Clinical Policy: Tisagenlecleucel (Kymriah)

Reference Number: CP.PHAR.361
Effective Date: 09.26.17
Last Review Date: 08.18
Line of Business: Commercial, Medicaid, HIM-Medical Benefit 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.
- Adult patients with relapsed or refractory (r/r) large B-cell lymphoma after two or more lines of systemic therapy including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, high grade B-cell lymphoma and DLBCL arising from follicular lymphoma.

Limitation(s) of use: Kymriah is not indicated for treatment of patients with primary central nervous system lymphoma.

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 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. Prescribed by or in consultation with an oncologist;
3. Age ≤ 25 years;
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, nilotinib, bosutinib, ponatinib)* at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced; **Prior authorization may be required for tyrosine kinase inhibitors*
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. Large B-Cell Lymphoma (must meet all)**:**
1. Diagnosis of large B-cell lymphoma;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Documentation of CD19 tumor expression;
5. Disease is refractory or member has relapsed after ≥ 2 lines of systemic therapy that includes Rituxan® and an anthracycline-containing regimen (e.g., doxorubicin);
6. Dose does not exceed 6.0×10^8 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)***

C. 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. All Indications in Section I:
1. 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. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. 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. Primary central nervous system lymphoma.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ALL: acute lymphoblastic leukemia
CAR: chimeric antigen receptor
CML: chronic myelogenous leukemia
DLBCL: diffuse large B-cell lymphoma
FDA: Food and Drug Administration
Ph+: Philadelphia chromosome positive

r/r: relapsed or refractory

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
Acute Lymphoblastic Leukemia		
imatinib mesylate (Gleevec®)	Adults with Ph+ ALL: 600 mg/day Pediatrics with Ph+ ALL: 340 mg/m^2/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
Bosulif® (bosutinib)	Ph+ CML: 500 mg per day	600 mg per day
Large B-Cell Lymphoma		
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
RGCVP (rituximab, gemcitabine, cyclophosphamide, vincristine, prednisone)	Varies	Varies
Second-Line Treatment Regimens		
Bendeka® (bendamustine) ± Rituxan (rituximab)	Varies	Varies

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
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
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

- Contraindications: none
- Boxed Warnings: cytokine release syndrome and neurological toxicities

Appendix D: 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]
- 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.

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
Large B-cell lymphoma	0.6 to 6.0 x 10^8 CAR-positive viable T cells IV	6.0 x 10^8 CAR-positive viable T-cells

*Kymriah should be administered at a certified healthcare facility.

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 Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; May 2018. Available at: https://www.us.kymriah.com/. Accessed May 10, 2018.
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.
6. National Comprehensive Cancer Network. B-Cell Lymphomas Version 04.2018. Available at: https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed May 23, 2018.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created.	09.26.17	11.17
Criteria added for new FDA indication: adult r/r DLBCL; policies combined for Commercial and Medicaid lines of business; added HIM-Medical Benefit; references reviewed and updated.	05.29.18	08.18

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.

For Health Insurance Marketplace members, when applicable, this policy applies only when the prescribed agent is on your health plan approved formulary. Request for non-formulary drugs must be reviewed using the formulary exception policy.

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