Clinical Policy: Ofatumumab (Arzerra, Kesimpta)

Reference Number: CP.PHAR.306
Effective Date: 02.01.17
Last Review Date: 11.23
Line of Business: Commercial, HIM, Medicaid

Coding Implications
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.

It is the policy of health plans affiliated with Centene Corporation® that Arzerra and Kesimpta are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Chronic Lymphocytic Leukemia (must meet all)**:**

1. Diagnosis of CLL;
2. Request is for Arzerra;
3. Prescribed by or in consultation with an oncologist or hematologist;
4. Age ≥ 18 years;
5. One of the following (a, b, c, or d):
   a. Both of the following (i and ii):
      i. Prescribed as first-line therapy in combination with chlorambucil;
      ii. Fludarabine-based therapy is considered inappropriate;
   b. Prescribed in combination with fludarabine and cyclophosphamide for relapsed disease;

c. Member is in complete or partial response after at least two lines of therapy for recurrent or progressive disease;
d. Disease is refractory to fludarabine and alemtuzumab;

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:
Medicaid/HIM – 6 months
Commercial – 6 months or to the member's renewal date, whichever is longer

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:
Medicaid/HIM – 6 months
Commercial – 6 months or to the member's renewal date, whichever is longer

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

**The criteria below do not apply to Arizona Complete Health Medicaid (AzCH-CCP) line of business. Please refer to AZ.CP.PHAR.1020 for multiple sclerosis requests for AzCH-CCP members.*

1. Diagnosis of one of the following (a, b, or c):
   a. Clinically isolated syndrome, and member is contraindicated to both, or has experienced clinically significant adverse effects to one, of the following at up to maximally indicated doses: an **interferon-beta agent** (Avonex®, Betaseron®/Extavia®†, Rebif®, or Plegridy®), **glatiramer** (Copaxone®, Glatopa®);
   b. Relapsing-remitting MS, and failure of all of the following at up to maximally indicated doses, unless clinically significant adverse effects are experienced or all are contraindicated (i, ii, iii, and iv):*
      i. **Dimethyl fumarate** (generic Tecfidera®);
      ii. **Teriflunomide** (generic Aubagio®);
      iii. **Fingolimod** (Gilenya®);
      iv. An **interferon-beta agent** (Avonex, Betaseron/Extavia†, Rebif, or Plegridy) or **glatiramer** (Copaxone, Glatopa);

**Prior authorization may be required for all disease modifying therapies for MS*

†Betaseron is preferred for the Commercial and HIM lines of business; Extavia is preferred for the Medicaid line of business

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 both 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:
Medicaid/HIM – 6 months
Commercial – 6 months or to the member's renewal date, whichever is longer

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I Other Than Multiple Sclerosis (must meet all)**:**

1. Currently receiving Arzerra via Centene benefit, 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 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:
Medicaid/HIM – 12 months
Commercial – 6 months or to the member's renewal date, whichever is longer

B. Multiple Sclerosis (must meet all)**:***
**The criteria below do not apply to Arizona Complete Health Medicaid (AzCH-CCP) line of business. Please refer to AZ.CP.PHAR.1020 for multiple sclerosis requests for AzCH-CCP members.*

1. Member meets one of the following (a or b):
   a. Currently receiving Kesimpta via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B)*;
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:
Medicaid/HIM –
If member has received < 1 year of total treatment – up to a total of 12 months of treatment
If member has received ≥ 1 year of total treatment – 12 months
Commercial – 6 months or to the member's renewal date, whichever is longer

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

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

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 policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents;

B. Primary progressive MS.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CLL: chronic lymphocytic leukemia
EDSS: Expanded Disability Status Scale
FDA: Food and Drug Administration
MS: multiple sclerosis
NCCN: National Comprehensive Cancer Network
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.

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
MS therapies		
teriflunomide (Aubagio)	7 mg or 14 mg PO QD	14 mg/day
Avonex, Rebif (interferon beta-1a)	*Avonex*: 30 mcg IM Q week *Rebif*: 22 mcg or 44 mcg SC TIW	*Avonex*: 30 mcg/week *Rebif*: 44 mcg TIW
Plegridy (peginterferon beta-1a)	125 mcg SC Q2 weeks	125 mcg/2 weeks
Betaseron, Extavia (interferon beta-1b)	250 mcg SC QOD	250 mg QOD
glatiramer acetate (Copaxone, Glatopa)	20 mg SC QD or 40 mg SC TIW	20 mg/day or 40 mg TIW

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
fingolimod (Gilenya)	0.5 mg PO QD	0.5 mg/day
dimethyl fumarate (Tecfidera)	120 mg PO BID for 7 days, followed by 240 mg PO BID	480 mg/day

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™), ublituximab-xiiy (Briumvi™), and ofatumumab (Kesimpta®).
- Of the disease-modifying therapies for MS that are FDA-labeled for clinically isolated syndrome, only the interferon products, glatiramer, and teriflunomide have demonstrated any efficacy in decreasing the risk of conversion to MS compared to placebo. This is supported by the American Academy of Neurology 2018 MS guidelines.
- In August 2020, Novartis announced their plan to transition Arzerra to an oncology patient access program will provide Arzerra at no cost to CLL patients in the U.S. Arzerra is no longer available for commercial purchase.

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 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	6 cycles

Drug Name	Indication	Dosing Regimen	Maximum Dose
		of subsequent 28-day cycles for a maximum of 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 and every 8 weeks thereafter for up to a maximum of 2 years	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	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 or 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 January 31, 2023.
2. Kesimpta Prescribing Information. East Hanover, NJ: Novartis; September 2022. Available at: www.kesimpta.com. Accessed January 31, 2023.
3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed January 31, 2023.
4. National Comprehensive Cancer Network. Waldenstrom's Macroglobulinemia/ Lymphoplasmacytic Lymphoma Version 1.2023. Available at: https://www.nccn.org/professionals/physician_gls/pdf/waldenstroms.pdf. Accessed January 31, 2023.
5. 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. Reaffirmed on September 18, 2021.
6. Genmab. Genmab announces plan to transition Arzerra (ofatumumab) to an oncology access program for chronic lymphocytic leukemia patients in the US. Press release published August 20, 2020. Available at: https://ir.genmab.com/news-releases/news-release-details/genmab-announces-plan-transition-arzerrar-ofatumumab-oncology/. Accessed January 31, 2023.

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, 10 mg (Arzerra)
J3590	Unclassified biologics (Kesimpta)
C9399	Unclassified drugs or biologicals (Kesimpta)

Reviews, Revisions, and Approvals	Date	P&T Approval Date
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; added Commercial line of business to the policy.	10.06.20	02.21
MS: Per November and December SDC and prior clinical guidance, removed redirection to Mayzent; for RRMS modified redirection to require generic dimethyl fumarate, Aubagio, Gilenya, and either an interferon-beta agent or glatiramer.	02.09.21	
2Q 2021 annual review: CLL/SLL- added specific requirements if request is for use as first-line therapy per NCCN and FDA; references to HIM.PHAR.21 revised to HIM.PA.154; references reviewed and updated.	02.10.21	05.21
2Q 2022 annual review: no significant changes; clarified B-cell lymphoma criteria per NCCN recommendations; clarified interferon-beta product redirections for each line of business per SDC; references reviewed and updated.	02.07.22	05.22
Template changes applied to other diagnoses/indications and continued therapy section.	09.21.22	
2Q 2023 annual review: for Arzerra, removed B-cell lymphoma criteria, SLL criteria, and off-label CLL uses per updated NCCN guidelines and limited commercial availability; for Kesimpta, applied template changes to continued therapy section, and for MS, to be inclusive of members continuing therapy from a different benefit, revised Medicaid/HIM continued approval duration to reference the	01.31.23	05.23

Reviews, Revisions, and Approvals	Date	P&T Approval Date
duration of total treatment received rather than the number of re-authorizations; references reviewed and updated.		
Per August SDC, added generic references to Aubagio and Gilenya redirections.	08.22.23	11.23

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.

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.