Reference number(s)
4467-A

STANDARD MEDICARE PART B MANAGEMENT

GAZYVA (obinutuzumab)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Chronic Lymphocytic Leukemia (CLL)
   Gazyva, in combination with chlorambucil, is indicated for the treatment of patients with previously untreated CLL.

2. Follicular Lymphoma
   1. Gazyva, in combination with bendamustine followed by Gazyva monotherapy, is indicated for the treatment of patients with follicular lymphoma who relapsed after, or are refractory to, a rituximab-containing regimen.
   2. Gazyva, in combination with chemotherapy followed by Gazyva monotherapy in patients achieving at least a partial remission, is indicated for the treatment of adult patients with previously untreated stage II bulky, III or IV follicular lymphoma.

B. Compendial Uses
1. Chronic lymphocytic leukemia/ small lymphocytic lymphoma (CLL/ SLL)
2. Follicular lymphoma
3. Marginal zone lymphomas
   a. Extranodal (gastric and non-gastric MALT lymphoma) marginal zone lymphoma
   b. Nodal marginal zone lymphoma
   c. Splenic marginal zone lymphoma
4. Histologic transformation of indolent lymphomas to diffuse large B-cell lymphoma
5. Mantle cell lymphoma
6. Diffuse large B-cell lymphoma
7. High-grade B-cell lymphomas (including high-grade B-cell lymphoma with translocations of MYC and BCL2 and/or BCL6 [double/triple hit lymphoma], high-grade B-cell lymphoma, not otherwise specified)
8. Burkitt lymphoma
9. HIV-related B-cell lymphomas
10. Post-transplant lymphoproliferative disorders
11. Castleman's disease
12. Hairy Cell Leukemia

All other indications will be assessed on an individual basis. Submissions for indications other than those enumerated in this policy should be accompanied by supporting evidence from Medicare approved compendia.

II. CRITERIA FOR INITIAL APPROVAL

A. Chronic Lymphocytic Leukemia (CLL) and Small Lymphocytic Lymphoma (SLL)
Authorization of 6 months may be granted for the treatment of CLL/SLL as a single agent or in combination with acalabrutinib, venetoclax, chlorambucil, bendamustine, high-dose methylprednisolone (HDMP), or ibrutinib.

B. Follicular Lymphoma (FL)
Authorization of 6 months, up to 30 months total, may be granted for the treatment of follicular lymphoma when any of the following criteria are met:
1. The requested medication will be used in combination with CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) regimen, CVP (cyclophosphamide, vincristine and prednisone) regimen, bendamustine, or lenalidomide as first line therapy.
2. The requested medication will be used as a single agent or in combination with lenalidomide, bendamustine, CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) or CVP (cyclophosphamide, vincristine, and prednisone) for subsequent therapy.
3. The requested medication will be used as maintenance therapy as a single agent.
4. The requested medication will be used as a substitute for rituximab in members experiencing intolerance or rare complications from rituximab such as mucocutaneous reactions including paraneoplastic pemphigus, Stevens-Johnson syndrome, lichenoid dermatitis, vesiculobullous dermatitis, and toxic epidermal necrolysis.

C. Extranodal Marginal Zone Lymphoma and Splenic Marginal Zone Lymphoma
Authorization of 6 months may be granted for the treatment of extranodal marginal zone lymphoma (gastric and non-gastric MALT lymphoma) or splenic marginal zone lymphoma when any of the following criteria are met:
1. The requested medication will be used as subsequent therapy in combination with bendamustine, or lenalidomide.
2. The requested medication will be used as maintenance therapy when the member has been previously treated with the requested medication and bendamustine.
3. The requested medication is used as a substitute for rituximab in members experiencing intolerance or rare complications from rituximab such as mucocutaneous reactions including paraneoplastic pemphigus, Stevens-Johnson syndrome, lichenoid dermatitis, vesiculobullous dermatitis, and toxic epidermal necrolysis.

D. Nodal Marginal Zone Lymphoma
Authorization of 6 months may be granted for the treatment of nodal marginal zone lymphoma when any of the following criteria are met:
1. The requested medication will be used as first-line therapy in combination with CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) regimen, CVP (cyclophosphamide, vincristine and prednisone) regimen, or bendamustine.
2. The requested medication will be used as subsequent therapy in combination with bendamustine, or lenalidomide.
3. The requested medication will be used as maintenance therapy when the member has been previously treated with the requested medication and bendamustine.
4. The requested medication is used as a substitute for rituximab in members experiencing intolerance or rare complications from rituximab such as mucocutaneous reactions including paraneoplastic

pemphigus, Stevens-Johnson syndrome, lichenoid dermatitis, vesiculobullous dermatitis, and toxic epidermal necrolysis.

E. Hairy Cell Leukemia
Authorization of 6 months may be granted in combination with vemurafenib as initial therapy for treatment of hairy cell leukemia in members who are unable to tolerate purine analogs.

A. Diffuse Large B-Cell Lymphoma when used as pre- treatment with glofitamab (Columvi)
Authorization of 1 month may be granted for treatment of diffuse large B-cell lymphoma when used as pre-treatment for up to 1 dose in cycle 1 of glofitamab therapy.

F. Histologic Transformation of indolent Lymphomas to Diffuse Large B-Cell Lymphoma, Mantle Cell Lymphoma, Diffuse Large B-Cell Lymphoma, High-Grade B-Cell Lymphomas(including high-grade B-cell lymphoma with translocations of MYC and BCL2 and/or BCL6 [double/triple hit lymphoma], high-grade B-cell lymphoma, not otherwise specified), Burkitt Lymphoma, HIV-Related B-Cell Lymphomas, Post-Transplant Lymphoproliferative Disorders, and Castleman's Disease
Authorization of 6 months may be granted for the treatment of histologic transformation of indolent lymphomas to diffuse large B-cell lymphoma, mantle cell lymphoma, diffuse large B-cell lymphoma, high-grade B-cell lymphomas (including high-grade B-cell lymphoma with translocations of MYC and BCL2 and/or BCL6 [double/triple hit lymphoma], high-grade B-cell lymphoma, not otherwise specified), Burkitt lymphoma, HIV-related B-cell lymphomas, post-transplant lymphoproliferative disorders, or Castleman's disease when the requested medication is used as a substitute for rituximab in members experiencing intolerance or rare complications from rituximab such as mucocutaneous reactions including paraneoplastic pemphigus, Stevens-Johnson syndrome, lichenoid dermatitis, vesiculobullous dermatitis, and toxic epidermal necrolysis.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must be currently receiving therapy with the requested agent.

A. **Follicular Lymphoma (FL)**
Authorization of 12 months, up to 30 months total may be granted when all of the following criteria are met:
1. The member is currently receiving therapy with the requested medication.
2. The requested medication is being used to treat an indication enumerated in Section II.
3. The member is receiving benefit from therapy. Benefit is defined as:
   i. No evidence of unacceptable toxicity while on the current regimen and
   ii. No evidence of disease progression while on the current regimen

B. Diffuse Large B-Cell Lymphoma when used as pre- treatment with glofitamab (Columvi)
All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria

C. **All other indications**
Authorization of 12 months, may be granted when all of the following criteria are met:
1. The member is currently receiving therapy with the requested medication.
2. The requested medication is being used to treat an indication enumerated in Section II.
3. The member is receiving benefit from therapy. Benefit is defined as:

i. No evidence of unacceptable toxicity while on the current regimen and
ii. No evidence of disease progression while on the current regimen

IV. APPENDIX

Re-challenge with the same anti-CD20 monoclonal antibody is not recommended and it is unclear if the use of an alternative anti-CD20 monoclonal antibody poses the same risk of recurrence.

V. SUMMARY OF EVIDENCE

The contents of this policy were created after examining the following resources:

1. The prescribing information for Gazyva and Columvi.
2. The available compendium
    a. National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium
    b. Micromedex DrugDex
    c. American Hospital Formulary Service- Drug Information (AHFS-DI)
    d. Lexi-Drugs
    e. Clinical Pharmacology
3. NCCN Guideline: Hairy cell leukemia
4. NCCN Guideline: Chronic lymphocytic leukemia/small lymphocytic lymphoma
5. NCCN Guideline: B-cell lymphomas

After reviewing the information in the above resources, the FDA-approved indications listed in the prescribing information for Gazyva are covered in addition to the following:

1. Chronic lymphocytic leukemia/ small lymphocytic lymphoma (CLL/ SLL)
2. Follicular lymphoma
3. Marginal zone lymphomas
    a. Extranodal (gastric and non-gastric MALT lymphoma) marginal zone lymphoma
    b. Nodal marginal zone lymphoma
    c. Splenic marginal zone lymphoma
4. Histologic transformation of indolent lymphomas to diffuse large B-cell lymphoma
5. Mantle cell lymphoma
6. Diffuse large B-cell lymphoma
7. High-grade B-cell lymphomas (including high-grade B-cell lymphoma with translocations of MYC and BCL2 and/or BCL6 [double/triple hit lymphoma], high-grade B-cell lymphoma, not otherwise specified)
8. Burkitt lymphoma
9. HIV-related B-cell lymphomas
10. Post-transplant lymphoproliferative disorders
11. Castleman's disease
12. Hairy Cell Leukemia

VI. EXPLANATION OF RATIONALE

Support for FDA-approved indications can be found in the manufacturer's prescribing information. Additionally, the prescribing information for Columvi supports using Gazyva as pretreatment prior to starting treatment with Columvi.

Support for the additional indications listed in section V can be found in the NCCN Drugs and Biologics Compendium. Use of information in the NCCN Drugs and Biologics Compendium for off-label use of drugs and biologicals in an anti-cancer chemotherapeutic regimen is supported by the Medicare Benefit Policy Manual, Chapter 15, section 50.4.5 (Off-Label Use of Drugs and Biologicals in an Anti-Cancer Chemotherapeutic Regimen).

VII. REFERENCES

1. Gazyva [package insert]. South San Francisco, CA: Genentech, Inc.; July 2022.
2. Columvi [package insert]. South San Francisco, CA: Genentech, Inc.; June 2023.
3. The NCCN Drugs & Biologics Compendium® © 2023 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed June 2, 2023.