Clinical Policy Title:	tisagenlecleucel
Policy Number:	RxA.183
Drug(s) Applied:	Kymriah®
Original Policy Date:	02/07/2020
Last Review Date:	10/19/2023
Line of Business Policy Applies to:	All lines of business (except Medicare)

Criteria

I. Initial Approval Criteria

A. Acute Lymphoblastic Leukemia (must meet all)**:**

1. Diagnosis of B-cell precursor ALL;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≤ 25 years;
4. Documentation of CD19 tumor expression;
5. Recent (within the last 30 days) documentation of one of the following (a or b):
   a. Absolute lymphocyte count (ALC) of 500/µL or greater;
   b. CD3 (T-cells) cell count of ≥ 150/µL if ALC < 500/µL;
6. Request meets one of the following (a, b, or c):
   a. Disease is refractory* or member has had more than or equal to 2 relapses for Philadelphia chromosome positive or Philadelphia chromosome negative;
   *Refractory is defined as failure to achieve a complete response following induction therapy with more than or equal to 2 cycles of standard chemotherapy regimen (primary refractory) or after 1 cycle of standard chemotherapy for relapsed leukemia (chemorefractory);
   b. If Disease is Philadelphia chromosome positive: Trial and failure of two (2) lines of chemotherapy that included two (2) tyrosine kinase inhibitors (e.g., imatinib, Sprycel®, Tasigna®, Bosulif®, Iclusig®) at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
   *Prior authorization may be required for tyrosine kinase inhibitors
   c. Member has relapsed following hematopoietic stem cell transplantation (HSCT) and must be six (6) months or greater since HSCT at the time of Kymriah® infusion;
7. Member does not have active or primary central nervous system (CNS) disease;
8. Kymriah is not prescribed concurrently with other CAR T-cell immunotherapy (e.g., Abecma, Breyanzi, Tecartus, Yescarta);
9. Dose does not exceed (a or b):
   a. Weight of 50 kg or less: 5.0 x 10^6 chimeric antigen receptor CAR-positive viable T cells per kg of body weight;
   b. Weight greater than 50 kg: 2.5 x 10^8 CAR-positive viable T cells.

Approval Duration

Commercial: 3 months (1 dose only)

Medicaid: 3 months (1 dose only)

This clinical policy has been developed to authorize, modify, or determine coverage for individuals with similar conditions. Specific care and treatment may vary depending on individual need and benefits covered by the plan. This policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. This document may contain prescription brand name drugs that are trademarks of pharmaceutical manufacturers that are not affiliated with RxAdvance.

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B. Large B-Cell Lymphoma (must meet all)**:**

1. Diagnosis of one of the following (a, b or c):
   a. Diffuse large B-cell lymphoma arising from follicular lymphoma;
   b. Histologic transformation of nodal marginal zone lymphoma to DLBCL;
   c. High-grade B-cell lymphomas (including High-grade B-cell lymphomas with translocations of MYC and BCL2 and/or BCL6 (double/triple hit lymphoma));
2. Member has one of the following B cell lymphoma subtype (a, or b) (off-label);
   a. Acquired immunodeficiency syndrome (AIDS)-related B-cell lymphomas;
   b. Monomorphic post-transplant lymphoproliferative disorders;
3. Prescribed by or in consultation with an oncologist or hematologist;
4. Age ≥ 18 years;
5. Recent (within the last 30 days) ALC of 300/µL or greater;
6. Disease is refractory or member has relapsed after more than or equal to 2 lines of systemic therapy that includes rituximab and one anthracycline-containing regimen (e.g., doxorubicin);
   *Prior authorization may be required.
7. Member does not have active or primary CNS disease;
8. Kymriah is not prescribed concurrently with other CAR T-cell immunotherapy (e.g., Abecma, Breyanzi, Tecartus, Yescarta);
9. Dose does not exceed 6.0 x 10^8 CAR-positive viable T cells.

Approval Duration
Commercial: 3 months (1 dose only)
Medicaid: 3 months (1 dose only)

C. Follicular Lymphoma (must meet all):

1. Diagnosis of FL grade 1 and 2;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. Request meets one of the following (a or b):
   a. Disease is relapsed/refractory after ≥ 2 lines of systemic therapy that includes a combination of an anti-CD20 monoclonal antibody (e.g., rituximab or Gazyva®) and an alkylating agent (e.g., bendamustine, cyclophosphamide, chlorambucil);
      *Prior authorization may be required.
   b. Member has relapsed following hematopoietic stem cell transplantation (HSCT) and must be six (6) months or greater since HSCT at the time of Kymriah® infusion;
5. Member does not have active CNS involvement by malignancy;
6. Kymriah is not prescribed concurrently with other CAR T-cell immunotherapy (e.g., Abecma, Breyanzi, Tecartus, Yescarta);
7. Dose does not exceed a single administration of 6 x 10^8 CAR-positive viable T cells.

Approval Duration
Commercial: 3 months (1 dose only)
Medicaid: 3 months (1 dose only)

II. Continued Therapy Approval

A. All Indications in Section I

1. Continued therapy will not be authorized as tisagenlecleucel is indicated to be dosed one time only.

Approval Duration
Not applicable

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References

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2. National Comprehensive Cancer Network. B-Cell Lymphomas Version 5.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf. Accessed January 18, 2023.
3. National Comprehensive Cancer Network. Central Nervous System Cancers Version 2.2022. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cns.pdf. Accessed January 18, 2023.
4. Schuster SJ, Bishop MR, Tam CS, et al. Tisagenlecleucel in adult relapsed or refractor diffuse large B-cell lymphoma. N Engl J Med 2019; 380(1): 45-56. Available at: https://www.nejm.org/doi/full/10.1056/nejmoa1804980. Accessed January 18, 2023.
5. National Comprehensive Cancer Network. Pediatric Acute Lymphoblastic Leukemia Version 1.2022. Available at https://www.nccn.org/professionals/physician_gls/pdf/ped_all.pdf. Accessed January 18, 2023.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
Policy reviewed 1. Clinical Policy Title was updated. 2. Drug(s) Applied was updated. 3. Line of Business Policy Applies to was update to all lines of business. 4. Initial Approval criteria: Commercial and Medicaid approval duration were updated. 5. References were updated.	07/14/2020	09/14/2020
Policy was reviewed. 1. Initial approval criteria I.B.1 updated to include the indication of “Histologic transformation of nodal marginal zone lymphoma to DLBCL”. 2. Initial approval criteria I.B.2 was updated to include off label indications. 3. References were reviewed and updated	03/02/2021	06/10/2021
Policy was reviewed. 1. Initial Approval Criteria I.A.6.a was updated to add Philadelphia chromosome negative. 2. Initial Approval Criteria B.1.c was added: High-grade B-cell lymphomas (including High-grade B-cell lymphomas with translocations of MYC and BCL2	01/13/2022	04/18/2022

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and/or BCL6 (double/triple hit lymphoma)); 3. Initial Approval Criteria I.B.a was removed : High-grade B-cell lymphomas (including High-grade B-cell lymphomas with translocations of MYC and BCL2 and/or BCL6 (double/triple hit lymphoma)); 4. References were reviewed and updated.		
Policy was reviewed: 1. Initial Approval Criteria, I.C: Updated to include approval criteria for indication, Follicular Lymphoma. 2. Initial Approval Criteria I.A.8, I.B.8, I.C.6: Updated to add Kymriah is not prescribed concurrently with other CAR T-cell immunotherapy (e.g., Abecma, Breyanzi, Tecartus, Yescarta). 3. References were reviewed and updated.	01/18/2023	04/13/2023
Policy was reviewed.	10/19/2023	10/19/2023

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