PROVIDER POLICIES & PROCEDURES

CAR T- CELL THERAPY

The primary purpose of this document is to assist providers enrolled in the Connecticut Medical Assistance Program (CMAP) with the information needed to support a medical necessity determination for CAR T-cell therapy. By clarifying the information needed for prior authorization of services, HUSKY Health hopes to facilitate timely review of requests so that individuals obtain the medically necessary care they need as quickly as possible.

Chimeric antigen receptor T (CAR-T) cells are a form of genetically modified autologous immunotherapy. Each dose is a customized treatment created using an individual's own T-cells. The individual's T-cells are collected and sent to a manufacturing center where they are genetically modified to include a specific protein (a chimeric antigen receptor or CAR) that directs T- cells to target and kill the leukemia or lymphoma cells that have a specific antigen (CD19) on the surface. Once the cells are modified, they are infused back into the patient as therapy.

KYMRIAH™ (tisagenlecleucel)
KYMRIAH is a CD 19-directed genetically modified autologous T cell immunotherapy 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, and adult patients with relapsed or refractory large B-cell lymphoma including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, high grade B-cell lymphoma and DLBCL arising from follicular lymphoma. KYMRIAH is not indicated for the treatment of patients with primary central nervous system lymphoma.

YESCARTA® (axicabtagene ciloleucel)
Yescarta is a CD 19-directed genetically modified autologous T cell immunotherapy indicated for the treatment of adult patients with relapsed or refractory large B-cell lymphoma 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 from follicular lymphoma. YESCARTA is not indicated for the treatment of patients with primary central nervous system lymphoma.

Both KYMRIAH and YESCARTA have a boxed warning for cytokine release syndrome (CRS) and neurological toxicities and are available only through a program under a Risk Evaluation and Mitigation Strategy (REMS). Healthcare facilities that dispense and administer KYMRIAH or YESCARTA must be enrolled and must comply with REMS requirements. Certified facilities must have on-site, immediate access to tocilizumab to treat CRS as needed.

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CLINICAL GUIDELINE

KYMRIAH

Coverage decisions for the use of KYMRIAH will be made in accordance with the DSS definition of Medical Necessity. The following criteria are guidelines *only*. Coverage decisions are based on an assessment of the individual and their unique clinical needs. If the guidelines conflict with the definition of Medical Necessity, the definition of Medical Necessity shall prevail. In addition to the guidelines listed below, KYMRIAH will be considered medically necessary if the use for the individual is supported by CMS approved Compendia (per Section 1861(t)(2)(B)(ii)(I) of the Social Security Act).

I. KYMRIAH will be considered medically necessary for individuals that meet the following criteria:

A. The individual has been diagnosed with relapsed/refractory B-cell precursor acute lymphoblastic leukemia; **AND**
   a. The individual is ≤ 25 years of age;
      AND
   b. The individual's condition is refractory or in second or later relapse;
      i. The individual has been treated with 1 or more cycles of systemic therapy without a complete response, **OR**
      ii. The individual has achieved a complete response and experienced multiple relapses following standard chemotherapy; **AND**
      iii. For individuals with Philadelphia chromosome (Ph) positive disease;
         1. has failed two prior trials of tyrosine kinase inhibitor (TKI) therapy, **OR**
         2. has a contraindication or intolerance to TKI therapy;

   AND
   c. The individual will receive a lymphodepleting chemotherapy regimen within two weeks preceding Kymriah infusion.
   AND
   d. The patient-specific IV infusion dose is based on the following:
      i. Patients ≤ 50kg: 0.2 to 5.0 x 10^6 CAR-positive viable T-cells per kg body weight
      ii. Patients > 50kg: 0.1 to 2.5 x 10^8 CAR-positive viable T-cells.

OR

B. The individual has been diagnosed with relapsed/refractory B-cell lymphoma including any of the following:
   - Diffuse large B-cell lymphoma (DLBCL) not otherwise specified; **OR**
   - High grade B-cell lymphoma; **OR**
   - Diffuse large B-cell lymphoma (DLBCL) arising from follicular lymphoma.

   AND
   a. The individual is > 18 years of age;
   AND
   b. The individual has experienced disease progression following a trial of two or more lines of systemic therapy; including an anthracycline chemotherapy agent and an anti-CD20 antibody;
   AND
   c. The individual will receive a lymphodepleting chemotherapy regimen:

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i. Fludarabine with cyclophosphamide, or bendamustine within 2 to 11 days preceding Kymriah infusion; **OR**
ii. the patient is unable to receive lymphodepleting chemotherapy if WBC count is less than or equal to 1 x 10^9/L within one week prior to Kymriah infusion;

AND

d. The patient-specific IV infusion dose does not exceed 6.0 x 10^8 CAR-positive viable T cells;

AND

C. The individual has confirmed CD19 tumor expression; **AND**
D. The individual has been screened for HBV, HCV, and HIV and the individual currently does not have an clinically significant active infection; **AND**
E. The individual does not have primary central nervous system lymphoma; **AND**
F. The individual does not have any FDA labeled contraindications; **AND**
G. The individual has not previously been treated with CAR-T cell therapy, other genetically modified T cell therapy, or KYMRIAH; **AND**
H. The individual will receive KYMRIAH at a treatment center that is certified to administer KYMRIAH.

CLINICAL GUIDELINE

YESCARTA

Coverage decisions for the use of YESCARTA will be made in accordance with the DSS definition of Medical Necessity. The following criteria are guidelines *only*. Coverage decisions are based on an assessment of the individual and their unique clinical needs. If the guidelines conflict with the definition of Medical Necessity, the definition of Medical Necessity shall prevail. In addition to the guidelines listed below, YESCARTA will be considered medically necessary if the use for the individual is supported by CMS approved Compendia (per Section 1861(t)(2)(B)(ii)(I) of the Social Security Act).

YESCARTA will be considered medically necessary for individuals that meet the following criteria:

A. The individual has been diagnosed with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy including:
   - Diffuse large B-cell lymphoma (DLBCL) not otherwise specified, **OR**
   - Primary mediastinal large B-cell lymphoma, **OR**
   - High grade B-cell Lymphoma, **OR**
   - Diffuse large B-cell lymphoma (DLBCL) arising from follicular lymphoma;

   AND
B. The individual is > 18 years of age;
   AND
C. The individual has experienced disease progression following a trial of two or more lines of systemic therapy; including an anthracycline chemotherapy agent and an anti-CD20 antibody;
   AND
D. The individual will receive a lymphodepleting chemotherapy regimen of cyclophosphamide and fludarabine on the fifth, fourth and third day before infusion of Yescarta;
   AND
E. The individual will not be treated with more than 2 x 10^8 CAR-positive viable T cells. If the

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individual is under 100kg in weight, they will receive weight-based dosing 2 x 10^6 CAR-positive viable T cells per kg body weight; **AND**

F. The individual has confirmed CD19 tumor expression; **AND**
G. The individual has been screened for HBV, HCV, and HIV and the individual currently does not have an clinically significant active infection; **AND**
H. The individual does not have primary central nervous system lymphoma; **AND**
I. The individual does not have any FDA labeled contraindications; **AND**
J. The individual has not previously been treated with CAR-T cell therapy, other genetically modified T cell therapy, or YESCARTA; **AND**
K. The individual will receive YESCARTA at a treatment center that is certified to administer YESCARTA

NOTE: EPSDT Special Provision
Early and Periodic Screening, Diagnosis, and Treatment (EPSDT) is a federal Medicaid requirement that requires the Connecticut Medical Assistance Program (CMAP) to cover services, products, or procedures for Medicaid enrollees under 21 years of age where the service or good is medically necessary health care to correct or ameliorate a defect, physical or mental illness, or a condition identified through a screening examination. The applicable definition of medical necessity is set forth in Conn. Gen. Stat. Section 17b-259b (2011) [ref. CMAP Provider Bulletin PB 2011-36].

PROCEDURE
Prior authorization of KYMRIAH and YESCARTA is required. Coverage determinations will be based upon a review of requested and/or submitted case-specific information.

The following information is needed to review requests for KYMRIAH and YESCARTA:

1. Fully completed State of Connecticut, Department of Social Services HUSKY Health Program **KYMRIAH or YESCART Prior Authorization** Request form (to include physician's order and signature);
2. Clinical information supporting the medical necessity of the treatment as outlined above; and
3. Other information as requested.

Requesting Authorization
Requests for the prior authorization of KYMRIAH and YESCARTA must be submitted by the ordering physician and faxed to the number listed on the request form. Questions regarding this form should be directed to the HUSKY Health Program Utilization Management Department at 1.800.440.5071 (select option for medical authorizations).

Initial Authorization
If approved, authorization will be given for 1 dose only.

Reauthorization
Not applicable

EFFECTIVE DATE
This Policy for the prior authorization of KYMRIAH and YESCARTA for individuals covered under the HUSKY Health Program is effective May 1, 2019.

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LIMITATIONS
One time dose per lifetime

CODES:

Code	Definition
Q2041	Axicabtagene ciloleucel, up to 200 million autologous anti-CD19 CAR positive T cells, including leukapheresis and dose preparation procedures, per therapeutic dose
Q2042	Tisagenlecleucel, up to 600 million CAR-positive viable T cells, including leukapheresis and dose preparation procedures, per therapeutic dose

DEFINITIONS

1. **HUSKY A**: Connecticut children and their parents or a relative caregiver; and pregnant women may qualify for HUSKY A (also known as Medicaid). Income limits apply.
2. **HUSKY B**: Uninsured children under the age of 19 in higher income households may be eligible for HUSKY B (also known as the Children's Health Insurance Program) depending on their family income level. Family cost-sharing may apply.
3. **HUSKY C**: Connecticut residents who are age 65 or older or residents who are ages 18-64 and who are blind, or have another disability, may qualify for Medicaid coverage under HUSKY C (this includes Medicaid for Employees with Disabilities (MED-Connect), if working). Income and asset limits apply.
4. **HUSKY D**: Connecticut residents who are ages 19-64 without dependent children and who: (1) do not qualify for HUSKY A; (2) do not receive Medicare; and (3) are not pregnant, may qualify for HUSKY D (also known as Medicaid for the Lowest-Income populations).
5. **HUSKY Health Program**: The HUSKY A, HUSKY B, HUSKY C, HUSKY D and HUSKY Limited Benefit programs, collectively.
6. **HUSKY Limited Benefit Program or HUSKY, LBP**: Connecticut's implementation of limited health insurance coverage under Medicaid for individuals with tuberculosis or for family planning purposes and such coverage is substantially less than the full Medicaid coverage.
7. **Medically Necessary or Medical Necessity**: (as defined in Connecticut General Statutes § 17b-259b) Those health services required to prevent, identify, diagnose, treat, rehabilitate or ameliorate an individual's medical condition, including mental illness, or its effects, in order to attain or maintain the individual's achievable health and independent functioning provided such services are: (1) Consistent with generally-accepted standards of medical practice that are defined as standards that are based on (A) credible scientific evidence published in peer-reviewed medical literature that is generally recognized by the relevant medical community, (B)recommendations of a physician-specialty society, (C) the views of physicians practicing in relevant clinical areas, and (D) any other relevant factors; (2) clinically appropriate in terms of type, frequency, timing, site, extent and duration and considered effective for the individual's illness, injury or disease; (3) not primarily for the convenience of the individual, the individual's health care provider or other health care providers; (4) not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of the individual's illness, injury or disease; and (5) based on an assessment of the individual and his or her medical condition.
8. **Prior Authorization**: A process for approving covered services prior to the delivery of the service or initiation of the plan of care based on a determination by CHNCT as to whether the requested service is medically necessary.

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ADDITIONAL RESOURCES AND REFERENCES:

Hartmann J, Schüler-Lenz M, Bondanza A, Buchholz CJ. Clinical development of CAR T cells challenges and opportunities in translating innovative treatment concepts. EMBO Mol Med. 2017 August 1.

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UpToDate. Treatment of relapsed or refractory acute lymphoblastic leukemia in adults. Last updated 6/28/2018.

UpToDate. Treatment of relapsed or refractory diffuse large B cell lymphoma. Last updated 01/08/2018.

U.S. Food and Drug Administration. Approved Risk Evaluation and Mitigation Strategies (REMS) – KYMRIAH (tisagenlecleucel). Updated 05/01/2018. Available at: https://www.accessdata.fda.gov/scripts/cder/rems/index.cfm?event=IndvRemsDetails.page&REMS=3688 Accessed on November 1, 2018.

U.S. Food and Drug Administration. Approved Risk Evaluation and Mitigation Strategies (REMS) – Yescarta (axicabtagene ciloeucel). Updated 10/18/2017. Available at: https://www.accessdata.fda.gov/scripts/cder/rems/index.cfm?event=IndvRemsDetails.page&REMS=375 Accessed on November 1, 2018.

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PUBLICATION HISTORY

Status	Date	Action Taken
Original publication	December 2018	Approved at the December 12, 2018 Medical Reviewer meeting. Approved by the CHNCT Clinical Quality Subcommittee on March 18, 2019. Approved by DSS on March 27, 2019.

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