Clinical Policy: Ofatumumab (Arzerra)
Reference Number: PA.CP.PHAR.306
Effective Date: 01/18
Last Review Date: 10/30/2019

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

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
It is the policy of Pennsylvania Health and Wellness ® 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. Prescribed by or in consultation with an oncologist or hematologist;
      3. Request meets one of the following (a or b):
         a. Dose does not exceed the maximum indicated in section IV;
         b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

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

   Approval duration: 6 months

   B. Waldenstrom’s Macroglobulinemia/Lymphoplasmacytic Lymphoma (off-label)
      (must meet all):
      1. Diagnosis of Waldenstrom’s macroglobulinemia/lymphoplasmacytic lymphoma (WM/LPL);
      2. Prescribed by or in consultation with an oncologist or hematologist;
      3. Member is rituximab-intolerant;
      4. Disease is progressive, relapsed, or unresponsive to primary therapy (see Appendix B for examples);
      5. Request meets one of the following (a or b):
a. Dose does not exceed the maximum indicated in section IV;
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

C. Other diagnoses/indications: Refer to PA.CP.PMN.53

II. Continued Approval
A. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (must meet all):
   1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
   2. Member is responding positively to therapy;
   3. If request is for a dose increase, request meets one of the following (a or b):
      a. New dose does not exceed the maximum indicated in section IV;
      b. 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 Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies; or
   2. Refer to PA.CP.PMN.53

III. 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
WM/LPL: Waldenstrom’s macroglobulinemia/lymphoplasmacytic lymphoma

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

<table>
<thead>
<tr>
<th>Examples of Primary Therapy for WM/LPL</th>
<th>Dosing Regimen</th>
<th>Dose Limit/Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treanda®, Bendeka® (bendamustine)/Rituxan® (rituximab)</td>
<td>Varies</td>
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</tr>
<tr>
<td>bortezomib (Velcade®)/dexamethasone/ Rituxan® (rituximab)</td>
<td>Varies</td>
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Examples of Primary Therapy for WM/LPL | Dosing Regimen | Dose Limit/Maximum Dose
---|---|---
Rituxan® (rituximab)/cyclophosphamide/dexamethasone | Varies | Varies

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/BoxedWarnings
- Contraindication(s): none
- Boxed warning(s): hepatitis B virus reactivation and progressive multifocal leukoencephalopathy

IV. Dosage and Administration

<table>
<thead>
<tr>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
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<tr>
<td>Previously untreated CLL</td>
<td>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</td>
<td>12 cycles</td>
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<td>Relapsed CLL</td>
<td>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</td>
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<td>Extended treatment in CLL</td>
<td>300 mg on Day 1 followed by 1,000 mg 1 week later on Day 8, followed by 1,000 mg 7 weeks later and every 8 weeks thereafter for up to a maximum of 2 years</td>
<td>2 years</td>
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<tr>
<td>Refractory CLL</td>
<td>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</td>
<td>Refer to dosing regimen</td>
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V. Product Availability
Vial, single-use for intravenous infusion: 100 mg/5 mL, 1,000 mg/50 mL

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.

Appendices

Appendix A: Abbreviation/Acronym Key

CLL: chronic lymphocytic leukemia  
SLL: small lymphocytic lymphoma

FDA: Food and Drug Administration  
WM/LPL: Waldenstrom’s macroglobulinemia/lymphoplasmacytic lymphoma

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Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): none
- Boxed warning(s): hepatitis B virus reactivation and progressive multifocal leukoencephalopathy

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.

<table>
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<th>HCPCS Codes</th>
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<tr>
<td>J9999</td>
<td>Not otherwise classified, antineoplastic drug</td>
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CLINICAL POLICY
Ofatumumab

Reviews, Revisions, and Approvals

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<tr>
<td>4Q 2018 annual review: no significant changes; summarized NCCN and FDA-approved uses for improved clarity; added specialist involvement in care; updated</td>
<td>07/18</td>
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<tr>
<td>4Q 2019 annual review: No changes per Statewide PDL implementation</td>
<td>10/30/19</td>
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References