BlueCross BlueShield Federal Employee Program

GAZYVA (obinutuzumab)

RATIONALE FOR INCLUSION IN PA PROGRAM

Background

Gazyva (obinutuzumab) is a monoclonal antibody intended to be used for treatment of patients with chronic lymphocytic leukemia (CLL), follicular lymphoma (FL), gastric or nongastric MALT lymphoma, splenic marginal zone lymphoma, or nodal marginal zone lymphoma. Gazyva works by helping certain cells in the immune system attack cancer cells. In particular, Gazyva targets the CD20 antigen expressed on the surface of the pre-B and mature B lymphocytes (1-4).

Regulatory Status

FDA-approved indications: Gazyva is a CD20-directed cytolytic antibody and is indicated: (1,5)

1. In combination with chlorambucil, for the treatment of patients with previously untreated chronic lymphocytic leukemia
2. In combination with bendamustine followed by Gazyva monotherapy, for the treatment of patients with follicular lymphoma (FL) who relapsed after, or are refractory to, a rituximab-containing regimen
3. In combination with chemotherapy followed by Gazyva monotherapy in patients achieving at least a partial remission, for the treatment of adult patients with previously untreated stage II bulky, III or IV follicular lymphoma.
4. In combination with zanubrutinib, for the treatment of relapsed or refractory follicular lymphoma (FL) after two or more lines of systemic therapy.

Off-Label Uses: (2-4)

1. Chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL)
    a. First-line therapy in patients without del(17p)/TP53
    b. First-line therapy in patients with del(17p)/TP53
    c. First-line therapy when used with Calquence (acalabrutinib)
    d. Patients unable to tolerate purine analogs as a single agent or in combination with chlorambucil
    e. Patients with relapsed or refractory disease as a single agent
2. Gastric MALT lymphoma in patients who relapsed after, or are refractory to, a rituximab-containing regimen and in combination with bendamustine
3. Nongastric MALT lymphoma in patients who relapsed after, or are refractory to, a rituximab-containing regimen and in combination with bendamustine

4. Splenic marginal zone lymphoma in patients who relapsed after, or are refractory to, a rituximab-containing regimen and in combination with bendamustine
5. Nodal Marginal Zone Lymphoma who relapsed after, or are refractory to, a rituximab-containing regimen and in combination with bendamustine

Gazyva carries a boxed warning regarding hepatitis B virus (HBV) reactivation and progressive multifocal leukoencephalopathy (PML). Patients must be screened for HBV infection before treatment initiation. Positive patients must be monitored during and after Gazyva treatment. In the event of HBV reactivation, discontinue Gazyva and concomitant medications (1). Patients presenting with new onset or changes to pre-existing neurologic manifestations should be evaluated for the diagnosis of PML. Evaluation of PML includes, but is not limited to, consultation with a neurologist, brain MRI, and lumbar puncture. Discontinue Gazyva therapy and consider discontinuation or reduction of any concomitant chemotherapy or immunosuppressive therapy in patients who develop PML (1).

Gazyva can cause severe and life-threatening infusion reactions. Patients should be premedicated with acetaminophen, antihistamine and a glucocorticoid and closely monitored during the entire infusion (1).

Acute renal failure, hyperkalemia, hypocalcemia, hyperuricemia, and/or hyperphosphatemia from Tumor Lysis Syndrome (TLS) can occur within 12-24 hours after the first infusion. Patients with high tumor burden and/or high circulating lymphocyte count (>25 x 10^9/L) are at greater risk for TLS and should receive appropriate tumor lysis prophylaxis with anti-hyperuricemics (e.g., allopurinol) and hydration beginning 12-24 hours prior to the infusion of Gazyva. For treatment of TLS, correct electrolyte abnormalities, monitor renal function, and fluid balance, and administer supportive care, including dialysis as indicated (1).

Serious bacterial, fungal, and new or reactivated viral infections can occur during and following Gazyva therapy. Do not administer Gazyva to patients with an active infection. Patients with a history of recurring or chronic infections may be at increased risk of infection (1).

Gazyva has been shown to cause life threatening neutropenia and thrombocytopenia. Patients must be continuously monitored for infection, thrombocytopenia, and hemorrhagic events. In patients with Grade 3 or 4 neutropenia, consider administration of granulocyte colony-stimulating factors (G-CSF) and/or dose delays of Gazyva. Patients with severe and long lasting (>1 week) neutropenia are

strongly recommended to receive antimicrobial prophylaxis until resolution of neutropenia to Grade 1 or 2. Antiviral and antifungal prophylaxis should be considered as well. In patients with Grade 3 or 4 thrombocytopenia, platelet counts should be monitored frequently. Management of hemorrhage may require blood product support (1).

The safety and efficacy of immunization with live or attenuated viral vaccines during or following Gazyva therapy have not been studied. Immunization with live virus vaccines is not recommended during treatment and until B-cell recovery (1).

The safety and effectiveness of Gazyva in patients less than 18 years of age have not been established (1).

Summary

Gazyva (obinutuzumab) is a monoclonal antibody intended to be used for treatment of patients with previously untreated chronic lymphocytic leukemia (CLL)/small lymphocytic lymphoma (SLL), follicular lymphoma (FL), gastric or nongastric MALT lymphoma, splenic marginal zone lymphoma, or nodal marginal zone lymphoma. Gazyva carries a boxed warning regarding hepatitis B virus (HBV) reactivation and progressive multifocal leukoencephalopathy (PML). Gazyva can cause severe and life-threatening infusion reactions. Serious bacterial, fungal, and new or reactivated viral infections can occur during and following Gazyva therapy. Do not administer Gazyva to patients with an active infection. Gazyva has been shown to cause life-threatening neutropenia and thrombocytopenia. The safety and efficacy of immunization with live or attenuated viral vaccines during or following Gazyva therapy has not been studied. The safety and efficacy of Gazyva in patients less than 18 years of age have not been established (1-5).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Gazyva while maintaining optimal therapeutic outcomes.

References

1. Gazyva [package insert]. South San Francisco, CA: Genentech, Inc.; July 2022.
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3. NCCN Clinical Practice Guidelines in Oncology® Chronic Lymphocytic Leukemia/ Small Lymphocytic Lymphoma (Version 3.2024). National Comprehensive Cancer Network, Inc. March 2024. Accessed on May 14, 2024.
4. NCCN Clinical Practice Guidelines in Oncology® B-cell Lymphomas (Version 2.2024). National Comprehensive Cancer Network, Inc. April 2024. Accessed on May 14, 2024.
5. Brukinsa [package insert]. San Mateo, CA: BeiGene USA, Inc.; March 2024.