Medical Drug Clinical Criteria

Subject:	Arzerra (ofatumumab)		
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Overview

This document addresses the use of Arzerra (ofatumumab). Arzerra is a monoclonal antibody directed against the surface antigen CD20 and is used to treat chronic lymphocytic leukemia (CLL). Ofatumumab is also available as Kesimpta, a subcutaneous injection approved by the FDA for relapsing multiple sclerosis. Kesimpta is addressed in a separate clinical criteria (ING-CC-0174).

The FDA approved indications for Arzerra in CLL include as a first line agent in combination with chlorambucil for treatment of previously untreated patients for whom fludarabine-based therapy is considered inappropriate. It is also approved in combination with fludarabine and cyclophosphamide for patients with relapsed disease, or as a single agent for those refractory to fludarabine and alemtuzumab. Arzerra is also approved as extended therapy. For extended therapy, Arzerra was studied as a maintenance treatment for 24 months in patients who were in complete or partial response after at least 2 lines of prior therapy. Chronic lymphocytic leukemia (CLL) and small lymphocytic lymphoma (SLL) are different manifestations of the same disease and are managed in much the same way.

Other Uses

The National Comprehensive Cancer Network® (NCCN) provides additional recommendations with a category 2A level of evidence for the use of Arzerra. These include the use in CLL/SLL as a first line therapy in combination with bendamustine; however, supportive text indicates this recommendation comes from one non-comparative phase 2 study (Flinn 2016). In 2023, NCCN no longer recommend these addtional uses in B-cell Lymphomas and CLL/SLL.

NCCN also recommends the use of Arzerra in Waldenström's Macroglobulinemia/Lymphoplasmacytic Lymphoma in those intolerant to rituximab, supported by an open-label, single arm phase 2 study. NCCN also lists a 2A recommendation for Arzerra as a substitute for rituximab in patients experiencing rare mucocutaneous reactions; however, it is unclear if the use of an alternative anti-CD20 antibody poses the same risk of recurrence (B-cell Lymphomas Guideline).

Arzerra (ofatumumab) has a black box warning for hepatitis B reactivation which, in some cases, results in fulminant hepatitis, hepatic failure, and death. Arzerra also has a black box warning for progressive multifocal leukoencephalopathy which can occur in patients receiving CD20-directed antibodies, including Arzerra.

Definitions and Measures

Complete Response (CR): The disappearance of all signs of cancer as a result of treatment; also called complete remission; does not indicate the cancer has been cured.

Line of Therapy:

- First-line therapy: The first or primary treatment for the diagnosis, which may include surgery, chemotherapy, radiation therapy or a combination of these therapies.
- Second-line therapy: Treatment given when initial treatment (first-line therapy) is not effective or there is disease progression.
- Third-line therapy: Treatment given when both initial (first-line therapy) and subsequent treatment (second-line therapy) are not effective or there is disease progression.

Maintenance therapy: Designed to maintain a condition to prevent a relapse.

One line of therapy: Single line of therapy.

Partial response (PR): A decrease in the size of a tumor, or in the amount of cancer in the body, resulting from treatment; also called partial remission.

Progressive Disease (PD): Cancer that is growing, spreading, or getting worse.

Refractory Disease: Illness or disease that does not respond to treatment.

Relapse or recurrence: After a period of improvement, during which time a disease (for example, cancer) could not be detected, the return of signs and symptoms of illness or disease. For cancer, it may come back to the same place as the original (primary) tumor or to another place in the body.

Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Arzerra (ofatumumab)

Requests for Arzerra (ofatumumab) may be approved if the following criteria are met:

I. Individual has a diagnosis of chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) (Label; NCCN 2A); **AND**
II. Individual is using for one of the following:
    A. As first line therapy in combination with chlorambucil; **OR**
    B. Treatment of relapsed or refractory CLL/SLL, as a single agent and only in one line of therapy, *or* in combination with fludarabine and cyclophosphamide;
    OR
    C. As maintenance treatment for up to 24 months when the following criteria are met:
        1. Treatment is following at least 2 lines of therapy for relapsed or progressive disease; **AND**
        2. A complete or partial response has been achieved.

Requests for Arzerra (ofatumumab) may not be approved for the following:

I. Treatment of Waldenström's macroglobulinemia/lymphoplasmacytic lymphoma; **OR**
II. Treatment of multiple sclerosis; **OR**
III. All other indications, not included above.

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS

J9302	Injection, ofatumumab, 10 mg [Arzerra]

ICD-10 Diagnosis

C83.00-C83.09	Small cell B-cell lymphoma [specified as small lymphocytic lymphoma]
C91.10-C91.12	Chronic lymphocytic leukemia of B-cell type

Document History

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Document History:

- 02/24/2023 – Annual Review: No changes. Coding Reviewed: No changes.
- 02/25/2022 – Annual Review: Update references. Minor wording and formatting criteria updates. Coding Reviewed: No changes.
- 02/19/2021 – Annual Review: Update may not be approved section to include multiple sclerosis. Coding Reviewed: No changes.
- 02/21/2020 – Annual Review: No changes. Coding reviewed: No changes.
- 05/17/2019– Annual Review: First review of Arzerra clinical criteria. Wording and formatting updates. Add criteria for use with fludarabine and cyclophosphamide for relapse or refractory disease. Coding Reviewed: No changes.

References

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5. Furman RR, eradat H, Switzky JC, et al. A phase 2 trial of ofatumumab in subjects with Waldenstrom's macroglobulinemia [abstract]. Blood 2010; 116: Abstract 1795.
6. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2022; Updated periodically.
7. NCCN Clinical Practice Guidelines in Oncology™. © 2019 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: http://www.nccn.org/index.asp. Accessed on December 29, 2022.
    a. Waldenstr̈om Macroglobulinemia/Lymphoplasmacytic Lympoma. V1.2023. Revised July 6, 2022.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.