Clinical Policy: Ofatumumab (Arzerra)

Reference Number: CP.PHAR.306
Effective Date: 02/17
Last Review Date: 02/17

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
The intent of the criteria is to ensure that patients follow selection elements established by Centene® clinical policy for ofatumumab (Arzerra®).

Policy/Criteria
It is the policy of health plans affiliated with Centene Corporation® 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. Meets a or b:
   a. FDA-approved use, one of the following:
      i. Untreated CLL/SLL: In combination with chlorambucil when fludarabine-based therapy is considered inappropriate;
      ii. Relapsed CLL/SLL: In combination with fludarabine and cyclophosphamide;
      iii. Recurrent or progressive CLL/SLL: If complete/partial response has been achieved after ≥ 2 lines of therapy;
      iv. CLL/SLL refractory to fludarabine and alemtuzumab;
   b. Off-label NCCN recommended use, one of the following:
      i. Untreated CLL/SLL:
         a) Without del(17p)/TP53 mutation: First-line therapy in combination with chlorambucil in any of the following:
            1) Older patients (e.g., age ≥ 65 years);
            2) Younger patients (e.g., age < 65 years) with significant comorbidities;
            3) Frail patients unable to tolerate purine analogs (e.g., fludarabine);
      ii. Relapsed or refractory CLL/SLL:
         a) With or without del(17p)/TP53 mutation: as a single agent;
         b) Without del(17p)/TP53 mutation: in combination with FC (fludarabine, cyclophosphamide) in younger patients (e.g., age < 65 years) without significant comorbidities.

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

Approval duration: 3 months

B. Other diagnoses/indications: Refer to CP.PHAR.57 – Global Biopharm Policy.

1. The following off-label NCCN recommended uses for Arzerra, meeting NCCN categories 1, 2a, or 2b, are approved per the CP.PHAR.57 Global Biopharm Policy:
   a. Waldenstrom's macroglobulinemia/lymphoplasmacytic lymphoma.

II. Continued Approval

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

1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Member has none of the following reasons to discontinue:
   a. Disease progression or unacceptable toxicity;
   b. Anaphylactic reaction to Arzerra;
   c. Progressive multifocal leukoencephalopathy;
   d. Hepatitis B virus reactivation.

Approval duration: 6 months

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

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy; or
2. Refer to CP.PHAR.57 - Global Biopharm Policy.

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.

FDA Approved Indications:
Arzerra (ofatumumab) is a CD20-directed cytotoxic monoclonal antibody/intravenous formulation indicated:

- in combination with chlorambucil, for the treatment of previously untreated patients with 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.

Appendices
Appendix A: Abbreviation Key
CLL: Chronic lymphocytic leukemia
SLL: Small lymphocytic lymphoma

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.

HCPCS Codes	Description
J9999	Not otherwise classified, antineoplastic drug

Reviews, Revisions, and Approvals	Date	Approval Date
Policy split from CP.PHAR.182.Excellus Oncology.	01/17	02/17

References
1. Arzerra prescribing information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; August 2016. Available at www.arzerra.com. Accessed November 4, 2016.
2. Ofatumumab. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.NCCN.org. Accessed November 4, 2016.
3. Chronic lymphocytic leukemia/small lymphocytic lymphoma (Version 1.2017). In: National Comprehensive Cancer Network Guidelines. Available at NCCN.org. Accessed January 4, 2017.

of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

Note: For Medicare members, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs and LCDs should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at http://www.cms.gov for additional information.