RXADVANCE
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Clinical Policy Title:	ofatumumab
Policy Number:	RxA.585
Drug(s) Applied:	Arzerra®
Original Policy Date:	03/06/2020
Last Review Date:	12/07/2020
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.

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 hematologist;
3. Age 18 years of age or older;
4. 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 hematologist;
3. Age 18 years of age or older;
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 hematologist;
4. Age 18 years of age or older;
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 • Imbruvica® (ibrutinib) ± rituximab • 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 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.

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 September 23, 2020.
2. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed September 23, 2020.
3. National Comprehensive Cancer Network. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Version 4.2020. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cll.pdf. Accessed September 23, 2020.
4. National Comprehensive Cancer Network. Waldenstrom's Macroglobulinemia/Lymphoplasmacytic Lymphoma Version 1.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/waldenstroms.pdf. Accessed September 23, 2020.
5. National Comprehensive Cancer Network. B-Cell Lymphomas Version 4.2020. Available at: https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf . Accessed September 23, 2020.
6. Micromedex® Healthcare Series [Internet database]. Greenwood Village, Colo: Thomson Healthcare. Updated periodically. Accessed September 23, 2020

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