Clinical Policy Title:	ofatumumab
Policy Number:	RxA.585
Drug(s) Applied:	Arzerra®
Original Policy Date:	03/06/2020
Last Review Date:	10/19/2022
Line of Business Policy Applies to:	All lines of business

Background

Ofatumumab (Arzerra®) is a CD20-directed cytolytic monoclonal antibody. Ofatumumab 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.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
ofatumumab (Arzerra®)	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

Drug Name	Indication	Dosing Regimen	Maximum Dose
ofatumumab (Arzerra®)	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	12 doses

Dosage Forms

- Single-use vial: 100 mg/5 mL, 1,000 mg/50 mL

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

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

1. Diagnosis of CLL or small lymphocytic lymphoma (SLL);
2. Prescribed by or in consultation with an oncologist or a hematologist;
3. Age ≥ 18 years;
4. If request is for use as first line therapy, one of the following (a or b):
   a. Prescribed in combination with bendamustine, and there is no del(17)/TP53 mutation;
   b. Prescribed in combination with chlorambucil, and fludarabine-based therapy is considered inappropriate;
5. Request meets one of the following (a or b): *
   a. Dose does not exceed the maximum dose indicated in Dosing Information;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).
   *Prescribed regimen must be FDA-approved or recommended by NCCN.

Approval Duration
Commercial: 6 months
Medicaid: 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 a hematologist;
3. Age ≥ 18 years;
4. Member is rituximab-intolerant;
5. Request is for second-line or subsequent therapy (see Appendix B for examples of prior therapy);
6. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).*
   *Prescribed regimen must be FDA-approved or recommended by NCCN.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

C. B-Cell Lymphomas (off-label) (must meet all)**:**

1. Diagnosis of one of the following B-cell lymphoma subtypes (a-j):
   a. Follicular lymphoma;
   b. Marginal zone lymphoma ((i, ii, iii, or iv):
      i. Splenic marginal zone lymphoma;
      ii. Gastric MALT lymphoma;
      iii. Nongastric MALT lymphoma;
      iv. Nodal marginal zone lymphoma;
   c. Histologic transformation of marginal zone lymphoma to diffuse large B-cell lymphoma;
   d. Diffuse large B-cell lymphoma;
   e. High-grade B-cell lymphoma;
   f. Mantle cell lymphoma;
   g. Castleman's disease;
   h. Post-transplant lymphoproliferative disorder;
   i. AIDS-related B-cell lymphoma;
   j. Burkitt lymphoma;
2. Used as a substitute* for Rituxan® (rituximab) or Gazyva® (obinutuzumab) in patients experiencing rare complications such as mucocutaneous reactions including paraneoplastic pemphigus, Stevens-Johnson syndrome, lichenoid dermatitis, vesiculobullous dermatitis, and toxic epidermal necrolysis;
   *Caution per NCCN Compendium, re-challenge with the same anti-CD20 monoclonal antibody is not recommended and it is unclear if the use of an alternative anti-CD20 monoclonal antibody poses the same risk of recurrence.
3. Prescribed by or in consultation with an oncologist or a hematologist;
4. Age ≥ 18 years;
5. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence). *
   *Prescribed regimen must be FDA-approved or recommended by NCCN.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

A. All Indications in Section I (must meet all):

1. Member is currently receiving medication that has been authorized by RxAdvance or member has met initial approval criteria for the covered indications and has received this medication for at least 30 days;
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 dose indicated in dosing information;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

*Prescribed regimen must be FDA-approved or recommended by NCCN

Approval Duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

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
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
WM/LPL primary therapy examples: • bendamustine/rituximab • bortezomib (Velcade®)/dexamethasone/rituximab • ibrutinib (Imbruvica®) ± rituximab • rituximab/cyclophosphamide/dexamethasone	Varies	Varies

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

APPENDIX C: Contraindications/Boxed Warnings
- Contraindication(s):
  - None reported

- Boxed Warning(s):
  - Hepatitis B virus reactivation, in some cases resulting in fulminant hepatitis, hepatic failure, and death.
  - Progressive multifocal leukoencephalopathy (PML) resulting in death.

APPENDIX D: General Information
- Do not administer IV push, IV bolus, or as a subcutaneous injection.
- While ofatumumab is no longer commercially available, it may be obtained for clinical use in patients with CLL.

References
1. Arzerra® Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; August 2016. Available at: https://www.novartis.us/sites/www.novartis.us/files/arzerra.pdf. Accessed July 29, 2022.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed July 29, 2022.
3. National Comprehensive Cancer Network. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Version 1. 2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cll.pdf . Accessed July 29, 2022.
4. National Comprehensive Cancer Network. Waldenstrom's Macroglobulinemia/Lymphoplasmacytic Lymphoma

Version 1.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/waldenstroms.pdf . Accessed July 29, 2022.
5. National Comprehensive Cancer Network. B-Cell Lymphomas Version 5.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf .Accessed July 29, 2022.
6. Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Available at: https://www.micromedexsolutions.com/micromedex2/librarian/CS/8A6852/PFActionId/pf.HomePage/ssl/true . Accessed July 29, 2022.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	1/2020	03/06/2020
Policy was reviewed: 1. Clinical policy title updated 2. Line of business policy applies to was updated to All lines of business 3. Continued Therapy criteria II.A.1 was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance..." 4. Appendix D added with general information. 5. Reference reviewed and updated.	09/23/2020	12/07/2020
Policy was reviewed: 1. Statement about provider sample ‘‘The provision of provider samples does not guarantee coverage…” was added to Clinical Policy 2. Statement about drug listing format in Appendix B is updated to "Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand, Brand name® when the drug is available by brand only and generic name when the drug is available by generic only". 3. References were reviewed and updated.	10/09/2021	12/07/2021
Policy was reviewed:	07/29/2022	10/19/2022

1. Initial Approval Criteria I.A.4: Updated to add If request is for use as first line therapy, one of the following (a or b): a. Prescribed in combination with bendamustine, and there is no del(17)/TP53 mutation; b. Prescribed in combination with chlorambucil, and fludarabine-based therapy is considered inappropriate; 2. References were reviewed and updated.		