Utilization Review Policy 161

POLICY: Oncology (Injectable – CD20-Directed Antibody) – Gazyva Utilization Management Medical Policy

- Gazyva® (obinutuzumab intravenous infusion – Genentech)

EFFECTIVE DATE: 1/1/2021
LAST REVISION DATE: 12/17/2025

COVERAGE CRITERIA FOR: All Aspirus Medicare Plans

OVERVIEW

Gazyva, a CD20-directed antibody, is indicated for the treatment of:[1]

- **Chronic lymphocytic leukemia**, in combination with chlorambucil in previously untreated patients.
- **Follicular lymphoma**, in combination with bendamustine followed by Gazyva monotherapy, for patients who relapse or are refractory to a rituximab containing regimen.
- **Follicular lymphoma, stage II bulky, III or IV**, in combination with chemotherapy, followed by Gazyva monotherapy for patients achieving at least a partial remission, in previously untreated patients.
- Active **lupus nephritis**, in adults who are receiving standard therapy.

Dosing

The approved dosing regimen for Gazyva recommends up to 6 cycles (6 months) of therapy for chronic lymphocytic leukemia.[1] For follicular lymphoma, the FDA approved dosing regimen for Gazyva recommends up to 6 months (six 28-day cycles or up to eight 21-day cycles) of therapy. Patients with relapsed or refractory follicular lymphoma who achieve stable disease, or a complete or partial response; or patients with previously untreated follicular lymphoma who achieve a complete or partial response, should continue Gazyva monotherapy for up to 2 years.

In the GADOLIN study, adults with rituximab refractory non-Hodgkin lymphoma were randomized to treatment with Gazyva 1,000 mg on Days 1, 8, and 15 of Cycle 1 and on Day 1 of Cycles 2 through 6 plus bendamustine 90 mg/m^2 on Days 1 and 2 of Cycles 1 through 6 or bendamustine 120 mg/m^2 on Days 1 and 2 of Cycles 1 through 6 (28-day cycles).[2] Patients without disease progression in the Gazyva plus bendamustine group could receive maintenance therapy with Gazyva 1,000 mg once every 2 months for up to 2 years. Patients in the Gazyva and bendamustine group had significantly longer progression-free survival than the bendamustine monotherapy group.

Guidelines

Gazyva is addressed in National Comprehensive Cancer Network guidelines:

- **B-cell lymphomas:** Guidelines (version 3.2025 – August 18, 2025) recommend Gazyva for the first-line and second-line treatment of follicular lymphoma or nodal marginal zone lymphoma in combination with CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone), CVP (cyclophosphamide, vincristine, and prednisone), bendamustine, or lenalidomide; as third-line

and subsequent treatment in combination with Brukinsa® (zanubrutinib capsule); or as single agent maintenance treatment.[3,5] The guidelines also recommend Gazyva as first-line treatment of nodal marginal zone lymphoma; second-line or maintenance therapy for nodal marginal zone lymphoma, extranodal marginal zone lymphoma of the stomach, extranodal marginal zone lymphoma of nongastric sites, and splenic marginal zone lymphoma. Gazyva, in combination with Venclexta® (venetoclax tablets) and Brukinsa, is recommended for the first-line treatment of mantle cell lymphoma with TP53 mutation; and can also be substituted for rituximab in mantle cell lymphoma. Gazyva is also recommended as a substitute for rituximab products (Rituxan, biosimilars) in patients with intolerance or experiencing rare complications, regardless of histology. Finally, Gazyva is recommended as pretreatment, 7 days prior to the administration of Columvi™ (glofitamab-gxbm intravenous infusion) for the treatment of diffuse large B-cell lymphoma (DLBCL), histologic transformation of indolent lymphomas to DLBCL, high-grade B-cell lymphoma, HIV-related B-cell lymphoma, and post-transplant lymphoproliferative disorders.

- **Castleman Disease:** Guidelines (version 1.2026 – November 24, 2025) recommend Gazyva as a substitute for rituximab products (Rituxan, biosimilars) in patients with intolerance or experiencing rare complications.[3,8]
- **Chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL):** Guidelines (version 1.2026 – October 10, 2025) recommend Gazyva for the first-line treatment of CLL/SLL without del(17p)/TP53 mutation in patients with indications for treatment, Gazyva is recommended in combination with bendamustine, chlorambucil, Calquence® (acalabrutinib capsules), Venclexta, Imbruvica® (ibrutinib capsules and tablets), high-dose methylprednisolone; or as a single-agent.[3,4] Gazyva is also recommended as a single agent or in combination with Venclexta, Calquence, or high-dose methylprednisolone for the first-line treatment of CLL/SLL with del(17p)/TP53 mutation; as second-line or subsequent treatment in combination with Venclexta for CLL/SLL with or without del(17p)/TP53 mutation; as a single agent or in combination with high-dose methylprednisolone for relapsed or refractory CLL/SLL without del(17p)/TP53 mutation; in combination with high-dose methylprednisolone for relapsed or refractory CLL/SLL with del(17p)/TP53 mutation; and in combination with Venclexta for retreatment for late relapse after a period of remission in patients with or without del(17p)/TP53 mutations.
- **Hairy Cell Leukemia:** Guidelines (version 2.2026 – December 2, 2025) recommend Gazyva in combination with Zelboraf® (vemurafenib tablets) for initial treatment in patients who cannot tolerate purine analogs including frail patients and those with active infections.[3,6]

Lupus Nephritis

Guidelines for the management of lupus nephritis from Kidney Disease: Improving Global Outcomes (KDIGO) [2024] include consideration of anti-CD20 therapy (e.g., rituximab, obinutuzumab) for patients with Class III or IV biopsy-confirmed lupus nephritis who have an inadequate response or intolerance to standard induction regimens.[9] Anti-CD20 agents are not recommended as initial therapy; rather, they are reserved for refractory or relapsing disease.

The 2024 American College of Rheumatology lupus nephritis guidelines recommend anti-CD20 therapy, such as rituximab or obinutuzumab, only for patients with refractory or relapsing disease who do not respond to standard induction regimens (e.g., mycophenolate, cyclophosphamide, belimumab, or calcineurin inhibitors).[10]

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Gazyva. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indications. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Gazyva as well as the monitoring required for adverse events and long-term efficacy, approval requires Gazyva to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Gazyva is recommended in those who meet one of the following criteria:

FDA-Approved Indications

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1. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma. Approve for 6 months if the patient meets ALL of the following (A and B):

A) Patient is ≥ 18 years of age; AND

B) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve the following dosing (A, B, C, and D):

A) Each individual dose must not exceed 1,000 mg administered by intravenous infusion; AND

B) The first dose is divided and administered on Day 1 (100 mg) and Day 2 (900 mg) of Cycle 1; AND

C) Patient receives a maximum of two additional doses in Cycle 1; AND

D) Patient receives a maximum of one dose in each subsequent 28-day cycle.

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2. Follicular Lymphoma. Approve for 6 months if the patient meets ALL of the following (A, B, and C):

A) Patient is ≥ 18 years of age; AND

B) Gazyva is used in ONE of the following situations (i, ii, iii, iv, v, or vi):

- **i.** In combination with chemotherapy; OR
  Note: Examples include CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone), CVP (cyclophosphamide, vincristine, and prednisone), or bendamustine.
- **ii.** In combination with lenalidomide; OR
- **iii.** As a single agent for second-line and subsequent therapy; OR
- **iv.** In combination with Brukinsa (zanubrutinib capsules) for third-line and subsequent therapy; OR
- **v.** For maintenance treatment following Gazyva in combination with chemotherapy; OR
- **vi.** Patient experienced an adverse event or intolerance to a rituximab product; AND
  Note: Examples of adverse events or intolerance includes paraneoplastic pemphigus, Stevens-Johnson syndrome, lichenoid dermatitis, vesiculobullous dermatitis, toxic epidermal necrolysis. Examples of rituximab products include Rituxan and biosimilars.

C) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve the following dosing (A, B, and C):
A) Each individual dose must not exceed 1,000 mg administered by intravenous infusion; AND
B) Patient receives a maximum of three doses in Cycle 1; AND
C) Patient receives a maximum of one dose in each subsequent cycle (21-day cycle, 28-day cycle, or 2-month cycle).

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3. Lupus Nephritis. Approve for the duration noted if the patient meets ONE of the following (A or B):
A) Initial Therapy. Approve for 6 months if the patient meets ALL of the following (i, ii, iii, and iv):
i. Patient is ≥ 18 years of age; AND
ii. Diagnosis of lupus nephritis has been confirmed on biopsy; AND
Note: For example, World Health Organization class III, IV, or V lupus nephritis.
iii. The medication is being used concurrently with an immunosuppressive regimen; AND
Note: Examples of an immunosuppressive regimen include azathioprine, cyclophosphamide, leflunomide, methotrexate, mycophenolate mofetil and/or a systemic corticosteroid.
iv. The medication is prescribed by or in consultation with a nephrologist or rheumatologist; OR
B) Patient is Currently Receiving Gavzyva. Approve for 1 year if the patient meets ALL of the following (i, ii, and iii):
i. The medication is being used concurrently with an immunosuppressive regimen; AND
Note: Examples of an immunosuppressive regimen include azathioprine, cyclophosphamide, leflunomide, methotrexate, mycophenolate mofetil and/or a systemic corticosteroid.
ii. According to the prescriber, patient has responded to the medication.
Note: Examples of a response include improvement in organ dysfunction, reduction in flares, reduction in corticosteroid dose, reduction in proteinuria, decrease in anti-dsDNA titers, and improvement in complement levels (i.e., C3, C4).
iii. The medication is prescribed by or in consultation with a nephrologist or rheumatologist.

Dosing. Approve 1,000 mg administered intravenously once, then 1,000 mg intravenously at Week 2, 24, and 26, followed by 1,000 mg intravenously every 6 months.

Other Uses with Supportive Evidence

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4. Hairy Cell Leukemia. Approve for 6 months if the patient meets ALL of the following (A, B, C, D, and E):
A) Patient is ≥ 18 years of age; AND
B) Patient is unable to tolerate purine analog therapy; AND
Note: Examples of purine analogs include cladribine and pentostatin.
C) Gazyva is used as initial therapy; AND
D) Gazyva is used in combination with Zelboraf (vemurafenib tablets); AND
E) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve the following dosing (A, B, and C):
A) Each individual dose must not exceed 1,000 mg given by intravenous infusion; AND
B) Patient receives a maximum of three doses in Cycle 1; AND
C) Patient receives a maximum of one dose in each subsequent cycle (28-day cycle or 2-month cycle).

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5. Marginal Zone Lymphoma. Approve for 6 months if the patient meets ALL of the following (A, B, and C):
Note: Includes nodal marginal zone lymphoma, splenic marginal zone lymphoma, extranodal marginal zone lymphoma of the stomach, or extranodal marginal zone lymphoma of nongastric sites (noncutaneous).
A) Patient is ≥ 18 years of age; AND
B) Gazyva is used in ONE of the following situations (i, ii, iii, or iv):
i. First-line therapy for nodal marginal zone lymphoma only; OR
ii. Second-line or subsequent therapy for recurrent or progressive disease; OR
iii. Maintenance therapy for rituximab refractory disease; OR
iv. Patient experienced an adverse event or intolerance to a rituximab product; AND
Note: Examples of adverse events or intolerance includes paraneoplastic pemphigus, Stevens-Johnson syndrome, lichenoid dermatitis, vesiculobullous dermatitis, toxic epidermal necrolysis. Examples of rituximab products include Rituxan and biosimilars.
C) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve the following dosing (A, B, and C):
A) Each individual dose must not exceed 1,000 mg given by intravenous infusion; AND
B) Patient receives a maximum of three doses in Cycle 1; AND
C) Patient receives a maximum of one dose in each subsequent cycle (28-day cycle or 2 month cycle).

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6. Mantle Cell Lymphoma. Approve for 6 months if the patient meets ALL of the following (A, B, and C):
A) Patient is ≥ 18 years of age; AND
B) Gazyva is used in ONE of the following situations (i or ii):
i. Induction therapy for TP53 mutated disease in combination with Venclexta (venetoclax tablets) and Brukinsa (zanubrutinib capsules); OR
ii. Gazyva may be substituted for a rituximab product; AND
C) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve the following dosing (A, B, and C):
A) Each individual dose must not exceed 1,000 mg given by intravenous infusion; AND
B) Patient receives a maximum of three doses in Cycle 1; AND
C) Patient receives a maximum of one dose in each subsequent cycle (28-day cycle or 2 month cycle).

7. Other B-Cell Lymphomas. Approve for 6 months if the patient meets ALL of the following (A, B, and C):

Note: Includes diffuse large B-cell lymphoma (DLBCL), histologic transformation of indolent lymphomas to DLBCL, high-grade B-cell lymphoma, Burkitt lymphoma, HIV-related B-cell lymphoma, post-transplant lymphoproliferative disorders, Castleman's disease.

A) Patient is ≥ 18 years of age; AND

C) Patient meets ONE of the following (i or ii):

i. A single dose of Gazyva is used as pretreatment before the first dose of Columvi (glofitamab-gxbm intravenous infusion); OR

ii. Patient experienced an adverse event or intolerance to a rituximab product; AND
Note: Examples of adverse events or intolerance includes paraneoplastic pemphigus, Stevens-Johnson syndrome, lichenoid dermatitis, vesiculobullous dermatitis, toxic epidermal necrolysis. Examples of rituximab products include Rituxan and biosimilars.

D) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve ONE of the following dosing (A or B):

A) Pretreatment before Columvi: Approve a single 1,000 mg dose administered by intravenous infusion; OR

B) Approve the following for the treatment of other B-cell lymphomas (i, ii, and iii):

i. Each individual dose must not exceed 1,000 mg given by intravenous infusion; AND

ii. Patient receives a maximum of three doses in Cycle 1; AND

iii. Patient receives a maximum of one dose in each subsequent cycle (28-day cycle, or 2-month cycle).

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Gazyva is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Gazyva® intravenous infusion [prescribing information]. South San Francisco, CA: Genentech; October 2025.
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3. The NCCN Drugs and Biologics Compendium. © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on December 12, 2025. Search term: obinutuzumab.
4. The NCCN Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Clinical Practice Guidelines in Oncology (version 1.2026 – October 10, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on December 12, 2025.
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6. The NCCN Hairy Cell Leukemia Clinical Practice Guidelines in Oncology (version 2.2026 – December 2,, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on December 12, 2025.
7. Columvi™ intravenous infusion [prescribing information]. South San Francisco, CA: Genentech; June 2023.
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9. Kidney Disease: Improving Global Outcomes (KDIGO) Lupus Nephritis Work Group. KDIGO 2024 Clinical Practice Guideline for the management of Lupus Nephritis. *Kidney Int*. 2024;105(1S):S1-S69.
10. Sammaritano L, Askanase A, Bermas B, et al. 2024 American College of Rheumatology (ACR) Guidelines for the Screening, Treatment, and Management of Lupus Nephritis. Published: May 7, 2025. Available at: https://rheumatology.org/lupus-guideline. Accessed: October 21, 2025.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	**Hairy Cell Leukemia:** Added new condition of approval.	11/16/2022
Selected Revision	**Other B-Cell Lymphomas:** A single dose of Gazyva is used as pretreatment before the first dose of Columvi (glofitamab intravenous infusion) was added as an additional option of approval. Dosing was updated with regimen for pretreatment before Columvi administration.	08/16/2023
Annual Revision	**Marginal Zone Lymphoma:** Removed gastric mucosa-associated lymphoid tissue (MALT) lymphoma and nongastric MALT lymphoma from Note and added extranodal marginal zone lymphoma of the stomach and extranodal marginal zone lymphoma of nongastric sites (noncutaneous). **Other B-Cell Lymphomas:** Added histologic transformation of indolent lymphomas to diffuse large B-cell lymphoma.	12/06/2023
Aspirus P&T Review	Policy reviewed and approved by Aspirus P&T committee. Annual review process	09/16/2024
Annual Revision	**Follicular Lymphoma:** Added in combination with lenalidomide, as a single agent for second-line and subsequent therapy, and in combination with Brukinsa (zanubrutinib capsules) for third-line and subsequent therapy, as additional options for approval. **Marginal Zone Lymphoma:** Added maintenance therapy for rituximab refractory disease as an additional option for approval. **Mantle Cell Lymphoma:** Added new condition of approval. **Other B-cell Lymphomas:** Removed mantle cell lymphoma from list of examples of B-cell lymphomas.	12/04/2024
Update	04/08/2025: The policy name was changed from "Oncology (Injectable) – Gayzva UM Medical Policy" to "Oncology (Injectable – CD20-Directed Antibody) – Gayzva UM Medical Policy".	N/A
Aspirus P&T Review	Policy reviewed and approved by Aspirus P&T committee. Annual review process	09/15/2025
Selected Revision	**Lupus Nephritis**: New condition of approval added. A new dosing limitation was added.	11/05/2025
Annual Revision	No criteria changes.	12/17/2025