Medical Policy:

Gazyva® (obinutuzumab) Intravenous

POLICY NUMBER	LAST REVIEW	ORIGIN DATE
MG.MM.PH.147	April 7, 2025	

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 polymorphoneclear neutrophils (PMNs), produces radical oxygen, and mediates phagocytosis by binding to CD16A and CD16B NA1 and NA2 isoforms.

Length of Authorization

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:

- 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.

Dosing Limits [Medical Benefit]

Max Units (per dose and over time):

1. **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

2. **All other indications**

   Loading dose:

   - 100 billable units days 1, 8, 15 of cycle 1 (21 days)

   Maintenance Dose:

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

Guideline

I. Initial Approval Criteria

Gazyva *may be considered medically necessary if one of the below conditions are met* ***AND*** *use is consistent with the medical necessity criteria that follows:*

1. **Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL)**
   - A. Used as first-line therapy; **AND**
     - i. Used in combination with chlorambucil; **OR**
     - ii. Used in combination with acalabrutinib; **OR**
     - iii. Used in combination with venetoclax; **OR**
     - iv. Used as a single agent**; **OR**
     - v. Used in combination with bendamustine for disease without del(17p)/TP53 mutation** (excluding use in frail patients); **OR**
     - vi. Used in combination with high-dose methylprednisolone for disease with del(17p)/TP53 Mutation**; **OR**
   - B. Used as subsequent therapy; **AND**
     - i. Used as a single agent; **AND**
       a. Used for disease without del(17p)/TP53 mutation; **AND**
       b. Used for relapsed or refractory disease after prior BTK inhibitor (e.g., ibrutinib, acalabrutinib, zanubrutinib, pirtobrutinib)- and venetoclax-based regimens; **OR**
     - ii. Used in combination with high-dose methylprednisolone; **AND**
       a. Used for disease with del(17p)/TP53; **AND**
       b. Used for relapsed or refractory disease after prior BTK inhibitor (e.g., ibrutinib, acalabrutinib, zanubrutinib, pirtobrutinib)- and venetoclax-based regimens; **OR**
     - iii. Used in combination with venetoclax (if previously used); **AND**
       a. 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*

2. **Follicular Lymphoma**
   - A. Patient is > 18 years of age; **AND**

B. Used as first-line therapy; **AND**
    i. Used in combination with chemotherapy [e.g., bendamustine or CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) or CVP (cyclophosphamide, vincristine, prednisone)]; **OR**
C. Used as second-line and subsequent therapy for no response, relapsed, refractory, or progressive disease (if not previously given); **AND**
    i. Used in combination with chemotherapy [e.g., bendamustine or CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) or CVP (cyclophosphamide, vincristine, prednisone)]; **OR**
    ii. Used in combination with lenalidomide; **OR**
    iii. Used as a single agent; **OR**
D. Used as third-line and subsequent therapy for no response, relapsed, or progressive disease; **AND**
    i. Used in combination with zanubrutinib; **OR**
E. Used as a single agent for maintenance therapy; **AND**
    i. Used as first-line extended therapy following chemoimmunotherapy; **OR**
    ii. Used as second-line extended therapy for rituximab-refractory disease; **OR**
F. Used as a substitute for rituximab in patients with intolerance (including those experiencing severe hypersensitivity reactions requiring discontinuation of rituximab) or experiencing rare complications such as mucocutaneous reactions including paraneoplastic pemphigus, Stevens-Johnson syndrome, lichenoid dermatitis, vesiculobullous dermatitis, and toxic epidermal necrolysis

Limitations/Exclusions

Gazyva is not considered medically necessary for 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. Indications not supported by CMS recognized compendia or acceptable peer reviewed literature may be deemed as not approvable and therefore not reimbursable.

II. Renewal Criteria

Authorizations for CLL/SLL may NOT be renewed

Authorizations for other indications may be renewed based on the following criteria:

1. Patient continues to meet criteria in INITIAL APPROVAL CRITERIA; **AND**
2. Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread; **AND**
3. Absence of unacceptable toxicity from the drug including: progressive multifocal leukoencephalopathy (PML), hepatitis B reactivation, severe neutropenia/febrile neutropenia, severe thrombocytopenia, severe infusion reactions, hypersensitivity reactions, tumor lysis syndrome, etc.; **AND**
4. Length of therapy does not exceed 2 years.

Dosage/Administration

Indication	Dose
CLL/SLL	<u>Combination therapy:</u> 100 mg day 1, 900 mg day 2, then 1000 mg days 8 and 15 of Cycle 1 (loading doses) 1000 mg on Day 1 of Cycles 2-6 (28-day cycle) <u>Monotherapy:</u> 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: o Cycle 1 (28-day cycle): 1000 mg days 1, 8, and 15 o 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 o Cycle 1 (21-day cycle): 1000 mg days 1, 8, and 15 o Cycles 2-6 (21-day cycle): 1000 mg day 1 • Combination chemotherapy with CVP (cyclophosphamide, vincristine, prednisone) o Cycle 1 (21-day cycle): 1000 mg days 1, 8, and 15 o 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

Applicable Procedure Codes

Code	Description
J9301	Injection, obinutuzumab, 10 mg, 1 billable unit = 10 mg

Applicable NDCs

Code	Description
50242-0070-xx	Gazyva 1000 mg/ 40 ml single dose vial

ICD-10 Diagnoses

Code	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-lymphoma]
C91.10	Chronic lymphocytic leukemia of B-cell type not having achieved remission
C91.12	Chronic lymphocytic leukemia of B-cell type in relapse

Revision History

Company(ies)	DATE	REVISION
EmblemHealth & ConnectiCare	04/07/2025	Annual Review: Updated length of authorization and dosing chart. Initial criteria: Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL) Removed: "(excluding use in patients without del(17p)/TP53 mutation who are <65 years of age without significant comorbidities);" from the following: "Used as a single agent** (excluding use in patients without del(17p)/TP53 mutation who are <65 years of age without significant comorbidities)" Added: "Used in combination with high-dose methylprednisolone for disease with del(17p)/TP53 Mutation**; OR" Removed the following (some was reworded): "Used for disease without del(17p)/TP53 mutation; AND Used as a single agent (if not given as first-line therapy); AND Used for relapsed or refractory disease after prior BTK inhibitor (e.g., ibrutinib, calabrutinib, etc.)- and venetoclax-based regimens; OR Used in combination with venetoclax (if previously used as first-line therapy); AND Used as retreatment for relapsed disease after a period of remission" Added: "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 high-dose methylprednisolone; AND Used for disease with del(17p)/TP53; 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" Follicular Lymphoma Removed the following (some was reworded): Gazyva is used in ONE of the following situations (i, ii, or iii): In combination with chemotherapy; OR *Note: Examples include CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone), CVP (cyclophosphamide, vincristine, and prednisone), or bendamustine.* For maintenance treatment following Gazyva in combination with chemotherapy; OR Patient experienced an adverse event or intolerance to a rituximab product *Note: Examples of adverse events or intolerance includes paraneoplastic pemphigus, Stevens Johnson syndrome, lichenoid dermatitis, vesiculobullous dermatitis, toxic*

		*epidermal necrolysis. Examples of rituximab products include Rituxan and biosimilars." Added: "*Used as first-line therapy; ANDUsed 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); 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 lenalidomide; OR Used as a single agent; OR Used as third-line and subsequent therapy for no response, relapsed, or progressive disease; AND Used in combination with zanubrutinib; OR Used as a single agent for maintenance therapy; AND Used as first-line extended therapy following chemoimmunotherapy; OR Used as second-line extended therapy for rituximab-refractory disease; OR Used as a substitute for rituximab in patients with intolerance (including those experiencing severe hypersensitivity reactions requiring discontinuation of rituximab) or experiencing rare complications such as mucocutaneous reactions including paraneoplastic pemphigus, Stevens-Johnson syndrome, lichenoid dermatitis, vesiculobullous dermatitis, and toxic epidermal necrolysis"
EmblemHealth & ConnectiCare	3/1/2024	Annual Review: Updated dosing limits for other indications, updated dosing chart. No criteria changes.
EmblemHealth & ConnectiCare	6/28/2023	Annual Review: <u>Dosing Limits:</u> Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (CLL/SLL) Loading Dose: Removed "10 billable units day 1, 90 billable units day 2, 100 billable units days 8, 15 of cycle 1 (28 days)" Added "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: Removed "100 billable units every 28 days" Added "200 billable units every 21 days " <u>Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL): Initial</u> Criteria: Removed "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 c. In combination with chlorambucil for disease without del(17p)/TP53 mutation in members age ≥65 years, in younger members with significant comorbidities, or in frail patients unable to tolerate purine analogs." Added " a. Used as first-line therapy; AND i. Used in combination with chlorambucil †; OR ii. Used in combination with acalabrutinib; OR iii. Used in combination with venetoclax; OR iv. Used as a single agent (excluding use in patients without del(17p)/TP53 mutation who are <65 years of age without significant comorbidities); OR v. Used in combination with bendamustine for disease without del(17p)/TP53 mutation (excluding use in frail patients); OR b. Used as subsequent therapy; AND i. Used for disease without del(17p)/TP53 mutation; AND a) Used as a single agent (if not given as first-line therapy); AND 1) Used for relapsed or refractory disease after prior BTK inhibitor (e.g., ibrutinib, calabrutinib, etc.)- and venetoclax-based regimens; OR b) Used in combination with venetoclax (if previously used as first-line therapy); AND

		1) Used as retreatment for relapsed disease after a period of remission" Removed Non-Hodgkin Lymphoma Criteria Added Follicular Lymphoma indication and Criteria Limitations and Exclusions: removed: "Treatment with Gazyva (obinutuzumab) exceeds the total duration limit of 6 cycles."
EmblemHealth & ConnectiCare	6/17/20022	Transferred policy to new template
EmblemHealth & ConnectiCare	7/15/2019	Annual review

References

1. Gazyva prescribing information. Genentech, Inc. South San Francisco, CA 2016.
2. Clinical Pharmacology Elsevier Gold Standard. 2017.
3. Micromedex® Healthcare Series: Thomson Micromedex, Greenwood Village, Co. 2017.
4. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium. 2017.
5. AHFS Drug Information. American Society of Health-Systems Pharmacist or Wolters Kluwer Lexi-Drugs. Bethesda, MD. 2017.