# Drug Monograph

Drug Name: **Tecartus® (brexucabtagene autoleucel) suspension for intravenous infusion**
Drug Class: **(CAR)-T Cell Therapy Agents**
Prepared For: MO HealthNet
Prepared By: Conduent

☒ **New Criteria** ☐ **Revision of Existing Criteria**

## Executive Summary

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| **Purpose:** | The purpose of this monograph is to provide a review of new therapy to determine whether the reviewed drug should be made available on an open access basis to prescribers, require a clinical edit or require prior authorization for use. |
| **Dosage Forms:** | Tecartus is available as a cell suspension for infusion. Tecartus comprises a suspension of $2 \times 10^6$ CAR-positive viable T cells per kg of body weight, with a maximum of $2 \times 10^8$ CAR-positive viable T cells in approximately 68 mL suspension in an infusion bag. |
| **Manufacturer:** | Kite Pharma, Inc., Santa Monica, CA 90404 |
| **Summary of Findings:** | The efficacy of Tecartus was demonstrated in a single-arm, open-label multicenter trial of adult patients with relapsed or refractory mantle cell lymphoma (MCL). The primary endpoint was objective response rate. 87% of the 60 patients in the primary efficacy analysis had an objective response and 62% had a complete response. The median time to response was 28 days (range: 24 to 92 days) with a median follow-up time for duration of response of 8.6 months. |

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| **Status Recommendation:** | ☒ Clinical Edit<br>☐ Open Access | ☐ PA Required<br>☐ PDL |
| **Type of PA Criteria:** | ☒ Appropriate Indications<br>☐ No PA Required | ☐ Non-Preferred<br>☐ Preferred |

## Purpose

The purpose of this monograph is to provide a review of new therapy to determine whether the reviewed drug should be considered a prior authorization drug, a clinical edit drug or an open access drug. While prescription expenditures are increasing at double-digit rates, payers are evaluating ways to control these costs by influencing prescriber behavior and guide appropriate medication usage. This review will assist in the achievement of qualitative and economic goals related to health care resource utilization. Restricting the use of certain medications can reduce costs by requiring documentation of appropriate indications for use, and where appropriate, encourage the use of less expensive agents within a drug class.

## Introduction [1]

Mantle cell lymphoma (MCL) is a type of B-cell non-Hodgkin lymphoma that affects the lymph nodes, causing them to grow and release cancer cells into the blood and lymphatic systems. Often diagnosed in advanced stages, it tends to spread quickly and resist treatment more than some other forms of lymphoma. The American Cancer Society estimates that MCL accounts for about 5% of B-cell lymphomas or around 3,800 new cases in the U.S. per year. Most often diagnosed after the age of 60, it affects more men than women.

## Dosage Form [2]

Tecartus is available as a cell suspension for infusion. Tecartus comprises a suspension of $2 \times 10^6$ CAR-positive viable T cells per kg of body weight, with a maximum of $2 \times 10^8$ CAR-positive viable T cells in approximately 68 mL suspension in an infusion bag.

## Manufacturer [2]

Kite Pharma, Inc., Santa Monica, CA 90404.

## Indication(s) [2]

Tecartus is a CD19-directed genetically modified autologous T cell immunotherapy indicated for the treatment of adult patients with relapsed or refractory MCL.

## Clinical Efficacy [2,3] (mechanism of action/pharmacology, comparative efficacy)

Tecartus, a CD19-directed genetically modified autologous T cell immunotherapy, binds to CD19-expressing cancer cells and normal B cells. Studies demonstrated that following anti-CD19 CAR T cell engagement with CD19-expressing target cells, the CD28 and CD3-zeta co-stimulatory domains activate downstream signaling cascades that lead to T cell activation, proliferation, acquisition of effector functions, and secretion of inflammatory cytokines and chemokines. This sequence of events leads to killing of CD19-expressing cells.

Pharmacokinetics:
Following infusion of Tecartus, anti-CD19 CAR T cells exhibited an initial rapid expansion followed by a decline to near baseline levels by three months. Peak levels of anti-CD19 CAR T cells occurred within the first seven to 15 days after infusion.

 

Clinical Trials Experience

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| **STUDY DESIGN** | Single-arm, open-label multicenter trial (n=74) |
| **INCLUSION CRITERIA** | • Adults 18 years and older<br>• Relapsed or refractory MCL<br>• Previously treated with: anthracycline or bendamustine-containing chemotherapy, an anti-CD20 monoclonal antibody therapy and Ibrutinib or acalabrutinib |
| **EXCLUSION CRITERIA** | • Patients with active or serious infections<br>• Prior allogeneic hematopoietic stem cell transplant (HSCT)<br>• Detectable cerebrospinal fluid malignant cells or brain metastases<br>• Any history of central nervous system (CNS) lymphoma or CNS disorders |
| **TREATMENT REGIMEN** | Patients underwent leukapheresis and optional bridging therapy, followed by conditioning chemotherapy consisting of fludarabine 30 mg/m$^2$/day and cyclophosphamide 500 mg/m$^2$/day intravenous (IV) infusion for 3 days followed by a single infusion of Tecartus at a targeted dose of 2 x 10$^6$ CAR T cells/kg. |
| **RESULTS** | The primary endpoint was the percentage of patients with an objective response (complete or partial response) as assessed by an independent radiologic review committee according to the Lugano classification. The primary efficacy analysis was conducted after 60 patients had been treated and followed for 7 months.<br><br>87% of the 60 patients in the primary efficacy analysis had an objective response and 62% had a complete response. The median time to response was 28 days (range: 24 to 92 days) with a median follow-up time for duration of response of 8.6 months. |
| **SAFETY** | Common adverse events of grade 3 or higher were cytopenias (in 94% of the patients) and infections (in 32%). Grade 3 or higher cytokine release syndrome and neurologic events occurred in 15% and 31% of patients, respectively; none were fatal. Two grade 5 infectious adverse events occurred. |

## Contraindications [(2)]

- None

## Warnings and Precautions [(2)]

- Black Box Warning: Cytokine Release Syndrome (CRS), including fatal or life-threating reactions, may occur in patients receiving Tecartus
- Black Box Warning: Neurologic toxicities, including life-threatening reactions, may occur in patients receiving Tecartus
- Because of the risk of CRS and neurological toxicities, Tecartus is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS)
- Hypersensitivity reactions may occur during infusion
- Serious or life-threatening infections may occur after Tecartus infusion
- Prolonged cytopenias may occur for several weeks following Tecartus infusion
- B cell aplasia and hypogammaglobulinemia may occur

 

- Secondary malignancies may occur
- Due to the potential for neurologic events, including altered mental status or seizures, patients receiving Tecartus are at risk for altered or decreased consciousness or coordination in the eight weeks following infusion. Patients should refrain from driving and engaging in hazardous occupations or activities during this initial period

## Adverse Effects [2]

| Most common, ≥ 10% | Any grade (%) | Grade 3 or Higher (%) |
|---|---|---|
| **Coagulopathy** | 10 | 2 |
| **Tachycardia** | 45 | 0 |
| **Bradycardia** | 10 | 0 |
| **Non-ventricular arrhythmias** | 10 | 4 |
| **Nausea** | 35 | 1 |
| **Constipation** | 29 | 0 |
| **Diarrhea** | 28 | 5 |
| **Abdominal pain** | 17 | 0 |
| **Oral pain** | 16 | 0 |
| **Vomiting** | 13 | 0 |
| **Dysphagia** | 10 | 2 |
| **Pyrexia** | 94 | 15 |
| **Fatigue** | 48 | 1 |
| **Chills** | 41 | 0 |
| **Edema** | 35 | 2 |
| **Pain** | 17 | 2 |
| **Cytokine release syndrome** | 91 | 18 |
| **Hypogammaglobulinemia** | 16 | 1 |
| **Infection – pathogen unspecified** | 43 | 24 |
| **Viral infections** | 18 | 4 |
| **Bacterial infections** | 13 | 6 |
| **Decreased appetite** | 26 | 0 |
| **Musculoskeletal pain** | 37 | 2 |
| **Motor dysfunction** | 17 | 4 |
| **Encephalopathy** | 51 | 24 |
| **Tremor** | 38 | 2 |
| **Headache** | 35 | 1 |
| **Aphasia** | 20 | 7 |
| **Dizziness** | 18 | 6 |
| **Neuropathy** | 13 | 2 |
| **Insomnia** | 21 | 0 |
| **Delirium** | 18 | 5 |
| **Anxiety** | 16 | 0 |
| **Renal insufficiency** | 18 | 9 |
| **Decreased urine output** | 11 | 1 |
| **Hypoxia** | 40 | 20 |
| **Cough** | 38 | 0 |
| **Dyspnea** | 24 | 6 |
| **Pleural effusion** | 21 | 5 |

 

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| **Rash** | 22 | 4 |
| **Hypotension** | 57 | 27 |
| **Hypertension** | 18 | 11 |
| **Thrombosis** | 17 | 4 |

## Drug Interactions [(2)]

- None specified

## Dosage and Administration [(2)]

Each single infusion bag of Tecartus contains a suspension of chimeric antigen receptor (CAR)-positive T cells in approximately 68 mL. The dose is $2 \times 10^6$ CAR-positive viable T cells per kg body weight, with a maximum of $2 \times 10^8$ CAR-positive viable T cells.

Tecartus is for autologous use only. The patient's identity must match the patient identifiers on the Tecartus cassette and infusion bag.

## Cost

| Generic Name | Brand Name | Manufacturer | Cost/infusion bag** |
|---|---|---|---|
| Brexucabtagene autoleucel | Tecartus | Kite Pharma | $373,000/one time infusion |

** Maximum Allowable Cost

## Conclusion

Tecartus, a chimeric antigen receptor (CAR)-T cell therapy, is the first cell-based gene therapy approved for treatment of adult patients with relapsed or refractory MCL. This indication is approved under accelerated approval based on overall response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial. Tecartus is administered as a one-time IV infusion. Each dose of Tecartus is a customized treatment created using a patient's own immune system to help fight the lymphoma. The patient's T cells, a type of white blood cell, are collected and genetically modified to include a new gene that facilitates the targeting and killing of the lymphoma cells. These modified T cells are then infused back into the patient. The safety and efficacy of Tecartus was established in a single-arm, open-label trial of adult patients with relapsed or refractory MCL. The primary endpoint was objective response rate. The complete remission rate after treatment with Tecartus was 62%, with an objective response rate of 87%. Tecartus carries a boxed warning for CRS and neurologic toxicities. Other warnings and precautions of Tecartus include hypersensitivity reactions, severe infections, prolonged cytopenias, hypogammaglobulinemia, secondary malignancies, and effects on ability to drive and operate machinery. Tecartus is available only through a restricted REMS program. The most common non-laboratory adverse reactions (≥ 20%) with Tecartus use were pyrexia, CRS, hypotension, encephalopathy, fatigue, tachycardia, arrhythmia, infection – pathogen unspecified, chills, hypoxia, cough, tremor, musculoskeletal pain, headache, nausea, edema, motor dysfunction, constipation, diarrhea, decreased appetite, dyspnea, rash, insomnia, pleural effusion, and aphasia.

 

## Recommendation

The MO Healthnet Division recommends adding this drug to the (CAR)-T Cell Therapy clinical edit.

## References


1) FDA Approved Drugs: August 2020 Tecartus Approved for Mantle Cell Lymphoma. https://express-scripts.com/corporate/articles/fda-approved-drugs-august-2020. Accessed November 3, 2020.
2) Product Information: Tecartus (brexucabtagene autoleucel). Kite Pharma, Inc., Santa Monica, CA 90404.
3) Wang M, Munoz J, et al. KTE-X19 CAR T-Cell Therapy in Relapsed or Refractory Mantle-Cell Lymphoma. N Engl J Med. 2020 Apr 2;382(14):1331-42.


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