Ofatumumab (Arzerra®)

NDC CODE(S) 00078-0669-XX ARZERRA 20MG/ML Solution (NOVARTIS)
00078-0690-XX ARZERRA 20MG/ML Solution (NOVARTIS)

DESCRIPTION

Ofatumumab is an IgG1κ human monoclonal antibody which binds specifically to the CD20 molecule. The CD20 molecule is expressed on the surface of B lymphocytes, both of normal cells and on those of B-cell chronic lymphocytic leukemia. After binding with ofatumumab, the CD20 molecule remains on the B-cell surface resulting in cell lysis and destruction of the diseased and normal B-cells. While the exact cause of cell lysis is not known, complement-dependent cytotoxicity and antibody-dependent, cell mediated cytotoxicity are likely mechanisms.

POLICY

- Ofatumumab for the treatment of the following is considered ***medically necessary*** if the medical appropriateness criteria are met. **(See Medical Appropriateness below.)**
  - B Cell Lymphomas
  - Chronic lymphocytic leukemia /Small Lymphocytic Lymphoma (CLL/SLL)
  - Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma
- Ofatumumab for the treatment of other conditions/diseases is considered ***investigational.***

MEDICAL APPROPRIATENESS

INITIAL APPROVAL CRITERIA

- Patient is at least 18 years old; **AND**

Universal Criteria

- Patient must be screened for HBV infection (i.e., HBsAg and anti-HBc) prior to initiating therapy; **AND**
- Must not be administered concurrently with live vaccines; **AND**

Chronic Lymphocytic Leukemia (CLL)/Small Lymphocytic Lymphoma (SLL)

- Used as first-line therapy in combination with chlorambucil; **OR**
- Used as first-line therapy in combination with bendamustine; **AND**
  - Patient does not have del(17p)/TP53 mutation; **AND**
  - Patient is not considered to be frail with significant comorbidities; **OR**
- Used for relapsed or refractory disease; **AND**
  - Used as a single agent; **OR**
  - Used in combination with fludarabine and cyclophosphamide (FC); **OR**
- Used as extended treatment in patients with complete or partial response after 2 or more lines of therapy; **AND**
  - Used as a single agent

B-Cell Lymphomas

- Used as a substitute for rituximab or obinutuzumab in patients experiencing rare complications such as mucocutaneous reactions including paraneoplastic pemphigus, Stevens-Johnson syndrome, lichenoid dermatitis, vesiculobullous dermatitis, and toxic epidermal necrolysis; **AND**
- Patient has any of the following:
  - Follicular Lymphoma (low grade 1-2)
  - MALT Lymphoma (Gastric or Non-Gastric)
  - Marginal Zone Lymphoma (Splenic or Nodal)
  - Diffuse Large B-Cell Lymphoma (DLBCL)
  - Histologic Transformation of Nodal Marginal Zone Lymphoma to DLBCL
  - Mantle Cell Lymphoma
  - High Grade B-Cell Lymphomas
  - Burkitt Lymphoma
  - AIDS Related B Cell Lymphomas
  - Post-Transplant Lymphoproliferative Disorders
  - Castleman's Disease

Waldenström's Macroglobulinemia/Lymphoplasmacytic Lymphoma

- Used as a single agent OR as part of combination therapy; **AND**
- Patient is intolerant to rituximab; **AND**
  - Patient has previously failed primary therapy; OR
  - Patient has progressive or relapsed disease

RENEWAL CRITERIA

- Patient continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in the Initial Approval Criteria; **AND**
- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: Hepatitis B virus reactivation/infection, progressive multifocal leukoencephalopathy, severe infusion reactions, tumor lysis syndrome, cytopenias (neutropenia, anemia, and thrombocytopenia), etc.

DOSAGE/ADMINISTRATION

INDICATION	DOSE
CLL/SLL (First-line)	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 (Refractory)	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)	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)	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
NHL	1,000 mg weekly for 4 doses, then 1,000 mg every 8 weeks for 4 doses
Waldenström's/ Lymphoplasmacytic lymphoma	**Cycle 1:** 300 mg on day 1, then 1,000 mg weekly for weeks 2 through 4; OR 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-treatment 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.

LENGTH OF AUTHORIZATION

Coverage will be provided for 6 months with renewal subject to the following:
- CLL/SLL (first-line) may be renewed to allow for a total of 12 cycles
- CLL/SLL (relapsed or refractory) may not be renewed (unless the provisions for extended treatment have been met)
- CLL/SLL (extended treatment) may be renewed to provide for a total of 2 years of therapy
- NHL/FL may be renewed to provide up to a total of 8 doses
- Waldenström's Macroglobulinemia/Lymphoplasmacytic lymphoma may be renewed to allow for up to a total of 3 cycles

DOSING LIMITS

Max Units (per dose and over time) [HCPCS Unit]:

CLL/SLL:
First-Line
- 30 billable units on day 1 and 100 billable units on day 8; then
- 100 billable units every 28 days for up to 11 doses

Refractory
- 30 billable units on day 1; then
- 200 billable units weekly x 7 doses; then
- 200 billable units every 28 days x 4 doses

Relapsed
- 30 billable units on day 1 and 100 billable units on day 8; then
- 100 billable units every 28 days for up to 5 doses

Extended Treatment
- 30 billable units on day 1 and 100 billable units on day 8; then
- 100 billable units 7 weeks later and every 8 weeks thereafter

NHL/FL
- 100 billable units every 7 days x 4 doses
- 100 billable units every 8 weeks thereafter

Waldenström's Macroglobulinemia / Lymphoplasmacytic Lymphoma
- 30 billable units on day 1; then
- 200 billable units every 7 days x 4 doses

APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

BlueCross BlueShield of Tennessee's Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

IMPORTANT REMINDER

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the Medical Policy and a health plan, the express terms of the health plan will govern.

ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

SOURCES

1. Arzerra [package insert]. East Hanover, NJ; Novartis Pharmaceuticals Corporation, August 2016. Accessed February 2021.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) ofatumumab. National Comprehensive Cancer Network, 2021. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed February 2021.
3. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma. Version 2.2021. National Comprehensive Cancer Network, 2021. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed February 2021.
4. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) Waldenström's Macroglobulinemia/Lymphoplasmacytic Lymphoma. Version 1.2021. National Comprehensive Cancer Network, 2021. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed February 2021.
5. Furman RR, Eradat H, DiRienzo CG, et al. A phase II trial of ofatumumab in subjects with Waldenström's macroglobulinemia. Blood. 2011;118:3701
6. Wierda WG, Kipps TJ, Mayer J, et al. Ofatumumab as single-agent CD20 immunotherapy in fludarabine-refractory chronic lymphocytic leukemia. J Clin Oncol 2010;28:1749-1755
7. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) B-Cell Lymphomas. Version 2.2021. National Comprehensive Cancer Network, 2021. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed February 2021.
8. Rosenbaum CA, Jung SH, Pitcher B, et al. Phase 2 multicentre study of single-agent ofatumumab in previously untreated follicular lymphoma: CALGB 50901 (Alliance). Br J Haematol. 2019 Feb 5.

9. Van Imhoff GW, McMillan A, Matasar MJ et al. Ofatumumab Versus Rituximab Salvage Chemoimmunotherapy in Relapsed or Refractory Diffuse Large B-Cell Lymphoma: The ORCHARRD Study. J Clin Oncol 2017;35 (5):544-551.
10. Furman RR, Eradat HA, DiRienzo CG, et al. Once-weekly ofatumumab in untreated or relapsed Waldenström's macroglobulinaemia: an open-label, single-arm, phase 2 study. Lancet Haematol. 2017 Jan;4(1):e24-e34. doi: 10.1016/S2352-3026(16)30166-1. Epub 2016 Dec 1.
11. Hillmen P, Robak T, Janssens A, et al. Chlorambucil plus ofatumumab versus chlorambucil alone in previously untreated patients with chronic lymphocytic leukaemia (COMPLEMENT 1): a randomised, multicentre, open-label phase 3 trial. Lancet. 2015 May 9;385(9980):1873-83. doi: 10.1016/S0140-6736(15)60027-7. Epub 2015 Apr 14.
12. Robak T, Warzocha K, Govind Babu K, et al. Ofatumumab plus fludarabine and cyclophosphamide in relapsed chronic lymphocytic leukemia: results from the COMPLEMENT 2 trial. Leuk Lymphoma. 2017 May;58(5):1084-1093. doi: 10.1080/10428194.2016.1233536. Epub 2016 Oct 12.
13. van Oers MH, Kuliczkowski K, Smolej L, et al. Ofatumumab maintenance versus observation in relapsed chronic lymphocytic leukaemia (PROLONG): an open-label, multicentre, randomised phase 3 study. Lancet Oncol. 2015 Oct;16(13):1370-9. doi: 10.1016/S1470-2045(15)00143-6. Epub 2015 Sep 13.
14. Lemery SJ, Zhang J, Rothmann MD, et al. U.S. Food and Drug Administration Approval: Ofatumumab for the Treatment of Patients with Chronic Lymphocytic Leukemia Refractory to Fludarabine and Alemtuzumab. 10.1158/1078-0432.CCR-10-0570 Published September 2010.
15. Lexi-Comp Online. (2021, February). AHFS DI. *Ofatumumab*. Retrieved April 13, 2021 from Lexi-Comp Online with AHFS.
16. MICROMEDEX Healthcare Series. Drugdex Drug Evaluations. (2021, March). *Ofatumumab*. April 13, 2021 from MICROMEDEX Healthcare Series.

EFFECTIVE DATE 8/31/2021

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