

Clinical Policy: Obinutuzumab (Gazyva)

Reference Number: PA.CP.PHAR.305

Effective Date: 01/2018

Last Review Date: 10/2025

Description

Obinutuzumab (Gazyva[®]) is a CD20-directed cytolytic antibody.

FDA Approved Indication(s)

Gazyva is indicated on combination with:

- Chlorambucil, for the treatment of patients with previously untreated chronic lymphocytic leukemia (CLL)
- 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
- 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

Policy/Criteria

It is the policy of PA Health & Wellness[®] that Gazyva is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (must meet all):

1. Diagnosis of CLL or small lymphocytic lymphoma (SLL);
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age \geq 18 years;
4. If prescribed for second-line or subsequent therapy, one of the following (a, b or c):
 - a. Prescribed as a single agent;
 - b. Prescribed in combination with Venclexta[®];
 - c. Other NCCN recommendations listed as category 1, 2A, or 2B;
5. Request meets one of the following (a or b):
 - a. After initial loading doses, dose does not exceed 1,000 mg per 28-day cycle;
 - b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 12 months

B. B-Cell Lymphomas and Tumors with B-Cell Predominance (must meet all):

1. Diagnosis of one of the following B-cell lymphoma subtypes (a, b or c):
 - a. Castleman disease;
 - b. Follicular lymphoma (FL);
 - c. Other B-cell lymphomas (off-label, i-viii):
 - i. Marginal zone lymphoma (1, 2, or 3):
 - 1) Splenic marginal zone lymphoma;
 - 2) Nodal marginal zone lymphoma;
 - 3) Extranodal marginal zone lymphoma (a or b):

- a) Gastric MALT lymphoma;
 - b) Nongastric MALT lymphoma;
 - ii. Histologic transformation of indolent lymphomas to diffuse large B-cell lymphoma (DLBCL);
 - iii. DLBCL;
 - iv. High-grade B-cell lymphoma;
 - v. Mantle cell lymphoma;
 - vi. Post-transplant lymphoproliferative disorders;
 - vii. HIV-related B-cell lymphoma;
 - viii. Burkitt lymphoma;
2. Prescribed by or in consultation with an oncologist or hematologist;
 3. Age \geq 18 years;
 4. One of the following (a-f):
 - a. Gazyva is prescribed as a substitute* for rituximab in patients experiencing intolerance to rituximab (including severe hypersensitivity reactions requiring discontinuation) or rare complications such as mucocutaneous reactions including paraneoplastic pemphigus, Stevens-Johnson syndrome, lichenoid dermatitis, vesiculobullous dermatitis, and toxic epidermal necrolysis;
**Re-challenge with the same anti-CD20 monoclonal antibody is not recommended and it is unclear if the use of an alternative anti-CD20 monoclonal antibody poses the same risk of recurrence.*
 - b. For FL: Gazyva is requested for one of the following uses (i, ii, iii or iv):
 - i. First line therapy in combination with bendamustine, lenalidomide, or as a component of CHOP or CVP or Revlimid;
 - ii. Second-line or subsequent therapy (*see Appendix B for examples of prior therapy*);
 - iii. Maintenance therapy as a single agent if disease is rituximab-refractory or following chemoimmunotherapy;
 - iv. Third-line and subsequent therapy in combination with Brukinsa;
 - c. For marginal zone lymphomas: Gazyva is requested for one of the following uses (i, ii, or iii):
 - i. Maintenance therapy if disease is rituximab-refractory, recurrent, and has been treated with Gazyva and bendamustine;
 - ii. Second-line or subsequent therapy in combination with chemotherapy or Revlimid (*see Appendix B for examples of prior therapy*);
 - iii. Nodal marginal zone lymphoma only: First line therapy in combination with bendamustine, lenalidomide, or as a component of CHOP or CVP;
 - d. For all subtypes other than FL and marginal zone lymphoma, Gazyva is prescribed for second-line or subsequent therapy prior to Columvi™ for one of the following subtypes (i-vi):
 - i. Histologic transformation of indolent lymphomas to DLBCL;
 - ii. DLBCL;
 - iii. High-grade B-cell lymphoma;
 - iv. Mantle cell lymphoma;
 - v. Post-transplant lymphoproliferative disorders;
 - vi. HIV-related B-cell lymphoma;

- e. For mantle cell lymphoma, and prescribed in combination with Venclexta and Brukinsa[®]: Both of the following (i and ii):
 - i. Disease is positive for TP53 mutation;
 - ii. A clinical trial is not available (*a clinical trial is strongly recommended*)
- f. Other NCCN recommendations listed as category 1, 2A, or 2B;
- 5. Request meets one of the following (a or b):
 - a. After initial loading doses, dose does not exceed 1,000 mg per 28-day cycle;
 - b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 12 months

C. Hairy Cell Leukemia (off-label) (must meet all):

- 1. Diagnosis of hairy cell leukemia;
- 2. Prescribed by or in consultation with an oncologist or hematologist;
- 3. Age \geq 18 years;
- 4. Prescribed in one of the following ways (a, b or c):
 - a. As a single agent;
 - b. As initial therapy in combination with Zelboraf[®] (vemurafenib) and member is unable to tolerate purine analogs (e.g., cladribine, pentostatin);
 - c. Other NCCN recommendations listed as category 1, 2A, or 2B;
- 5. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

Approval duration: 12 months

D. Other diagnoses/indications: Refer to PA.CP.PMN.53

II. Continued Approval

A. All Indications in Section I (must meet all):

- 1. Currently receiving medication via PA Health & Wellness benefit or member has previously met all initial approval criteria; or the Continuity of Care policy (PA.PHARM.01) applies;
- 2. Member is responding positively to therapy;
- 3. If request is for a dose increase, request meets one of the following (a or b):
 - a. After initial loading doses, new dose does not exceed 1,000 mg per 28-day cycle;
 - b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2):

- 1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy; or the Continuity of Care policy (PA.PHARM.01) applies; or
- 2. Refer to PA.CP.PMN.53

III. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CLL: chronic lymphocytic leukemia	NCCN: National Comprehensive Cancer Network
DLBCL: diffuse large B-cell lymphoma	NHL: non-Hodgkin lymphoma
FDA: Food and Drug Administration	SLL: small lymphocytic lymphoma
FL: follicular lymphoma	
MALT: mucosa-associated lymphoid tissue	

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
FL and Marginal Zone Lymphomas <i>Examples of first-line, second-line and subsequent therapies:</i> <ul style="list-style-type: none"> • bendamustine + rituximab • RCHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone) • RCVP (rituximab, cyclophosphamide, vincristine, prednisone) • <u>Single-agent examples:</u> rituximab; Leukeran[®] (chlorambucil) ± rituximab; cyclophosphamide ± rituximab; Revlimid[®] (lenalidomide) ± rituximab; Aliqopa[®] (copanlisib) 	Varies	Varies

Therapeutic alternatives are listed as Brand name[®] (generic) when the drug is available by brand name only and generic (Brand name[®]) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): patients with known hypersensitivity reactions (e.g., anaphylaxis) to obinutuzumab or any of the excipients, including serum sickness with prior obinutuzumab use
- Boxed warning(s): hepatitis B virus reactivation and progressive multifocal leukoencephalopathy

IV. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
CLL	100 mg IV on day 1, 900 mg IV on day 2 of cycle 1, then 1,000 mg IV on days 8 and 15 of cycle 1; begin the next cycle of therapy on day 29. For cycles 2 to 6, give obinutuzumab 1,000 mg IV on day 1 repeated every 28 days.	See regimen

Indication	Dosing Regimen	Maximum Dose
FL	<p>1,000 mg IV on day 1, 8 and 15 of Cycle1, 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.</p> <p>For patients with relapsed or refractory FL, administer Gazyva in combination with bendamustine in six 28-day cycles. Patients who achieve stable disease, complete response, or partial response to the initial 6 cycles should continue on Gazyva 1,000 mg as monotherapy for up to two years.</p> <p>For patients with previously untreated FL, administer Gazyva with one of the following chemotherapy regimens:</p> <ul style="list-style-type: none"> • Six 28-day cycles in combination with bendamustine • Six 21-day cycles in combination with CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone), followed by 2 additional 21-day cycles of Gazyva alone • Eight 21-day cycles in combination with CVP (cyclophosphamide, vincristine, prednisone) <p>Patients with previously untreated FL who achieve a complete response or partial response to the initial 6 or 8 cycles should continue on Gazyva 1,000 mg as monotherapy for up to two years.</p>	See regimen

V. Product Availability

Single-dose vial: 1,000 mg/40 mL (25 mg/mL)

VI. References

1. Gazyva Prescribing Information. South San Francisco, CA: Genentech, Inc.; July 2022. Available at: <https://www.gazyva.com/>. Accessed July 07, 2025.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed August 24, 2025.
3. National Comprehensive Cancer Network. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Version 3.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cll.pdf. Accessed August 24, 2025.
4. National Comprehensive Cancer Network. B-Cell Lymphomas Version 3.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed August 24, 2025.
5. National Comprehensive Cancer Network. Hairy Cell Leukemia Version 1.2026. Available at: https://www.nccn.org/professionals/physician_gls/pdf/hairy_cell.pdf. Accessed August 24, 2025.
6. National Comprehensive Cancer Network. Castleman disease Version 2.2025. Available at: https://www.nccn.org/professionals/physician_gls/pdf/castleman.pdf. Accessed September 4, 2025.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J9301	Injection, obinutuzumab, 10 mg

Reviews, Revisions, and Approvals	Date
4Q 2018 annual review: summarized NCCN and FDA-approved uses for improved clarity; added specialist involvement in care; separated FL and off-label MZL into individual criteria sets; removed primary cutaneous B-cell lymphomas as a covered off-label indication (not listed in the NCCN compendium for Gazyva); updated continued therapy section to include language for continuity of care; references reviewed and updated.	07/2018
4Q 2019 annual review: No changes per Statewide PDL implementation 01-01-2020	10/2019
4Q 2020 annual review: NCCN recommended uses added for B-cell lymphomas; FDA/NCCN dosing limitation added, references reviewed and updated.	10/2020
4Q 2021 annual review: for CLL/SLL, added additional requirements if used as second-line or subsequent therapy per NCCN; for nodal marginal zone lymphoma, added option for use as first line therapy per NCCN; for B-cell lymphomas, clarified that I.B.5 does not apply to marginal zone lymphoma; references reviewed and updated.	10/2021
4Q 2022 annual review: added criteria for FL for first- and second-line therapy, maintenance therapy, and as a rituximab substitute as supported by NCCN; replaced “in combination with bendamustine” for second-line treatment in marginal zone lymphoma with “in combination with chemotherapy” as NCCN supports several regimens; references reviewed and updated.	10/2022
4Q 2023 annual review: for CLL/SLL added combination therapy option with Venclexta per NCCN; for FL added “in combination with chemotherapy” for second-line or subsequent therapy; for FL and MZL simplified combination regimens and agents to “chemotherapy” to align with NCH criteria; added criteria for NCCN-supported indication of hairy cell leukemia; revised terminology from “AIDS-Related B-Cell Lymphomas” to “HIV-Related B-Cell Lymphomas” per NCCN; references reviewed and updated.	10/2023
4Q 2024 annual review: added Commercial line of business for use in medical coverage determinations; for CLL/SLL removed requirement for del(17p)/TP53-negative status per NCCN Compendium; for B-cell lymphomas, added option for Gazyva monotherapy prior to Columvi administration for specific lymphomas and for FL removed requirement for	10/2024

Reviews, Revisions, and Approvals	Date
<p>combination chemotherapy in second line and subsequent therapy per NCCN; for hairy cell leukemia, clarified that member must be unable to tolerate purine analogs per NCCN and removed active infection as an option for criteria consolidation; references reviewed and updated.</p>	
<p>4Q 2025 annual review: for CLL/SLL indication and combination therapy with Venclexta, removed requirement for previous combination use as first-line therapy per NCCN; for section header “Follicular and Other B-Cell Lymphomas,” revised to “B-Cell Lymphomas and Tumors with B-Cell Predominance” to capture indication for Castleman disease; for indication of histologic transformation of marginal zone lymphoma to DLBCL, revised indication language from marginal zone lymphoma to indolent lymphomas per NCCN; for certain B-cell neoplasms where Gazyva is prescribed prior to Columvi administration, removed monotherapy requirement, revised third-line to for second-line therapy, and added mantle cell lymphoma indication per NCCN; for FL and marginal zone lymphomas, add combination therapy with Revlimid option per NCCN; for mantle cell lymphoma, added option for in combination with Venclexta and Brukinsa per NCCN; added monotherapy option for hairy cell leukemia per NCCN; revised all initial approval durations to 12 months; references reviewed and updated.</p>	<p>10/2025</p>