



POLICY NUMBER UM ONC_1259	SUBJECT Gazyva™ (obinutuzumab)		DEPT/PROGRAM UM Dept	PAGE 1 OF 4
DATES COMMITTEE REVIEWED 02/11/14, 11/02/14, 04/11/16, 02/06/17, 02/01/18, 02/07/19, 12/11/19, 01/08/20	APPROVAL DATE January 8, 2020	EFFECTIVE DATE January 8, 2020	COMMITTEE APPROVAL DATES (latest version listed last) 02/11/14, 11/02/14, 04/11/16, 02/06/17, 02/01/18, 02/07/19, 12/11/19, 01/08/20	
PRIMARY BUSINESS OWNER: UM APPROVED BY: Dr. Andrew Hertler		COMMITTEE/BOARD APPROVAL Utilization Management Committee		
URAC STANDARDS 7.3V HUM 1	NCQA STANDARDS UM 2		ADDITIONAL AREAS OF IMPACT	
CMS REQUIREMENTS	STATE/FEDERAL REQUIREMENTS		APPLICABLE LINES OF BUSINESS All	

I. PURPOSE

To define and describe the accepted indications for Gazyva (obinutuzumab) usage in the treatment of cancer

II. DEFINITIONS

Gazyva (obinutuzumab): is a recombinant fully humanized monoclonal antibody (IgG1 subclass) that targets the CD20 antigen on the surface of pre B- and mature B-lymphocytes and after binding causes B-cell lysis. B-cell depletion in peripheral blood is not directly correlated with depletion in solid organs or in malignant deposits and has not been shown to directly correlate to clinical response. It has been shown that obinutuzumab activates polymorphonuclear neutrophils (PMNs), produces radical oxygen, and mediates phagocytosis by binding to CD16A and CD16B NA1 and NA2 isoforms.

Gazyva (obinutuzumab) is FDA approved for the treatment of patients with previously untreated chronic lymphocytic leukemia (CLL) and is used in combination with chlorambucil. In addition, it is also FDA approved in combination with bendamustine followed by monotherapy for the treatment of patients with follicular lymphoma (FL) who relapsed after, or are refractory to, a rituximab-containing regimen. Also, 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.

Gazyva (obinutuzumab) is available as 1000 mg single use vials.

III. POLICY

New Century is responsible for processing all medication requests from network ordering providers. Medications not authorized by New Century may be deemed as not approvable and therefore not reimbursable.

Treatment request outside the approved FDA manufacturer labeling or CMS approved compendia must follow CMS Medicare Benefit Policy Manual Chapter 15. If references are not produced, delays may occur to the processing of such request.

Inclusion Criteria: Gazyva (obinutuzumab) may be considered medically necessary when any of the following selection criteria is met:

1. **Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL)**
 - a. The member has stage II-IV CD20 positive CLL/SLL, or if Stage 0-I disease, member must have bulky adenopathy, splenomegaly, OR systemic symptoms **AND**



- b. The member had no prior CLL therapy and Gazyva (obinutuzumab) is used in combination with chlorambucil/acalabrutinib/ ibrutinib/venetoclax/bendamustine OR
- c. As a single agent for relapsed or refractory disease.

2. Non-Hodgkin Lymphoma

- a. The member has follicular and nodal marginal zone, splenic marginal zone, gastric malt, and primary cutaneous B cell and Gazyva (obinutuzumab) is being used as any of the following:
 - i. In combination with CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone), CVP (cyclophosphamide, vincristine, and prednisone), or bendamustine (for follicular lymphoma only) OR
 - ii. As maintenance/consolidation therapy.

Exclusion Criteria: Gazyva (obinutuzumab) is not considered medically necessary when any of the following selection criteria is met:

1. The member has an active infection requiring systemic treatment.
2. Disease progression while taking Gazyva (obinutuzumab).
3. Dosing exceeds single dose limit of Gazyva (obinutuzumab) 1000 mg.
4. Treatment with Gazyva (obinutuzumab) exceeds the total duration limit of 6 cycles.
5. Indications not supported by CMS recognized compendia or acceptable peer reviewed literature may be deemed as not approvable and therefore not reimbursable.

IV. PROCEDURE

Requests for Gazyva (obinutuzumab) shall be reviewed for appropriateness per FDA approved product labeling, the National Comprehensive Cancer Network (NCCN) and American Society of Clinical Oncology (ASCO) clinical guidelines, or CMS approved compendia.

1. Dosage and Administration:

- a. The following premedications are recommended to reduce the risk of infusion reactions on days 1 and 2 of cycle 1 and for any prior infusion reactions on cycles 2-6:
 - i. Acetaminophen 650 to 1000 mg.
 - ii. Antihistamine (e.g., diphenhydramine 50 mg).
 - iii. IV glucocorticoid (dexamethasone 20 mg or methylprednisolone 80 mg). Hydrocortisone is not effective in reducing the rate of infusion reaction.
 - iv. Prophylactic hydration and anti-hyperuricemics to patients at high risk of tumor lysis syndrome.
- b. CLL Cycle 1: obinutuzumab 100 mg IV over 4 hours plus chlorambucil (0.5 mg/kg PO) on day 1, obinutuzumab 900 mg IV (rate, 50 mg/hr increased by 50 mg/hr increments every 30 minutes to a max rate of 400 mg/hr) on day 2, and then obinutuzumab 1000 mg IV (rate, 100 mg/hr and increased by 100 mg/hr increments every 30 minutes to a max rate of 400 mg/hr) on day 8 and day 15 plus chlorambucil (0.5 mg/kg PO) on day 15.
- c. CLL Cycles 2—6: obinutuzumab 1000 mg IV (rate, 100 mg/hr and increased by 100 mg/hr increments every 30 minutes to a max rate of 400 mg/hr) on day 1 plus chlorambucil (0.5 mg/kg PO) on day 1 and day 15, repeated every 28 days.



- d. The dose for follicular lymphoma is 1000 mg on day 1, 8 and 15 of Cycle 1, 1000 mg on day 1 of Cycles 2-6 or Cycles 2-8 repeated every 28 days, and then 1000 mg every 2 months for up to 2 years.

2. Dosage Adjustments

- a. Hematologic toxicity: interrupt therapy for grade 3 or 4 cytopenia.
- b. Infection: interrupt therapy if infection develops.
- c. Infusion reaction, grade 4: stop infusion and permanently discontinue therapy.
- d. Infusion reaction, grade 3: interrupt infusion and manage symptoms; resume at no more than half the rate after symptom resolution; permanently discontinue if grade 3 reaction occurs with rechallenge.
- e. Infusion reaction, grade 1 or 2: reduce infusion rate or interrupt infusion and manage symptoms; continue or resume infusion after symptom resolution; increase infusion rate at Increments and intervals appropriate for treatment cycle dose if no further symptoms develop.
- f. Nonhematologic toxicity: interrupt therapy for a grade 2 or higher nonhematologic toxicity.

3. Monitoring

- a. Evidence of tumor response indicates efficacy
- b. Hepatitis B infection; prior to initiating therapy.
- c. Laboratory and clinical signs of active HBV infection, in HBV carriers; throughout therapy and for several months following discontinuation of therapy.
- d. Blood counts include differential.
- e. Infusion reactions; during the entire infusion; more frequent monitoring during infusion and post-infusion period for patients with pre-existing cardiac or pulmonary conditions.
- f. Signs and symptoms of thrombocytopenia or hemorrhagic events; frequently and especially during the first treatment cycle.
- g. For treatment of TLS, correct electrolyte abnormalities, monitor renal function and fluid balance, and administer supportive care, including dialysis as indicated.

V. APPROVAL AUTHORITY

- 1. Review – UM Department
- 2. Final Approval – UM Committee

VI. ATTACHMENTS

None

VII. REFERENCES

- 1. Gazyva prescribing information. Genentech, Inc. South San Francisco, CA 2018.
- 2. Clinical Pharmacology Elsevier Gold Standard. 2020.
- 3. Micromedex® Healthcare Series: Thomson Micromedex, Greenwood Village, Co. 2020.
- 4. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium. 2020.



5. AHFS Drug Information. American Society of Health-Systems Pharmacist or Wolters Kluwer Lexi-Drugs s.
Bethesda, MD. 2020.