Clinical Policy: Obinutuzumab (Gazyva)

Reference Number: PA.CP.PHAR.305
Effective Date: 01/18
Last Review Date: 10/30/2019

Coding Implications
Revision Log

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)
- In combination with 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
- In combination with 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 Pennsylvania Health and 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 (i.e., small lymphocytic lymphoma [SLL]);
2. Prescribed by or in consultation with an oncologist or hematologist;
3. 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 Lymphoma (must meet all)**:**

1. Diagnosis of FL;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. 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. Marginal Zone Lymphoma (off-label) (must meet all):

1. Diagnosis of marginal zone lymphoma (i.e., gastric or nongastric MALT lymphoma, nodal marginal zone lymphoma, or splenic marginal zone lymphoma);

2. Prescribed by or in consultation with an oncologist or hematologist;
3. Member has used appropriate prior therapy (*see Appendix B for examples*)
4. Request meets one of the following:
   a. Dose does not exceed the maximum indicated in section IV;
   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

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

II. Continued Approval

A. All Indications (must meet all):

1. Currently receiving medication via Pennsylvania Health and 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 Pennsylvania Health and 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.

Examples of First-Line Therapy for Marginal Zone Lymphoma	Dosing Regimen	Dose Limit/ Maximum Dose
Treanda®, Bendeka® (bendamustine) + Rituxan® (rituximab)	Varies	Varies
RCHOP [Rituxan® (rituximab), cyclophosphamide, doxorubicin, vincristine (Vincasar PFS®), prednisone]	Varies	Varies
RCVP [Rituxan® (rituximab), cyclophosphamide, vincristine (Vincasar PFS®), prednisone]	Varies	Varies
Rituxan® (rituximab) (375 mg/m2 weekly for 4 doses) (preferred for SMZL)	Varies	Varies
Leukeran® (chlorambucil) + Rituxan® (rituximab)	Varies	Varies
cyclophosphamide + Rituxan® (rituximab)	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/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. Administer obinutuzumab in combination with chlorambucil (0.5 mg/kg orally on day 1 and 15) in cycles 1 to 6.	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.	See regimen

Indication	Dosing Regimen	Maximum Dose
	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.	

V. Product Availability

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

Background

Description/Mechanism of Action:

Obinutuzumab is monoclonal antibody that targets the CD20 antigen expressed on the surface of pre B- and mature B-lymphocytes. Upon binding to CD20, obinutuzumab mediates B-cell lysis through (1) engagement of immune effector cells, (2) by directly activating intracellular death signaling pathways (direct cell death), and/or (3) activation of the complement cascade. The immune effector cell mechanisms include antibody-dependent cellular cytotoxicity (ADCC) and antibody-dependent cellular phagocytosis. As an antibody with reduced fucose content, obinutuzumab induces greater ADCC activity than rituximab *in vitro* using human cancer cell lines. Obinutuzumab also demonstrated an increased ability to induce direct cell death when compared to rituximab. Obinutuzumab binds to FcγRIII 18 using purified proteins with a higher affinity than rituximab. Obinutuzumab and rituximab bind with similar affinity to overlapping epitopes on CD20.

Formulations:

Gazyva is available in 1,000 mg/40 mL (25 mg/mL) single-dose vials for intravenous administration following dilution.

Appendices

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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
J9999	Not otherwise classified, antineoplastic drugs

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	07/18	

Reviews, Revisions, and Approvals	Date	Approval Date
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.		
4Q 2019 annual review: No changes per Statewide PDL implementation 01-01-2020	10/30/19	

References

1. Gazyva Prescribing Information. South San Francisco, CA: Genentech, Inc.; November 2017. Available at: https://www.gazyva.com/. Accessed July 11, 2018.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed July 16, 2018.
3. National Comprehensive Cancer Network. Chronic lymphocytic leukemia/small lymphocytic lymphoma Version 5.2018. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cll.pdf. Accessed July 16, 2018.
4. National Comprehensive Cancer Network. B-cell lymphomas Version 4.2018. Available at: https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed July 16, 2018.