University of Michigan Health Plan

DRUG DETERMINATION POLICY

Title: DDP-38 CAR-T Cell Immunotherapy

Effective Date: 12/18/24

Important Information - Please Read Before Using This Policy

The following policy applies to health benefit plans administered by UM Health Plan and may not be covered by all UM Health Plan. Please refer to the member's benefit document for specific coverage information. If there is a difference between this general information and the member's benefit document, the member's benefit document will be used to determine coverage. For example, a member's benefit document may contain a specific exclusion related to a topic addressed in a coverage policy.

Benefit determinations for individual requests require consideration of:

1. The terms of the applicable benefit document in effect on the date of service.
2. Any applicable laws and regulations.
3. Any relevant collateral source materials, including coverage policies.
4. The specific facts of the situation.

Contact UM Health Plan Customer Service to discuss plan benefits more specifically.

1.0 Policy:

This policy describes the determination process for coverage of specific drugs.

This policy does not guarantee or approve benefits. Coverage depends on the specific benefit plan. Drug Determination Policies are not recommendations for treatment and should not be used as treatment guidelines.

2.0 Background or Purpose:

CAR-T cell immunotherapy is covered through the medical benefit based on approval by the Health Plan after review by a clinical pharmacist and the medical director. These criteria were developed and implemented to ensure appropriate use for the intended diagnoses and mitigation of toxicity, if possible.

3.0 Clinical Determination Guidelines:

Document the following with chart notes:

I. General Considerations

A. Appropriate medication use [must meet all listed below]:

1. Diagnosis: meets standard diagnostic criteria that designate signs, symptoms, and test results to support specific diagnosis.

2. FDA approval status [must meet one listed below]:

a. FDA approved: product, indication, and/or dosage regimen.

b. Non-FDA approved: compendium support (Lexicomp™, NCCN) for the use of a drug for a non-FDA-approved indication or dosage regimen.

3. Place in therapy: sequence of therapy supported by national or international accepted guidelines and/or studies (e.g., oncologic, infectious conditions).

B. Prescriber/site: oncologist; Certified Healthcare Facility enrolled in the specific CAR-T REMS; training has been given to providers on the management of cytokine release syndrome (CRS) and neurological toxicities.

C. Approval:

1. Initial: one-time infusion.
2. Re-approval: none.

D. Exclusions [meets one listed below]:

1. History of Allogeneic Stem Cell Transplantation (SCT), unless otherwise stated.
2. Central nervous system disorder: history of seizure disorder, cardiovascular ischemia or hemorrhage, dementia, cerebellar disease, or any autoimmune disease with central nervous system involvement.
3. Active Infection or inflammatory disorder.
4. Pregnancy.
5. Live vaccines: administered within two weeks prior to lympho-depleting chemotherapy.
6. Life expectancy: less than 12 weeks.

II. Kymriah intravenous (tisagenlecleucel IV).

A. Acute Lymphoblastic Leukemia [must meet all listed below]:

1. Age: three to 25 years.
2. Diagnosis and severity [must meet all listed below]:
   a. B-cell Precursor Acute Lymphoblastic Leukemia (ALL).
   b. CD19 tumor expression.
   c. Refractory to therapy or member has had at least two bone marrow relapses.
3. Other therapies: A trial of one therapeutic category listed below is required unless all are contraindicated. Trial must result in an inadequate response or severe adverse reaction.
   a. Autologous Stem Cell Transplant (SCT).
   b. Standard chemotherapy: two lines without complete response.
   c. Philadelphia chromosome-positive: two prior lines of tyrosine kinase inhibitor (TKI) therapy (e.g., imatinib, dasatinib, ponatinib).
4. Dosage regimen: Kymriah intravenous (tisagenlecleucel IV).
   a. Infuse two to 14 days after completion of lymphodepleting chemotherapy (cyclophosphamide and fludarabine).
   b. Dose: less than 50kg: 0.2 -5 x 10^6 CAR+ T cells per kg.; greater than 50kg: 0.1-2.5 10^8 CAR-positive T cells per kg.

B. Relapsed or Refractory Diffuse Large B-cell Lymphoma (DLBCL) [must meet all listed below]:

1. Age: at least 18 years.
2. Diagnosis and severity [must meet one listed below]:
   a. High-grade B-cell Lymphoma.
   b. DLBDL arising from follicular lymphoma.
   c. DLBL not otherwise specified.

3. Other therapies: A trial of one therapeutic category listed below is required unless all are contraindicated. Trial must result in an inadequate response or severe adverse reaction.
    a. Autologous Stem Cell Transplant (SCT).
    b. Standard chemotherapy: two lines without complete response.
4. Dosage regimen: Kymriah intravenous (tisagenlecleucel IV) [must meet both listed below]:
    a. Infuse two to 11 days after completion of lymphodepleting chemotherapy (cyclophosphamide and fludarabine or with bendamustine for cyclophosphamide intolerance or resistance to a previous cyclophosphamide regimen).
    b. Dose 0.6 to 6 x 108 CAR-positive viable T cells.

C. Follicular Lymphoma [must meet all listed below]:
1. Age: at least 18 years.
2. Diagnosis and severity: Relapsed or refractory Follicular Lymphoma after two or more lines of systemic therapy.
3. Other therapies: refractory to or relapse after the completion of two prior lines of systemic therapy that have National Comprehensive Cancer Network (NCCN) category of evidence and consensus of 2A or better.
4. Dosage regimen: Kymriah intravenous (tisagenlecleucel IV).
    i. Infused Kymriah two to six days after lymphodepleting chemotherapy with a fludarabine and cyclophosphamide regimen or a bendamustine regimen.
    ii. May omit lymphodepleting chemotherapy if white blood cell count is less than 1 x 10^9/L within one week prior to Kymriah infusion.

III. Yescarta intravenous (axicabtagene ciloleucel IV).

A. Large B-cell Non-Hodgkin Lymphoma (NHL) with CD 19 tumor expression [must meet all listed below]:
1. Age: at least 18 years.
2. Diagnosis and severity [must meet all listed below]:
    a. Diffuse large B-cell lymphoma (DLBCL).
    b. Primary mediastinal B-cell Lymphoma.
    c. High-grade B-cell lymphoma.
    d. Diffuse large B-cell lymphoma (DLBCL) arising from follicular lymphoma.
3. Other therapies: A trial of one therapeutic category listed below is required unless all are contraindicated. Trial must result in an inadequate response or severe adverse reaction.
    a. Autologous Stem Cell Transplant (SCT): progressed within one year post SCT.
    b. Standard chemotherapy: refractory to two lines, including anthracycline-based with an anti-CD 20 antibody.
    c. Follicular lymphoma transformation to diffuse B-cell lymphoma (DLBCL): refractory to two lines of chemotherapy.
4. Dosage regimen: Yescarta intravenous (axicabtagene ciloleucel IV).
    a. Infuse two to 14 days after completion of lymphodepleting chemotherapy (cyclophosphamide and fludarabine).

b. Target dose: 2 × 10^6 CAR-positive T cells per Kg; maximum dose: 2 × 108 CAR-positive T cells.

B. Follicular Lymphoma [must meet all listed below]:

1. Age: at least 18 years.
2. Diagnosis and severity: Relapsed or refractory Follicular Lymphoma after two or more lines of systemic therapy.
3. Other therapies: refractory to or relapse after the completion of two prior lines of systemic therapy that have National Comprehensive Cancer Network (NCCN) category of evidence and consensus of 2A or better.
4. Dosage regimen: Yescarta intravenous (axicabtagene ciloleucel IV).
   a. Infuse two to 14 days after completion of lymphodepleting chemotherapy (cyclophosphamide and fludarabine).
   b. Target dose: 2 x 10^6 CAR-positive T cells per kg body weight. Maximum of 2 x 10^8 CAR-positive T cells.

IV. Breyanzi intravenous (lisocabtageme maraleucel IV).

A. Relapsed or Refractory Diffuse Large B-cell Lymphoma (DLBCL) [must meet all listed below]:

1. Age: at least 18 years.
2. Diagnosis and severity [must meet one listed below]:
   a. High-grade B-cell Lymphoma.
   b. Follicular lymphoma grade 3B.
   c. Primary mediastinal large B-cell lymphoma.
   d. DLBL not otherwise specified (including DLBCL arising from indolent lymphoma).
3. Other therapies: A trial of one therapeutic category listed below is required unless all are contraindicated. Trial must result in an inadequate response or severe adverse reaction.
   a. Autologous and/or Allogeneic Stem Cell Transplant (SCT).
   b. Standard chemotherapy: two lines without complete response.
4. Dosage regimen: Breyanzi intravenous (lisocabtageme maraleucel IV).
   a. Infuse two to seven days after completion of three days of lymphodepleting chemotherapy (cyclophosphamide and fludarabine).
   b. Dose 50 to 110 x 106 CAR-T positive viable T cells.

V. Tecartus intravenous (brexucabtagene autoleucel IV).

A. Refractory mantle cell lymphoma.

1. Age: at least 18 years.
2. Diagnosis and severity. [must meet all listed below]:
   a. Refractory treatment or in second or later relapse.
   b. CD19-positive in the latest relapse as confirmed by immunohistochemistry or flow cytometry.
   c. The member has not received any prior FDA-approved CD19-directed therapy (e.g., Tecartus, Kymriah, or Yescarta).

d. The member has adequate organ and bone marrow function as determined by the treating oncologist or hematologist.

3. Other therapies: trials of one therapy from each group listed below are required unless contraindicated. Trials must result in an inadequate response or severe adverse reaction.

a. Tyrosine kinase inhibitor (BTKI) such (e.g., Ibrutinib, Acalabrutinib, Zanubrutinib.

b. The member has previously received Anti-CD20 monoclonal antibody therapy (e.g., rituximab, obinutuzumab).

c. Anthracycline- or benamustine-containing chemotherapy.

4. Dosage regimen:

a. Infuse two to four days after completion of chemotherapy (with fludarabine and cyclophosphamide).

b. Target dose: 2×10^6 CAR-positive viable T cells per kg body weight (Wang 2020); maximum dose: 2×10^8 CAR-positive viable T cells.

B. Acute Lymphoblastic Leukemia (ALL) [must meet all listed below]:

1. Age: at least 18 years.

2. Diagnosis and severity [must meet all listed below]:

a. B-cell Precursor ALL.

b. CD19 tumor expression.

c. Refractory to therapy or member has had at least two bone marrow relapses.

3. Other therapies: a trial of at least one therapy below is required unless all are contraindicated. Trials must result in an inadequate response or severe adverse reaction.

a. Allogenic Stem Cell Transplant (SCT).

b. Standard chemotherapy: two lines without complete response.

c. Philadelphia chromosome positive: two prior lines of tyrosine kinase inhibitor (TKI) therapy (e.g., imatinib, dasatinib, ponatinib).

4. Dosage regimen: Tecartus intravenous (brexucabtagene autoleucel IV).

a. Infuse two to four days after completion of chemotherapy (with fludarabine and cyclophosphamide).

b. Target dose: 2 × 106 CAR-positive viable T cells per kg body weight (Wang 2020); maximum dose: 2 × 108 CAR-positive viable T cells.

VI. Abecma intravenous (Idecabtagene Vicleucel IV) and Carvykti (ciltacabtagene autoleucel).

A. Multiple myeloma [must meet all listed below]:

1. Age: at least 18 years.

2. Diagnosis and severity.

a. Diagnosis: relapsed or refractory multiple myeloma without known central nervous system involvement.

3. Other therapies: Trials of at least four therapies listed below are required unless contraindicated. Trials must result in an inadequate response or severe adverse reaction:

a. Immunomodulatory agent (e.g., thalidomide, pomlidomide, lenalidomide).

b. Proteasome inhibitor (e.g., isatuximab or daratumumab).

c. Anti-CD38 monoclonal antibody (e.g., ixazomib, bortezomib, or carfilzomib).

4. Dosage regimen:
   a. Infuse two days after completion of chemotherapy (with fludarabine and cyclophosphamide).
   b. Abecma intravenous (Idecabtagene Vicleucel IV): Target dose: 300 to 460 × 106 CAR-positive viable T-cells. Delay idecabtagene vicleucel infusion up to seven days for unresolved serious adverse events.
   c. Carvykti (ciltacabtagene autoleucel): 0.5-1.0 x 106 CAR-positive viable T-cells per kg body weight, with a maximum dose of 1 x 108 CAR+ viable T cells per one-time infusion.

4.0 Codes:

COVERED CODES AND PRODCUTS				
Code	**Brand Name**	**Generic Name**	**Billing Units (1 unit)**	**Prior Approval**
Q2042	Kymriah	tisagenlecleucel	Up t 600 million CAR+ t cells	Y
Q2041	Yescarta	axicabta-gene ciloleuce	Up to 200 million CAR+ t cells	Y
Q2056	Carvykti	ciltacabtagene autoleucel	Up to 100 million CAR+ t cells	Y
Q2054	Breyanzi	Lisocabtagene maraeucel	Up to 110 million CAR+ t cells	Y
Q2055	Abecma	Idecabtagene Vicleuce	Up to 460 million CAR+ t cells	Y
Q2053	Tecartus	brexucabtagene autoleucel	Up to 200 million CAR+ t cells	Y

5.0 References, Citations, Resources & Associated Documents:

1. Kymriah [package insert] East Hanover, NJ Novartis Pharmaceuticals Corp, June 2024.
2. Yescarta [package insert] Santa Monica, CA; Kite Pharma, Inc. June 2024.
3. Chimeric Antigen Receptor-T cell therapy: Practical considerations for implementation in Europe. HemaSphere, 2018;2:1.
4. UpToDate® LexiDrug™, Hudson, Ohio: Wolters Kluwer, Inc.Kymriah, Yescarta, Breyanzi, Tecartus, Abcema, Carvykti accessed November 2024.
5. Management of immune-related adverse events in patients treated with chimeric antigen Receptor T-Cell therapy: ASCO Guideline. Journal of Clinical Oncology Nov 2021 https://ascopubs.org/doi/full/10.1200/JCO.21.01992
6. Carvykti [package insert]. Horsham, PA: Janssen Biotech, Inc.; April 2024.

7. Breyanzi [package insert]. Summit, NJ: Celgene Corporation, Bristol-Myers Squibb Company; May 2024.
8. Abecma [package insert]. Summit, NJ: Celgene Corporation, a Bristol-Myers Squibb Company; April 2024.
9. Tecartus [package insert]. Santa Monica, CA; Kite Pharma, Inc. June 2024.
10. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for B-Cell Lymphoma V.3.2024. © National Comprehensive Cancer Network, Inc. 2024. All rights reserved. Accessed [November 4, 2024].

6.0 Appendices:

None.

7.0 Revision History:

Original Effective Date: 06/27/2018

Next Review Date: 11/10/2025

Revision Date	Reason for Revision
9/19	Moved to new format; replaced abbreviations, corrected table
10/20	Annual review; revised criteria instructions and other therapies language; added diagnosis Relapsed or Refractory Diffuse Large B-cell Lymphoma (DLBCL), formatting, approved by P&T Committee 12/9/20
3/21	Off cycle review, added Breyanzi; approved at 4/28/21 P&T
10/21	Annual review; added drugs Tecartus and Abecma; reformatted, deleted ECOG performance status as exclusion, clarified life expectancy exclusion
10/22	Annual review; added reference
9/23	Annual Review; added Carvykti in line with PDL, clarified autologous vs allogenic stem cell transplant, updated formatting, updated coding section for Breyanzi, Abecma, and Tecartus, updated other therapies language, clarified four lines of therapy require for Abecma and Carvykti, added that review for these agents is by a clinical pharmacist and the medical director.
9/24	Annual review; removed Appendix I: Patient Safety and Monitoring. Added Follicular Lymphoma indication for Yescarta and Kymriah.