®) and a review of relevant professional society guidelines.

Obinutuzumab (Gazyva®) (1)
Study Design and Population
The efficacy of Gazyva was evaluated in REGENCY (NCT04221477), a Phase III, randomized, double-blind, placebo-controlled, parallel-group, multicenter study in 271 patients with International Society of Nephrology (ISN)/Renal Pathology Society (RPS) 2003 Class III or IV, with or without concomitant Class V lupus nephritis (LN), treated with standard therapy consisting of mycophenolate mofetil (MMF) and corticosteroids. Patients had active or active/chronic ISN/RPS 2003 Class III or IV, with or without concomitant Class V proliferative LN

determined by kidney biopsy, current or past positive antinuclear antibody (ANA), urine protein-to-creatinine ratio (UPCR) ≥ 1 g/g, and had received at least one dose of pulse intravenous (IV) methylprednisolone (≥ 250 mg) or equivalent treatment for LN during the 6 months prior to screening or during screening.

Patients with estimated glomerular filtration rate (eGFR) 50% of glomeruli on kidney biopsy, presence of rapidly progressive glomerulonephritis, evidence of active infection, receipt of anti-CD20 therapy < 9 months before or during screening, or receipt of cyclophosphamide, tacrolimus, ciclosporin, or voclosporin within 2 months of or during screening were excluded.

Patients were randomized 1:1 to receive Gazyva 1,000 mg (N=135) or placebo (N=136) intravenously, in combination with MMF 2-2.5 g/day and a tapering course of corticosteroids and were evaluated over 76 weeks. Patients randomized to receive Gazyva were further randomized in a 1:1 ratio to receive either Gazyva 1,000 mg IV on Day 1, Weeks 2, 24, 26, 50, and 52 (Arm 1), or Gazyva 1,000 mg IV on Day 1, Weeks 2, 24, 26, and 52 (Arm 2). The totality of the Gazyva efficacy data combining both treatment arms is shown in Table 1.

All patients received oral prednisone 0.5 mg/kg/day (maximum 60 mg/day) and remained at this dose until Week 2. Beginning on Day 15, prednisone was tapered to achieve a target dose of 5 mg/day by Week 24. Prednisone was maintained at a low dose (5 mg/day) from Week 24 until Week 80.

The median age of patients was 31 years, 85% were female, 58% were Hispanic or Latino, 48% were White, 19% were American Indian or Alaska Native, 15% were Black or African American and 6% were Asian. The distribution by kidney biopsy class was 39% Class III, 61% Class IV and 31% had concomitant Class V. Mean (standard deviation [SD]) eGFR at baseline 102.3 (±30.8) mL/min/1.73 m^2. Mean (SD) UPCR at baseline was 3.3 (±2.9) mg/mg with 42% of patients exhibiting UPCR ≥ 3 mg/mg at baseline.

Efficacy Results

The primary endpoint measure was proportion of patients who achieved complete renal response (CRR) at Week 76, defined as meeting all of the following criteria: UPCR < 0.5 g/g; eGFR ≥ 85% of baseline, as calculated using the 2009 Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation; with no occurrence of the following intercurrent events: rescue therapy, treatment failure, death or early study withdrawal.

Key secondary endpoint measures included: proportion of patients who achieved CRR with successful prednisone taper at Week 76 (defined as achievement of CRR at Week 76 without receiving prednisone > 7.5 mg/day or equivalent from Week 64 through Week 76), proportion of patients who achieved a proteinuric response at Week 76 (defined as achievement of UPCR < 0.8g/g and no occurrence of the following intercurrent events: rescue therapy, treatment failure, death or early study withdrawal) and proportion of patients who experience “renal-related events or deaths” through Week 76 (defined as occurrence of death, treatment failure,

≥ 50% increase in UPCR to a value ≥ 3 g/g and/or ≥ 30% decrease in eGFR to < 60 ml/min/1.73 m^2).

The proportion of patients achieving CRR at Week 76 was significantly greater in patients treated with Gazyva in combination with standard therapy compared to patients who received placebo plus standard therapy. There were also a higher proportion of patients who achieved CRR with successful prednisone taper at Week 76 and proteinuric response at Week 76 in the Gazyva plus standard therapy arm compared to the placebo plus standard therapy arm (see Table 1).

In the REGENCY study, patients who received Gazyva were less likely to experience the outcome of "renal-related event or death" compared with placebo. Fewer patients in the Gazyva arm experienced worsening kidney function or doubling of serum creatinine (see Table 2).

Table 1. Summary of Efficacy Results in Adult Patients with Active Lupus Nephritis (REGENCY Study)

	Gazyva + standard therapy (N=135)	**Placebo + standard therapy (N=136)**
Primary Endpoint		
Complete renal response (CRR) at Week 76 (%)	46.4 (38.0, 54.9)	33.1 (25.2, 41)
Treatment difference (95% CI)[a]	13.4 (2.0, 24.8)	
p-value	0.0232	
Components of CRR:		
UPCR < 0.5 g/g	64 (47.4%)	49 (36.0%)
eGFR ≥ 85% at baseline	113 (83.7%)	103 (75.7%)
No occurrence of intercurrent events	120 (88.9%)	102(75%)
Key Secondary Endpoints		
CRR with successful prednisone taper at Week 76 (%)	42.7 (34.3, 51.1)	30.9 (23.1, 38.7)
Treatment difference (95% CI)	11.9 (0.6, 23.2)	
p-value	0.0421	
Proteinuric response at Week 76 (%)	55.5 (47.1, 64)	41.9 (33.6, 50.2)
Treatment difference (95% CI)	13.7 (2.0, 25.4),	
p-value	0.0227	

CI: confidence interval; CRR: complete renal response; eGFR: estimated glomerular filtration rate; UPCR: urine protein-to-creatinine ratio.

[a] Primary and key secondary endpoints were analyzed using the Cochran-Mantel-Haenszel (CMH) test, adjusted for stratification factors race and region. Multiple Imputation handled missing data. For the primary endpoint CRR and the key secondary endpoint CRR with successful prednisone taper, missing data (not due to an Intercurrent Event [ICE]) occurred in four patients in the Gazyva arm and one in the placebo arm. For the key secondary endpoint proteinuric response, four Gazyva patients and two placebo patients had non-ICE-related missing data.

Table 2. Renal-Related Event or Death in Adult Patients with Active Lupus Nephritis (REGENCY Study) by Week 76

	Week 0-76		Hazard Ratio (HR) vs. Placebo (95% CI) Week 76
	Gazyva + standard therapy (N=135)	Placebo + standard therapy (N=136)	
Renal-Related Event or Death			
Number (%) of patients with event	24 (17.8%)	46 (33.8%)	
Time to event			0.5 (0.3, 0.8)
Components of Renal-Related Event or Death Endpoint			
Percentage of patients with:			
Death	3 (2.2%)	1 (0.7%)	
Treatment failure[a]	6 (4.4%)	25 (18.4%)	
End-stage renal disease (ESRD)[1]	0	2 (1.5%)	
Clinically significant, sustained worsening in UPCR and/or eGFR from Week 24[2]	5 (3.7%)	22(16.2%)	
Rescue Therapy except corticosteroid-only rescue[3]	5 (3.7%)	22 (16.2%)	
Worsening proteinuria[b]	17 (12.6%)	18 (13.2%)	
Worsening eGFR[c]	7 (5.2%)	20 (14.7%)	
Additional Renal-Related Events			
Percentage of patients with event			
Doubling of serum creatinine from baseline through Week 76	4 (3.0%)	8 (5.9%)	

CI: confidence interval; eGFR: estimated glomerular filtration rate; UPCR: urine protein-to-creatinine ratio.

[a] Treatment failure was prospectively defined as any of the following: 1) new ESRD or need for chronic dialysis or renal transplantation, 2) clinically significant, sustained worsening in UPCR and/or eGFR from Week 24 onward that leads the investigator to conclude the patient failed the randomized treatment period, or 3) receipt of rescue therapy, except corticosteroid-only rescue.

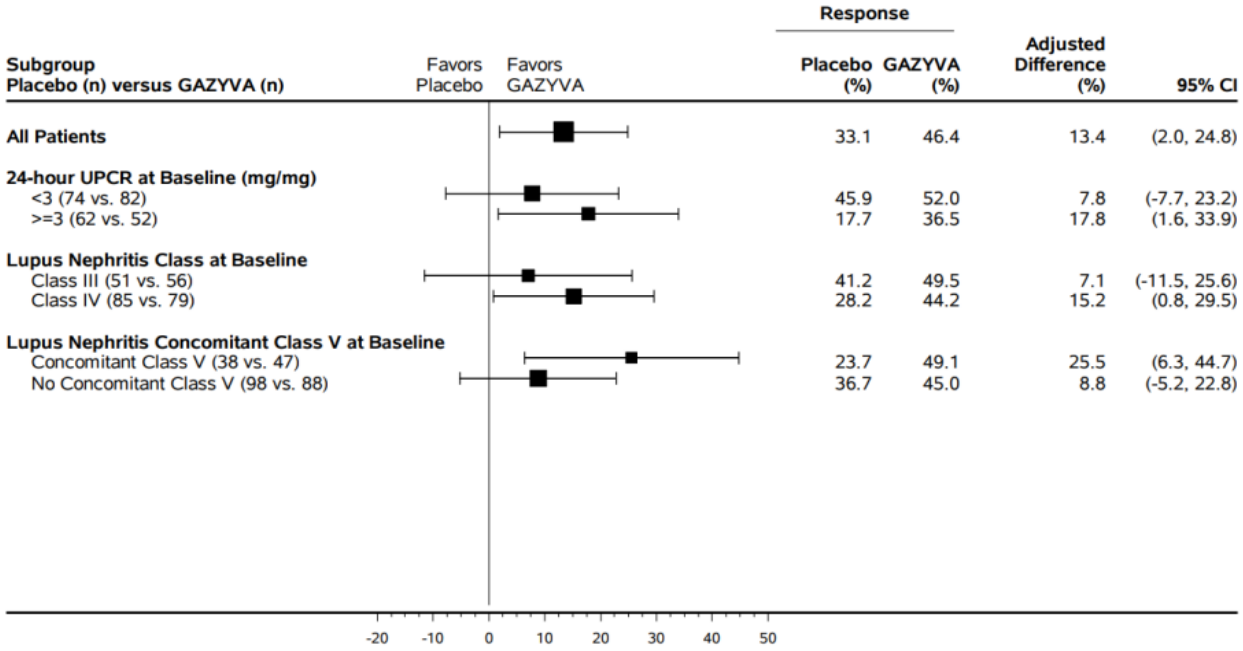
[b] Worsening proteinuria was prospectively defined as a confirmed ≥ 50% increase in UPCR to a value ≥ 3 g/g.

[c] Worsening eGFR was prospectively defined as confirmed ≥ 30% decrease in eGFR to a value < 60mL/min/1.73m^2.

Subgroup Analyses

In pre-specified subgroup efficacy analyses, the primary endpoint in patients was examined based on 24-hour UPCR at baseline (< 3 g/g or ≥ 3 g/g), lupus nephritis class at baseline (Class III or IV), and concomitant Class V at baseline. The results are displayed in Figure 1 below.

Figure 1. Forest Plot of CRR at Week 76 on Baseline Disease Characteristics, Efficacy-Evaluable Patients



Subgroup findings should be interpreted with caution due to small sample sizes and overlapping subgroups.
All patients received standard of care, consisting of MMF and corticosteroids, as per protocol.

CI: confidence interval; CRR: complete renal response; MMF: mycophenolate mofetil; UPCR: urine protein-to-creatinine ratio.

Practice Guidelines and Position Statements

European League Against Rheumatism (EULAR) and the American College of Rheumatology (ACR) Classification Criteria for Systemic Lupus Erythematosus

In 2019, updated classification criteria for systemic lupus erythematosus (SLE) jointly supported by EULAR and the ACR were issued. Multiple classification domains were specified. Antinuclear antibodies (ANA) as well as SLE-specific antibodies anti-double-stranded DNA (anti-dsDNA) or anti-Smith (Anti-Sm) antibodies were among the laboratory tests supporting the criteria for a SLE diagnosis. (6)

Coding

Procedure codes on Medical Policy documents are included **only** as a general reference tool for each policy. **They may not be all-inclusive.**

The presence or absence of procedure, service, supply, or device codes in a Medical Policy document has no relevance for determination of benefit coverage for members or reimbursement for providers. **Only the written coverage position in a Medical Policy should be used for such determinations.**

Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member's benefit contract or Summary Plan Description (SPD) for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

CPT Codes	None

HCPCS Codes	J9301

*Current Procedural Terminology (CPT®) ©2025 American Medical Association: Chicago, IL.

References

U.S. Food and Drug Administration Label:

1. Prescribing Label: GAZYVA® (obinutuzumab) injection, for intravenous use. December 2025. Available at <https://www.accessdata.fda.gov> (accessed on February 3, 2026).

Other:

2. Horowitz, DM. Systemic lupus erythematosus. Medline Plus. Updated Jan 28, 2025. Available at <https://www.medlineplus.gov> (accessed February 4, 2026).
3. Musa R, Rout P, Qurie A. Lupus Nephritis. [Updated January 16, 2025]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 January. Available at <https://www.ncbi.nlm.nig.gov> (accessed February 4, 2026).
4. Wu C, Wang Y, Chen S, et al. Obinutuzumab in systemic lupus erythematosus: a real-world experience. Front Immunol. Nov 19 2025; 16:1702550. PMID 41346585
5. Fanouriakis A, Kostopoulou M, Anders HJ, et al. EULAR recommendations for the management of systemic lupus erythematosus with kidney involvement: 2025 update. Ann Rheum Dis. Jan 2026; 85(1):75-90. PMID 41107121.
6. Aringer M, Costenbader KH, Daikh DI, et al. 2019 EULAR/ACR Classification Criteria for Systemic Lupus Erythematosus. Arthritis Rheumatol. Sep 2019; 71(9):1400-1412. PMID 31385462

Centers for Medicare and Medicaid Services (CMS)

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare and Medicaid Services (CMS) does not have a national Medicare coverage position. Coverage may be subject to local carrier discretion.

A national coverage position for Medicare may have been developed since this medical policy document was written. See Medicare's National Coverage at <https://www.cms.hhs.gov>.

Policy History/Revision

Date	Description of Change
07/15/2026	New medical document. Obinutuzumab (Gazyva®) may be considered medically necessary for the treatment of adults with active lupus nephritis when ALL of the following criteria are met: The individual has a diagnosis of systemic lupus erythematosus (SLE) as confirmed by laboratory testing

	documenting the presence of autoantibodies (e.g., antinuclear antibodies [ANA], anti-double-stranded DNA [anti-dsDNA] antibodies, and/or anti-Smith [anti-Sm] antibodies); and The individual is currently receiving standard therapy (e.g., mycophenolate mofetil (MMF), azathioprine, cyclophosphamide, leflunomide, and/or hydroxychloroquine); and The individual has been diagnosed with Class III-V lupus nephritis. Obinutuzumab (Gazyva®) is considered experimental, investigational and/or unproven for all other non-Food and Drug Administration approved indications.