

5.21.03

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| Section: | Prescription Drugs | Effective Date: | April 1, 2021 |
| Subsection: | Antineoplastic Agents | Original Policy Date: | December 1, 2011 |
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Last Review Date: March 12, 2021

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

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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** in patients 18 years of age or older for the treatment of chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) or for the treatment of Waldenstrom's macroglobulinemia/lymphoplasmacytic lymphoma and if the conditions indicated below are met.

Arzerra may be considered **investigational** in patients less than 18 years of age and for all other indications.

Prior-Approval Requirements

Age 18 years of age or older

Diagnoses

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

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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 fluridarabine 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

Patients 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

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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 2.2021. December 2020.
3. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Waldenstrom's macroglobulinemia/Lymphoplasmacytic Lymphoma. Version 1.2021. September 2020.
4. The NCCN Drugs & Biologics Compendium™ 2021 National Comprehensive Cancer Network, Inc.

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 |

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| | 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 section 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 fludarabine 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 |

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 12, 2021 and is effective on April 1, 2021.