Kymriah (tisagenlecleucel) is a non-preferred product and will only be considered for coverage under the medical benefit when the following criteria are met:

Members must be clinically diagnosed with one of the following disease states and meet their individual criteria as stated.

### ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) – for autologous use only

For **initial** authorization:
1. Member is 3-25 years of age and has documentation of CD19 tumor expression; AND
2. Member has B-cell acute lymphoblastic leukemia that is refractory or in second or later relapse as defined by one of the following:
   a) 2nd or greater Bone Marrow (BM) relapse;
   b) Any BM relapse after allogeneic stem cell transplantation (SCT) and must be > 6 months from SCT at the time of CAR-T cell immunotherapy infusion;
   c) Refractory as defined by not achieving a complete remission (CR) after 2 cycles of a standard chemotherapy regimen or chemorefractory as defined by not achieving a CR after 1 cycle of standard chemotherapy for relapse leukemia;
   d) Member with Philadelphia chromosome positive (Ph+) acute lymphoblastic leukemia that is intolerant to or have failed 2 lines of tyrosine kinase inhibitor (TKI) therapy (e.g. imatinib mesylate (Gleevec), dasatinib (Sprycel), nilotinib (Tasigna) or ponatinib (Iclusig)), or if TKI therapy is contraindicated;
   e) Member is not eligible for allogeneic SCT; AND
3. Member has been screened for hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV) prior to collection of cells (leukapheresis); AND
4. Healthcare facility/provider has enrolled in the Kymriah REMS and has training on the management of cytokine release syndrome (CRS) and neurological toxicities; AND
5. Member must be premedicated with acetaminophen and an H1-antihistamine, and tocilizumab (Actemra) must be available in healthcare facility prior to infusion; AND
6. Member has a life expectancy > 12 weeks; AND
7. Member does not have history of ALL of the following:
   a) Prior CAR-T therapy;
   b) Concomitant genetic syndrome (e.g., Fanconi anemia, Kostmann syndrome, Shwachman syndrome or any other known bone marrow failure syndrome);
   c) Burkitt's lymphoma/leukemia;
   d) Malignancy, except carcinoma in situ of the skin or cervix treated with curative intent and with no evidence of active disease;
   e) Prior treatment with gene therapy product;
f) Presence of Grade 2 to 4 acute or extensive chronic graft-versus-host disease (GVHD);
g) Active or latent hepatitis B or active hepatitis C or HIV.

8. **Dosage allowed:** Weight 50 kg or less: administer 0.2 to 5.0 x 10^6 CAR-positive viable T cells per kg body weight intravenously. Weight above 50 kg: administer 0.1 to 2.5 x 10^8 total CAR-positive viable T cells (non-weight based) intravenously.

*If member meets all the requirements listed above, the medication will be approved for 3 months.*

For **reauthorization**:
1. Kymriah will not be reauthorized for continued therapy.

### LARGE B-CELL LYMPHOMA – for autologous use only

For **initial** authorization:
1. **Member is being use for adult member (18 years old or older) with has relapsed or refractory large B-cell lymphoma (diffuse large B-cell lymphoma (DLBCL) not otherwise specified, high grade B-cell lymphoma, or DLBCL arising from follicular lymphoma); AND**
2. **Member has received ≥ 2 lines of chemotherapy, including rituximab and anthracycline, or relapsed following autologous hematopoietic stem cell transplantation (HSCT); AND**
3. **Member does not have ALL of the following:**
   a) Active central nervous system malignancy;
   b) Prior allogenic HSCT;
   c) ECOG performance status ≥ 2;
   d) Creatinine clearance < 60;
   e) Alanine aminotransferase > 5 times normal;
   f) Cardiac ejection fraction < 45%
   g) Absolute lymphocyte concentration less than 300/µL;
   h) Active replication of or prior infection with hepatitis B or active hepatitis C (HCV RNA positive);
   i) HIV positive; AND
4. **Healthcare facility/provider has enrolled in the Kymriah REMS and has training on the management of cytokine release syndrome (CRS) and neurological toxicities; AND**
5. **Member must be premedicated with acetaminophen and an H1-antihistamine, and tocilizumab (Actemra) must be available in healthcare facility prior to infusion; AND**
6. **Member has a life expectancy > 12 weeks; AND**
7. **Member has not received prior CAR-T therapy.**
8. **Dosage allowed:** Administer 0.6 to 6.0 x 10^8 CAR-positive viable T cells.

*If member meets all the requirements listed above, the medication will be approved for 3 months.*

For **reauthorization**:
1. Kymriah will not be reauthorized for continued therapy.

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CareSource considers Kymriah (tisagenlecleucel) not medically necessary for the treatment of the following disease states based on a lack of robust clinical controlled trials showing superior efficacy compared to currently available treatments:

- Primary central nervous system lymphoma

<table>
<thead>
<tr>
<th>DATE</th>
<th>ACTION/DESCRIPTION</th>
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<tbody>
<tr>
<td>10/24/2017</td>
<td>New policy for Kymriah created.</td>
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<tr>
<td>08/27/2018</td>
<td>New indication of Large B-cell lymphoma was added. Criteria expanded for ALL diagnosis for member’s disease history requirement.</td>
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</tbody>
</table>
References:

6. NCCN Guidelines. Acute Lymphoblastic Leukemia. V.1.2018

Effective date: 09/07/2018
Revised date: 08/27/2018