Prior Authorization Review Panel

CHC-MCO Policy Submission

A separate copy of this form must accompany each policy submitted for review.
Policies submitted without this form will not be considered for review.

Plan: PA Health & Wellness	**Submission Date: 11/01/2022**
Policy Number: PA.CP.PHAR.305	**Effective Date: 01/2018** **Revision Date: 10/2022**
Policy Name: Obinutuzumab (Gazyva)	

Type of Submission – Check all that apply:

- ☐ **New Policy**
- ✓ **Revised Policy***
- ☐ **Annual Review - No Revisions**
- ☐ **Statewide PDL -** *Select this box when submitting policies for Statewide PDL implementation and when submitting policies for drug classes included on the Statewide PDL.*

***All revisions to the policy must be highlighted using track changes throughout the document.**

Please provide any changes or clarifying information for the policy below:

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.

Name of Authorized Individual (Please type or print): **Venkateswara R. Davuluri, MD**	**Signature of Authorized Individual:**

Clinical Policy: Obinutuzumab (Gazyva)

Reference Number: PA.CP.PHAR.305
Effective Date: 01/2018
Last Review Date: 10/2022

Coding Implications
Revision Log

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 ≥ 18 years;
4. If prescribed for second-line or subsequent therapy, both of the following (a and b):
   a. Prescribed as a single agent;
   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*).

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. Follicular lymphoma (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-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;
   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 lymphoma – 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;
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*).

Approval duration: 6 months

C. 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.LTSS.PA.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.LTSS.PA.01) applies; or
2. Refer to PA.CP.PMN.53

III. 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 *Examples of first-line, second-line and subsequent therapies:* • bendamustine + rituximab	Varies	Varies

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
• 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)		

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/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 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. 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,	See regimen

Indication	Dosing Regimen	Maximum Dose
	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.	

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 August 2, 2022.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed August 2, 2022
3. National Comprehensive Cancer Network. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Version 3.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cll.pdf. Accessed August 2, 2022
4. National Comprehensive Cancer Network. B-Cell Lymphomas Version 5.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed August 2, 2022

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	Approval 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	

Reviews, Revisions, and Approvals	Date	Approval Date
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	