Clinical Policy: Ofatumumab (Arzerra, Kesimpta)

Reference Number: ERX.SPA.265
Effective Date: 12.01.18
Last Review Date: 05.22
Line of Business: Commercial, Medicaid

Revision Log

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

Description
Ofatumumab (Arzerra®, Kesimpta®) 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

Kesimpta is indicated for the treatment of relapsing forms of multiple sclerosis (MS), to include clinically isolated syndrome, relapsing-remitting disease, and active secondary progressive disease, in adults.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Arzerra and Kesimpta are **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. Request is for Arzerra;
3. Prescribed by or in consultation with an oncologist or hematologist;
4. Age ≥ 18 years;
5. If request is for use as first line therapy, one of the following (a or b):
   a. Prescribed in combination with bendamustine, and there is no del(17)/TP53 mutation;
   b. Prescribed in combination with chlorambucil, and fludarabine-based therapy is considered inappropriate;
6. 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*).

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

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. Request is for Arzerra;
3. Prescribed by or in consultation with an oncologist or hematologist;
4. Age ≥ 18 years;
5. Member is rituximab-intolerant;
6. Request is for second-line or subsequent therapy (*see Appendix B for examples of prior therapy*);
7. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).*
   **Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration: 6 months

C. B-Cell Lymphomas (off-label) (must meet all)**:**

1. Diagnosis of one of the following B-cell lymphoma subtypes (a-j):
   a. Follicular lymphoma;
   b. Marginal zone lymphoma (i, ii, iii, or iv):
      i. Splenic marginal zone lymphoma;
      ii. Gastric MALT lymphoma;
      iii. Nongastric MALT lymphoma;
      iv. Nodal marginal zone lymphoma;
   c. Histologic transformation of nodal marginal zone lymphoma to diffuse large B-cell lymphoma;
   d. Diffuse large B-cell lymphoma;
   e. High-grade B-cell lymphoma;
   f. Mantle cell lymphoma;
   g. Castleman disease;
   h. Post-transplant lymphoproliferative disorder;
   i. AIDS-related B-cell lymphoma;
   j. Burkitt lymphoma;
2. Request is for Arzerra;
3. Prescribed by or in consultation with an oncologist or hematologist;
4. Age ≥ 18 years;
5. Used as a substitute* for rituximab or Gazyva® (obinutuzumab) in members with intolerance or experiencing rare complications such as mucocutaneous reactions including paraneoplastic pemphigus, Stevens-Johnson syndrome, lichenoid dermatitis, vesiculobullous dermatitis, and toxic epidermal necrolysis;
   **Caution per NCCN Compendium, re-challenge with the same anti-CD20 monoclonal antibody is not recommended and it is unclear if the use of an alternative anti-CD20 monoclonal antibody poses the same risk of recurrence.*
6. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).*
   **Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration: 6 months

D. Multiple Sclerosis (must meet all)**:**

1. Diagnosis of one of the following (a, b, or c):
   a. Clinically isolated syndrome;
   b. Relapsing-remitting MS;
   c. Secondary progressive MS;
2. Request is for Kesimpta;
3. Prescribed by or in consultation with a neurologist;
4. Age ≥ 18 years;
5. Kesimpta is not prescribed concurrently with other disease modifying therapies for MS (*see Appendix D*);
6. Documentation of baseline number of relapses per year and expanded disability status scale (EDSS) score;

7. At the time of request, member does not have active hepatitis B infection (positive results for hepatitis B surface antigen and anti-hepatitis B virus tests);
8. Dose does not exceed the following:
   a. Initial dose: 20 mg, followed by 20 mg doses 1 and 2 weeks later;
   b. Maintenance dose: 20 mg every 4 weeks.

Approval duration: 6 months

E. Other diagnoses/indications

1. Refer to ERX.PA.01 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 Other Than Multiple Sclerosis (must meet all)**:**

1. Currently receiving Arzerra via a health plan affiliated with Envolve Pharmacy Solutions, or documentation supports that member is currently receiving Arzerra for a covered indication and has received this medication for at least 30 days;
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 V;
   b. New dose is supported by practice guideline or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration: 12 months

B. Multiple Sclerosis (must meet all)**:**

1. Currently receiving Kesimpta via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
2. Member meets one of the following (a or b):
   a. If member has received < 1 year of total treatment: Member is responding positively to therapy;
   b. If member has received ≥ 1 year of total treatment: Member meets one of the following (i, ii, iii, or iv):
      i. Member has not had an increase in the number of relapses per year compared to baseline;
      ii. Member has not had ≥ 2 new MRI-detected lesions;
      iii. Member has not had an increase in EDSS score from baseline;
      iv. Medical justification supports that member is responding positively to therapy;
3. Kesimpta is not prescribed concurrently with other disease modifying therapies for MS (*see Appendix D*);
4. If request is for a dose increase, new dose does not exceed 20 mg every 4 weeks.

Approval duration: first re-authorization: 6 months**; second and subsequent re-authorizations:** 12 months

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

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 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 – ERX.PA.01 or evidence of coverage documents;

B. Primary progressive MS.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CLL: chronic lymphocytic leukemia
FDA: Food and Drug Administration
EDSS: Expanded Disability Status Scale
MS: multiple sclerosis
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 and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
WM/LPL primary therapy examples: • bendamustine/rituximab • bortezomib (Velcade®)/dexamethasone/ rituximab • Imbruvica® (ibrutinib) ± rituximab • 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/Boxed Warnings

- Contraindication(s):
  - Arzerra: none reported
  - Kesimpta: active hepatitis B virus infection
- Boxed warning(s):
  - Arzerra: hepatitis B virus reactivation, progressive multifocal leukoencephalopathy
  - Kesimpta: none reported

Appendix D: General Information

- Disease-modifying therapies for MS are: glatiramer acetate (Copaxone®, Glatopa®), interferon beta-1a (Avonex®, Rebif®), interferon beta-1b (Betaseron®, Extavia®), peginterferon beta-1a (Plegridy®), dimethyl fumarate (Tecfidera®), diroximel fumarate (Vumerity®), monomethyl fumarate (Bafiertam™), fingolimod (Gilenya®, Tascenso ODT™), teriflunomide (Aubagio®), alemtuzumab (Lemtrada®), mitoxantrone (Novantrone®), natalizumab (Tysabri®), ocrelizumab (Ocrevus®), cladribine (Mavenclad®), siponimod (Mayzent®), ozanimod (Zeposia®), ponesimod (Ponvory™), and ofatumumab (Kesimpta®).

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Ofatumumab (Arzerra)	Previously untreated CLL	In combination with chlorambucil: 300 mg IV on Day 1 followed by 1,000 mg on Day 8 (Cycle 1). Then 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	12 cycles
	Relapsed CLL	In combination with fludarabine and cyclophosphamide: 300 mg IV on Day 1 followed by 1,000 mg on Day 8 (Cycle 1). Then 1,000 mg on Day 1 of subsequent 28-day cycles for a maximum of 6 cycles	6 cycles
	Extended treatment in CLL	300 mg IV on Day 1 followed by 1,000 mg 1 week later on Day 8, followed by 1,000 mg 7	2 years

Drug Name	Indication	Dosing Regimen	Maximum Dose
		weeks later and every 8 weeks thereafter for up to a maximum of 2 years	
	Refractory CLL	300 mg IV 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	12 doses
Ofatumumab (Kesimpta)	MS	20 mg SC at weeks 0, 1, and 2, followed by 20 mg SC monthly starting at week 4	20 mg

VI. Product Availability

Drug Name	Availability
Ofatumumab (Arzerra)	Single-use vials: 100 mg/5 mL, 1,000 mg/50 mL
Ofatumumab (Kesimpta)	Single-dose prefilled Sensoready pen and prefilled syringe: 20 mg/0.4 mL

VII. References

1. Arzerra Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; August 2016. Available at https://www.us.arzerra.com. Accessed February 7, 2022.
2. Kesimpta Prescribing Information. East Hanover, NJ: Novartis; August 2020. Available at: www.kesimpta.com. Accessed February 4, 2022.
3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. February 7, 2022.
4. National Comprehensive Cancer Network. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Version 2.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cll.pdf. Accessed February 7, 2022.
5. National Comprehensive Cancer Network. Waldenstrom's Macroglobulinemia/Lymphoplasmacytic Lymphoma Version 2.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/waldenstroms.pdf. Accessed February 7, 2022.
6. National Comprehensive Cancer Network. B-Cell Lymphomas Version 5.2021. Available at: https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed February 7, 2022.
7. Rae-Grant A, Day GS, Marrie RA, et al. Practice guideline: disease-modifying therapies for adults with multiple sclerosis – report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. Neurology. 2018;90(17):777-88.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	07.11.18	11.18
4Q 2019 annual review: NCCN recommendations for B-cell lymphomas added; FDA/NCCN dosing limitation added; 12 doses added as maximum per PI for refractory CLL; Arzerra use in WM/LPL restated as second-line or subsequent therapy; references reviewed and updated.	08.27.19	11.19
4Q 2020 annual review: no significant changes; references reviewed and updated.	08.11.20	11.20
RT2: added new subcutaneous dosage form Kesimpta to the policy for the treatment of multiple sclerosis; added primary progressive MS as a diagnosis not covered.	10.06.20	02.21
2Q 2021 annual review: CLL/SLL- added specific requirements if request is for use as first-line therapy per NCCN and FDA; MS: removed re-directions per current formulary status; references reviewed and updated.	02.08.21	05.21
2Q 2022 annual review: no significant changes; clarified B-cell lymphoma criteria per NCCN recommendations; references reviewed and updated.	02.07.22	05.22

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.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. 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.