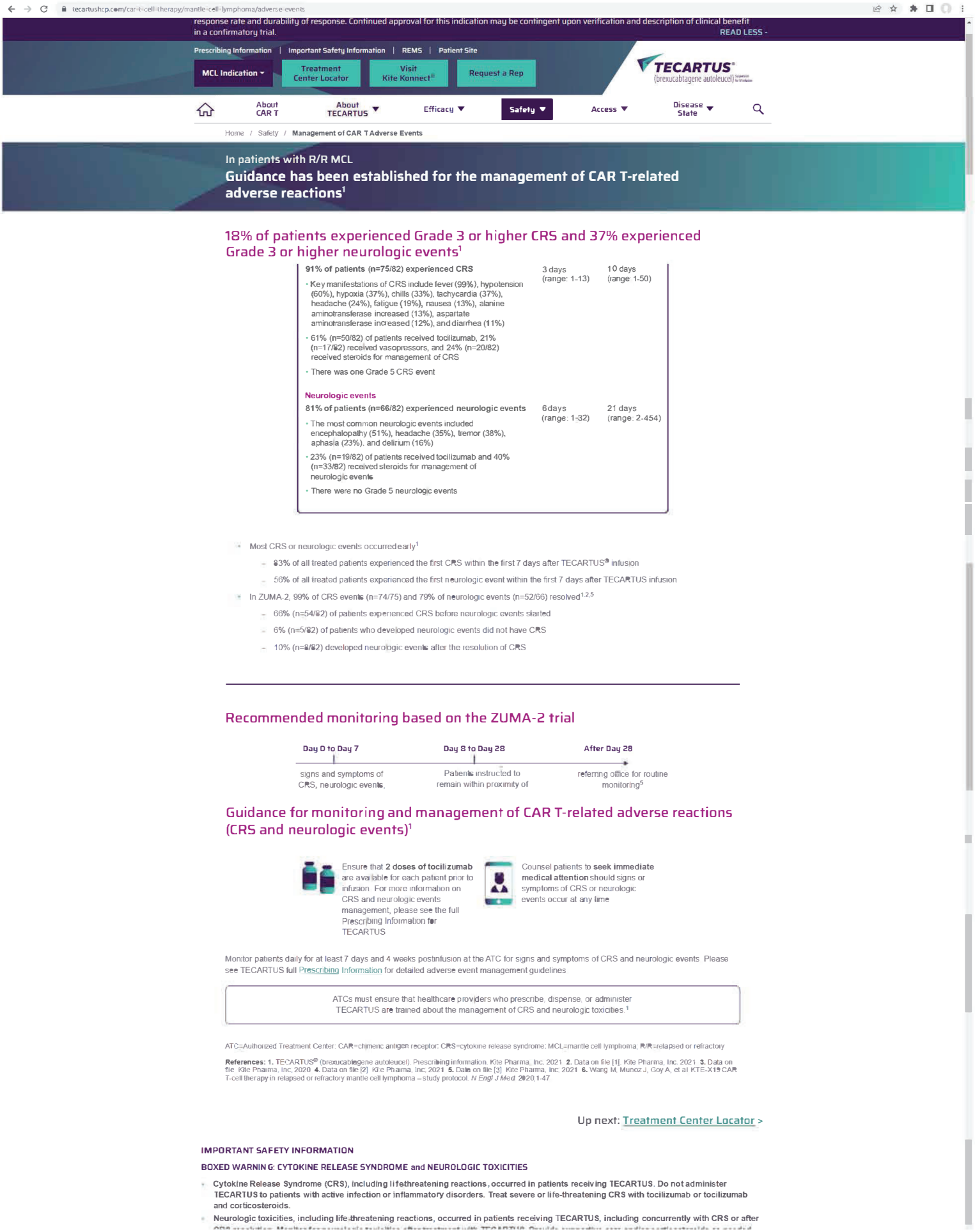
Screenshot from Applicant's website www.tecartushcp.com/car-t-cell-therapy/mantle-cell-lymphoma/adverse-events downloaded on February 6, 2023 displaying the mark in use



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 fatal or life-threatening reactions, occurred following treatment with TECARTUS. CRS occurred in 91% (75/82) of patients with MCL, including ≥ Grade 3 CRS in 18% of patients. Among the patients with MCL who died after receiving TECARTUS, one patient had a fatal CRS event. The median time to onset of CRS was 3 days (range: 1 to 13 days) and the median duration of CRS was 10 days (range: 1 to 50 days) for patients with MCL.

Among patients with CRS, the key manifestations (>10%) included fever (93%), hypotension (62%), tachycardia (59%), chills (32%), hypoxia (31%), headache (21%), fatigue (20%), and nausea (13%). Serious events associated with CRS included hypotension, fever, hypoxia, tachycardia, and dyspnea.

Ensure that a minimum of 2 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 7 days at the certified healthcare facility, and for 4 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 fatal or life-threatening, occurred following treatment with TECARTUS. Neurologic events occurred in 81% (66/82) of patients with MCL, including ≥ Grade 3 in 37% of patients. The median time to onset for neurologic events was 6 days (range: 1 to 32 days) with a median duration of 21 days (range: 2 to 454 days) in patients with MCL. Neurologic events resolved for 119 out of 134 (89%) patients treated with TECARTUS. The onset of neurologic events can be concurrent with CRS following resolution of CRS or in the absence of CRS. 91% of all treated patients experienced the first CRS or neurological event within the first 7 days after TECARTUS infusion.

The most common neurologic events (>10%) included encephalopathy (57%), headache (37%), tremor (34%), confusional state (26%), aphasia (23%), delirium (17%), dizziness (15%), anxiety (14%), and agitation (12%). Serious events (≥ 2%) including encephalopathy, aphasia, confusional state, and seizures occurred after treatment with TECARTUS.

Monitor patients daily for at least 7 days at the certified healthcare facility and for 4 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 in 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 2 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).

Hemophagocytic Lymphohistiocytosis/Macrophage Activation Syndrome (HLH/MAS), including life-threatening reactions, occurred following treatment with TECARTUS. HLH/MAS occurred in 4% (3/78) of patients with ALL. Two patients experienced Grade 3 events and 1 patient experienced a Grade 4 event. The median time to onset for HLH/MAS was 8 days (range: 6 to 9 days) with a median duration of 5 days (range: 2 to 8 days). All 3 patients with HLH/MAS had concurrent CRS symptoms and neurologic events after TECARTUS infusion. Treatment of HLH/MAS should be administered per institutional standards.

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. Infections (all grades) occurred in 56% (46/82) of patients with MCL. 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 with MCL 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.

In immunosuppressed patients, life-threatening and fatal opportunistic infections have been reported. The possibility of rare infectious etiologies (e.g., fungal and viral infections such as HHV-6 and progressive multifocal leukoencephalopathy) should be considered in patients with neurologic events and appropriate diagnostic evaluations should be performed.

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 patients with MCL, Grade 3 or higher cytopenias not resolved by Day 30 following TECARTUS infusion occurred in 55% (45/82) of patients and included thrombocytopenia (38%), neutropenia (37%), and anemia (17%). Monitor blood counts after TECARTUS infusion.

Hypogammaglobulinemia and B-cell aplasia can occur in patients receiving treatment with TECARTUS. Hypogammaglobulinemia was reported in 16% (13/82) of patients with MCL. 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 6 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 one 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 fever, CRS, hypotension, encephalopathy, fatigue, tachycardia, arrhythmia, infection with pathogen unspecified, chills, hypoxia, cough, tremor, musculoskeletal pain, headache, nausea, edema, motor dysfunction, constipation, diarrhea, decreased appetite, dyspnea, rash, insomnia, pleural effusion, and aphasia.

Please see full Prescribing Information, including **BOXED WARNING** and Medication Guide.

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.

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