# Clinical Criteria

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| **Subject:** | Gazyva (obinutuzumab) | | |
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## Overview

This document addresses the use of Gazyva (obinutuzumab). Gazyva is a monoclonal antibody directed against the surface antigen CD20 and is used to treat chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL) and follicular lymphoma (FL).

Gazyva is FDA approved in combination with chlorambucil for previously untreated CLL. CLL and SLL are different manifestations of the same disease and are managed in much the same way. The National Comprehensive Cancer Network® (NCCN) provides additional recommendations with a category 2A level of evidence for the use of Gazyva. NCCN recommends it to be used as first line treatment for patients without del (17p) mutation, in combination with either chlorambucil or bendamustine. NCCN also recommends Gazyva first line as a single agent for those with del (17p) mutation (2A recommendation) and for frail patients without del (17p) mutation (2B recommendation). It is also recommended as a single agent in patients without del (17p) mutation in relapsed or refractory disease. Venetoclax was recently granted FDA approval for treatment of CLL/SLL based on a study of Gazyva in combination with venetoclax as first line therapy in those with CLL/SLL with or without del (17p) mutation. NCCN recommends this combination regimen be used in those with del (17p) mutation or in those without del (17p) mutation who are frail, age ≥65 years, or with significant comorbidities.

Gazyva is also FDA approved to treat follicular lymphoma (FL), a type of B-cell lymphoma. It is indicated in combination with bendamustine followed by monotherapy for up to 2 years for treatment of FL which has relapsed after or is refractory to a rituximab-containing regimen. It is also approved in combination with bendamustine, CHOP regimen, or CVP regimen followed by monotherapy for up to 2 years for previously untreated FL.

### Other Uses

NCCN guideline for B-cell Lymphomas include 2A recommendations for the use of Gazyva for multiple types of refractory non-Hodgkin lymphomas (gastric MALT lymphoma, nodal marginal zone lymphoma, nongastric MALT lymphoma, and splenic marginal zone lymphoma). The rationale cited for the above 2A indications is from an open label randomized phase 2 trial comparing the efficacy and safety of rituximab to Gazyva as both induction and maintenance therapy in indolent NHLs (Sehn 2015). This trial recruited few patients with non-follicular lymphoma, so efficacy results were only presented for the subgroup of patients with follicular lymphoma. NCCN also lists a 2A recommendation for Gazyva as a substitute for rituximab in patients experiencing rare mucocutaneous reactions; however it is unclear if the use of an alternative anti-CD20 antibody poses the same risk of recurrence. NCCN and other compendia do not support the use of Gazyva for treatment of diffuse large B-cell lymphoma and mantle-cell lymphoma.

Gazyva has a black box warning for hepatitis B (HBV) reactivation which, in some cases, results in fulminant hepatitis, hepatic failure, and death. Gazyva and concomitant medications should be discontinued in the event of HBV reactivation. Gazyva also has a black box warning for progressive multifocal leukoencephalopathy (PML), including fatal PML, which can occur in patients receiving Gazyva.

### Definitions and Measures

CHOP regimen: Cyclophosphamide, doxorubicin, vincristine, and prednisone

CVP regimen: Cyclophosphamide, vincristine, and prednisone

Del (17p) mutation: A cytogenetic abnormality which reflects the loss of the TP53 gene and is frequently associated with mutations in the remaining TP53 allele, and is associated with short treatment-free interval, short median survival, and poor response to chemotherapy

Follicular Lymphoma: A type of B-cell non-Hodgkin lymphoma, a cancer of the immune system that is usually indolent (slow-growing). The tumor cells grow as groups to form nodules. There are several subtypes of follicular lymphoma.

Line of Therapy:

- First-line therapy: The first or primary treatment for the diagnosis, which may include surgery, chemotherapy, radiation therapy or a combination of these therapies.
- Second-line therapy: Treatment given when initial treatment (first-line therapy) is not effective or there is disease progression.
- Third-line therapy: Treatment given when both initial (first-line therapy) and subsequent treatment (second-line therapy) are not effective or there is disease progression.

Maintenance therapy: Designed to maintain a condition to prevent a relapse.

Non-Hodgkin Lymphoma (NHL): A group of malignant solid tumors or lymphoid tissues.

One line of therapy: Single line of therapy.

Refractory Disease: Illness or disease that does not respond to treatment.

Relapse or recurrence: After a period of improvement, during which time a disease (for example, cancer) could not be detected, the return of signs and symptoms of illness or disease. For cancer, it may come back to the same place as the original (primary) tumor or to another place in the body.

## Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

**Gazyva (obinutuzumab)**

Requests for Gazyva (obinutuzumab) may be approved if the following criteria are met:

I. Individual has a diagnosis of chronic lymphocytic leukemia/small lymphocytic lymphoma; **AND**
II. Individual is using for one of the following:
    A. In combination with chlorambucil or bendamustine for first-line treatment in individuals without del (17p) mutation (Label, NCCN 2A); **OR**
    B. In combination with venetoclax for first-line treatment for the following:
        1. Individuals with del (17p) mutation (NCCN 2A); **OR**
        2. Individuals without del (17p) mutation who are frail, age ≥65 years, or with significant comorbidities (NCCN 2A); **OR**
    ~~B.~~C. As a single agent for first-line treatment in individuals who are frail *or* with del (17p) mutation (NCCN 2A); **OR**
    ~~C.~~D. As a single agent for treatment of relapsed/refractory disease without del (17p) mutation (NCCN 2A);

**OR**

III. Individual has a diagnosis of follicular lymphoma; **AND**
IV. Individual is using in combination with one of the following regimens *and* as monotherapy, for up to 24 months or until disease progression, following the listed combination therapy regimens:
    A. Cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP regimen); **OR**
    B. Cyclophosphamide, vincristine, and prednisone (CVP regimen); **OR**
    C. Bendamustine.

Requests for Gazyva may not be approved for the following:

I. All other indications not included above; **OR**
II. Treatment of diffuse large B-cell lymphoma and mantle-cell lymphoma.

## Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

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| **J9301** | Injection, obinutuzumab, 10 mg [Gazyva] |

*ICD-10 Diagnosis*

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| **C82.00-C82.99** | Follicular lymphoma |
| **C83.00-C83.09** | Small cell B-cell lymphoma |
| **C91.10-C91.12** | Chronic lymphocytic leukemia of B-cell type |

## Document History

Revised: 06/10/2019
Document History:

- 06/10/2019 – Select Review: Add combination treatment with venetoclax for CLL based on venetoclax labeling and NCCN recommendations. Coding reviewed: No changes.
- 05/17/2019 – Annual Review: First review of Gazyva clinical criteria. Minor wording and formatting changes. Add references for off label criteria. Coding reviewed: No changes.

## References


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