Gazyva® (obinutuzumab)
(Intravenous)

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I. Length of Authorization [1,7-13,16,18]

Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (CLL/SLL):

- Combination therapy is limited to six (6) 28-day cycles and may NOT be renewed.
- Single-agent therapy is limited to eight (8) 21-day cycles and may NOT be renewed.

B-Cell Lymphomas:

- Diffuse Large B-Cell lymphoma (DLBCL) pretreatment for glofitamab-gxbm: Coverage is limited to a single dose and may NOT be renewed.
- All other indications: Coverage is provided for six (6) months and may be renewed for up to a maximum of two (2) years of maintenance therapy.

Hairy Cell Leukemia:

- Combination therapy with vemurafenib is limited to three (3) 28-day cycles and may NOT be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Gazyva 1000 mg/40 mL single-dose vial: 2 vials every 21 days (6 vials for the initial 21-day cycle only)

B. Max Units (per dose and over time) [HCPCS Unit]:

Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (CLL/SLL):

- Loading Dose: 10 billable units day 1, 90 billable units day 2, 100 billable units day 3, 200 billable units days 8 and 15 of Cycle 1 (21 days)
- Maintenance Dose: 200 billable units every 21 days

B-Cell Lymphomas:

- Loading Dose: 100 billable units x 3 weekly doses for Cycle 1 (21 days)

- Maintenance Dose: 100 billable units every 21 days for 8 cycles; then every 2 months for 2 years

Hairy Cell Leukemia

- Cycle 2 (28-day cycle): 100 billable units x 3 weekly doses
- Cycles 3-4 (28-day cycle): 100 billable units every 28 days

III. Initial Approval Criteria [1]

Coverage is provided in the following conditions:

- Patient is at least 18 years of age; **AND**

Universal Criteria [1]

- Patient does not have an active infection, including clinically important localized infections; **AND**
- Patient has not received a live vaccine within 28 days prior to starting treatment and live vaccines will not be administered concurrently while on treatment; **AND**
- Patient has been screened for the presence of hepatitis B virus (HBV) infection (i.e., HBsAg and anti-HBc) prior to initiating therapy and patients with evidence of current or prior HBV infection will be monitored for HBV reactivation during treatment; **AND**

Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (CLL/SLL) † ‡ Φ [1,2,8,9,11,12,14,66e]

- Used as first-line therapy; **AND**
  - Used in combination with chlorambucil for disease without del(17p)/TP53 mutation; **AND**

▪ Use of obinutuzumab in combination with chlorambucil will be restricted to patients with a contraindication or intolerance to obinutuzumab + acalabrutinib or obinutuzumab + venetoclax; **OR**

  - Used in combination with acalabrutinib; **OR**
  - Used in combination with venetoclax; **OR**
  - Used as a single agent**; **OR**
  - Used in combination with bendamustine for disease without del(17p)/TP53 mutation** *(excluding use in frail patients)*; **OR**
  - Used in combination with high-dose methylprednisolone for disease with del(17p)/TP53 mutation**; **OR**
- Used as subsequent therapy; **AND**
  - Used as a single agent; **AND**
    - Used for disease without del(17p)/TP53 mutation; **AND**

        - Used for relapsed or refractory disease after prior BTK inhibitor (e.g., ibrutinib, acalabrutinib, zanubrutinib, pirtobrutinib)- and venetoclax-based regimens; **OR**
    - Used in combination with venetoclax (if previously used); **AND**
        - Used as treatment for relapse after a period of remission

***Consider when BTK inhibitor (e.g., ibrutinib, acalabrutinib, zanubrutinib, pirtobrutinib) and venetoclax are not available or contraindicated or rapid disease de-bulking is needed*

B-Cell Lymphomas † ‡ [1,2,15,18,19]

- Follicular Lymphoma (Grade 1-2) **† ‡Φ**
    - Used as first-line therapy; **AND**
        - Used in combination with chemotherapy [e.g., bendamustine or CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) or CVP (cyclophosphamide, vincristine, prednisone)]; **OR**
    - Used as second-line and subsequent therapy for no response, relapsed, refractory, or progressive disease (if not previously given) after prior treatment with a rituximab-containing regimen; **AND**
        - Used in combination with bendamustine; **OR**
        - Used in combination with lenalidomide; **OR**
    - Used as third-line and subsequent therapy for no response, relapsed, or progressive disease after prior treatment with an anti-CD20 antibody and an alkylating agent; **AND**
        - Used in combination with zanubrutinib; **OR**
    - Used as a single agent for maintenance therapy; **AND**
        - Used as first-line extended therapy in patients who achieved at least a partial response following obinutuzumab in combination with chemotherapy; **OR**
        - Used as second-line extended therapy following combination therapy with obinutuzumab and either bendamustine or lenalidomide for rituximab-refractory disease; **OR**
- Extranodal Marginal Zone Lymphoma(of Non-Gastric Sites [Non-Cutaneous] or of the Stomach) or Marginal Zone Lymphoma (Splenic or Nodal) **‡**
    - Used as first-line therapy *(Nodal Marginal Zone Lymphoma only)*; **AND**
        - Used in combination with chemotherapy [e.g., bendamustine or CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) or CVP (cyclophosphamide, vincristine, prednisone)]; **OR**
    - Used in combination with bendamustine (if not previously treated with bendamustine); **AND**
        - Used as second-line therapy for disease recurrence following initial management of splenomegaly with rituximab (*Splenic Marginal Zone Lymphoma only*); **OR**

        - Used as subsequent therapy after prior treatment with rituximab for relapsed, refractory, or progressive disease; **OR**
    - Used as a single agent for maintenance as second-line extended therapy for rituximab-refractory patients treated with obinutuzumab and bendamustine for recurrent disease
- Diffuse Large B-Cell lymphoma (DLBCL)
    - Used as pretreatment prior to glofitamab-gxbm administration; **AND**
        - Patient has relapsed or refractory disease

Hairy Cell Leukemia ‡ [2]

- Used as initial therapy; **AND**
- Used in combination with vemurafenib; **AND**
- Patient is unable to tolerate purine analogs including frail patients and those with active infection

Preferred therapies and recommendations are determined by review of clinical evidence. NCCN category of recommendation is taken into account as a component of this review. Regimens deemed equally efficacious (i.e., those having the same NCCN categorization) are considered to be therapeutically equivalent.

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); Φ Orphan Drug

IV. Renewal Criteria [1]

Coverage may be renewed based upon the following criteria:

- Patient continues to meet the universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: severe neutropenia/febrile neutropenia, severe thrombocytopenia, severe infusion-related reactions, hypersensitivity reactions including serum sickness, tumor lysis syndrome (TLS), disseminated intravascular coagulation (DIC), etc.; **AND**
- Patient has been evaluated for the presence of progressive multifocal leukoencephalopathy (PML) and has been found to be negative; **AND**

CLL/SLL [8-12]

- Coverage may NOT be renewed

B-Cell Lymphomas (maintenance treatment) [1,7,13]

- Patient has not exceeded a maximum of two (2) years of therapy

Diffuse Large B-Cell lymphoma (pretreatment for glofitamab-gxbm) [18]

- Coverage may NOT be renewed

Hairy Cell Leukemia [16]

- Coverage may NOT be renewed

V. Dosage/Administration [1,7-13,16-18]

Indication	Dose
CLL/SLL	Combination therapy: • Cycle 1 (28-day cycle): 100 mg day 1, 900 mg day 2, then 1000 mg days 8 and 15 • Cycles 2-6 (28-day cycle): 1000 mg on day 1 Monotherapy: • Cycle 1 (21-day cycle): 100 mg day 1, 900 mg day 2, then 1000 mg days 8 and 15 • Cycles 2-8 (21-day cycle): 1000 mg on day 1 -OR- • Cycle 1 (21-day cycle): 100mg day 1, 900 mg day 2, 1000 mg day 3, 2000 mg days 8 and 15 • Cycles 2-8 (21-day cycle): 2000 mg on day 1

B-Cell Lymphomas	Initial combination therapy with chemotherapy:
	• Combination chemotherapy with bendamustine:
	  ○ Cycle 1 (28-day cycle): 1000 mg days 1, 8, and 15
	  ○ Cycles 2-6 (28-day cycle): 1000 mg day 1
	• Combination chemotherapy with CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone), followed by 2 additional 21-day cycles of Gazyva alone
	  ○ Cycle 1 (21-day cycle): 1000 mg days 1, 8, and 15
	  ○ Cycles 2-6 (21-day cycle): 1000 mg day 1
	• Combination chemotherapy with CVP (cyclophosphamide, vincristine, prednisone)
	  ○ Cycle 1 (21-day cycle): 1000 mg days 1, 8, and 15
	  ○ Cycles 2-8 (21-day cycle): 1000 mg day 1
	Initial combination therapy with lenalidomide:
	• Cycle 1 (28-day cycle): 1000 mg days 8, 15, and 22
	• Cycles 2-6 (28-day cycle): 1000 mg day 1
	Initial combination therapy with zanubrutinib:
	• Cycle 1 (28-day cycle): 1000 mg days 1, 8, and 15
	• Cycle 2-6 (28-day cycle): 1000 mg day 1
	Initial Monotherapy:
	• 1000 mg once a week for 4 weeks on days 1, 8, 15, and 22
	Maintenance therapy for use after initial combination therapy or monotherapy:
	• 1000 mg every 8 weeks for up to two years (12 doses) as monotherapy

	• **NOTE:** When initial therapy is given in combination with lenalidomide, the first year of maintenance therapy will be given with lenalidomide, followed by an additional year of monotherapy Pretreatment for glofitamab-gxbm • Cycle 1: 1000 mg as a single dose on day 1
Hairy Cell Leukemia	Initial combination therapy with vemurafenib: • Cycle 2 (28-day cycle): 1000 mg on days 1, 8, and 15 • Cycles 3-4 (28-day cycle): 1000 mg on day 1

VI. Billing Code/Availability Information

HCPCS Code:

- J9301 – Injection, obinutuzumab, 10 mg; 1 billable unit = 10 mg

NDC:

- Gazyva 1000 mg/ 40 mL single-dose vial: 50242-0070-xx

VII. References (STANDARD)

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Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C82.00	Follicular lymphoma grade I unspecified site
C82.01	Follicular lymphoma grade I lymph nodes of head, face, and neck
C82.02	Follicular lymphoma grade I intrathoracic lymph nodes
C82.03	Follicular lymphoma grade I intra-abdominal lymph nodes
C82.04	Follicular lymphoma grade I lymph nodes of axilla and upper limb
C82.05	Follicular lymphoma grade I lymph nodes of inguinal region and lower limb
C82.06	Follicular lymphoma grade I intrapelvic lymph nodes
C82.07	Follicular lymphoma grade I spleen
C82.08	Follicular lymphoma grade I lymph nodes of multiple sites
C82.09	Follicular lymphoma grade I extranodal and solid organ sites
C82.10	Follicular lymphoma grade II unspecified site
C82.11	Follicular lymphoma grade II lymph nodes of head, face, and neck
C82.12	Follicular lymphoma grade II intrathoracic lymph nodes
C82.13	Follicular lymphoma grade II intra-abdominal lymph nodes
C82.14	Follicular lymphoma grade II lymph nodes of axilla and upper limb
C82.15	Follicular lymphoma grade II lymph nodes of inguinal region and lower limb
C82.16	Follicular lymphoma grade II intrapelvic lymph nodes
C82.17	Follicular lymphoma grade II spleen
C82.18	Follicular lymphoma grade II lymph nodes of multiple sites
C82.19	Follicular lymphoma grade II extranodal and solid organ sites
C82.20	Follicular lymphoma grade III unspecified site
C82.21	Follicular lymphoma grade III lymph nodes of head, face, and neck

C82.22	Follicular lymphoma grade III intrathoracic lymph nodes
C82.23	Follicular lymphoma grade III intra-abdominal lymph nodes
C82.24	Follicular lymphoma grade III lymph nodes of axilla and upper limb
C82.25	Follicular lymphoma grade III lymph nodes of inguinal region and lower limb
C82.26	Follicular lymphoma grade III intrapelvic lymph nodes
C82.27	Follicular lymphoma grade III spleen
C82.28	Follicular lymphoma grade III lymph nodes of multiple sites
C82.29	Follicular lymphoma grade III extranodal and solid organ sites
C82.30	Follicular lymphoma grade IIIa unspecified site
C82.31	Follicular lymphoma grade IIIa lymph nodes of head, face, and neck
C82.32	Follicular lymphoma grade IIIa intrathoracic lymph nodes
C82.33	Follicular lymphoma grade IIIa intra-abdominal lymph nodes
C82.34	Follicular lymphoma grade IIIa lymph nodes of axilla and upper limb
C82.35	Follicular lymphoma grade IIIa lymph nodes of inguinal region and lower limb
C82.36	Follicular lymphoma grade IIIa intrapelvic lymph nodes
C82.37	Follicular lymphoma grade IIIa spleen
C82.38	Follicular lymphoma grade IIIa lymph nodes of multiple sites
C82.39	Follicular lymphoma grade IIIa extranodal and solid organ sites
C82.40	Follicular lymphoma grade IIIb unspecified site
C82.41	Follicular lymphoma grade IIIb lymph nodes of head, face, and neck
C82.42	Follicular lymphoma grade IIIb intrathoracic lymph nodes
C82.43	Follicular lymphoma grade IIIb intra-abdominal lymph nodes
C82.44	Follicular lymphoma grade IIIb lymph nodes of axilla and upper limb
C82.45	Follicular lymphoma grade IIIb lymph nodes of inguinal region and lower limb
C82.46	Follicular lymphoma grade IIIb intrapelvic lymph nodes
C82.47	Follicular lymphoma grade IIIb spleen
C82.48	Follicular lymphoma grade IIIb lymph nodes of multiple sites
C82.49	Follicular lymphoma grade IIIb extranodal and solid organ sites
C82.50	Diffuse follicle center lymphoma unspecified site
C82.51	Diffuse follicle center lymphoma lymph nodes of head, face, and neck
C82.52	Diffuse follicle center lymphoma intrathoracic lymph nodes
C82.53	Diffuse follicle center lymphoma intra-abdominal lymph nodes
C82.54	Diffuse follicle center lymphoma lymph nodes of axilla and upper limb
C82.55	Diffuse follicle center lymphoma lymph nodes of inguinal region and lower limb
C82.56	Diffuse follicle center lymphoma intrapelvic lymph nodes
C82.57	Diffuse follicle center lymphoma spleen

C82.58	Diffuse follicle center lymphoma lymph nodes of multiple sites
C82.59	Diffuse follicle center lymphoma extranodal and solid organ sites
C82.60	Cutaneous follicle center lymphoma unspecified site
C82.61	Cutaneous follicle center lymphoma lymph nodes of head, face, and neck
C82.62	Cutaneous follicle center lymphoma intrathoracic lymph nodes
C82.63	Cutaneous follicle center lymphoma intra-abdominal lymph nodes
C82.64	Cutaneous follicle center lymphoma lymph nodes of axilla and upper limb
C82.65	Cutaneous follicle center lymphoma lymph nodes of inguinal region and lower limb
C82.66	Cutaneous follicle center lymphoma intrapelvic lymph nodes
C82.67	Cutaneous follicle center lymphoma spleen
C82.68	Cutaneous follicle center lymphoma lymph nodes of multiple sites
C82.69	Cutaneous follicle center lymphoma extranodal and solid organ sites
C82.80	Other types of follicular lymphoma unspecified site
C82.81	Other types of follicular lymphoma lymph nodes of head, face, and neck
C82.82	Other types of follicular lymphoma intrathoracic lymph nodes
C82.83	Other types of follicular lymphoma intra-abdominal lymph nodes
C82.84	Other types of follicular lymphoma lymph nodes of axilla and upper limb
C82.85	Other types of follicular lymphoma lymph nodes of inguinal region and lower limb
C82.86	Other types of follicular lymphoma intrapelvic lymph nodes
C82.87	Other types of follicular lymphoma spleen lymph nodes of multiple sites
C82.88	Other types of follicular lymphoma lymph nodes of multiple sites
C82.89	Other types of follicular lymphoma extranodal and solid organ sites
C82.90	Follicular lymphoma, unspecified site
C82.91	Follicular lymphoma, unspecified lymph nodes of head, face, and neck
C82.92	Follicular lymphoma, unspecified intrathoracic lymph nodes
C82.93	Follicular lymphoma, unspecified intra-abdominal lymph nodes
C82.94	Follicular lymphoma, unspecified lymph nodes of axilla and upper limb
C82.95	Follicular lymphoma, unspecified lymph nodes of inguinal region and lower limb
C82.96	Follicular lymphoma, unspecified intrapelvic lymph nodes
C82.97	Follicular lymphoma, unspecified spleen
C82.98	Follicular lymphoma, unspecified lymph nodes of multiple sites
C82.99	Follicular lymphoma, unspecified extranodal and solid organ sites
C83.00	Small cell B-cell lymphoma unspecified site
C83.01	Small cell B-cell lymphoma lymph nodes of head, face, and neck
C83.02	Small cell B-cell lymphoma intrathoracic lymph nodes
C83.03	Small cell B-cell lymphoma intra-abdominal lymph nodes

C83.04	Small cell B-cell lymphoma lymph nodes of axilla and upper limb
C83.05	Small cell B-cell lymphoma lymph nodes of inguinal region and lower limb
C83.06	Small cell B-cell lymphoma intrapelvic lymph nodes
C83.07	Small cell B-cell lymphoma spleen
C83.08	Small cell B-cell lymphoma lymph nodes of multiple sites
C83.09	Small cell B-cell lymphoma extranodal and solid organ sites
C83.80	Other non-follicular lymphoma unspecified site
C83.81	Other non-follicular lymphoma lymph nodes of head, face, and neck
C83.82	Other non-follicular lymphoma intrathoracic lymph nodes
C83.83	Other non-follicular lymphoma intra-abdominal lymph nodes
C83.84	Other non-follicular lymphoma lymph nodes of axilla and upper limb
C83.85	Other non-follicular lymphoma lymph nodes of inguinal region and lower limb
C83.86	Other non-follicular lymphoma intrapelvic lymph nodes
C83.87	Other non-follicular lymphoma spleen
C83.88	Other non-follicular lymphoma lymph nodes of multiple sites
C83.89	Other non-follicular lymphoma extranodal and solid organ sites
C85.80	Other specified types of non-Hodgkin lymphoma, unspecified site
C85.81	Other specified types of non-Hodgkin lymphoma, lymph nodes of head, face, and neck
C85.82	Other specified types of non-Hodgkin lymphoma, intrathoracic lymph nodes
C85.83	Other specified types of non-Hodgkin lymphoma, intra-abdominal lymph nodes
C85.84	Other specified types of non-Hodgkin lymphoma, lymph nodes of axilla and upper limb
C85.85	Other specified types of non-Hodgkin lymphoma, lymph nodes of inguinal region and lower limb
C85.86	Other specified types of non-Hodgkin lymphoma, intrapelvic lymph nodes
C85.87	Other specified types of non-Hodgkin lymphoma, spleen
C85.88	Other specified types of non-Hodgkin lymphoma, lymph nodes of multiple sites
C85.89	Other specified types of non-Hodgkin lymphoma, extranodal and solid organ sites
C88.4	Extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue [MALT-
C91.10	Chronic lymphocytic leukemia of B-cell type not having achieved remission
C91.12	Chronic lymphocytic leukemia of B-cell type in relapse
C91.40	Hairy cell leukemia not having achieved remission
C91.42	Hairy cell leukemia, in relapse
Z85.72	Personal history of non-Hodgkin's lymphomas

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

The preceding information is intended for non-Medicare coverage determinations. Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determinations

(NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications, including any preceding information, may be applied at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC