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Section:	Prescription Drugs	**Effective Date:**	January 1, 2016
Subsection:	Antineoplastic Agents	**Original Policy Date:**	January 1, 2014
Subject:	Gazyva	**Page:**	1 of 5

Last Review Date: December 3, 2015

Gazyva

Description

Gazyva (obinutuzumab)

Background
Gazyva is a monoclonal antibody intended to be used with chlorambucil to treat patients with previously untreated chronic lymphocytic leukemia (CLL) (1). CLL and small lymphocytic lymphoma (SLL) are B- cell lymphomas that are essentially the same disease. In SLL, the cancer cells are primarily in the lymph nodes, whereas in CLL, they are in the bloodstream and bone marrow (2). Gazyva works by helping certain cells in the immune system attack cancer cells. Gazyva targets the CD20 antigen expressed on the surface of the pre B- and mature B-lymphocytes (1).

Each dose of Gazyva is 1000 mg, administered intravenously, with the exception of the first infusions in cycle 1, which are administered on day 1 (100 mg) and day 2 (900 mg). Gazyva to be administered during 6 treatment cycles each of 28 days duration (1).

Regulatory Status
FDA-approved indication: Gazyva is a CD20-directed cytolytic antibody and is indicated, in combination with chlorambucil, for the treatment of patients with previously untreated chronic lymphocytic leukemia (1).

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 in combination with chlorambucil has been shown to cause neutropenia and thrombocytopenia. Patients must be continuously monitored for infection. Patients with neutropenia are strongly recommended to receive antimicrobial prophylaxis throughout the treatment period. Antiviral and antifungal prophylaxis should be considered. Platelet counts and bleeding should be monitored. 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 has 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 pediatric patients has not been established (1).

Related policies
Arzerra, Rituxan, Imbruvica Zydelig

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Gazyva may be considered **medically necessary** in patients that are 18 years of age and older with untreated chronic lymphocytic leukemia (CLL)/ small lymphocytic lymphoma (SLL) when used in combination with chlorambucil; screened and monitored for hepatitis B and reactivation; monitored for signs and symptoms of progressive multifocal leukoencaphalopathy (PML); and patient does not have any active infection.

Gazyva is considered **investigational** in patients that are less than 18 years of age and in patients who have been previously treated for CLL or SLL or when not used in combination with chlorambucil.

Prior-Approval Requirements

Age 18 years of age or older

Diagnosis

Patient must have the following:

CD20-positive chronic lymphocytic leukemia (CLL) / small lymphocytic lymphoma (SLL)

AND ALL of the following:

1. Patient has not been previously treated for CLL/SLL
2. Used in combination with chlorambucil
3. Absence of active infection
4. Patient has or will be screened for hepatitis B prior to initiation of therapy and will be continued to be monitored during treatment if positive
5. Patient will be monitored for signs and symptoms of progressive multifocal leukoencephalopathy (PML)

Prior – Approval *Renewal* Requirements

None

Policy Guidelines

Pre - PA Allowance
None

Prior - Approval Limits
Duration 12 months

Prior – Approval *Renewal* Limits
None

Rationale

Summary
Gazyva is a monoclonal antibody intended to be used with chlorambucil to treat patients with previously untreated chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL). 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. Acute renal failure, hyperkalemia, hypocalcemia, hyperuricemia, and/or hyperphosphatemia from Tumor Lysis Syndrome (TLS) can occur within 12-24 hours after the first infusion. 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 in combination with chlorambucil has been shown to cause 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 pediatric patients has not been established (1-2).

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. September 2015.
2. Chronic Lymphocytic Leukemia/ Small Lymphocytic Lymphoma (CLL/SLL); http://www.lymphoma.org/site/pp.asp?c=bkLTKaOQLmK8E&b=6300147

Policy History

Date	Action
November 2013	Addition to PA
March 2014	Annual review
December 2014	Annual editorial review and reference update
December 2015	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 3, 2015 and is effective January 1, 2016.

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