Clinical Policy: Ofatumumab (Arzerra)

Reference Number: LA.PHAR.306
Effective Date: 07.10.24
Last Review Date: 11.24.25~~11.14.24~~
Line of Business: Medicaid

Coding Implications
Revision Log

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

****Please note: This policy is for medical benefit****

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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 (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of Louisiana Healthcare Connections® that Arzerra is **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: 6 months

B. ~~**Waldenstrom's Macroglobulinemia/Lymphoplasmacytic Lymphoma (off-label)**~~ **Multiple Sclerosis** (must meet all~~):~~**:**

1. Diagnosis of ~~Waldenstrom's macroglobulinemia/lymphoplasmacytic lymphoma (WM/LPL);~~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*
   c. Secondary progressive MS;
2. Request is for Arzerra;
3. Prescribed by or in consultation with ~~an oncologist or hematologist~~a neurologist;
4. Age ≥ 18 years;
5. ~~Member is rituximab-intolerant;~~
6. ~~6.~~5. ~~Request is for second-line or subsequent therapy (*see Appendix* ~~At the time of request, member does not have active hepatitis B *for examples of prior therapy*~~infection (positive results for hepatitis B surface antigen and anti-hepatitis B virus tests);
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.*~~
6. 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

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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 LA.PMN.255.

~~**C.A. 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 LA.PMN.255~~

~~2.~~ 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:~~ LA.PMN.53 ~~for Medicaid~~.

II. Continued Therapy

A. ~~All Indications in Section I Other Than Multiple Sclerosis~~Chronic Lymphocytic Leukemia (must meet all):

1. Currently receiving Arzerra via Louisiana Healthcare Connections 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: 12 months

B. 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 LA.PMN.255; or

~~**B.A. 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 LA.PMN.255~~

~~2.~~ 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~~: LA.PMN.53 ~~for Medicaid~~.

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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~~ies~~ LA.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
fingolimod (Gilenya)	0.5 mg PO QD	0.5 mg/day

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Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
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
- Boxed warning(s):
  - Arzerra: hepatitis B virus reactivation, progressive multifocal leukoencephalopathy

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®, and biosimilar Tyruko®), ocrelizumab (Ocrevus®), ocrelizumab/hyaluronidase-ocsq (Ocrevus Zunovo™), cladribine (Mavenclad®), siponimod (Mayzent®), ozanimod (Zeposia®), ponesimod (Ponvory™), and 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	6 cycles

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Drug Name	Indication	Dosing Regimen	Maximum Dose
		(Cycle 1). Then 1,000 mg IV on Day 1 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

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VI. Product Availability

Drug Name	Availability
Ofatumumab (Arzerra)	Single-use vials: 100 mg/5 mL, 1,000 mg/50 mL

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VII. References

1. Arzerra Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; August 2016. Available at https://www.us.arzerra.com. Accessed January ~~11, 2024~~23, 2025.
2. ~~Kesimpta Prescribing Information. East Hanover, NJ: Novartis; January 2024. Available at: www.kesimpta.com. Accessed February 1, 2024~~.
~~3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed January 31, 2024.~~
~~4. National Comprehensive Cancer Network. Waldenstrom's Macroglobulinemia/ Lymphoplasmacytic Lymphoma Version 2.2024. Available at: https://www.nccn.org/professionals/physician_gls/pdf/waldenstroms.pdf. Accessed January 31, 2024.~~
~~5.~~3. Rae-Grant A, Day GS, Marrie RA, et al. Practice guideline recommendations summary: 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.~~788. Full guideline available at: https://www.aan.com/Guidelines/home/GetGuidelineContent/898. Reaffirmed on ~~September 18, 2021~~October 19, 2024.
~~6.~~4. 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 February ~~1, 2024~~12, 2025.

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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)

Reviews, Revisions, and Approvals	Date	LDH Approval Date
Policy created	05.09.23	08.28.23
Annual Review; removed B-cell lymphoma criteria, SLL criteria, and off-label CLL uses per updated NCCN guidelines and limited commercial availability; Added generic references to Aubagio and Gilenya redirections.	02.21.24	07.10.24
No significant changes; references reviewed and updated.	11.14.24	01.27.25
Annual review: for Arzerra, removed Waldenstrom's macroglobulinemia/lymphoplasmacytic lymphoma criteria as this off-label use is no longer supported by NCCN and removed primary therapeutic examples for Appendix B; for MS continued therapy, modified approval duration from "if member has received < 1 year of total treatment – up to a total of 12 months of treatment and if member has received > 1 year of total treatment – 12 months" to "12 months"; references reviewed and updated.	11.24.25	

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. LHCC 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.

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,

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contract of insurance, etc.), as well as to state and federal requirements and applicable LHCC administrative policies and procedures.

This clinical policy is effective as of the date determined by LHCC. 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. LHCC 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.

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