Clinical Policy: Obinutuzumab (Gazyva)

Reference Number: CP.PHAR.305
Effective Date: 02/17
Last Review Date: 02/17

Coding Implications
Revision Log

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

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

Policy/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 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 CP.PHAR.57 – Global Biopharm Policy.

II. Continued Approval

A. All Indications (must meet all):
1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
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 Centene benefit and documentation supports positive response to therapy; or
2. Refer to 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
Policy split from CP.PHAR.182 Excellus Oncology.	01/17	02/17

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.

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.

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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.

Note: For Medicare members, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs and LCDs should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at http://www.cms.gov for additional information.

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