# Clinical Policy: Obinutuzumab (Gazyva)

Reference Number: CP.PHAR.305
Effective Date: 02.01.17
Last Review Date: 11.24
Line of Business: Commercial, HIM, Medicaid

Coding Implications
Revision Log

**See Important Reminder at the end of this policy for important regulatory and legal information.**

## Description

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

## FDA Approved Indication(s)

Gazyva is indicated in 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 FL

## Policy/Criteria

*Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.*

It is the policy of health plans affiliated with Centene Corporation® 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 ≥ 18 years;
4. If prescribed for second-line or subsequent therapy, prescribed as a single agent or in combination with Venclexta® (if combination previously used as first-line therapy);
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*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

**Approval duration:**
**HIM/Medicaid –** 6 months
**Commercial –** 6 months or to the member's renewal date, whichever is longer

**B. Follicular and Other B-Cell Lymphomas** (must meet all):
1. Diagnosis of one of the following B-cell lymphoma subtypes (a or b):
   a. FL;
   b. Other B-cell lymphomas (off-label):
      i. Marginal zone lymphoma (a, b, or c):
         a) Splenic marginal zone lymphoma;
         b) Nodal marginal zone lymphoma;
         c) Extranodal marginal zone lymphoma (1 or 2):
            1) Gastric MALT lymphoma;
            2) Nongastric MALT lymphoma;
      ii. Histologic transformation of marginal zone lymphoma to diffuse large B-cell lymphoma;
      iii. Diffuse large B-cell lymphoma;
      iv. High-grade B-cell lymphoma;
      v. Mantle cell lymphoma;
      vi. Castleman's disease;
      vii. Post-transplant lymphoproliferative disorders;
      viii. HIV-related B-cell lymphoma;
      ix. Burkitt lymphoma;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. For FL: Gazyva is requested for one of the following uses (a, b, c, or d):
   a. First line therapy in combination with chemotherapy;
   b. Second-line or subsequent therapy (*see Appendix B for examples of prior therapy*);
   c. Maintenance therapy as a single agent if disease is rituximab-refractory or following chemotherapy;
   d. As a substitute* for rituximab in patients experiencing 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.*
5. For marginal zone lymphomas: Gazyva is requested for one of the following uses (a, b, c, or d):
   a. Maintenance therapy if disease is rituximab-refractory, recurrent, and has been treated with Gazyva and bendamustine;
   b. Second-line or subsequent therapy in combination with chemotherapy (*see Appendix B for examples of prior therapy*);
   c. As a substitute* for rituximab in patients experiencing 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.*

d. Nodal marginal zone lymphoma only: First line therapy in combination with chemotherapy;

6. For all subtypes other than FL and marginal zone lymphoma, one of the following (a or b):
   a. Gazyva is requested as a substitute* for rituximab in patients experiencing 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. Gazyva is prescribed as a single agent for third-line or subsequent therapy prior to Columvi™ for one of the following subtypes (i-v):
      i. Histologic transformation of marginal zone lymphoma to diffuse large B-cell lymphoma;
      ii. Diffuse large B-cell lymphoma;
      iii. High-grade B-cell lymphoma;
      iv. Post-transplant lymphoproliferative disorders;
      v. HIV-related B-cell lymphoma;
7. 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*).

   **Prescribed regimen must be FDA-approved or recommended by NCCN.*

**Approval duration:**
**HIM/Medicaid –** 6 months
**Commercial –** 6 months or to the member's renewal date, whichever is longer

**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 ≥ 18 years;
4. Prescribed as initial therapy in combination with Zelboraf® (vemurafenib);
5. Member is unable to tolerate purine analogs (e.g., cladribine, pentostatin);
6. 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).*

   **Prescribed regimen must be FDA-approved or recommended by NCCN*

**Approval duration:**
**HIM/Medicaid –** 6 months
**Commercial –** 6 months or to the member's renewal date, whichever is longer

**D. Other diagnoses/indications** (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business:

CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or

b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

## II. Continued Therapy

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

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Gazyva for a covered indication and has received this medication for at least 30 days;
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*).

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

**Approval duration:**
**HIM/Medicaid –** 12 months
**Commercial –** 6 months or to the member's renewal date, whichever is longer

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

**III. Diagnoses/Indications for which coverage is NOT authorized:**

**A.** Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

**IV. Appendices/General Information**

*Appendix A: Abbreviation/Acronym Key*

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

*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 for all relevant lines of business and may require prior authorization.*

| Drug Name | Dosing Regimen | Dose Limit/ Maximum Dose |
|---|---|---|
| **FL and Marginal Zone Lymphomas**<br>*Examples of first-line, second-line and subsequent therapies:*<br>• bendamustine + rituximab<br>• RCHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone)<br>• RCVP (rituximab, cyclophosphamide, vincristine, prednisone)<br>• Single-agent examples: 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

**V. 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, | See regimen |

| Indication | Dosing Regimen | Maximum Dose |
|---|---|---|
| | give obinutuzumab 1,000 mg IV on day 1 repeated every 28 days. | |
| FL | 1,000 mg IV 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.<br><br>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.<br><br>For patients with previously untreated FL, administer Gazyva with one of the following chemotherapy regimens:<br>• Six 28-day cycles in combination with bendamustine<br>• Six 21-day cycles in combination with CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone), followed by 2 additional 21-day cycles of Gazyva alone<br>• Eight 21-day cycles in combination with CVP (cyclophosphamide, vincristine, prednisone)<br>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. | See regimen |

## VI. Product Availability

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

## VII. References

1. Gazyva Prescribing Information. South San Francisco, CA: Genentech, Inc.; July 2022. Available at: https://www.gazyva.com/. Accessed July 19, 2024.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed August 21, 2024.
3. National Comprehensive Cancer Network. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Version 3.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cll.pdf. Accessed August 21, 2024.
4. National Comprehensive Cancer Network. B-Cell Lymphomas Version 2.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed August 21, 2024.
5. National Comprehensive Cancer Network. Hairy Cell LeukemiaVersion 2.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/hairy_cell.pdf. Accessed August 21, 2024.

**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 | P&T Approval Date |
|---|---|---|
| 4Q 2020 annual review: no significant changes; references reviewed and updated. | 08.11.20 | 11.20 |
| 4Q 2021 annual review: replaced HIM-Medical Benefit with HIM; 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. | 06.28.21 | 11.21 |
| 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. Template changes applied to other diagnoses/indications. | 08.04.22 | 11.22 |
| 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. | 08.09.23 | 11.23 |
| 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 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 | 07.19.24 | 11.24 |

| Reviews, Revisions, and Approvals | Date | P&T Approval Date |
|---|---|---|
| an option for criteria consolidation; references reviewed and updated. | | |

**Important Reminder**

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

**Note:**
**For Medicaid members**, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.