

Clinical Policy: Ofatumumab (Arzerra)

Reference Number: PA.CP.PHAR.306

Effective Date: 01/18

Last Review Date: 10/30/2019

[Coding Implications](#)

[Revision Log](#)

Description

The intent of the criteria is to ensure that patients follow selection elements established by Pennsylvania Health and Wellness[®] clinical policy for ofatumumab (Arzerra[®]).

FDA Approved Indication(s)

Arzerra is indicated:

- In combination with chlorambucil, for the treatment of previously untreated patients with chronic lymphocytic leukemia (CLL) for whom fludarabine-based therapy is considered inappropriate
- In combination with fludarabine and cyclophosphamide for the treatment of patients with relapsed CLL
- For extended treatment of patients who are in complete or partial response after at least two lines of therapy for recurrent or progressive CLL
- For the treatment of patients with CLL refractory to fludarabine and alemtuzumab

Policy/Criteria

It is the policy of Pennsylvania Health and Wellness[®] that Arzerra is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma* (must meet all):

1. Diagnosis of chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL);
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Request meets one of the following (a or b):
 - a. Dose does not exceed the maximum indicated in section IV;
 - b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**CLL and SLL, non-Hodgkin lymphoma (NHL) subtypes, are different manifestations of the same disease.³*

Approval duration: 6 months

B. Waldenstrom's Macroglobulinemia/Lymphoplasmacytic Lymphoma (off-label) (must meet all):

1. Diagnosis of Waldenstrom's macroglobulinemia/lymphoplasmacytic lymphoma (WM/LPL);
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Member is rituximab-intolerant;
4. Disease is progressive, relapsed, or unresponsive to primary therapy (*see Appendix B for examples*);
5. Request meets one of the following (a or b):

- a. Dose does not exceed the maximum indicated in section IV;
- b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

Approval duration: 6 months

C. Other diagnoses/indications: Refer to PA.CP.PMN.53

II. Continued Approval

A. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (must meet all):

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a or b):
 - a. New dose does not exceed the maximum indicated in section IV;
 - b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2):

1. Currently receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies; or
2. Refer to PA.CP.PMN.53

III. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CLL: chronic lymphocytic leukemia

FDA: Food and Drug Administration

NCCN: National Comprehensive Cancer
Network

SLL: small lymphocytic lymphoma

WM/LPL: Waldenstrom's

macroglobulinemia/lymphoplasmacytic
lymphoma

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Examples of Primary Therapy for WM/LPL	Dosing Regimen	Dose Limit/ Maximum Dose
Treanda®, Bendeka® (bendamustine)/Rituxan® (rituximab)	Varies	Varies
bortezomib (Velcade®)/dexamethasone/ Rituxan® (rituximab)	Varies	Varies

Examples of Primary Therapy for WM/LPL	Dosing Regimen	Dose Limit/ Maximum Dose
Rituxan [®] (rituximab)/cyclophosphamide/dexamethasone	Varies	Varies

Therapeutic alternatives are listed as Brand name[®] (generic) when the drug is available by brand name only and generic (Brand name[®]) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): none
- Boxed warning(s): hepatitis B virus reactivation and progressive multifocal leukoencephalopathy

IV. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Previously untreated CLL	In combination with chlorambucil: 300 mg IV on Day 1 followed by 1,000 mg IV on Day 8 (Cycle 1). Then 1,000 mg IV on Day 1 of subsequent 28-day cycles for a minimum of 3 cycles until best response or a maximum of 12 cycles	12 cycles
Relapsed CLL	In combination with fludarabine and cyclophosphamide: 300 mg IV on Day 1 followed by 1,000 mg IV on Day 8 (Cycle 1). Then 1,000 mg IV on Day 1 of subsequent 28-day cycles for a maximum of 6 cycles	6 cycles
Extended treatment in CLL	300 mg on Day 1 followed by 1,000 mg 1 week later on Day 8, followed by 1,000 mg 7 weeks later and every 8 weeks thereafter for up to a maximum of 2 years	2 years
Refractory CLL	300 mg initial dose, followed 1 week later by 2,000 mg weekly for 7 doses, followed 4 weeks later by 2,000 mg every 4 weeks for 4 doses	Refer to dosing regimen

V. Product Availability

Vial, single-use for intravenous infusion: 100 mg/5 mL, 1,000 mg/50 mL

Background

Description/Mechanism of Action:

Arzerra (ofatumumab) is a CD20-directed cytotoxic monoclonal antibody that binds specifically to both the small and large extracellular loops of the CD20 molecule. The CD20 molecule is expressed on normal B lymphocytes (pre-B-to mature B-lymphocyte) and on B-cell CLL. The CD20 molecule is not shed from the cell surface and is not internalized following antibody binding. The Fab domain of ofatumumab binds to the CD20 molecule and the Fc domain mediates immune effector functions to result in B-cell lysis *in vitro*. Data suggest that possible mechanisms of cell lysis include complement-dependent cytotoxicity and antibody-dependent, cell-mediated cytotoxicity.

Formulations:

Arzerra is available in 100 mg/5 mL (20 mg/mL) and 1,000 mg/50 mL (20 mg/mL) single-use vials for intravenous administration following dilution.

Appendices

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bortezomib (Velcade [®])/dexamethasone/ Rituxan [®] (rituximab)	Varies	Varies
Rituxan [®] (rituximab)/cyclophosphamide/dexamethasone	Varies	Varies

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Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): none
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Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPSC Codes	Description
J9999	Not otherwise classified, antineoplastic drug

Reviews, Revisions, and Approvals	Date	Approval Date
4Q 2018 annual review: no significant changes; summarized NCCN and FDA-approved uses for improved clarity; added specialist involvement in care; updated	07/18	
4Q 2019 annual review: No changes per Statewide PDL implementation 01-01-2020	10/30/19	

References

1. Arzerra Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; August 2016. Available at <https://www.us.arzerra.com/>. Accessed July 11, 2018.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed July 11, 2018.
3. National Comprehensive Cancer Network. Chronic lymphocytic leukemia/small lymphocytic lymphoma (Version 5.2018). Available at: https://www.nccn.org/professionals/physician_gls/pdf/cll.pdf. Accessed July 11, 2018.
4. National Comprehensive Cancer Network. Waldenstrom's macroglobulinemia/lymphoplasmacytic lymphoma (Version 1.2018). Available at: https://www.nccn.org/professionals/physician_gls/pdf/waldenstroms.pdf. Accessed July 16, 2018.