Clinical Policy: Obinutuzumab (Gazyva)

Reference Number: LA.PHAR.305
Effective Date: 11.04.23
Last Review Date: 04.22.24 ~~06.15.23~~
Line of Business: Medicaid

Coding Implications
Revision Log

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

Please note: This policy is for medical benefit

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 Louisiana Healthcare Connections 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, both of the following (a and b):
   a. Prescribed as a single agent~~;~~ or in combination with Venclexta® (if combination previously used as first-line therapy);
   b. Disease does not have del(17p)/TP53 mutation;
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: 6 months

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. ~~AIDS~~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 ~~bendamustine, lenalidomide, or as a component of CHOP or CVP~~chemotherapy;
   b. Second-line or subsequent therapy in combination with chemotherapy (*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 ~~bendamustine or as a component of CHOP or CVP~~chemotherapy;

6. For all subtypes other than FL and marginal zone lymphoma: 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.*
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: 6 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 ≥ 18 years;
4. Prescribed as initial therapy in combination with Zelboraf® (vemurafenib);
5. Member is either unable to tolerate purine analogs (e.g., cladribine, pentostatin) or has active infection;
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*

~~C.~~ **Approval duration: 6 months**

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

~~1.~~ 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 LA.PMN.255

~~2.~~ 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: LA.PMN.53 for Medicaid.

II. Continued Therapy

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

1. Currently receiving medication via Louisiana Healthcare Connections 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):*

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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: 12 months

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 LA.PMN.255
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: LA.PMN.53 for Medicaid.

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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 policy – LA.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

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

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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 *Examples of first-line, second-line and subsequent therapies:* • bendamustine + rituximab • RCHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone) • RCVP (rituximab, cyclophosphamide, vincristine, prednisone) • 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/SLL	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
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. 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. For patients with previously untreated FL, administer Gazyva with one of the following chemotherapy regimens: • 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) 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 ~~August 2, 2022~~June 28, 2023.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed August 2, ~~2022~~2023.
3. National Comprehensive Cancer Network. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Version 3.~~2022~~2023. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cll.pdf. Accessed August ~~2, 2022~~9, 2023.
4. National Comprehensive Cancer Network. B-Cell Lymphomas Version 5.~~2022~~2023. Available at: https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed August ~~2, 2022~~9, 2023.
5. National Comprehensive Cancer Network. Hairy Cell LeukemiaVersion 1.2023. Available at: https://www.nccn.org/professionals/physician_gls/pdf/hairy_cell.pdf. Accessed August 9, 2023

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	LDH Approval Date
Converted corporate to local policy.	06.15.23	10.05.23
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.	04.22.24	

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. LHCC 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.

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 LHCC administrative policies and procedures.

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