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: 02/01/2020**
Policy Number: PA.CP.PHAR.362	**Effective Date: 01/01/2018** **Revision Date: 01/15/2020**
Policy Name: Axicabtagene Ciloleucel (Yescarta)	

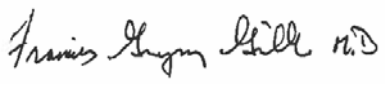
Type of Submission – Check all that apply:

- ☐ **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 requirement in Section IA to confirm "Member does not have active or primary central nervous system (CNS) disease" to align with clinical trial exclusion criteria and NCCN recommendations; added to Section III "Active or primary CNS disease"; Appendix D was updated to include information related to CNS disease;; references reviewed and updated.

Name of Authorized Individual (Please type or print):	**Signature of Authorized Individual:**
Francis G. Grillo, MD	

Clinical Policy: Axicabtagene Ciloleucel (Yescarta)

Reference Number: PA.CP.PHAR.362
Effective Date: 10.31.17
Last Review Date: 01.20

Revision Log

Description
Axicabtagene ciloleucel (Yescarta™) is a CD19-directed, genetically modified, autologous T cell immunotherapy.

FDA Approved Indication(s)
Yescarta is indicated for the treatment of adult patients with relapsed or refractory large B-cell lymphoma (LBCL) after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, primary mediastinal large B-cell lymphoma, high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma.

Limitation of use: Yescarta is not indicated for the treatment of patients with primary central nervous system (CNS) lymphoma.

Policy/Criteria
Provider must submit documentation (which may include office chart notes and lab results) supporting that member has met all approval criteria

It is the policy of health plans affiliated with PA Health & Wellness that Yescarta is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Large B-Cell Lymphoma (must meet all)**:**

1. Diagnosis of large B-cell lymphoma;
2. Age ≥18;
3. Prescribed by or in consultation with an oncologist;
4. Recent (within the last 30 days) absolute lymphocyte count (ALC) ≥ 100/µL;
5. Disease is refractory or member has relapsed after ≥ 2 lines of systemic therapy that includes Rituxan® and one anthracycline-containing regimen (e.g., doxorubicin);
   **Prior authorization may be required for Rituxan*
6. Member does not have active or primary CNS disease;
7. Dose does not exceed 2 x 10^8 CAR-positive viable T cells.

Approval duration: 3 months *(1 dose only, with 4 doses of tocilizumab (Actemra) at up to 800 mg per dose)*

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Large B-Cell Lymphoma: Not Applicable
Continued therapy will not be authorized as Yescarta is indicated to be dosed one time only.

B. Other diagnoses/indications:

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.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 policy – PA.CP.PMN.53 for Medicaid or evidence of coverage documents.

B. Active or primary CNS disease

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ALC: absolute lymphocyte count
CAR: chimeric antigen receptor
CNS: central nervous system
CRS: cytokine release syndrome
DLBCL: diffuse large B-cell lymphoma
FDA: Food and Drug Administration
LBCL: large B-cell 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
First-Line Treatment Regimens		
RCHOP (Rituxan® (rituximab), cyclophosphamide, doxorubicin, vincristine, prednisone)	Varies	Varies
RCEPP (Rituxan® (rituximab), cyclophosphamide, etoposide, prednisone, procarbazine)	Varies	Varies
RCDOP (Rituxan® (rituximab), cyclophosphamide, liposomal doxorubicin, vincristine, prednisone)	Varies	Varies
DA-EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicine) + Rituxan® (rituximab)	Varies	Varies
RCEOP (Rituxan® (rituximab), cyclophosphamide, etoposide, vincristine, prednisone)	Varies	Varies

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
RGCVP (Rituxan®, gemcitabine, cyclophosphamide, vincristine, prednisone)	Varies	Varies
Second-Line Treatment Regimens		
Bendeka® (bendamustine) ± Rituxan® (rituximab)	Varies	Varies
CEPP (cyclophosphamide, etoposide, prednisone, procarbazine) ± Rituxan® (rituximab)	Varies	Varies
CEOP (cyclophosphamide, etoposide, vincristine, prednisone) ± Rituxan® (rituximab)	Varies	Varies
DA-EPOCH ± Rituxan® (rituximab)	Varies	Varies
GDP (gemcitabine, dexamethasone, cisplatin) ± Rituxan® (rituximab)	Varies	Varies
gemcitabine, dexamethasone, carboplatin ± Rituxan® (rituximab)	Varies	Varies
GemOx (gemcitabine, oxaliplatin) ± Rituxan® (rituximab)	Varies	Varies
gemcitabine, vinorelbine ± Rituxan® (rituximab)	Varies	Varies
lenalidomide ± Rituxan® (rituximab)	Varies	Varies
Rituxan® (rituximab)	Varies	Varies
DHAP (dexamethasone, cisplatin, cytarabine) ± Rituxan® (rituximab)	Varies	Varies
DHAX (dexamethasone, cytarabine, oxaliplatin) ± Rituxan® (rituximab)	Varies	Varies
ESHAP (etoposide, methylprednisolone, cytarabine, cisplatin) ± Rituxan® (rituximab)	Varies	Varies
ICE (ifosfamide, carboplatin, etoposide) ± Rituxan® (rituximab)	Varies	Varies
MINE (mesna, ifosfamide, mitoxantrone, etoposide) ± Rituxan® (rituximab)	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): none reported
- Boxed warning(s): cytokine release syndrome (CRS), neurologic toxicities

Appendix D: General Information

- The ZUMA-1 trial included only patients that received prior anti-CD20 antibody therapy and an anthracycline-containing regimen. Patients with an ALC < 100/µL were excluded.
- CRS, including fatal or life-threatening reactions, occurred in patients receiving Yescarta. Do not administer Yescarta to patients with active infection or inflammatory disorders. Treat severe or life-threatening CRS with tocilizumab or tocilizumab and corticosteroids.

- Neurologic toxicities, including fatal or life-threatening reactions, occurred in patients receiving Yescarta, including concurrently with CRS or after CRS resolution. Monitor for neurologic toxicities after treatment with Yescarta. Provide supportive care and/or corticosteroids, as needed.
- The ZUMA-1 trial inclusion criteria required a MRI of the brain showing no evidence of CNS lymphoma. Patients with detectable cerebrospinal fluid malignant cells, or brain metastases, or with a history of cerebrospinal fluid malignant cells or brain metastases were excluded. For primary DLBCL of the CNS (i.e., primary CNS lymphoma), NCCN treatment guidelines for CNS cancers recommend a high-dose methotrexate induction based regimen or whole brain radiation therapy, which consolidation therapy with high-dose chemotherapy with stem cell rescue, high-dose cytarabine with or without etoposide, low dose whole brain radiation therapy, or continuation with monthly high-dose methotrexate-based regimen.
- Yescarta is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the Yescarta REMS.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Large B-Cell Lymphoma	Target dose: 2×10^6 CAR-positive viable T cells per kg body weight	2×10^8 CAR-positive viable T cells

VI. Product Availability

Single-dose unit infusion bag: frozen suspension of genetically modified autologous T cells labeled for the specific recipient

VII. References

1. Yescarta Prescribing information. Santa Monica, CA: Kite Pharma, Inc.; May 2019. Available at www.yescarta.com. Accessed October 31, 2019.
2. Data on File. Kite Pharma - Yescarta: Primary Results of the Pivotal ZUMA-1 Phase 2 Study. MRC-00038. October 2017.
3. National Comprehensive Cancer Network. B-cell Lymphomas Version 5.2019. Available at: https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed October 31, 2019.
4. National Comprehensive Cancer Network Drug and Biologics Compendium. Available at http://www.nccn.org/professionals/drug_compendium. Accessed October 31, 2019.
5. National Comprehensive Cancer Network. Central Nervous System Cancers Version 3.2019. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cns.pdf. Accessed October 31, 2019.
6. Neelapu SS, Locke FL, Bartlett NL, et al. Axicabtagene Ciloleucel CAR T-Cell Therapy in Refractory Large B-Cell Lymphoma. NEJM 2017; 377: 2531-44.

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
Q2041	Axicabtagene Ciloleucel, up to 200 Million Autologous Anti-CD19 CAR T Cells, Including Leukapheresis And Dose Preparation Procedures, Per Infusion

Reviews, Revisions, and Approvals	Date	P&T Approval Date
2Q 2019 annual review: removed requirement for CD19 tumor expression; added minimum ALC requirement per clinical trial exclusion criteria; added hematologist prescriber option; references reviewed and updated.	04/19	
1Q 2020 annual review: Added requirement in Section IA to confirm "Member does not have active or primary central nervous system (CNS) disease" to align with clinical trial exclusion criteria and NCCN recommendations; added to Section III "Active or primary CNS disease"; Appendix D was updated to include information related to CNS disease; references reviewed and updated.	01/2020	