



JENNIFER KENT
DIRECTOR

State of California—Health and Human Services Agency
Department of Health Care Services



EDMUND G. BROWN JR.
GOVERNOR

DATE: September 10, 2018

N.L.: 10-0718
Index: Benefits

TO: ALL COUNTY CALIFORNIA CHILDREN SERVICES (CCS) PROGRAM ADMINISTRATORS, MEDICAL CONSULTANTS, INTEGRATED SYSTEMS OF CARE DIVISION (ISCD) STAFF, AND THE GENETICALLY HANDICAPPED PERSONS PROGRAM (GHPP)

SUBJECT: TISAGENLECLEUCEL (KYMRIAH™)

I. PURPOSE

The purpose of this Numbered Letter (N.L.) is to establish CCS Program policy regarding the authorization of tisagenlecleucel (Kymriah), as a treatment of B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory or in second or later relapse.

II. BACKGROUND

ALL is a cancer of the blood and bone marrow characterized by the development and proliferation of large numbers of immature lymphocytes. ALL arises from malignant transformation of progenitor B- or T-cell cells in the bone marrow into leukemic cells. It is characterized by the accumulation of lymphoblasts in the bone marrow or in various extramedullary sites¹. ALL is the most common cancer in children and represents 25 percent of cancer diagnoses in children younger than 15 years of age.² Every year, ALL is diagnosed in approximately 3,100 patients aged 20 years or younger.³ B-cell leukemia is the most common form of ALL.

The Federal Food and Drug Administration (FDA) approved tisagenlecleucel on August 30, 2017, as the first in class of Chimeric Antigen Receptor T cell therapy (CAR-T) for patients up to 25 years of age with B-cell precursor acute lymphoblastic leukemia that is refractory or in second or later relapse. Tisagenlecleucel suspension is a CD19-directed genetically modified autologous T-cell immunotherapy, which involves reprogramming a patient's own T cells with a transgene encoding a chimeric

¹ <https://www.cancer.gov/types/leukemia/hp/adult-all-treatment-pdq>

² https://www.cancer.gov/types/leukemia/hp/child-all-treatment-pdq#cit/section_1.5

³ FDA News Release: FDA Approval Brings First Gene Therapy to the United States, August 30, 2017

antigen receptor (CAR) to identify and eliminate CD19-expressing malignant and normal cells.

Upon binding to CD19-expressing cells, the CAR transmits a signal to promote T-cell expansion, activation, target cell elimination and persistence of the CAR-positive T cells. The CAR-T process involves the following steps:

1. Leukapheresis.
2. Cryopreservation and sending cells to the manufacturer.
3. Programming of the cells.
4. Return of the programmed CAR-T cells to the treatment center.
5. Preparation of the client with lymphodepleting chemotherapy.
6. Infusion of the CAR-T cells.

III. POLICY

Effective the date of this letter, tisagenlecleucel is a CCS Program benefit when the following criteria are met:

- A. The client meets the CCS Program residential, financial and medical eligibility criteria;
- B. The client has a diagnosis of B-cell precursor ALL, refractory or in second or later relapse;
- C. The client's care is under the supervision and monitoring of a CCS Program paneled physician at an approved hematology/oncology Specialty Care Center (SCC) that has:
 1. Accreditation by the Foundation for the Accreditation of Cellular Therapy (FACT) for immune effector cell therapy;
 2. Current Risk Evaluation and Mitigation Strategy (REMS) certification, known as Kymriah REMS, including the use of tocilizumab for cytokine release syndrome, if it occurs; and

3. Agreed to monitor response to treatment using the Clinical Remission (CR) Criteria that was used in the ELIANA Study.⁴

D. The request for tisagenlecleucel is for:

1. Inpatient or outpatient administration of tisagenlecleucel.
2. The FDA approved:
 - a. Indication: Client with B-cell precursor ALL that is refractory or in second or later relapse.
 - b. Dosage.
 - (1) For patients 50 kg or less, administer 0.2 to 5.0 x 10⁶ total CAR-positive viable T cells per kg body weight intravenously.
 - (2) For patients above 50 kg, administer 0.1 to 2.5 x 10⁸ total CAR-positive viable T cells (non-weight based) intravenously.
3. CCS clients up to age 21 are eligible.

E. The client is assigned one of the following ICD-10-CM codes:

1. C91.00, Acute lymphoblastic leukemia not having achieved remission,
2. C91.02, Acute lymphoblastic leukemia, in relapse.

IV. POLICY IMPLEMENTATION

- A. Tisagenlecleucel (Kymriah) requires a separate authorization to the outpatient SCC, even if administered while inpatient;
- B. Tisagenlecleucel (Kymriah) requires a separate authorization;
- C. Requesting CCS Program providers must submit:

⁴ Maude SL, Laetsch TW, Buechner J, Rives S, Boyer M, Bittencourt H, Bader P, Verneris MR, Stefanski HE, Myers GD, Qayed M, De Moerloose B, Hiramatsu H, Schlis K, Davis KL, Martin PL, Nemecek ER, Yanik GA, Peters C, Baruchel A, Boïssel N, Mechinaud F, Balduzzi A, Krueger J, June CH, Levine BL, Wood P, Taran T, Leung M, Mueller KT, Zhang Y, Sen K, Lebwohl D, Pulsipher MA, Grupp SA. Tisagenlecleucel in Children and Young Adults with B-Cell Lymphoblastic Leukemia. *N Engl J Med.* 2018 Feb 1;378(5):439-448. doi: 10.1056/NEJMoa1709866., Supplementary Appendix

1. A CCS Program Service Authorization Request (SAR) to their county CCS Program office or to the ISCD Special Populations Authorization Unit along with:
 - a. A copy of the prescription or physician order from the CCS Program approved hematology/oncology SCC; and
 - b. Progress notes from the SCC documenting/providing:
 - (1) Status of ALL.
 - (2) Latest relevant laboratory values.
 - (3) Past ALL treatments.
 - (4) No active infection.
 - (5) No active inflammatory disorder(s).
 - c. Documentation establishes that the SCC has:
 - (1) FACT accreditation for immune effector cell therapy.
 - (2) Risk Evaluation and Mitigation Strategy (REMS) certification, known as Kymriah REMS
 - (3) Has the drug, tocilizumab, available to use if needed for treatment of cytokine release syndrome
 - (4) Supportive care if needed.
- D. SCC must bill tisagenlecleucel using the UB-04 claim form.
- E. Submit copy of manufacturer's payment invoice for tisagenlecleucel with the claim.
- F. SCC must bill with HCPCS code Q2040 or until a permanent HCPCS is released.
- G. Q2040 = **Tisagenlecleucel, up to 250 million (or 2.5×10^8) CAR-positive viable T cells.**
- H. SAR Units is limited to 1 (one).
- I. The provider is reimbursed by the manufacturer for leukapheresis and should not submit an authorization request for leukapheresis to the CCS Program.

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J. The State CCS Program Medical Director or designee will review exceptions on a case-by-case basis.

If you have any questions regarding this N.L., please contact Jill Abramson, M.D., M.P.H, by telephone at (916) 713-8388 or by e-mail at Jill.Abramson@dhcs.ca.gov.

Sincerely,

ORIGINAL SIGNED BY

Sarah Eberhardt-Rios, Division Chief
Integrated Systems of Care Division

Enclosure: Clinical Remission (CR) Criteria

Enclosure: Clinical Remission (CR) Criteria

CR classification requires all of the following criteria be met: < five percent lymphoblasts in bone marrow by morphology, circulating blasts <one percent in peripheral blood, no evidence of extramedullary disease, neutrophils $>1.0 \times 10^9/L$, platelets $>100 \times 10^9/L$, and no platelet and/or neutrophil transfusions within seven days of peripheral blood sample for disease assessment.

CR with incomplete blood count recovery (CRi) defined by all criteria for CR, except that patients had ≥ 1 of the following: neutrophils $\leq 1.0 \times 10^9/L$, platelets $\leq 100 \times 10^9/L$, or platelet/neutrophil transfusions within seven days of peripheral blood sample for disease assessment.