Clinical Policy: Tisagenlecleucel (Kymriah)

Reference Number: CP.HNMC.XX
Effective Date: 09.26.17
Last Review Date: 11.17
Line of Business: Medicaid – Medi-Cal

Revision Log

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

Description
Tisagenlecleucel (Kymriah™) is a CD19-directed genetically modified autologous T-cell immunotherapy.

FDA Approved Indication(s)
Kymriah is indicated for the treatment of patients up to 25 years of age with B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory or in second or later relapse.

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 Centene Corporation® that Kymriah is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Acute Lymphoblastic Leukemia (must meet all)**:**

1. Diagnosis of B-cell precursor ALL;
2. Age ≤ 25;
3. Prescribed by or in consultation with an oncologist;
4. Documentation of CD19 tumor expression;
5. Disease is refractory or member has had ≥ 2 relapses;
6. If disease is Philadelphia chromosome positive, failure of 2 tyrosine kinase inhibitors *(e.g. imatinib, dasatinib)* at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
7. Dose does not exceed (a or b):
   a. Weight ≤ 50 kg: 5.0×10^6 chimeric antigen receptor (CAR)-positive viable T cells per kg of body weight;
   b. Weight > 50 kg: 2.5×10^8 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 CP.PHAR.57 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Acute Lymphoblastic Leukemia: Not Applicable
Continued therapy will not be authorized as Kymriah is indicated to be dosed one time only.

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Refer to CP.PHAR.57 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

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 – CP.PHAR.57 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ALL: acute lymphoblastic leukemia
CAR: chimeric antigen receptor
CML: chronic myelogenous leukemia
FDA: Food and Drug Administration
Ph+: Philadelphia chromosome positive

Appendix B: General Information

- Refractory ALL is defined as complete remission not achieved after 2 cycles of standard chemotherapy or 1 cycle of standard chemotherapy due to relapsed leukemia.[2]

Appendix C: Black Bock Warning: Cytokine Release Syndrome And Neurological Toxicities

- Cytokine Release Syndrome (CRS), including fatal or life-threatening reactions, occurred in patients receiving Kymriah. Do not administer Kymriah to patients with active infection or inflammatory disorders. Treat severe or life-threatening CRS with tocilizumab.
- Neurological toxicities, which may be severe or life-threatening, can occur following treatment with Kymriah, including concurrently with CRS. Monitor for neurological events after treatment with Kymriah. Provide supportive care as needed.
- Kymriah is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the Kymriah REMS.

Appendix D: Therapeutic Alternatives

Drug	Dosing Regimen	Dose Limit/ Maximum Dose
imatinib mesylate (Gleevec®)	Adults with Ph+ ALL: 600 mg/day Pediatrics with Ph+ ALL: 340 mg/m2/day	Adults:800 mg/day Pediatrics: 600 mg/day
Sprycel® (dasatinib)	140 mg per day	180 mg per day
Iclusig® (ponatinib)	45 mg per day	45 mg per day
Tasigna® (nilotinib)	Resistant or intolerant Ph+ CML-CP and CML-AP: 400 mg twice per day	800 mg/day

Drug	Dosing Regimen	Dose Limit/ Maximum Dose
Bosulif® (bosutinib)	Ph+ CML: 500 mg per day	600 mg per 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.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
ALL	50 kg or less: 0.2 to 5.0 x 10^6 CAR-positive viable T cells per kg of body weight IV Above 50 kg: 0.1 to 2.5 x 10^8 CAR-positive viable T cells IV	50 kg or less: 0.2 to 5.0 x 10^6 CAR-positive viable T cells per kg of body weight Above 50 kg: 0.1 to 2.5 x 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. Kymriah Package Insert. East Hanover, NJ: Novartis Pharmaceuticals Corporation; August 2017. Available at: https://www.us.kymriah.com/. Accessed August 30, 2017.
2. Data on File. Novartis Pharmaceuticals Corporation; East Hanover, NJ.
3. National Comprehensive Cancer Network. Acute Lymphoblastic Leukemia Version 3.2017. Available at https://www.nccn.org/. Accessed September 13, 2017.
4. National Comprehensive Cancer Network. Adolescent and Young Adult (AYA) Oncology. Version 1.2017. Available at https://www.nccn.org/. Accessed September 13, 2017.
5. National Comprehensive Cancer Network Drug and Biologics Compendium. Available at https://www.nccn.org/. Accessed September 13, 2017.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created.	09.26.17	11.17
HNMC version drafted from the commercial criteria. Revised section 1A5 to list only HNMC formulary Tyrosine Kinase inhibitors.	10.23.17	
Criterion I.A.5 was omitted in error. It is now added to reflect what is approved by corporate for all other lines of business.	01.12.18	

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.