MetroPlus Health

Policy and Procedure

Title: Breyanzi (lisocabtagene maraleucel)	Division: Medical Management Department: Utilization Management
Approval Date: 1/31/2023	LOB: Medicaid, HIV SNP, HARP, CHP, MetroPlus Gold, Goldcare I&II, Essential Plan, QHP
Effective Date: 1/31/2023	Policy Number: UM-MP347
Review Date: 1/30/2024	Cross Reference Number:
Retired Date:	Page 1 of 11

I. POLICY DESCRIPTION:

Medical Oncology – Anti-CD19 CAR-T immunotherapy, Breyanzi (lisocabtagene maraleucel)

II. RESPONSIBLE PARTIES:

Medical Management Administration, Utilization Management, Integrated Care Management, Pharmacy, Claim Department, Providers Contracting.

III. DEFINITIONS:

Breyanzi (lisocabtagene maraleucel) is an autologous genetically modified immunotherapy that targets cancer and normal B cells that express an antigen called CD19. The patient's T cells are collected and modified to have a chimeric antigen receptor (CAR), which will allow them to identify and eliminate CD19 expressing cells. The CAR consists of a FMC63 monoclonal antibody-derived single chain variable fragment (scFv), a hinge region called IgG4, CD28 transmembrane domain, 4-1BB (CD137) costimulatory doman and a CD3 zeta activation domain. Once the CAR binds to CD19 it will induce T cell activation and proliferation, release of pro-inflammatory cytokines and cytotoxic killing of the target cells.

Breyanzi is currently approved by the FDA for the treatment of adult patients who have relapsed or refractory large B-cell lymphoma after using at least 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.

IV. POLICY:

For the Medicare and UltraCare lines of business, MetroPlusHealth determines medical necessity based on applicable Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD).

For all non-Medicare LOBs:

Breyanzi will be considered medically necessary once the following coverage criteria is met. Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.
https://www.cms.gov/medicare-coverage-database/search.aspx

INITIAL REQUEST:

1. **Large B-cell lymphoma (LBCL) that is refractory or in relapse:**
   A. Member is 18 years of age or older;
   AND

B. Member has a diagnosis of relapsed or refractory large B-cell lymphoma (LBCL) including ANY one of the following:
- **a.** Diffuse large B-cell lymphoma (DLBCL) not otherwise specified including DLBCL arising from indolent lymphoma;

OR
- **b.** High-grade B-cell lymphoma;

OR
- **c.** Primary mediastinal large B-cell lymphoma;

OR
- **d.** Follicular lymphoma grade 3B;

OR
- **e.** AIDS-related B-cell lymphoma;

OR
- **f.** Monomorphic posttransplant lymphoproliferative disorder (B-cell type);

AND

C. Member has received prior treatment with at least two lines of therapy, including at least one drug from ALL of the following drug classes unless contraindicated:
- **a.** Anthracycline [e.g., Doxorubicin (Adriamycin, Rubex)];

AND
- **b.** Anti CD-20 monoclonal antibody [e.g., Rituximab (Rituxan, Ruxience, Truxima) or Obinutuzumab (Gazyva)];

AND

D. Member has an Eastern Cooperative Oncology Group (ECOG) score < 2;

AND

E. Member does not have ANY one of the following:
- **a.** Diagnosis of central nervous system lymphoma;

OR
- **b.** History of primary malignancy that has not been in remission for at least 2 years prior to Breyanzi consideration;

OR
- **c.** History or presence of clinically relevant CNS pathology **[**e.g., seizure disorders, paresis, aphasia, stroke, severe brain injuries, organic brain syndrome, cerebellar disease, dementia, Parkinson's disease, and or psychosis];

OR
- **d.** Active inflammatory disorder;

OR

e. Active uncontrolled infection including human immunodeficiency virus (HIV), Hepatitis B or C and Cytomegalovirus (CMV);

OR

f. Autoimmune disease requiring immunosuppression;

AND

F. Member has not received allogenic hematopoetic stem cell transplantation (HSCT) in last 90 days prior to leukapheresis;

AND

G. Member will not receive live vaccines 6 weeks prior to lymphodepleting chemotherapy and during administration of Breyanzi and until immune recovery after treatment;

AND

H. Member does not have ANY one the following lab criteria:

a. Creatinine clearance < 30 mL/min;

OR

b. Alanine aminotransferase > 5 times the upper limit of normal;

OR

c. Left ventricular ejection fraction (LVEF) < 40%;

AND

I. Member has no prior use of CAR-T therapy including Breyanzi;

AND

J. ONE of the following:

a. Member has no prior use of CD-19 targeted therapy;

OR

b. If member has used a previous CD-19 targeted therapy they must re-biopsy and have a CD-19 positive disease

AND

K. Breyanzi will not be given concurrently with other CAR-T immunotherapies [Kymriah (Tisagenlecleucel), Yescarta (Axicabtagene ciloleucel), Tecartus (brexucabtagene autoleucel)];

AND

L. Breyanzi will be prescribed by the consultation of a hematologist or oncologist;

AND

M. Member has adequate vascular access for leukapheresis procedure**;**

AND

N. Member has adequate bone marrow function to receive lymphodepleting chemotherapy as determined by the prescriber;

AND

O. Breyanzi will be given accordingly based on the FDA approved dosing: Administered at least 2 days after completion of lymphodepleting chemotherapy as a single dose containing 50 to 110 x 10^6 CAR-postivie T cells consisting of CD4 and CD8 components;

AND

P. Member will receive Breyanzi at a healthcare facility enrolled in the Breyanzi REMS and are aware of how to manage cytokine release syndrome and neurological toxicities (See Appindices A and B)

Initial Duration of Approval: *One single dose per lifetime*

RENEWAL REQUEST:
Breyanzi will not be renewed for additional requests as this is a single dose therapy.

Renewal Duration of Approval: *Not Applicable*

V. LIMITATIONS/ EXCLUSIONS:

- Breyanzi is considered to be experimental and investigational if prescribed for indications that have not been approved by the FDA.
- Repeat infusions of breyanzi are considered to be experimental and investigational because there have been no established studies to demonstrate effectiveness.

VI. APPLICABLE PROCEDURE CODES:

CPT	Description
Q2054	Lisocabtagene maraleucel, up to 110 million autologous anti-CD19 car-positive viable T cells, including leukapheresis and dose preparation procedures, per therapeutic dose

VII. APPLICABLE DIAGNOSIS CODES:

CODE	Description
C82.40- C82.49	Follicular lymphoma grade IIIb
C82.50- C82.59	Diffuse follicle center lymphoma
C83.30- C83.39	Diffuse large B-cell lymphoma
C83.90- C83.99	Non-follicular (diffuse) lymphoma

C85.10- C85.19	Unspecified B-cell lymphoma
C85.20- C85.29	Mediastinal (thymic) large B-cell lymphoma
D47.Z1	Post-transplant lymphoproliferative disorder (PTLD)
Z51.12	Encounter for antineoplastic immunotherapy

VIII. REFERENCES:

1. Breyanzi (lisocabtagene maraleucel) [prescribing information]. Bothell, WA: Juno Therapeutics Inc; January 2024.
2. Juno Therapeutics, a Subsidiary of Celgene. A Phase 1, Multicenter, Open-Label Study of JCAR017, CD19-targeted Chimeric Antigen Receptor (CAR) T Cells, for Relapsed and Refractory (R/R) B-cell Non-Hodgkin Lymphoma (NHL). clinicaltrials.gov. Published November 21, 2022. Accessed December 23, 2022. https://clinicaltrials.gov/ct2/show/NCT02631044?term=02631044&draw=2&rank=1

IX. APPENDICES:

Appendix A: CRS Grading and Management Guidance

CRS Grade	Tocilizumab	Corticosteroids*
Grade 1 Fever	If less than 72 hours after infusion, consider tocilizumab 8 mg/kg IV over 1 hour (MAX 800 mg). If 72 hours or more after infusion, treat symptomatically.	If less than 72 hours after infusion, consider dexamethasone 10 mg IV every 24 hours. If 72 hours or more after infusion, treat symptomatically.

Grade 2 Symptoms require and respond to moderate intervention. Oxygen requirement less than 40% fraction of inspired oxygen (FiO2), or hypotension responsive to fluids or low dose of one vasopressor, or Grade 2 organ toxicity.	Administer tocilizumab 8 mg/kg IV over 1 hour (not to exceed 800 mg). Repeat tocilizumab every 8 hours as needed if not responsive to intravenous fluids or increasing supplemental oxygen. **Limit tocilizumab to a maximum of 3 doses in a 24-hour period; maximum total of 4 doses.**	If less than 72 hours after infusion, administer dexamethasone 10 mg IV every 12 to 24 hours. If 72 hours or more after infusion, consider dexamethasone 10 mg IV every 12 to 24 hours.
	If no improvement within 24 hours or rapid progression, repeat tocilizumab and escalate dose and frequency of dexamethasone 10 to 20 mg IV every 6 to 12 hours. If no improvement or continued rapid progression, maximize dexamethasone, switch to high-dose methylPREDNISolone 2 mg/kg if needed. After 2 doses of tocilizumab, consider alternative immunosuppressants. **Do not exceed 3 doses of tocilizumab in 24 hours, or 4 doses in total.**	
Grade 3 Symptoms require and respond to aggressive intervention. Oxygen requirement 40% FiO2 or greater, or hypotension requiring high-dose or multiple	Administer tocilizumab 8 mg/kg IV over 1 hour (not to exceed 800 mg). Repeat tocilizumab every 8 hours as needed if not responsive to intravenous fluids or increasing supplemental oxygen. **Limit tocilizumab to a maximum of 3 doses in a 24-hour period; maximum total of 4 doses.**	Administer dexamethasone 20 mg IV every 12 hours.

<table>
<tr><td rowspan="2">vasopressors, or Grade 3 organ toxicity, or Grade 4 transaminitis.</td><td colspan="2">If no improvement within 24 hours or rapid progression of CRS, repeat tocilizumab and escalate dose and frequency of dexamethasone 10 to 20 mg IV every 6 to 12 hours.

If no improvement or continued rapid progression, maximize dexamethasone, switch to high-dose methylPREDNISolone 2 mg/kg if needed. After 2 doses of tocilizumab, consider alternative immunosuppressants. Do not exceed 3 doses of tocilizumab in 24 hours, or 4 doses in total.</td></tr>
<tr><td rowspan="2">Grade 4

Life-threatening symptoms

Requirements for ventilator support or continuous veno-venous hemodialysis (CVVHD) or Grade 4 organ toxicity (excluding transaminitis).</td><td>Administer tocilizumab 8 mg/kg IV over 1 hour (not to exceed 800 mg).

Repeat tocilizumab every 8 hours as needed if not responsive to intravenous fluids or increasing supplemental oxygen.

Limit tocilizumab to a maximum of 3 doses in a 24-hour period; maximum total of 4 doses.</td><td>Administer dexamethasone 20 mg IV every 6 hours.</td></tr>
<tr><td colspan="2">If no improvement within 24 hours or rapid progression of CRS, escalate tocilizumab and corticosteroid use.

If no improvement or continued rapid progression, maximize dexamethasone, switch to high-dose methylPREDNISolone 2 mg/kg if needed.

After 2 doses of tocilizumab, consider alternative immunosuppressants. Do not exceed 3 doses of tocilizumab in 24 hours, or 4 doses in total.</td></tr>
<tr><td colspan="3">*If corticosteroids are initiated, continue corticosteroids for at least 3 doses or until complete resolution of symptoms, and consider corticosteroid taper.</td></tr>
</table>

Appendix B: Neurologic Toxicity Grading and Management Guidance

Neurologic Toxicity Grade	Corticosteroids and Antiseizure Medications
Grade 1	Start non-sedating, antiseizure medicines (eg, levetiracetam) for seizure prophylaxis.

	If 72 hours or more after infusion, observe the patient. If less than 72 hours after infusion, consider dexamethasone 10 mg IV every 12 to 24 hours for 2 to 3 days.
Grade 2	Start non-sedating, antiseizure medicines (eg, levetiracetam) for seizure prophylaxis. Administer dexamethasone 10 mg IV every 12 hours for 2 to 3 days, or longer for persistent symptoms. Consider taper for a total steroid exposure of greater than 3 days. If no improvement after 24 hours or worsening of neurologic toxicity, increase the dose and/or frequency of dexamethasone up to a maximum of 20 mg IV every 6 hours. If no improvement after another 24 hours, rapidly progressing symptoms, or life-threatening complications arise, give methylPREDNISolone 2 mg/kg loading dose, followed by 2 mg/kg divided 4 times a day; taper within 7 days.
Grade 3	Start non-sedating, antiseizure medicines (eg, levetiracetam) for seizure prophylaxis. Administer dexamethasone 10 to 20 mg IV every 8 to 12 hours. Steroids are not recommended for isolated Grade 3 headaches. If no improvement after 24 hours or worsening of neurologic toxicity, escalate to methylprednisolone (dose and frequency as per Grade 2). If cerebral edema is suspected, consider hyperventilation and hyperosmolar therapy. Give high-dose methylPREDNISolone 1 to 2 g, repeat every 24 hours if needed; taper as clinically indicated and cyclophosphamide 1.5 g/m(2).
Grade 4	Start non-sedating, antiseizure medicines (eg, levetiracetam) for seizure prophylaxis. Administer dexamethasone 20 mg IV every 6 hours.

	If no improvement after 24 hours or worsening of neurologic toxicity, escalate to methylPREDNISolone (dose and frequency as per Grade 2). If cerebral edema is suspected, consider hyperventilation and hyperosmolar therapy. Give high-dose methylPREDNISolone 1 to 2 g, repeat every 24 hours if needed; taper as clinically indicated, and cyclophosphamide 1.5 g/m(2).

REVISION LOG:

REVISIONS	DATE
Creation date	1/31/2023

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Annual update	1/22/2024
Update LOBs to remove Medicare and Ultracare	8/12/2024

Approved: **Date:** David Ackman Digitally signed by David Ackman Date: 2024.08.29 10:01:36 -04'00'	**Approved:** **Date:**
David Ackman, MD **VP of Medical Director**	**Sanjiv Shah, MD** **Chief Medical Officer**

Medical Guideline Disclaimer:

Property of Metro Plus Health Plan. All rights reserved. The treating physician or primary care provider must submit MetroPlus Health Plan clinical evidence that the patient meets the criteria for the treatment or surgical procedure. Without this documentation and information, Metroplus Health Plan will not be able to properly review the request for prior authorization. The clinical review criteria expressed in this policy reflects how MetroPlus Health Plan determines whether certain services or supplies are medically necessary. MetroPlus Health Plan established the clinical review criteria based upon a review of currently available clinical information(including clinical outcome studies in the peer-reviewed published medical literature, regulatory status of the technology, evidence-based guidelines of public health and health research agencies, evidence-based guidelines and positions of leading national health professional organizations, views of physicians practicing in relevant clinical areas, and other relevant factors). MetroPlus Health Plan expressly reserves the right to revise these conclusions as clinical information changes, and welcomes further relevant information. Each benefit program defines which services are covered. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered andor paid for by MetroPlus Health Plan, as some programs exclude coverage for services or supplies that MetroPlus Health Plan considers medically necessary. If there is a discrepancy between this guidelines and a member's benefits program, the benefits program will govern. In addition, coverage may be mandated by applicable legal requirements of a state, the Federal Government or the Centers for Medicare & Medicaid Services (CMS) for Medicare and Medicaid members.
All coding and website links are accurate at time of publication.

MetroPlus Health Plan has adopted the herein policy in providing management, administrative and other services to our members, related to health benefit plans offered by our organization.