Kymriah (tisagenlecleucel)
(Intravenous)

Document Number: IC-0319

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I. Length of Authorization

Coverage will be provided for one treatment course (1 dose of Kymriah) and may not be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [Pharmacy Benefit]:

- N/A

B. Max Units (per dose and over time) [Medical Benefit]:

B-Cell Precursor Acute Lymphoblastic Leukemia (ALL)
- 1 billable unit (1 infusion of up to 250 million car-positive viable t-cells)

Large B-Cell Lymphoma
- 1 billable unit (1 infusion of up to 600 million car-positive viable t-cells)

III. Initial Approval Criteria

Coverage is provided in the following conditions:

- Patient does not have an active infection or inflammatory disorder; AND
- Patient has not received live vaccines within 6 weeks prior to the start of lymphodepleting chemotherapy and will not receive live vaccines until immune recovery following Kymriah treatment; AND
- Patient has been screened for hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV) in accordance with clinical guidelines prior to collection of cells (leukapheresis); AND
- Prophylaxis for infection has been followed according to local guidelines; AND
- Healthcare facility has enrolled in the Kymriah REMS and training has been given to providers on the management of cytokine release syndrome (CRS) and neurological toxicities; AND
- Patient has not received prior CAR-T therapy; AND

- Patient has not received prior anti-CD19 therapy, (e.g., blinatumomab, etc); AND
- Patient has CD19-positive disease; AND
- Used as single agent therapy (not applicable to lymphodepleting or bridging chemotherapy); AND
- Patient has a life expectancy > 12 weeks; AND

B-Cell Precursor Acute Lymphoblastic Leukemia (ALL) †

- Patient aged 3 to 25 years; AND
- Patient's disease is refractory or in second or later relapse defined as one of the following:
    - Second or greater bone marrow (BM) relapse; OR
    - Any BM relapse after allogeneic stem cell transplantation (SCT); OR
    - Primary refractory (not achieving a complete response after 2 cycles of standard chemotherapy) or chemorefractory (not achieving a complete response after 1 cycle of standard chemotherapy for relapsed disease); OR
    - Patients with Philadelphia chromosome (Ph)-positive disease have a contraindication, intolerance, or have failed two prior lines of tyrosine kinase inhibitor (TKI) therapy (e.g., imatinib, dasatinib, ponatinib, etc.); OR
    - Patient is not eligible for allogeneic SCT; AND
- Patient has a performance status (Karnofsky/Lansky) ≥ 50

Large B-Cell Lymphoma †

- Patient aged 18 years or greater; AND
- Patient has an ECOG performance status of 0-1; AND
- Patient does not have primary central nervous system lymphoma; AND
- Patient has one of the following aggressive B-cell non-Hodgkin lymphomas:
    - Diffuse large B-cell lymphoma (DLBCL) not otherwise specified; OR
    - High grade B-cell lymphoma; OR
    - DLBCL arising from follicular lymphoma (TFL); OR
    - Primary mediastinal large B-cell lymphoma; AND
- Patient's disease is relapsed or refractory and is defined as one of the following:
    - Relapse after autologous hematopoietic stem cell transplantation (HSCT); OR
    - Refractory disease to the most recent therapy; AND
- Therapy will be used as one of the following:
    - Used after two or more lines of systemic therapy, which included an anthracycline and an anti-CD20 monoclonal antibody (e.g., rituximab) [unless tumor is CD20-negative]; OR
    - Used as additional therapy for patients with intention to proceed to high-dose therapy who have partial response following second line therapy for relapsed or refractory disease; OR

- Used for treatment of disease that is in second or greater relapse

† FDA Approved Indication(s); ‡ Compendium Recommended Indication(s)

IV. Renewal Criteria

Coverage cannot be renewed.

V. Dosage/Administration

Indication	Dose
B-Cell Precursor ALL	Lymphodepleting chemotherapy: • Fludarabine (30 mg/m^2 intravenous daily for 4 days) and cyclophosphamide (500 mg/m^2 intravenous daily for 2 days starting with the first dose of fludarabine). Kymriah Infusion: • Infuse 2 to 14 days after completion of lymphodepleting chemotherapy • Kymriah is provided in a single-dose unit containing chimeric antigen receptor (CAR)-positive viable T cells* based on the patient weight reported at the time of leukapheresis: o Patients ≤ 50 kg: administer 0.2 to 5.0 x 10^6 CAR-positive viable T cells per kg body weight o Patients > 50 kg: administer 0.1 to 2.5 x 10^8 CAR-positive viable T cells
Large B-cell Lymphoma	Lymphodepleting chemotherapy: • Fludarabine (25 mg/m^2 intravenous daily for 3 days) and cyclophosphamide (250 mg/m^2 intravenous daily for 3 days starting with the first dose of fludarabine); OR • Bendamustine (90 mg/m^2 intravenous daily for 2 days) if the patient experienced a previous Grade 4 hemorrhagic cystitis with cyclophosphamide or demonstrates resistance to a previous cyclophosphamide containing regimen Kymriah Infusion: • Infuse 2 to 11 days after completion of lymphodepleting chemotherapy • Kymriah is provided in a single-dose unit containing chimeric antigen receptor (CAR)-positive viable T cells* based on the patient weight reported at the time of leukapheresis: o Administer 0.6 to 6.0 x 10^8 CAR-positive viable T cells
For autologous use only. For intravenous use only. • Kymriah is prepared from the patient's peripheral blood mononuclear cells, which are obtained via a standard leukapheresis procedure • One treatment course consists of lymphodepleting chemotherapy followed by a single infusion of Kymriah • Confirm availability of Kymriah prior to starting the lymphodepleting regimen. • Delay the infusion of Kymriah after lymphodepleting chemotherapy for unresolved serious adverse reactions from preceding chemotherapies (including pulmonary toxicity, cardiac toxicity, or hypotension), active uncontrolled infection, active graft versus host disease (GVHD), or worsening of leukemia burden.	

*See the Certificate of Analysis (CoA) for the actual number of chimeric antigen receptor (CAR)-positive T cells in the product.

- Store infusion bag in the vapor phase of liquid nitrogen (less than or equal to minus 120°C) in a temperature-monitored system. Thaw prior to infusion.
- In case of manufacturing failure, a second manufacturing may be attempted.
- Additional bridging chemotherapy may be necessary between leukapheresis and lymphodepleting chemotherapy.
- Tocilizumab must be available on site prior to infusion if needed for the treatment of CRS (2 doses minimum)
- Biosafety guidelines must be followed. Product contains human cells genetically modified with a lentivirus. Employ universal precautions when handling.

VI. Billing Code/Availability Information

Jcode:

- Q2042 – Tisagenlecleucel, up to 600 million car-positive viable t cells, including leukapheresis and dose preparation procedures, per therapeutic dose (effective 1/1/19)
- Q2040 – Tisagenlecleucel, up to 250 million car-positive viable t cells, including leukapheresis and dose preparation procedures, per infusion (inactive 1/1/19)

NDC:

- Kymriah suspension for intravenous infusion (Ped ALL); 1 infusion bag (10 to 50 mL): 00078-0846-xx
- Kymriah suspension for intravenous infusion (DLBCL); 1 infusion bag (10 to 50 mL): 00078-0958-xx

VII. References

1. Kymriah [package insert]. East Hanover, NJ; Novartis Pharmaceuticals Corp., May 2018. Accessed October 2018.
2. Porter DL, Hwang WT, Frey NV, et al. Chimeric antigen receptor T cells persist and induce sustained remissions in relapsed refractory chronic lymphocytic leukemia. Sci Transl Med. 2015 Sep 2;7(303):303ra139. doi: 10.1126/scitranslmed.aac5415.
3. Schuster S, Bishop MR, Constantine T, et al. Global Pivotal Phase 2 Trial of the CD19-Targeted Therapy CTL019 In Adult Patients with Relapsed or Refractory (R/R) Diffuse Large B-Cell Lymphoma (DLBCL)—An Interim Analysis. Clinical Lymphoma, Myeloma and Leukemia, Volume 17 , S373 - S374.
4. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) tisagenlecleucel. National Comprehensive Cancer Network, 2018. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed October 2018.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C83.30	Diffuse large B-cell lymphoma unspecified site

C83.31	Diffuse large B-cell lymphoma, lymph nodes of head, face, and neck
C83.32	Diffuse large B-cell lymphoma intrathoracic lymph nodes
C83.33	Diffuse large B-cell lymphoma intra-abdominal lymph nodes
C83.34	Diffuse large B-cell lymphoma lymph nodes of axilla and upper limb
C83.35	Diffuse large B-cell lymphoma, lymph nodes of inguinal region and lower limb
C83.36	Diffuse large B-cell lymphoma intrapelvic lymph nodes
C83.37	Diffuse large B-cell lymphoma, spleen
C83.38	Diffuse large B-cell lymphoma lymph nodes of multiple sites
C83.39	Diffuse large B-cell lymphoma extranodal and solid organ sites
C85.20	Mediastinal (thymic) large B-cell lymphoma unspecified site
C85.21	Mediastinal (thymic) large B-cell lymphoma lymph nodes of head, face, and neck
C85.22	Mediastinal (thymic) large B-cell lymphoma intrathoracic lymph nodes
C85.23	Mediastinal (thymic) large B-cell lymphoma intra-abdominal lymph nodes
C85.24	Mediastinal (thymic) large B-cell lymphoma lymph nodes of axilla and upper limb
C85.25	Mediastinal (thymic) large B-cell lymphoma lymph nodes of inguinal region and lower limb
C85.26	Mediastinal (thymic) large B-cell lymphoma intrapelvic lymph nodes
C85.27	Mediastinal (thymic) large B-cell lymphoma spleen
C85.28	Mediastinal (thymic) large B-cell lymphoma lymph nodes of multiple sites
C85.29	Mediastinal (thymic) large B-cell lymphoma extranodal and solid organ sites
C91.00	Acute lymphoblastic leukemia not having achieved remission
C91.02	Acute lymphoblastic leukemia, in relapse

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD) and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at: http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto Government Benefit Administrators, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC