Prior Authorization Review Panel

CHC-MCO Policy Submission

A separate copy of this form must accompany each policy submitted for review.
Policies submitted without this form will not be considered for review.

Plan: PA Health & Wellness	**Submission Date: 02/01/2021**
Policy Number: PA.CP.PHAR.306	**Effective Date: 01/2018** **Revision Date: 01/2021**
Policy Name: Ofatumumab (Arzerra, Kesimpta)	

Type of Submission – Check all that apply:

- ☐ **New Policy**
- ✓ **Revised Policy***
- ☐ **Annual Review - No Revisions**
- ☐ **Statewide PDL -** *Select this box when submitting policies for Statewide PDL implementation and when submitting policies for drug classes included on the Statewide PDL.*

***All revisions to the policy must be highlighted using track changes throughout the document.**

Please provide any changes or clarifying information for the policy below:

Added new subcutaneous dosage form Kesimpta to the policy for the treatment of multiple sclerosis; added primary progressive MS as a diagnosis not covered

Name of Authorized Individual (Please type or print): **Auren Weinberg, MD**	**Signature of Authorized Individual:** 

Clinical Policy: Ofatumumab (Arzerra)

Reference Number: PA.CP.PHAR.306
Effective Date: 01/2018
Last Review Date: 01/2021

Coding Implications
Revision Log

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
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. Age ≥ 18 years;
4. Request is for Arzerra;
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

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. Age ≥ 18 years;

4. Request is for Arzerra;
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*).

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 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's disease;
   h. Post-transplant lymphoproliferative disorder;
   i. AIDS-related B-cell lymphoma;
   j. Burkitt lymphoma;
2. Used as a substitute* for Rituxan® (rituximab) or Gazyva® (obinutuzumab) in patients 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.*
3. Prescribed by or in consultation with an oncologist or hematologist;
4. Age ≥ 18 years;
5. Request is for Arzerra;
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*).

Approval duration: 6 months

D. Multiple Sclerosis: *If request is for Kesimpta for use in Multiple Sclerosis, please refer to PHW.PDL.043 Multiple Sclerosis Agents for prior authorization guidelines and visit https://papdl.com/preferred-drug-list to view all preferred/non-preferred Multiple Sclerosis agents included in the Pennsylvania Medical Assistance Program's Statewide preferred drug list.*

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

II. Continued Approval

A. All indications in Section I Other than Multiple Sclerosis (must meet all):

1. Currently receiving Arzerra 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. Multiple Sclerosis: *If request is for Kesimpta for use in Multiple Sclerosis, please refer to PHW.PDL.043 Multiple Sclerosis Agents for prior authorization guidelines and visit https://papdl.com/preferred-drug-list to view all preferred/non-preferred Multiple Sclerosis agents included in the Pennsylvania Medical Assistance Program's Statewide preferred drug list.*

C. 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
EDSS: Expanded Disability Status Scale
FDA: Food and Drug Administration
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 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	Varies	Varies

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
• rituximab/cyclophosphamide/dexamethasone		
MS therapies		
Aubagio (teriflunomide)	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 (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
Gilenya (fingolimod)	0.5 mg PO QD	0.5 mg/day
Tecfidera (dimethyl fumarate)	120 mg PO BID for 7 days, followed by 240 mg PO BID	480 mg/day
Mayzent (siponimod)	*All patients:* Day 1 and 2: 0.25 mg PO QD Day 3: 0.5 mg PO QD Day 4: 0.75 mg PO QD *CYP2C9 genotypes *1/*1, *1/*2, or *2/*2:* Day 5: 1.25 mg PO QD Day 6 and onward: 2 mg PO QD *CYP2C9 genotypes *1/*3 or *2/*3:* Day 5 and onward: 1 mg PO QD	2 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), teriflunomide (Aubagio), alemtuzumab (Lemtrada®), mitoxantrone (Novantrone®), natalizumab (Tysabri®), ocrelizumab (Ocrevus®), cladribine (Mavenclad®), siponimod (Mayzent), and ozanimod (Zeposia®).
- Of the disease-modifying therapies for MS that are FDA-labeled for clinically isolated syndrome, only the interferon products, glatiramer, and Aubagio have demonstrated any efficacy in decreasing the risk of conversion to MS compared to placebo. This is supported by the AAN 2018 MS guidelines.

IV. Dosage and Administration

	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 of subsequent 28-day cycles for a maximum of 6 cycles	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	Refer to dosing regimen
Ofatumumab (Kesimpta)	MS	20 mg SC at weeks 0, 1, and 2, followed by 20 mg SC monthly starting at week 4	20 mg

V. Product Availability

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

mL

VI. References

1. Arzerra Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; August 2016. Available at https://www.us.arzerra.com/. Accessed July 24, 2020.

2. Kesimpta Prescribing Information. East Hanover, NJ: Novartis; August 2020. Available at: www.kesimpta.com. Accessed August 31, 2020.
3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed July 24, 2020.
4. National Comprehensive Cancer Network. Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma Version 4.2020. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cll.pdf. Accessed July 24, 2020.
5. National Comprehensive Cancer Network. Waldenstrom's Macroglobulinemia/Lymphoplasmacytic Lymphoma Version 2.2020. Available at: https://www.nccn.org/professionals/physician_gls/pdf/waldenstroms.pdf. Accessed July 24, 2020.
6. National Comprehensive Cancer Network. B-Cell Lymphomas Version 2.2020. Available at: https://www.nccn.org. Accessed July 24, 2020.
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.

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 100 mg/5 mL

Reviews, Revisions, and Approvals	Date	Approval Date
4Q 2018 annual review: no significant changes; summarized NCCN and FDA-approved uses for improved clarity; added specialist involvement in care; updated	07/18	
4Q 2019 annual review: No changes per Statewide PDL implementation 01-01-2020	10/30/19	
4Q 2020 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.	10/2020	
Added new subcutaneous dosage form Kesimpta to the policy for the treatment of multiple sclerosis; added primary progressive MS as a diagnosis not covered	01/2021	