

SmartPA Criteria Proposal

Drug/Drug Class:	CAR-T Cell Therapy Clinical Edit
First Implementation Date:	June 21, 2018
Proposed Date:	June 16, 2022
Prepared for:	MO HealthNet
Prepared by:	MO HealthNet/Conduent
Criteria Status:	<input type="checkbox"/> Existing Criteria <input checked="" type="checkbox"/> Revision of Existing Criteria <input type="checkbox"/> New Criteria

Executive Summary

Purpose: Ensure appropriate utilization and control of CAR-T Cell Therapies

Why Issue Selected: CAR-T Cell Therapy is a form of immunotherapy where a patient's T-cells are collected and genetically engineered to produce chimeric antigen receptors (CAR) on the cell surface, allowing the modified T-cells to recognize an antigen on target cancer cells.

Approved by the FDA in August 2017, Kymriah® (tisagenlecleucel) is indicated for the treatment of B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory or in second or later relapse in pediatric and young adult patients (up to 25 years of age); Kymriah is also indicated for the treatment of adult patients with relapsed or refractory 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. In May 2022, Kymriah was approved for the treatment of adults with relapsed or refractory follicular lymphoma (FL) after two or more lines of systemic therapy.

FDA approved in October 2017, Yescarta® (axicabtagene ciloleucel) is indicated for the treatment of adult patients with relapsed or refractory large B-cell lymphoma after one or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, primary mediastinal large B-cell lymphoma, high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma. In March 2021, Yescarta received another FDA indication for adult patients with relapsed or refractory follicular lymphoma (FL) after two or more lines of systemic therapy. In April 2022, Yescarta was approved for the treatment of adult patients with large B-cell lymphoma that is refractory to first line chemoimmunotherapy or that relapses within 12 months of first-line chemoimmunotherapy.

FDA approved in July 2020, Tecartus® (brexucabtagene autoleucel) is indicated for the treatment adult patients with relapsed or refractory mantle cell lymphoma (MCL) and for adult patients with relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL). Although previous systemic therapy for MCL is not noted in the indication, NCCN Guidelines state Tecartus is recommended for the treatment of adult patients with relapsed or refractory MCL only after chemoimmunotherapy and BTK inhibitor therapy.

Approved by the FDA in February 2021, Breyanzi® (lisocabtagene maraleucel) is indicated for the treatment of adult patients with relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified (including DLBCL arising from indolent lymphoma), high-grade B-cell lymphoma, primary mediastinal large B-cell lymphoma, and follicular lymphoma grade 3B.

FDA approved in March 2021, Abecma® (idecabtagene vicleucel) is indicated for treatment of adult patients with relapsed or refractory multiple myeloma after four or more prior lines of therapy, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody.

Approved by the FDA in February 2022, Carvykti™ (ciltacabtagene autoleucel) is indicated for the treatment of adult patients with relapsed or refractory multiple myeloma after four or more prior lines of therapy, including an immunomodulatory agents, a proteasome inhibitor, and an anti-CD38 monoclonal antibody.

All CAR-T cell therapies have boxed warnings concerning Cytokine Release Syndrome and neurologic toxicities with a REMS program. Abecma and Carvykti have additional boxed warnings for Hemophagocytic Lymphohistiocytosis/Macrophage Activation Syndrome (HLH/MAS) and prolonged cytopenias.

All requests for therapy will be reviewed by a Clinical Consultant.

Program-Specific Information:

Drug	Cost per infusion
ABECMA (IDECABTAGENE VICLEUCEL)	\$419,500.00 WAC
BREYANZI (LISOCABTAGENE MARALEUCEL)	\$410,300.00 WAC
CARVYKTI (CILTACABTAGENE AUTOLEUCEL)	\$465,000.00 WAC
KYMRIAH (TISAGENLECLEUCEL) – DLBCL	\$373,000.00 WAC
KYMRIAH (TISAGENLECLEUCEL) – PED ALL	\$475,000.00 WAC
TECARTUS (BREXUCABTAGENE AUTOLEUCEL)	\$399,000.00 WAC
YESCARTA (AXICABTAGENE CILOLEUCEL)	\$399,000.00 WAC

Type of Criteria: Increased risk of ADE Preferred Drug List
 Appropriate Indications Clinical Edit

Data Sources: Only Administrative Databases Databases + Prescriber-Supplied

Setting & Population

- Drug class for review: CAR-T Cell Therapies
- Age range: All appropriate MO HealthNet participants

Approval Criteria

- Prescribed by or in consultation with an oncologist, hematologist, or other specialist in the treated disease state **AND**
- Participant is currently not pregnant **AND**
- For Breyanzi:
 - Participant is aged ≥ 18 years **AND**
 - Documented diagnosis of relapsed or refractory large B-cell lymphoma, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified (including DLBCL arising from indolent

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- lymphoma), high-grade B-cell lymphoma, primary mediastinal large B-cell lymphoma, and follicular lymphoma grade 3B **AND**
 - Documentation of two or more previous lines of therapy for treated diagnosis
- For Kymriah:
 - Participant aged < 25 years **AND** documented diagnosis of B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory or in second or later relapse **OR**
 - Participant aged ≥ 18 years **AND** documented diagnosis of 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 **OR**
 - **Participant is aged ≥ 18 years AND documented diagnosis of relapsed or refractory follicular lymphoma (FL) after two or more previous lines of systemic therapy AND**
 - Documentation of two or more previous lines of systemic therapy for treated diagnosis
- For Yescarta:
 - **Documented diagnosis of large B-cell lymphoma that is refractory to first-line chemoimmunotherapy or that relapses within 12 months of first-line chemoimmunotherapy OR**
 - Documented diagnosis of relapsed or refractory large B-cell lymphoma after two or more lines of systemic therapy, including diffuse large B-cell lymphoma (DLBCL) not otherwise specified, primary mediastinal large B-cell lymphoma, high grade B-cell lymphoma, and DLBCL arising from follicular lymphoma **OR**
 - Documented diagnosis of relapsed or refractory follicular lymphoma (FL) **AND**
 - Participant aged ≥ 18 years **AND**
 - Documentation of **one** or more previous lines of systemic therapy for treated diagnosis
- For Tecartus:
 - Participant aged ≥ 18 years **AND**
 - Documented diagnosis of relapsed or refractory mantle cell lymphoma (MCL) **AND**
 - Documentation of two or more previous lines of systemic therapy for MCL, including chemoimmunotherapy and BTK inhibitor therapy **OR**
 - **Documented diagnosis of relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL)**
- For Abecma:
 - Participant is aged ≥ 18 years **AND**
 - Documented diagnosis of relapsed or refractory multiple myeloma **AND**
 - Documentation of four or more previous lines of therapy, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody
- **For Carvykti:**
 - **Participant aged ≥ 18 years AND**
 - **Documented diagnosis of relapsed or refractory multiple myeloma AND**
 - **Documentation of four or more previous lines of therapy, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 monoclonal antibody**

Denial Criteria

- Therapy will be denied if all approval criteria are not met
- Previous CAR-T Cell Therapy
- Participant has an active infection or inflammatory disorder

Billing Information

- The treating prescriber/facility may choose the method of administration most appropriate for the participant. The options available are:

- **Outpatient FFS Participant:** MHD FFS completes Prior Authorization for the drug, claim paid according to the current MHD drug reimbursement. All other expenses are paid for on a FFS basis.
 - The following are items that would be expected to be billed to MHD FFS (this list is used as an example and is not meant to be all inclusive): Apheresis, chemotherapy, cell engineering, antigen receptor T-Cell therapy (CAR-T), infusion, leukapheresis, preparative therapy. If any of these are included in the cost of the drug, they cannot be billed separately to MHD.
 - If the patient should require hospitalization due to cytokine release syndrome (CRS) or neurotoxicities after the CAR-T infusion, inpatient pre-certification is required, and payment will be made at the applicable rate for the facility as determined by established MHD regulations.
- **Outpatient MCO Participant:** MHD FFS completes Prior Authorization for the drug, drug claim paid according to the current MHD drug reimbursement. All other expenses are paid for by the MCO.
 - The following are items that would be expected to be billed to the participant MCO plan (this list is used as an example and is not meant to be all inclusive): Apheresis, chemotherapy, cell engineering, antigen receptor T-Cell therapy (CAR-T), infusion, leukapheresis, preparative therapy. If any of these are included in the cost of the drug, they cannot be billed separately to the MCO.
 - If the patient should require hospitalization due to cytokine release syndrome (CRS) or neurotoxicities after the CAR-T infusion, coverage of the hospital stay is the MCO plan responsibility and payment will be made at the applicable MCO rate for the facility as determined by established MCO provider agreement.
- **Inpatient FFS Participant:** MHD FFS completes Prior Authorization of the drug, MHD FFS covers the cost of the drug according to the current MHD drug reimbursement in addition to the hospital per diem. Medical provider costs are billed separately to FFS.
 - Pre-certification of the inpatient hospitalization is required for the CAR-T infusion; should the medical provider feel it is medically necessary to administer chemotherapy inpatient prior to CAR-T infusion, pre-certification is also required for those hospital days.
 - MHD FFS will reimburse the facility at the per diem rate during the participant's inpatient hospitalization. All other expenses will be reimbursed only if they are performed prior to the participant's inpatient stay and if they are not included in the cost of the drug. Examples of expenses expected prior to the inpatient hospitalization include, this list is not meant to be considered all inclusive: Apheresis, chemotherapy, cell engineering, leukapheresis, and preparative therapy.
 - If the patient should require subsequent hospitalization after the initial stay involving the therapy due to cytokine release syndrome or neurotoxicities, payment will be made at the applicable rate for the facility as determined by established MHD regulations.
- **Inpatient MCO Participant:** MHD FFS completes Prior Authorization of the drug, MHD FFS covers the cost of the drug according to the current MHD drug reimbursement. The MCO is responsible for the hospital stay and any medical provider costs.
 - The MCO will reimburse the facility at the per diem rate during the participant's inpatient hospitalization. All expenses, with the exception for the cost of the drug, are the responsibility of the MCO plan.
 - If the patient should require subsequent hospitalization after the initial stay involving the therapy, payment will be made at the applicable MCO per diem rate for the facility as determined by established MCO provider agreement.
- **The following apply to all scenarios above:**
 - Failure to get the prior authorization for the CAR-T therapy prior to administration will result in no payment for the CAR-T therapy.
 - During the prior authorization for the CAR-T therapy the provider must determine if the participant will receive the CAR-T therapy as an inpatient or outpatient service.
 - There will be no additional \$100,000 reimbursement for hospitalization or treatment in any of the above scenarios. The accompanying treatment will be paid for at the agreed upon provider rates.

- The CAR-T Therapy will only be paid for by MHD when the facility is approved by the manufacturer to administer the CAR-T therapy.
- All pre-therapy assessment and medical services, physician's charges, and outpatient follow-up care must be billed separately and will be reimbursed at current applicable MHD fee schedule or inpatient per diem rates.
- For experimental use of CAR-T therapy, when the manufacturer has provided the CAR-T drug through compassionate use or as part of a clinical trial, the facility will not be reimbursed for the drug by MHD FFS nor the MCO. All other medically necessary covered services associated with the CAR-T therapy, which are not part of the clinical trial, may be reimbursed according to the process selected by the treating prescriber and outlined above, according to the current hospital manual.

Required Documentation

Laboratory Results:
MedWatch Form:

Progress Notes:
Other:

Disposition of Edit

Denial: Exception code "0682" (Clinical Edit)
Rule Type: CE

Default Approval Period

2 months

References

- KYMRIA[®] (tisagenlecleucel) [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; August 2021.
- TECARTUS[®] (brexucabtagene autoleucel) [package insert]. Santa Monica, CA: Kite Pharma, Inc.; October 2021.
- YESCARTA[®] (axicabtagene ciloleucel) [package insert]. Santa Monica, CA: Kite Pharma, Inc.; April 2022.
- BREYANZI[®] (lisocabtagene maraleucel) [package insert]. Bothell, WA: June Therapeutics Inc., a Bristol-Myers Squibb Company; February 2021.
- ABECMA[®] (idecabtagene vicleucel) [package insert]. Summit, NJ: Celgene Corporation, a Bristol-Myers Squibb Company; March 2021.
- CARVYKTI[™] (ciltacabtagene autoleucel) [package insert]. Somerset, NJ: Janssen Biotech, Inc; February 2022.
- IPD Analytics. Oncology: Chimeric Antigen Receptor (CAR) T-cell Therapy. April 2017.
- IPD Analytics. New Drug Review: Tecartus (brexucabtagene autoleucel). August 2020.
- IPD Analytics. New Drug Review: Breyanzi (lisocabtagene maraleucel; liso-cel). February 2021.
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- Ogba N, Arwood N, Bartlett N, et al. Chimeric antigen receptor T-cell therapy. *J Natl Compr Canc Netw*. 2018; 16(9):1092-1106. doi: 10.6004/jnccn.2018.0073
- Mahadeo, K.M., Khazal, S.J., Abdel-Azim, H. et al. Management guidelines for paediatric patients receiving chimeric antigen receptor T cell therapy. *Nat Rev Clin Oncol* 16, 45–63 (2019)

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- National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines). Multiple Myeloma. Version 5.2022 – March 9, 2022. <https://www.nccn.org/>
- Wang M, et al. KTE-X19 CAR T-Cell Therapy in Relapsed or Refractory Mantle-Cell Lymphoma. N Engl J Med 2020;382:1331-42. DOI: 10.1056/NEJMoa1914347

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