VENTURA COUNTY
HEALTH CARE PLAN

UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Oncology (Injectable) – Gazyva Utilization Management Medical Policy
- Gazyva® (obinutuzumab intravenous infusion – Genentech)

REVIEW DATE: 10/20/2021

Overview
Gazyva is indicated for the treatment of:
- **Chronic lymphocytic leukemia**, in combination with chlorambucil in previously untreated patients.
- **Follicular lymphoma**, in combination with bendamustine followed by Gazyva monotherapy, for patients who relapse or are refractory to a rituximab containing regimen.
- **Follicular lymphoma, stage II bulky, III or IV**, in combination with chemotherapy, followed by Gazyva monotherapy for patients achieving at least a partial remission, in previously untreated patients.[1]

Dosing
The FDA approved dosing regimen for Gazyva recommends up to 6 cycles (6 months) of therapy for chronic lymphocytic leukemia.[1] For follicular lymphoma, the FDA approved dosing regimen for Gazyva recommends up to 6 months (six 28-day cycles or up to eight 21-day cycles) of therapy. Patients with relapsed or refractory follicular lymphoma who achieve stable disease, or a complete or partial response; or patients with previously untreated follicular lymphoma who achieve a complete or partial response, should continue Gazyva monotherapy for up to 2 years.

In the GADOLIN study, adult patients with rituximab refractory non-Hodgkin lymphoma were randomized to treatment with Gazyva 1,000 mg on Days 1, 8, and 15 of Cycle 1 and on Day 1 of Cycles 2 through 6 plus bendamustine 90 mg/m^2 on Days 1 and 2 of Cycles 1 through 6 or bendamustine 120 mg/m^2 on Days 1 and 2 of Cycles 1 through 6 (28-day cycles).[2] Patients without disease progression in the Gazyva plus bendamustine group could receive maintenance therapy with Gazyva 1,000 mg once every 2 months for up to 2 years. Patients in the Gazyva and bendamustine group had significantly longer progression-free survival than the bendamustine monotherapy group.

Guidelines
Gazyva is addressed in National Comprehensive Cancer Network guidelines:
- **B-cell lymphomas:** Guidelines (version 5.2021 – September 22, 2021) recommend Gazyva for the first-line and second-line treatment of follicular lymphoma (grade 1 or 2) in combination with CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone), CVP (cyclophosphamide, vincristine, and prednisone), bendamustine, or Revlimid (lenalidomide capsules); or as single agent maintenance treatment.[3,5] The guidelines also recommend Gazyva as second-line or maintenance therapy for gastric and nongastric mucosa-associated lymphoid tissue (MALT) lymphoma, nodal marginal zone lymphoma, and splenic marginal zone lymphoma. Gazyva is also recommended as a substitute for rituximab products (Rituxan and biosimilars) in patients with intolerance or experiencing rare complications, regardless of histology.
- **Chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL):** Guidelines (version 1.2022 – September 8, 2021) recommend Gazyva for the first-line treatment of CLL/SLL without del(17p)/TP53 mutation in combination with bendamustine.[3,4] For first-line treatment of CLL/SLL without del(17p)/TP53 mutation in patients ≥ 65 years of age and younger patients with

significant comorbidities, Gazyva is recommended in combination with Calquence® (acalabrutinib capsules), Venclexta® (venetoclax tablets), high-dose methylprednisolone, chlorambucil, or Imbruvica® (ibrutinib capsules and tablets); or as a single agent. For first-line treatment of CLL/SLL without del(17p)/TP53 mutation in patients < 65 years of age without significant comorbidities, Gazyva is recommended in combination with Calquence, Venclexta, or high-dose methylprednisolone. Gazyva is also recommended as a single agent or in combination with Venclexta or Calquence for the first-line treatment of CLL/SLL with del(17p)/TP53 mutation; and as a single agent or in combination with high-dose methylprednisolone for relapsed or refractory CLL/SLL without del(17p)/TP53 mutation.

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Gazyva. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indications. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Gazyva as well as the monitoring required for adverse events and long-term efficacy, approval requires Gazyva to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Gazyva is recommended in those who meet one of the following criteria:

FDA-Approved Indications

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1. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma. Approve for 6 months if the patient meets the following criteria (A and B):

A) Patient is ≥ 18 years of age; AND

B) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve the following dosing (A, B, C, and D):

A) Each individual dose must not exceed 1,000 mg administered by intravenous infusion; AND

B) The first dose is divided and administered on Day 1 (100 mg) and Day 2 (900 mg) of Cycle 1; AND

C) Patient receives a maximum of two additional doses in Cycle 1; AND

D) Patient receives a maximum of one dose in each subsequent 28-day cycle.

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2. Follicular Lymphoma. Approve for 6 months if the patient meets the following criteria (A, B, and C):

A) Patient is ≥ 18 years of age; AND

B) Gazyva is used in ONE of the following situations (i, ii, or iii):

i. In combination with chemotherapy; OR
Note: Examples include CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone), CVP (cyclophosphamide, vincristine, and prednisone), or bendamustine.

ii. For maintenance treatment following Gazyva in combination with chemotherapy; OR

iii. Patient experienced an adverse event or intolerance to a rituximab product; AND
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.

C) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve the following dosing (A, B, and C):
A) Each individual dose must not exceed 1,000 mg administered by intravenous infusion; AND
B) Patient receives a maximum of three doses in Cycle 1; AND
C) Patient receives a maximum of one dose in each subsequent cycle (21-day cycle, 28-day cycle, or 2 month cycle).

Other Uses with Supportive Evidence

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3. Marginal Zone Lymphoma. Approve for 6 months if the patient meets the following criteria (A, B, and C):
Note: Includes nodal marginal zone lymphoma, splenic marginal zone lymphoma, gastric mucosa-associated lymphoid tissue (MALT) lymphoma, or nongastric MALT lymphoma.
A) Patient is ≥ 18 years of age; AND
B) Gazyva is used in ONE of the following situations (i, ii, or iii):
i. First-line therapy for nodal marginal zone lymphoma only; OR
ii. Second-line or subsequent therapy for recurrent or progressive disease; OR
iii. Patient experienced an adverse event or intolerance to a rituximab product; AND
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.
C) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve the following dosing (A, B, and C):
A) Each individual dose must not exceed 1,000 mg given by intravenous infusion; AND
B) Patient receives a maximum of three doses in Cycle 1; AND
C) Patient receives a maximum of one dose in each subsequent cycle (28-day cycle or 2 month cycle).[2]

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4. Other B-Cell Lymphomas. Approve for 6 months if the patient meets the following criteria (A, B, and C):
Note: Includes diffuse large B-cell lymphoma, mantle cell lymphoma, high-grade B-cell lymphoma, Burkitt lymphoma, AIDS-related B-cell lymphoma, post-transplant lymphoproliferative disorders, Castleman's disease.
A) Patient is ≥ 18 years of age; AND
B) Patient experienced an adverse event or intolerance to a rituximab product; AND
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.
C) The medication is prescribed by or in consultation with an oncologist.
Dosing. Approve the following dosing (A, B, and C):
A) Each individual dose must not exceed 1,000 mg given by intravenous infusion; AND
B) Patient receives a maximum of three doses in Cycle 1; AND
C) Patient receives a maximum of one dose in each subsequent cycle (28-day cycle, or 2 month cycle).[2]

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Gazyva is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Gazyva® intravenous infusion [prescribing information]. South San Francisco, CA: Genentech; March 2020.
2. Sehn LH, Chua N, Mayer J, et al. Obinutuzumab plus bendamustine versus bendamustine monotherapy in patients with rituximab-refractory indolent non-Hodgkin lymphoma (GADOLIN): a randomized, controlled, open-label, multicenter, phase 3 trial. *Lancet Oncol*. 2016;17:1081-1093.
3. The NCCN Drugs and Biologics Compendium. © 2021 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on October 14, 2021. Search term: obinutuzumab.
4. The NCCN Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Clinical Practice Guidelines in Oncology (version 1.2022 – September 8, 2021). © 2021 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on October 14, 2021.
5. The NCCN B-Cell Lymphomas Clinical Practice Guidelines in Oncology (version 5.2021 – September 22, 2021). © 2021 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on October 14, 2021.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	10/14/2020
Annual Revision	**Follicular Lymphoma:** Add examples of rituximab products to the Note. **Marginal Zone Lymphoma:** To the criteria that Gazyva will be used in one of the following situations, added additional requirement that Gazyva is used for first-line therapy for nodal marginal zone lymphoma only. Added examples of rituximab products to Note. **Other B-Cell Lymphomas:** Added examples of rituximab products to Note.	10/20/2021