Kymriah

Description

Kymriah (tisagenlecleucel)

Background
Kymriah is a genetically-modified autologous T cell immunotherapy indicated for the treatment of B-cell precursor acute lymphoblastic leukemia (ALL), that is refractory or in second or later relapse. Kymriah is also indicated for the treatment of refractory or relapsed diffuse large B-cell lymphoma (DLBCL) in adult patients. Each dose of Kymriah is a customized treatment created using an individual patient’s own T-cells, a type of white blood cell known as a lymphocyte. The patient’s T-cells are collected and sent to a manufacturing center where they are genetically modified to include a new gene that contains a specific protein (a chimeric antigen receptor or CAR) that directs the T-cells to target and kill leukemia cells that have a specific antigen (CD19) on the surface. Once the cells are modified, they are infused back into the patient to kill the cancer cells (1).

Regulatory Status
FDA-approved indication: Kymriah is a CD19-directed genetically modified autologous T cell immunotherapy indicated for the treatment of (1):

1. Patients up to 25 years of age with B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory or in second or later relapse.
2. 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.
Limitations of use for DLBCL:
Kymriah is not indicated for treatment of patients with primary central nervous system lymphoma.

Kymriah has a boxed warning for cytokine release syndrome (CRS) and neurological toxicities. Patients with an active infection or inflammatory disorders should not receive Kymriah and monitoring for neurological events should be done after treatment of Kymriah (1).

Kymriah is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS). Healthcare facilities that dispense and administer Kymriah must be enrolled and comply with the REMS requirements. Certified healthcare facilities must have on-site, immediate access to tocilizumab (Actemra), and ensure that a minimum of two doses of tocilizumab are available for each patient for administration within 2 hours after Kymriah infusion, if needed for treatment of CRS (1).

Serious infections, including life-threatening or fatal infections, occurred in patients after Kymriah infusion. Hepatitis B virus (HBV) reactivation, in some cases resulting in fulminant hepatitis, hepatic failure, can occur in patients treated with drugs directed against B cells. Perform screening for HBV, HCV, and HIV in accordance with clinical guidelines before collection of cells for manufacturing (1).

The safety and efficacy of Kymriah has not been established in patients above 25 years of age with relapsed or refractory (r/r) B-cell acute lymphoblastic. The safety and efficacy of Kymriah has not been established in pediatric patients with relapsed or refractory DLBCL (1).

Related policies
Yescarta

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Kymriah may be considered medically necessary for patients 25 years of age and younger with B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory or relapsed, or for patients 18 years and older for the treatment of relapsed or refractory diffuse large B-cell lymphoma (DLBCL), and if the conditions indicated below are met.

Kymriah may be considered investigational for all other indications.
Prior-Approval Requirements

Diagnoses

Patient must have **ONE** of the following:

1. Refractory or relapsed B-cell precursor acute lymphoblastic leukemia (ALL)
   a. Patient must be 25 years of age or younger
   b. Documentation of CD19 tumor expression in bone marrow or peripheral blood
   c. Lymphoblasts ≥ 5%
   d. Patient must have received a regimen containing **ONE** of the following, as part of their initial therapy for ALL:
      i. 2 lines of tyrosine kinase inhibitor therapy (TKI)
      ii. 2 cycles of a standard chemotherapy regimen
   e. Patient has had prior stem cell transplantation that has disease progression 6 months post stem cell infusion

   AND **NONE** of the following:
   a. Burkitt lymphoma
   b. Grade 2 to 4 graft-versus-host disease (GvHD)
   c. Concomitant genetic syndrome with the exception of Down syndrome
   d. Allogenic cellular therapy within 6 weeks prior to Kymriah infusion
   e. Active central nervous system malignancy

2. Refractory or relapsed diffuse large B-cell lymphoma (DLBCL)
   a. Patients must be 18 years of age or older
   b. Patient must have received **TWO** or more lines of systemic therapy including:
      i. Anti-CD20 monoclonal antibody for CD20-positive tumor
      ii. Anthracycline-containing chemotherapy regimen
      iii. Transformed follicular lymphoma **ONLY**: prior chemotherapy for follicular lymphoma and subsequently had chemorefractory disease after transformation to diffuse large B-cell lymphoma
   c. Patient has had prior autologous stem cell transplantation (ASCT) that has disease progression 6 months post stem cell infusion **OR** is ineligible for autologous stem cell transplant (ASCT)
   d. **NO** active central nervous system malignancy
AND ALL of the following for BOTH indications:
1. Absence of active infection (including TB, HBV, HCV, and HIV)
2. Patient is not at risk for HBV infection OR patient is at risk for HBV infection and HBV infection has been ruled out or treatment for HBV infection has been initiated
3. Prescriber agrees to monitor the patient for signs and symptoms of cytokine release syndrome (CRS) and administer tocilizumab (Actemra) if needed
4. Prescriber agrees to monitor the patient for signs and symptoms of neurological toxicities
5. Prescriber is enrolled in Kymriah REMS Access program
6. NO dual therapy with another CD19-directed CAR-T cell therapy treatment (Yescarta) or any other gene therapy

Prior – Approval Renewal Requirements
None

Policy Guidelines

Pre – PA Allowance
None

Prior - Approval Limits
Duration One infusion bag per Lifetime

Rationale

Summary
Kymriah is an autologous T cell immunotherapy and is intended for B-cell precursor acute lymphoblastic leukemia (ALL) refractory or in second or later relapse. Kymriah may also be used to treat adult relapsed or refractory diffuse large B-cell lymphoma (DLBCL). Kymriah may cause cytokine release syndrome (CRS) and neurological toxicities. Kymriah should not be administered in patients with an active infection or any inflammatory disorders (1).

References
5.21.101

Section: Prescription Drugs
Subsection: Antineoplastic Agents
Subject: Kymriah

Effective Date: October 1, 2019
Original Policy Date: September 8, 2017
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Policy History

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<td>September 2017</td>
<td>Addition to PA</td>
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<tr>
<td>December 2017</td>
<td>Annual editorial review</td>
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<td>Change in the age requirement from 2 through 25 to 25 yrs. of age and</td>
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<tr>
<td>March 2018</td>
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<td>Removal of the word “autologous” from stem cell requirement and patient</td>
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<td>May 2018</td>
<td>Addition of the diagnosis of refractory or relapsed diffuse large B-cell</td>
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<td>lymphoma (DLBCL) in patients 18 years of age or older to criteria.</td>
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Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on September 13, 2019 and is effective on October 1, 2019.