

DRAFT Medical Coverage Policy | Tisagenlecleucel (Kymriah)



EFFECTIVE DATE:XXXXXX
POLICY LAST UPDATED: XXXXXXXX

OVERVIEW

KYMRIAH™ (tisagenlecleucel) is a prescription cancer treatment used in patients up to 25 years old who have acute lymphoblastic leukemia (ALL) that is either relapsing (went into remission, then came back) or refractory (did not go into remission with other leukemia treatments). KYMRIAH is made from your own white blood cells.

MEDICAL CRITERIA

BlueCHiP for Medicare and Commercial

Kymriah (tisagenlecleucel) is medically necessary when ALL of the following are met:

1. The patient has a diagnosis of relapsed/refractory B-cell precursor acute lymphoblastic leukemia (ALL) (note: the patient must meet all aspects of the diagnosis as indicated)
AND
2. The prescriber has confirmed the patient has CD19 tumor expression
AND
3. The patient is 25 years of age or younger
AND
4. BOTH of the following:
 - a. ONE of the following:
 - i. The patient did not achieve complete response (CR) following 2 cycles of standard chemotherapy **OR**
 - ii. The patient is in the second or later relapse following treatment with 2 or more cycles of standard chemotherapy**AND**
 - b. If the patient is Philadelphia Chromosome positive (Ph+), ONE of the following:
 - i. The patient has failed treatment with 2 or more tyrosine kinase inhibitors (TKI) indicated for ALL **OR**
 - ii. The patient has intolerance, hypersensitivity, or contraindications to TKI agents indicated for ALL**AND**
5. The patient does not have active uncontrolled infection including Hepatitis B, Hepatitis C, or HIV infection
AND
6. The patient does not have active central nervous system (CNS) malignancy involvement (i.e. white blood cell (WBC) count greater than or equal to 5 cells/mcl in the cerebral spinal fluid (CSF) with presence of lymphoblasts)
AND
7. The patient does not have any FDA labeled contraindications to the requested agent
AND
8. The patient has not previously been treated with gene therapy including the requested agent

Approval: 1 treatment course per lifetime

PRIOR AUTHORIZATION

Prior authorization is required for BlueCHiP for Medicare and recommended for Commercial Products

POLICY STATEMENT

BlueCHiP for Medicare and Commercial

Kymriah (tisagenlecleucel) is medically necessary when the above criteria has been met

COVERAGE

Benefits may vary between groups and contracts. Please refer to the appropriate Benefit Booklet, Evidence of Coverage or Subscriber Agreement for applicable physician administered infusion drug benefits/coverage.

BACKGROUND

Acute Lymphoblastic Leukemia (ALL)

Acute Lymphoblastic Leukemia is characterized by the proliferation of immature lymphoid cells in the bone marrow, peripheral blood, and other organs. The incidence of ALL in the United States is 1.58 cases per 100,000 individuals per year and the median age at diagnosis is 15 years.³ Risk factors for developing ALL include older age (over 70 years), exposure to chemotherapy or radiation, and presence of genetic disorders (e.g. Down syndrome). A diagnosis of ALL can be made when there is demonstration of greater than or equal to 20% bone marrow lymphoblasts upon hematopathology review of bone marrow aspirate. Following the diagnosis of ALL, a genetic characterization (e.g. determining presence of Philadelphia chromosome) is completed to aid in optimal risk stratification and treatment planning. Immunophenotypic classification of ALL should also be completed. Acute lymphoblastic leukemia can be classified into the following 3 groups based on immunophenotype: precursor B-cell ALL, mature B-cell ALL, and T-cell ALL. Tisagenlecleucel is indicated for precursor B-cell ALL.

Treatment of ALL represents one of the most complex and intensive programs in cancer therapy.³ Initial treatment includes induction therapy with a combination of vincristine, anthracyclines (e.g. daunorubicin, doxorubicin), and corticosteroids with or without L-asparaginase and/or cyclophosphamide. Additionally, intrathecal antimetabolites such as methotrexate, cytarabine, and/or 6-mercaptopurine are often included at induction therapy for CNS prophylaxis. The goal of induction therapy is to achieve complete remission (CR). Patients who do not achieve CR following induction therapy are considered to have primary refractory disease. 15% of ALL patients fall within this category. For patients who achieve CR, postinduction consolidation therapy followed by maintenance therapy is recommended.³

Treatment options for patients who have primary refractory ALL or have relapsed following initial or subsequent CR may be managed using repeat chemotherapy (in combination with tyrosine kinase inhibitor for patients who are Philadelphia Chromosome positive), blinatumomab, or tisagenlecleucel (for refractory ALL or second or later relapsed ALL).

Kymriah (tisagenlecleucel)

Tisagenlecleucel is an antigen-specific autologous immunotherapy comprising of T cells that have been genetically-modified to target cells that express CD19. CD19 is an antigen expressed on the surface of B-cells and tumors derived from B-cells. The tisagenlecleucel chimeric antigen receptor (CAR) protein consists of an extracellular portion that has a murine anti-CD-19 single chain antibody fragment and an intracellular portion that contains T cell signaling and co-stimulatory domains. The intracellular domains play critical roles in tisagenlecleucel's functions including T cell activation and anti-tumor activity.

Diagnosis of ALL requires demonstration of equal to or greater than 20% bone marrow lymphoblasts on a hematology review of bone marrow aspirate

Efficacy

The efficacy of tisagenlecleucel is based on results of a phase 2, open label, multicenter single-arm trial in pediatric and young adult patients with refractory/relapsed (R/R) B-cell precursor ALL. The trial enrolled patients who had primary refractory disease (defined as failure to achieve complete response after two cycles

of standard chemotherapy) or had two or more relapses. Key exclusion criteria included history of prior treatment with any gene therapy, presence of CNS involvement as defined by NCCN guidelines (i.e. white blood cell (WBC) count greater than or equal to 5 cells/mcl in the cerebral spinal fluid (CSF) with presence of lymphoblasts), and presence of active infection including hepatitis B, hepatitis C, and HIV.

The trial enrolled 88 patients of whom 63 received a single dose of tisagenlecleucel and were therefore evaluable for efficacy. The 63 evaluable patients included 6 patients (10%) patients who had primary refractory disease, 30 patients (48%) who had one prior stem cell transplantation, and 5 patients (8%) had two stem cell transplantations. Of the 63 patients, 35 patients were males and 28 patients were females. The median age was 12 years (range, 3-23 years). Seventy-three percent of patients were white, 10% were Asian, and 17% were of other races. All 63 evaluable patients received tisagenlecleucel that was manufactured at the manufacturer's United States facility.

The primary endpoint of the trial was overall remission rate (ORR), defined as a best overall response rate (BOR) of complete remission (CR) or complete remission with incomplete blood count recovery (CRi) assessed within 3 months following the infusion of tisagenlecleucel. The trial also evaluated the duration of CR, proportion of patients with CR and minimal residual disease (MRD). Among the 63 infused patients, 52 (83%) achieved CR/CRi, all of which were MRD-negative. With a median follow-up of 4.8 months from response, the median duration of CR/CRi was not reached (range: 1.2 to 14.1+ months). Median time to onset of CR/CRi was 29 days with onset of CR/CRi between 26 and 31 days for 50/52 (96%) responders. The stem cell transplantation rate among those who achieved CR/CRi was 12% (6/52).

CODING

There is not a specific HCPCS code for this drug. Claims must be filed with an unlisted HCPCS code and the NDC number.

RELATED POLICIES

Unlisted Procedures

PUBLISHED

Provider Update, December 2017

REFERENCES:

1. Kymriah prescribing information. Novartis. September 2017.
2. Kymriah Risk Evaluation and Mitigation Strategy (REMs)
3. NCCN Acute Lymphoblastic Leukemia treatment guidelines. Version 3.2017 – September 2017. Accessed September 2017.
4. KYMRIAHTM (tisagenlecleucel) <https://www.us.kymriah.com/acute-lymphoblastic-leukemia-children/>

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