Clinical Policy: Ofatumumab (Arzerra)

Reference Number: CP.PHAR.306
Effective Date: 02.01.17
Last Review Date: 11.17
Line of Business: Medicaid

Coding Implications
Revision Log

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

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

FDA Approved Indication(s)
Arzerra 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

Policy/Criteria
Provider must submit documentation (which may include office chart notes and lab results) supporting that member has met all approval 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 CLL or small lymphocytic lymphoma (SLL);
2. Meets a or b:
   a. FDA-approved use, one of the following (i, ii, iii, or iv):
      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 or ii):
      i. Untreated CLL/SLL:

a) Without del(17p)/TP53 mutation: First-line therapy in any of the following:
1) Older patients (e.g., age ≥ 65 years) in combination with chlorambucil or bendamustine;
2) Younger patients (e.g., age < 65 years) (i or ii):
i. With significant comorbidities (*see Appendix B)*: with chlorambucil or bendamustine
ii. Without significant comorbidities: with bendamustine;
3) Frail patients unable to tolerate purine analogs (e.g., fludarabine);

ii. Relapsed or refractory CLL/SLL (a or b):
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 (i.e., age < 65 years) without significant comorbidities;

3. Request meets one of the following (a or b):
a. Dose does not exceed the maximum indicated in section V;
b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 6 months

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

B. Waldenstrom's Macroglobulinemia/Lymphoplasmacytic Lymphoma (off-label) (must meet all)**:**
1. Diagnosis of Waldenstrom's macroglobulinemia/lymphoplasmacytic lymphoma;
2. Member is rituximab-intolerant;
3. Disease is progressive, relapsed, or unresponsive to primary therapy;
4. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 6 months

C. Other diagnoses/indications
1. Refer to CP.PHAR.57 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**
1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy (e.g., no disease progression, no significant toxicity);
3. If request is for a dose increase, request meets one of the following (a or b):
a. For CLL/SLL only: New dose does not exceed the maximum indicated in section V;

b. For any indication: New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration: 12 months

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

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to CP.PHAR.57 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – CP.PHAR.57 evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CLL: chronic lymphocytic leukemia
FDA: Food and Drug Administration
NCCN: National Comprehensive Cancer Network
SLL: small lymphocytic lymphoma

Appendix B: General Information

- Cumulative Illness Rating Scale (CIRS), Charlson Comobidity Index, and the NCI Comorbidity Index are some of the scoring systems that can be used to assess comorbidities in patients with CLL. In these systems, the higher scores indicate greater comorbidity. Currently, there are no CIRS-based cutoffs for the ill-ness severity and comorbidity indices.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
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	2 years

	and every 8 weeks thereafter for up to a maximum of 2 years	
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	Refer to dosing regimen

VI. Product Availability

Vial, single-use for intravenous infusion: 100 mg/5 mL, 1,000 mg/50 mL

VII. References

1. Arzerra prescribing information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; August 2016. Available at www.arzerra.com. Accessed August 30, 2017.
2. Ofatumumab. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at www.NCCN.org. Accessed August 30, 2017.
3. Chronic lymphocytic leukemia/small lymphocytic lymphoma (Version 1.2018). In: National Comprehensive Cancer Network Guidelines. Available at NCCN.org. Accessed August 30, 2017.
4. Salvi F, Miller MD, Grilli A, et al. A manual of guidelines to score the modified cumulative illness rating scale and its validation in acute hospitalized elderly patients. J Am Geriatr Soc 2008; 56:1926-1931.

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
J9302	Injection, ofatumumab 100 mg/5 mL

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy split from CP.PHAR.182.Excellus Oncology.	01.17	02.17
Policy converted to new template. Annual Review. Safety criteria was applied according to the safety guidance discussed at CPAC and endorsed by Centene Medical Affairs. Added criteria for NCCN 2A rating and above recommended off-label use: Waldenstrom's macroglobulinemia/lymphoplasmacytic lymphoma. Authorization limits extended from 3 and 6 months to 6 and 12 months for initial and continued approval, respectively.	08.30.17	11.17

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence 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.

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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.