

Clinical Policy: Axicabtagene Ciloleucel (Yescarta)

Reference Number: CP.PHAR.362

Effective Date: 12.01.17

Last Review Date: 05.20

Line of Business: Commercial, HIM, Medicaid

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

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.*

**Efficacy of Yescarta has not been established in patients with a history of or current CNS lymphoma (see Appendix D)*

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 Yescarta is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

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

**Only for initial treatment dose; subsequent doses will not be covered.*

1. Diagnosis of LBCL;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age \geq 18 years;
4. Recent (within the last 30 days) absolute lymphocyte count (ALC) \geq 100/ μ L;
5. Disease is refractory or member has relapsed after \geq 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 a history of or current CNS disease;
7. Dose does not exceed 2×10^8 chimeric antigen receptor (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): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Large B-Cell Lymphoma

1. Continued therapy will not be authorized as Yescarta is indicated to be dosed one time only.

Approval duration: Not applicable

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): CP.CPA.09 for commercial, HIM.PHAR.21 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.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents;
- B. History of or current CNS disease.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ALC: absolute lymphocyte count	DLBCL: diffuse large B-cell lymphoma
CAR: chimeric antigen receptor	FDA: Food and Drug Administration
CNS: central nervous system	LBCL: large B-cell lymphoma
CRS: cytokine release syndrome	

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

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
DA-EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicine) + Rituxan [®] (rituximab)	Varies	Varies
RCEOP (Rituxan [®] (rituximab), cyclophosphamide, etoposide, vincristine, prednisone)	Varies	Varies
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.
- Bennani et al. 2019 reported on the real-world experience of 17 patients treated with Yescarta who had a history of secondary CNS involvement or had active CNS disease at time of CAR-T infusion. Among the 15 patients who received a Yescarta infusion, 10 had resolution of CNS involvement, and 5 had persistent active CNS disease at the time of infusion. The best overall response rates (complete and partial responses) at 30-days between the non-CNS and CNS cohorts were 75% vs 59% respectively (p = 0.15). Best overall response rates at month 6 were 41% vs 31% respectively (p = 0.60).
- 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
LBCL	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.
7. Bannani NN, Maurer MJ, Nastoupil LJ, et al. Experience with Axicabtagene Ciloleucel (Axi-cel) in Patients with Secondary CNS Involvement: Results from the US Lymphoma CAR T Consortium. Blood (2019); 134 (Supplement_1): 763.

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
Policy created.	10.31.17	11.17
Clarified requirement of one anthracycline-containing regimen among the two lines of systemic therapy; clarified that policy is for HIM medical benefit and not for pharmacy benefit	04.23.18	
1Q 2019 annual review: added minimum ALC requirement per clinical trial exclusion criteria; added hematologist prescriber option; references reviewed and updated.	09.25.18	02.19
Removed requirement for CD19 tumor expression.	02.19.19	05.19
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.	07.16.19	08.19
1Q 2020 annual review: no significant changes; replaced HIM-Medical Benefit with HIM line of business; references reviewed and updated.	10.31.19	02.20
Clarified history of or current CNS disease is an exclusion.	02.17.20	05.20

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.

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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.

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