BlueCross BlueShield
Federal Employee Program
Federal Employee Program®
750 9th St NW
Washington, D.C. 20001
202.942.1000
Fax 202.942.1125

5.21.003

Section:	Prescription Drugs	**Effective Date:**	April 1, 2024
Subsection:	Antineoplastic Agents	**Original Policy Date:**	December 1, 2011
Subject:	Arzerra	**Page:**	1 of 5

Last Review Date: March 8, 2024

Arzerra

Description

Arzerra (ofatumumab)

Background
Arzerra (ofatumumab) is a CD20-directed cytolytic monoclonal antibody indicated for the treatment of patients with chronic lymphocytic leukemia (CLL). All patients are pre-medicated with oral acetaminophen, oral or intravenous antihistamine and intravenous corticosteroid (1).

Regulatory Status
FDA-approved indications: Arzerra is a CD20-directed cytolytic monoclonal antibody indicated for: (1)

1. Treatment of patients with chronic lymphocytic leukemia (CLL) refractory to fludarabine and/or alemtuzumab or rituximab.
2. Extended treatment of patients who are in complete or partial response after at least two lines of therapy for recurrent or progressive CLL.
3. In combination with chlorambucil, for the treatment of previously untreated patients with chronic lymphocytic leukemia (CLL) for whom fludarabine-based therapy is considered inappropriate
4. In combination with flurdarabine and cyclophosphamide for the treatment of patients with relapsed chronic lymphocytic leukemia (CLL)

Off-Label Use:
Chronic lymphocytic leukemia (CLL) and small lymphocytic lymphoma (SLL) are different manifestations of the same disease yet are managed in similar fashions. Arzerra may be used in the treatment for small lymphocytic lymphoma. In addition, the NCCN Panel has included

newer agents, such as Arzerra, as therapy options for previously treated patients for Waldenstrom's macroglobulinemia/lymphoplasmacytic lymphoma who are intolerant to rituximab, either as a single agent or in combination therapy (2-4).

Boxed warnings include the possibility of developing progressive multifocal leukoencephalopathy (PML) and of HBV reactivation. Progressive multifocal leukoencephalopathy (PML), including fatal PML, can occur during treatment with Arzerra. If PML is suspected, Arzerra treatment should be discontinued. Arzerra has been shown to increase the risk of Hepatitis B infection and reactivation. High-risk patients should be screened. Arzerra should be discontinued in patients who develop or experience a reactivation of viral hepatitis (1).

Safety and effectiveness of Arzerra in patients less than 18 years of age have not been established (1).

Related policies
Gazyva, Rituximab, Rituxan Hycela

Policy

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

Arzerra may be considered **medically necessary** if the conditions indicated below are met.

Arzerra may be considered **investigational** for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:

1. Chronic Lymphocytic Leukemia (CLL) or Small Lymphocytic Lymphoma (SLL)
   AND ONE of the following:
   a. Previously untreated patients

i. Used in combination with chlorambucil in previously untreated patients

b. Relapsed or refractory
   i. Used in combination with flurdarabine and cyclophosphamide

c. Extended treatment in patients
   i. Complete or partial response after 2 previous therapies for recurrent or progressive CLL /SLL

2. Waldenstrom's macroglobulinemia/lymphoplasmacytic lymphoma
   a. Refractory or intolerant to rituximab

AND the following:
1. Hepatitis B virus screening before initiating treatment

Prior-Approval Renewal Requirements

Age 18 years of age or older

Diagnoses

Patient must have **ONE** of the following:
1. Chronic Lymphocytic Leukemia
2. Small Lymphocytic Lymphoma
3. Waldenstrom's macroglobulinemia/lymphoplasmacytic lymphoma

AND the following:
1. **NO** disease progression or unacceptable toxicity

Policy Guidelines

Pre-PA Allowance

None

Prior-Approval Limits

Duration 6 months

Prior-Approval Renewal Limits

Duration 12 months

Rationale

Summary
Arzerra (ofatumumab) is a CD20-directed cytolytic monoclonal antibody indicated for the treatment of patients with chronic lymphocytic leukemia (CLL). Off label uses include small lymphocytic lymphoma (SLL) and Waldenstrom's macroglobulinemia/lymphoplasmacytic lymphoma. Boxed warnings include the possibility of developing progressive multifocal leukoencephalopathy (PML) and of HBV reactivation. If PML is suspected, Arzerra treatment should be discontinued. Arzerra has been shown to increase the risk of Hepatitis B infection and reactivation. High-risk patients should be screened (1-4).

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

References
1. Arzerra [package Insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; August 2016.
2. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma. Version 1.2024. November 2023. Accessed on January 18, 2024.
3. National Comprehensive Cancer Network. NCCN Clinical Pratice Guidelines in Oncology: Waldenstrom's macroglobulinemia/Lymphoplasmacytic Lymphoma. Version 2.2024. December 2023. Accessed on January 18, 2024.
4. NCCN Drugs & Biologics Compendium® Ofatumumab 2024. National Comprehensive Cancer Network, Inc. Accessed on January 18, 2024.

Policy History

Date	Action
December 2011	New Policy
September 2012	Annual editorial and reference update
March 2013	Annual editorial and reference update
October 2013	Alemtuzumab (Campath) no longer commercially available. Addition of rituximab to criteria.
April 2014	Addition of a new indication for previously untreated with chronic lymphocytic leukemia (CLL) in combination with chlorambucil for whom fludarabine-based therapy is considered inappropriate

December 2014	Annual editorial review and reference update
December 2015	Annual review
January 2016	Addition new indications: extended treatment in patients with complete or partial response after 2 previous therapies for recurrent or progressive CLL, change to require only on prior therapy for CLL and SLL and Waldenstrom's macroglobulinemia/lymphoplasmacytic lymphoma in patients who are intolerant to rituximab Addition of renewal secton and duration of 12 months Policy changed from 5.04.03 to 5.21.03
March 2016	Annual review
June 2016	Annual review and reference update
September 2016	Annual review Addition of SLL to the CLL requirements Removal of one prior therapy for relapsed CLL and SLL and added used in combination with flurdarabine and cyclophosphamide
June 2017	Annual review and reference update
June 2018	Annual editorial review and reference update
June 2019	Annual review and reference update
March 2020	Annual review and reference update
June 2020	Annual review
March 2021	Annual editorial review and reference update Revised background and summary sections
March 2022	Annual review and reference update
December 2022	Annual review and reference update. Changed policy number to 5.21.003
March 2023	Annual review and reference update
March 2024	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 8, 2024 and is effective on April 1, 2024.