Clinical Policy: Obinutuzumab (Gazyva)

Reference Number: PA.CP.PHAR.305
Effective Date: 01/18
Last Review Date: 11/17

Coding Implications
Revision Log

Description
The intent of the criteria is to ensure that patients follow selection elements established by Pennsylvania Health and Wellness ® clinical policy for obinutuzumab (Gazyva®).

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 chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL);
2. Meets a or b:
   a. FDA-approved use:
      i. Untreated CLL/SLL in combination with chlorambucil;
   b. Off-label NCCN recommended use, one of the following:
      i. Untreated CLL/SLL:
         a) Without del(17p)/TP53 mutation: First-line therapy as a single agent or in combination with chlorambucil in any of the following populations:
            1) Older patients (e.g., age ≥ 65 years);
            2) Younger patients (e.g., age < 65 years) with significant comorbidities;
            3) Frail patients unable to tolerate purine analogs (e.g., fludarabine);
      ii. Relapsed or refractory CLL/SLL:
         b) Without del(17p)/TP53 mutation: As a single agent.

**CLL and SLL, non-Hodgkin lymphoma (NHL) subtypes, are different manifestations of the same disease.*[3]

Approval duration: 3 months

B. Non-Hodgkin Lymphomas

1. FDA-approved use (must meet all):
   a. Diagnosis of follicular lymphoma (FL);
   b. FL is relapsed or refractory following a rituximab-containing regimen;
   c. In combination with bendamustine followed by Gazyva monotherapy;
2. Off-label NCCN recommended use, one of the following:
   a. FL refractory or progressive: second-line or subsequent therapy in combination with bendamustine;
   b. FL rituximab refractory: maintenance therapy as second-line extended dosing;
   c. Gastric MALT lymphoma: second-line or subsequent therapy for recurrent or progressive disease in combination with bendamustine in patients with indications for treatment;

d. Gastric MALT lymphoma: maintenance therapy for rituximab refractory disease in patients with indications for treatment as second-line extended dosing;
e. Non-gastric MALT lymphoma: second-line or subsequent therapy for refractor or progressive disease in combination with bendamustine in patients with indications for treatment;
f. Non-gastric MALT lymphoma: Maintenance therapy for rituximab refractory disease in patients with indications for treatment as second-line extended dosing
g. Primary cutaneous B-cell lymphoma: Used for primary cutaneous marginal zone or follicle center lymphoma as therapy for very extensive or refractory generalized T3 cutaneous disease or as second-line or subsequent therapy with bendamustine for refractory or progressive generalized extra-cutaneous disease in patients with indications for treatment
h. Primary cutaneous B-cell lymphoma: Maintenance therapy for rituximab-refractory disease in patients with indications for treatment as second-line extended dosing
i. Splenic marginal zone lymphoma: Second-line or subsequent therapy for refractory or progressive disease in combination with bendamustine in patients with indications for treatment
j. Splenic marginal zone lymphoma: Maintenance therapy for rituximab refractory disease in patients with indications for treatment as second-line extended dosing

Approval duration: 3 months

C. Other diagnoses/indications: Refer to PA.CP.PHAR.57 – Global Biopharm Policy.

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 has none of the following reasons to discontinue:
   a. Disease progression or unacceptable toxicity;
   b. Progressive multifocal leukoencephalopathy;
   c. Hepatitis B virus reactivation.

Approval duration: 6 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.PHAR.57 - Global Biopharm Policy.

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.

FDA Approved Indications:
Gazyva (obinutuzumab) is a CD20-directed cytolytic antibody/intravenous formulation indicated for:

- Chronic lymphocytic leukemia (CLL):
  - In combination with chlorambucil, for the treatment of patients with previously untreated CLL;
- Follicular lymphoma (FL):
  - In combination with bendamustine followed by Gazyva monotherapy, for the treatment of patients with FL who relapsed after, or are refractory to, a rituximab-containing regimen.

Appendices
Appendix A: Abbreviation Key
ADCC: Antibody-dependent cellular cytotoxicity
CLL: Chronic lymphocytic leukemia
FL: Follicular lymphoma
MALT: Mucosa-associated lymphoid tissue
NHL: Non-Hodgkin lymphoma

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

References

1. Gazyva prescribing information. South San Francisco, CA: Genentech, Inc.; February 2016. Available at www.gazyva.com. Accessed November 4, 2016.
2. Obinutuzumab. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.NCCN.org. Accessed December 21, 2016.
3. Chronic lymphocytic leukemia/small lymphocytic lymphoma (Version 1.2017). In: National Comprehensive Cancer Network Guidelines. Available at NCCN.org. Accessed January 4, 2017.