NOW APPROVED

With FDA Breakthrough Therapy Designation[1]

TECARTUS™

(brexucabtagene autoleucel) Suspension for IV infusion

The first and only FDA-approved CAR T-cell therapy for adult patients with R/R MCL[1,2]

Learn more at TECARTUS.com

INDICATION

TECARTUS™ is a CD19-directed genetically modified autologous T cell immunotherapy indicated for the treatment of adult patients with relapsed or refractory mantle cell lymphoma (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.

IMPORTANT SAFETY INFORMATION

BOXED WARNING: CYTOKINE RELEASE SYNDROME and NEUROLOGIC TOXICITIES

- **Cytokine Release Syndrome (CRS), including life-threatening reactions, occurred in patients receiving TECARTUS. Do not administer TECARTUS to patients with active infection or inflammatory disorders. Treat severe or life-threatening CRS with tocilizumab or tocilizumab and corticosteroids.**
- **Neurologic toxicities, including life-threatening reactions, occurred in patients receiving TECARTUS, including concurrently with CRS or after CRS resolution. Monitor for neurologic toxicities after treatment with TECARTUS. Provide supportive care and/or corticosteroids as needed.**
- **TECARTUS is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the YESCARTA and TECARTUS REMS Program.**

Cytokine Release Syndrome (CRS), including life-threatening reactions, occurred following treatment with TECARTUS. In ZUMA-2, CRS occurred in 91% (75/82) of patients receiving TECARTUS, including ≥ Grade 3 CRS in 18% of patients. Among the patients who died after receiving TECARTUS, one had a fatal CRS event. The median time to onset of CRS was three days (range: 1 to 13 days) and the median duration of CRS was ten days (range: 1 to 50 days). Among patients with CRS, key manifestations (>10%) included fever (99%), hypotension (60%), hypoxia (37%), chills (33%), tachycardia (37%), headache (24%), fatigue (19%), nausea (13%), alanine aminotransferase increased (13%), aspartate aminotransferase increased (12%), and diarrhea (11%). Serious events associated with CRS included hypotension, fever, hypoxia, acute kidney injury, and tachycardia.

Ensure that a minimum of two doses of tocilizumab are available for each patient prior to infusion of TECARTUS. Following infusion, monitor patients for signs and symptoms of CRS daily for at least seven days at the certified healthcare facility, and for four weeks thereafter. Counsel patients to seek immediate medical attention should signs or symptoms of CRS occur at any time. At the first sign of CRS, institute treatment with supportive care, tocilizumab, or tocilizumab and corticosteroids as indicated.

Neurologic Toxicities, including those that were life-threatening, occurred following treatment with TECARTUS. In ZUMA-2, neurologic events occurred in 81% of patients, 37% of whom experienced Grade ≥3 adverse reactions. The median time to onset for neurologic events was six days (range: 1 to 32 days). Neurologic events resolved for 52 out of 66 (79%) patients with a median duration of 21 days (range: 2 to 454 days). Three patients had ongoing neurologic events at the time of death, including one patient with serious encephalopathy. The remaining unresolved neurologic events were either Grade 1 or Grade 2. Fifty-four (66%) patients experienced CRS by the onset of neurological events. Five (6%) patients did not experience CRS with neurologic events and eight patients (10%) developed neurological events after the resolution of CRS. 85% of all treated patients experienced the first CRS or neurological event within the first seven days after TECARTUS infusion.

The most common neurologic events (>10%) included encephalopathy (51%), headache (35%), tremor (38%), aphasia (23%), and delirium (16%). Serious events including encephalopathy, aphasia, and seizures occurred.

Monitor patients daily for at least seven days at the certified healthcare facility and for four weeks following infusion for signs and symptoms of neurologic toxicities and treat promptly.

REMS Program: Because of the risk of CRS and neurologic toxicities, TECARTUS is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the YESCARTA and TECARTUS REMS Program which requires that:

- Healthcare facilities that dispense and administer TECARTUS must be enrolled and comply with the REMS requirements. Certified healthcare facilities must have on-site, immediate access to tocilizumab, and ensure that a minimum of two doses of tocilizumab are available for each patient for infusion within two hours after TECARTUS infusion, if needed for treatment of CRS.
- Certified healthcare facilities must ensure that healthcare providers who prescribe, dispense, or administer TECARTUS are trained in the management of CRS and neurologic toxicities. Further information is available at www.YescartaTecartusREMS.com or 1-844-454-KITE (5483).

Hypersensitivity Reactions: Serious hypersensitivity reactions, including anaphylaxis, may occur due to dimethyl sulfoxide (DMSO) or residual gentamicin in TECARTUS.

Severe Infections: Severe or life-threatening infections occurred in patients after TECARTUS infusion. In ZUMA-2, infections (all grades) occurred in 56% of patients. Grade 3 or higher infections, including bacterial, viral, and fungal infections, occurred in 30% of patients. TECARTUS should not be administered to patients with clinically significant active systemic infections. Monitor patients for signs and symptoms of infection before and after infusion and treat appropriately. Administer prophylactic antimicrobials according to local guidelines

Febrile neutropenia was observed in 6% of patients after TECARTUS infusion and may be concurrent with CRS. In the event of febrile neutropenia, evaluate for infection and manage with broad-spectrum antibiotics, fluids, and other supportive care as medically indicated.

Viral Reactivation

Hepatitis B virus (HBV) reactivation, in some cases resulting in fulminant hepatitis, hepatic failure, and death, can occur in patients treated with drugs directed against B cells. Perform screening for HBV, HCV, and HIV in accordance with clinical guidelines before collection of cells for manufacturing.

Prolonged Cytopenias: Patients may exhibit cytopenias for several weeks following lymphodepleting chemotherapy and TECARTUS infusion. In ZUMA-2, Grade ≥ 3 cytopenias not resolved by Day 30 following TECARTUS infusion occurred in 55% of patients and included thrombocytopenia (38%), neutropenia (37%), and anemia (17%). Monitor blood counts after infusion.

Hypogammaglobulinemia and B-cell aplasia can occur in patients receiving treatment with TECARTUS. In ZUMA-2, hypogammaglobulinemia occurred in 16% of patients. Monitor immunoglobulin levels after treatment with TECARTUS and manage using infection precautions, antibiotic prophylaxis, and immunoglobulin replacement. The safety of immunization with live viral vaccines during or following TECARTUS treatment has not been studied. Vaccination with live virus vaccines is not recommended for at least six weeks prior to the start of lymphodepleting chemotherapy, during treatment, and until immune recovery following treatment with TECARTUS.

Secondary Malignancies may develop. Monitor life-long for secondary malignancies. In the event that it occurs, contact Kite at 1-844-454-KITE (5483) to obtain instructions on patient samples to collect for testing.

Effects on Ability to Drive and Use Machines: Due to the potential for neurologic events, including altered mental status or seizures, patients are at risk for altered or decreased consciousness or coordination in the 8 weeks following TECARTUS infusion. Advise patients to refrain from driving and engaging in hazardous activities, such as operating heavy or potentially dangerous machinery, during this period.

Adverse Reactions: The most common adverse reactions (incidence ≥ 20%) 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. Serious adverse reactions occurred in 66% of patients. The most common serious adverse reactions (> 2%) were encephalopathy, pyrexia, infection – pathogen unspecified, CRS, hypoxia, aphasia, renal insufficiency, pleural effusion, respiratory failure, bacterial infections, dyspnea, fatigue, arrhythmia, tachycardia, and viral infections.

Please see additional Important Safety Information throughout, and full Prescribing Information, including **BOXED WARNING** and Medication Guide.

References: 1. Kite, a Gilead Company [press release]. U.S. FDA approved Kite's TECARTUS™, the first and only CAR T treatment for relapsed or refractory mantle cell lymphoma. Published July 24, 2020. https://www.kitepharma.com/news/press-releases/2020/7/us-fda-approves-kites-tecartus-the-first-and-only-car-t-treatment-for-relapsed-or-refractory-mantle-cell-lymphoma. Accessed July 24, 2020. **2.** TECARTUS™ (brexucabtagene autoleucel). Prescribing information. Kite Pharma, Inc; 2020.

CAR=chimeric antigen receptor; MCL=mantle cell lymphoma; R/R=relapsed or refractory.

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