Medical Policy:

Arzerra® (ofatumumab) Intravenous

POLICY NUMBER	LAST REVIEW	ORIGIN DATE
MG.MM.PH.133	April 9, 2024	July 15, 2019

Definitions

Arzerra (ofatumumab): is a human IgG1-kappa monoclonal antibody that binds to the CD20 molecule on normal B lymphocytes and on B-cell chronic lymphocytic leukemia, resulting in B-cell lysis. The epitope which ofatumumab binds is different from the binding sites targeted by other CD20 antibodies that are currently available such as rituximab. Also, ofatumumab appears to have a slower off-rate and more stable CD20 binding as compared with rituximab. The slower off-rate and more stable binding may be responsible for ofatumumab's efficacy against cells with low CD20-antigen density and high expression of complement inhibitory molecules. In vitro, ofatumumab lyses rituximab-resistant Raji cells and CD20 low-expressing chronic lymphocytic leukemia cells in the presence of human plasma or unfractionated blood. Also, ofatumumab appears to be active against B- cell lymphoma/chronic lymphocytic leukemia cells with high expression of complement inhibitory molecules.

Length of Authorization

Coverage will be provided for 6 months and may be renewed.

Dosing Limits [Medical Benefit]

Max Units (per dose and over time) [Medical Benefit]:

- **CLL/SLL**
  1. First line
     a. 30 Billable units on day 1 and 100 billable units on day 8
     b. 100 Billable units every 28 days for up to 11 doses
  2. Single Agent Subsequent Therapy
     a. 30 Billable units on day 1; then
     b. 200 Billable units weekly x 7 doses; then
     c. 200 Billable units weekly every 28 days x 4 doses
  3. Relapsed
     a. 30 Billable units on day 1 and 100 billable units on day 8; then
     b. 100 Billable units every 28 days for up to 5 doses
  4. Extended Treatment
     a. 30 Billable units on day 1 and 100 billable units on day 8; then
     b. 100 Billable units 7 weeks later and every 8 weeks thereafter.
- **Waldenstrom's Macroglobulinemia**
     a. 30 Billable units on day 1; then
     b. 200 Billable units 7 weeks x 4 doses.

Guideline

I. Initial Approval Criteria

Arzerra *may be considered medically necessary if one of the below conditions are met* ***AND*** *use is consistent with the medical necessity criteria that follows:*

1. **Chronic Lymphocytic Leukemia (CLL)**
   A. As first line therapy in combination with chlorambucil or bendamustine in members who are unable to tolerate or has contraindications to fludarabine; **OR**
   B. As a single agent for members refractory to Fludara (fludarabine) AND Campath (alemtuzumab). *Refractoriness is defined as a failure to achieve at least a partial response, or disease progression during treatment or within 6 months of the last dose of at least 2 cycles of fludarabine and at least 12 doses of alemtuzumab;* **OR**
   C. In combination with fludarabine and cyclophosphamide for the treatment of patients with relapsed CLL ; **OR**
   D. For extended treatment of patients who are in complete or partial response after at least two lines of therapy for recurrent or progressive disease

2. **Waldenstrom's Macroglobulemia**
   A. Used as a single agent **OR** as part of combination therapy; **AND**
   B. Patient is intolerant to rituximab; **AND**
      i. Patient has previously failed primary therapy; **OR**
      ii. Patient has progressive or relapsed disease

Limitations/Exclusions

Arzerra (ofatumumab) is not considered medically necessary for when any of the following selection criteria is met:

1. Member has disease progression while taking Arzerra (ofatumumab).
2. Dosing exceeds single dose limit of Arzerra (ofatumumab) 2000 mg.
3. Treatment with Arzerra (ofatumumab) exceeds the maximum duration limit of 12 doses over 24 weeks for previously treated CLL or maximum 12 cycles for previously untreated CLL
4. Treatment with Arzerra (ofatumumab) exceeds the maximum duration limit of 2 years for extended treatment in CLL
5. Indications not supported by CMS recognized compendia or acceptable peer reviewed literature may be deemed as not approvable and therefore not reimbursable.

II. Renewal Criteria

1. Patient continues to meet criteria in Initial Approval Criteria; **AND**
2. Tumor response with stabilization of disease or decrease in size of tumor or tumor spread; **AND**
3. Absence of unacceptable toxicity from the drug. *Examples of unacceptable toxicity include the following: progressive multifocal leukoencephalopathy, severe infusion reactions, tumor lysis syndrome, cytopenias (neutropenia, anemia, and thrombocytopenia), etc.*

Dosage/Administration

Indication	Dose
CLL/SLL (First-line)	Administer 300 mg on Day 1, then 1,000 mg on Day 8, followed by 1,000 mg on Day 1 of subsequent 28-day cycles for a minimum of 3 cycles until best response or a maximum of 12 cycles
CLL/SLL (Single agent subsequent therapy	Administer 300 mg on Day 1, followed 1 week later by 2,000 mg given weekly x 7 doses (infusions 2 through 8), followed 4 weeks later by 2,000 mg every 4 weeks for 4 doses (infusions 9 through 12) for a total of 12 doses
CLL/SLL (Relapsed)	Administer 300 mg on Day 1, then 1,000 mg on Day 8, followed by 1,000 mg on Day 1 of subsequent 28-day cycles for a maximum of 6 cycles
CLL/SLL (Extended treatment)	Administer 300 mg on Day 1, then 1,000 mg on Day 8, followed by 1,000 mg 7 weeks later and every 8 weeks thereafter for up to a maximum of 2 years
Waldenström's/ Lymphoplasmacytic lymphoma	Cycle 1: • Administer 300 mg on day 1, then 1,000 mg weekly for weeks 2 through 4; OR • Administer 300 mg on day 1, then 2,000 mg weekly for weeks 2 through 5 Cycle 2-3: • Patients with stable disease or a minor response at week 16 of cycle 1 are eligible to receive a re-dosing cycle of 300 mg on day 1, then 2,000 mg for weeks 2 through 5. • Patients responding to cycle 1 or the redosing cycle who developed disease progression within 36 months can receive treatment with 300 mg on day 1, then 2,000 mg for weeks 2 through 5.

Applicable Procedure Codes

Code	Description
J9302	Injection, ofatumumab, 10 mg, 1 billable unit = 10 mg

Applicable NDCs

Code	Description
00078-0690-xx	Arzerra 1000 mg/50 ml single use vial
00078-0669-xx	Arzerra 100 mg/5 ml single use vial

ICD-10 Diagnoses

Code	Description
C83.00	Small cell B-cell lymphoma, unspecified site
C83.01	Small cell B-cell lymphoma, lymph nodes of head, face and neck
C83.02	Small cell B-cell lymphoma, intrathoracic lymph nodes
C83.03	Small cell B-cell lymphoma, intra-abdominal lymph nodes
C83.04	Small cell B-cell lymphoma, lymph nodes of axilla and upper limb
C83.05	Small cell B-cell lymphoma, lymph nodes of inguinal region and lower limb
C83.06	Small cell B-cell lymphoma, intrapelvic lymph nodes
C83.07	Small cell B-cell lymphoma, spleen
C83.08	Small cell B-cell lymphoma, lymph nodes of multiple sites
C83.09	Small cell B-cell lymphoma, extranodal and solid organ sites
C88.0	Waldenström macroglobulinemia
C91.10	Chronic lymphocytic leukemia of B-cell type not having achieved remission
C91.12	Chronic lymphocytic leukemia of B-cell type in relapse

Revision History

Company(ies)	DATE	REVISION
EmblemHealth & ConnectiCare	4/9/2024	Annual Review: Updated dosing limits, Initial Criteria: Chronic Lymphocytic Leukemia (CLL) Removed: "The member has stage III-IV CLL, or if Stage 0-II disease, member must have bulky adenopathy, splenomegaly, OR systemic symptoms AND"
EmblemHealth & ConnectiCare	8/1/2023	Annual Review: Chronic Lymphocytic Leukemia (CLL): Initial Criteria: Removed "Maintenance therapy as second-line extended dosing following complete or partial response to relapsed or refractory therapy." Added "in combination with fludarabine and cyclophosphamide for the treatment of patients with relapsed CLL ; **OR** for extended treatment of patients who are in complete or partial response after at least two lines of therapy for recurrent or progressive disease" Waldenstrom's Macroglobulemia: Initial Criteria: Removed "Given as a single agent salvage therapy to Rituxan – intolerant patients who don't respond to primary therapy." Added "Used as a single agent **OR** as part of combination therapy; AND C. Patient is intolerant to rituximab; **AND** iii. Patient has previously failed primary therapy; **OR** iv. Patient has progressive or relapsed disease" Updated dosing chart Removed ICD-10 Codes: Z85.72 Z85.79

EmblemHealth & ConnectiCare	3/23/2022	Transferred policy to new template
EmblemHealth & ConnectiCare	7/15/2019	Annual review – no changes

References

1. Arzerra prescribing information. GSK, Research Triangle Park, NC. 2016.
2. Clinical Pharmacology Elsevier Gold Standard. 2018.
3. Micromedex® Healthcare Series: Thomson Micromedex, Greenwood Village, Co. 2018.
4. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium.2018
5. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD. 2018.