YESCARTA®
(axicabtagene ciloleucel) Suspension for IV infusion

TECARTUS®
(brexucabtagene autoleucel) suspension for infusion

Important Safety Information for Healthcare Professionals to Minimize the Risks of Cytokine Release Syndrome and Serious Neurologic Adverse Reactions

THIS WILL ALLOW QUICK IDENTIFICATION OF NEW SAFETY INFORMATION. HEALTHCARE PROFESSIONALS ARE ASKED TO REPORT ANY SUSPECTED ADVERSE REACTIONS.

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LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

ALL	Acute lymphoblastic leukemia
CAR T	Chimeric antigen receptor T-cell
CD	Cluster of differentiation
CNS	Central nervous system
CRS	Cytokine release syndrome
DLBCL	Diffuse large B-cell lymphoma
FL	Follicular lymphoma
HCP	Healthcare professional
HLH/MAS	Hemophagocytic lymphohistiocytosis/macrophage activation syndrome
ICANS	Immune effector cell-associated neurotoxicity syndrome
LBCL	Large B-cell lymphoma
MCL	Mantle cell lymphoma
PAC	Patient Alert Card

1. WHAT IS YESCARTA AND TECARTUS

- Yescarta (axicabtagene ciloleucel) and Tecartus (brexucabtagene autoleucel) are engineered autologous T cell immunotherapy product that binds to CD19 expressing cancer cells and normal B cells. Following anti CD19 chimeric antigen receptor T cell (CAR T) engagement with CD19 expressing target cells, the CD28 co stimulatory domains and CD3 zeta signaling domain 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 apoptosis and necrosis of CD19 expressing target cells.
- Yescarta is indicated for the treatment of adult patients with large B cell lymphoma (LBCL) that is refractory to first line chemoimmunotherapy or that relapses within 12 months of first line chemoimmunotherapy. In addition, Yescarta is authorized for the treatment of adult patients with relapsed or refractory LBCL 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 (FL) and adult patients with relapsed or refractory FL after two or more lines of systemic therapy.
- Tecartus is indicated for the treatment of adult patients with relapsed or refractory mantle cell lymphoma (MCL) and adult patients with relapsed or refractory B-cell precursor acute lymphoblastic leukemia (ALL).
- Yescarta and Tecartus administration can result in severe, life threatening, and fatal reactions like cytokine release syndrome (CRS) and serious neurologic adverse reactions, also known as immune effector cell associated neurotoxicity syndrome (ICANS). As a result, these products will only be supplied to hospitals and associated certified centers where healthcare professionals (HCPs) have completed training and have on site, immediate access to tocilizumab.

2. PURPOSE OF THE EDUCATIONAL MATERIAL FOR YESCARTA AND TECARTUS

This guide is intended to provide information on CRS and serious neurologic adverse reactions/ICANS associated with the use of Yescarta and Tecartus, including guidance on monitoring, management of symptoms, and reporting of these adverse reactions.

Review the Yescarta and Tecartus Summary of Product Characteristics for HCPs for a more detailed description of these risks as well as other risks and read this HCP Educational Material prior to prescribing.

All patients or their caregivers must be given a Patient Alert Card (PAC) to educate them about the symptoms of CRS and serious neurologic adverse reactions/ICANS and the need to report the symptoms to their treating physician immediately. Treating HCPs should also advise their patients to keep the PACs with them at all times and show it to any HCP who may treat them.

The information in this guide is provided by Gilead for HCPs who are involved in the treatment of patients with Yescarta or Tecartus. To obtain copies of the PAC, contact Gilead Medical Information at askgileadME@gilead.com.

HCPs are asked to report any suspected adverse reactions. To report an adverse reaction associated with Yescarta or Tecartus, please contact the National Pharmacovigilance Center (NPC) – Saudi Food and Drug Authority (SFDA) call center 19999, e-mail: npc.drug@sfda.gov.sa, or website: https://ade.sfda.gov.sa/, or contact the Gilead patient safety department e-mail: DrugSafety.KSA@Gilead.com.

3. HOW TO USE THIS GUIDE

This guide will help you to:

- Identify patients with CRS or serious neurologic adverse reactions/ICANS
- Learn the importance of excluding alternate causes for the reported symptoms
- Grade the severity of the CRS or serious neurologic adverse reactions/ICANS
- Provide treatment of the CRS or serious neurologic adverse reactions/ICANS according to the severity grade, as shown in this guide

4. IMPORTANT POINTS TO CONSIDER BEFORE YOU ADMINISTER YESCARTA OR TECARTUS

- To mitigate the risks associated with Yescarta or Tecartus, clinical facilities must be specifically certified prior to ordering the product. As a part of the certification process, HCPs will be trained on the Educational Materials; the treatment center is responsible for ensuring training of appropriate personnel.
- Yescarta and Tecartus must be administered in a certified healthcare setting.

  The certified healthcare facility must ensure the availability of at least 2 doses of tocilizumab (an interleukin-6 receptor inhibitor) per patient for infusion within 2 hours after Yescarta or Tecartus infusion, if needed for treatment of CRS.

Guidance on managing CRS

Table 1. Signs and Symptoms Associated with CRS

CYTOKINE RELEASE SYNDROME (CRS)

Any organ can be affected by CRS.

The following are common signs and symptoms:

Pyrexia	Chills
Tiredness	Renal impairment
Cardiac failure	Headache
Tachycardia	Malaise
Cardiac arrhythmias	Transaminitis
Dyspnea	Nausea
Hypoxia	Diarrhea
Capillary leak syndrome	Hypotension

Yescarta

Key manifestations of CRS (≥ 10%) in all patients combined included fever, hypotension, tachycardia, hypoxia, chills, headache, and fatigue. Serious events that may be associated with CRS include cardiac arrhythmias (including atrial fibrillation and ventricular tachycardia), cardiac arrest, cardiac failure, renal insufficiency, respiratory failure, capillary leak syndrome, multi-organ failure, and hemophagocytic lymphohistiocytosis/macrophage activation syndrome (HLH/MAS).

Prophylactic treatment with corticosteroids was administered in a cohort study for 3 days beginning on the day of infusion with Yescarta, with no patients developing Grade 3 or higher CRS. Therefore, consider the risk and benefits of prophylactic corticosteroids in the context of pre-existing comorbidities for the individual patient and the potential for the risk of Grade 4 and prolonged neurologic toxicities.

Tumor necrosis factor antagonists are not recommended for management of CRS associated with Yescarta.

Tecartus

Among patients with CRS, the key manifestations (>10%) were similar in MCL and ALL and included fever (93%), hypotension (62%), tachycardia (59%), chills (32%), hypoxia (31%), headache (21%), fatigue (20%), and nausea (13%). Serious events associated with CRS in MCL and ALL combined (≥ 2%) included hypotension, fever, hypoxia, tachycardia, and dyspnea.

Yescarta and Tecartus

CRS has been known to be associated with end organ dysfunction (e.g., hepatic, renal, cardiac, and pulmonary). In addition, worsening of underlying organ pathologies can occur in the setting of CRS. Patients with medically significant cardiac dysfunction should be managed by standards of critical care and measures such as echocardiography should be considered. HLH/MAS presents with symptoms similar to CRS. Evaluation for HLH/MAS should be considered in patients with severe or unresponsive CRS.

Yescarta and Tecartus continue to expand and persist following administration of tocilizumab and corticosteroids.

Yescarta or Tecartus should not be administered to patients with active infections or inflammatory disease until these conditions have resolved. Diagnosis of CRS requires excluding alternative causes of systemic inflammatory response, including infection. In the event of febrile neutropenia, evaluate for infection and manage with broad spectrum antibiotics, fluids and other supportive care as medically indicated.

Treatment algorithms have been developed to ameliorate some of the CRS symptoms experienced by patients following Yescarta or Tecartus treatment (see Table 3 for Yescarta and Table 4 for Tecartus for more details).

Table 2 describes the grading of CRS according to the Lee criteria*:

Table 2. CRS Grading (Excluding Neurologic Adverse Reactions)

Lee Grade	Symptoms
Grade 1	Symptoms require symptomatic treatment only (e.g., fever, nausea, fatigue, headache, myalgia, malaise)
Grade 2	Symptoms require and respond to moderate intervention Oxygen requirement < 40% FiO2 or Hypotension responsive to fluids or low dose of one vasopressor or Grade 2 organ toxicity
Grade 3	Symptoms require and respond to aggressive intervention Oxygen requirement ≥ 40% FiO2 or Hypotension requiring high dose or multiple vasopressors or Grade 3 organ toxicity or Grade 4 transaminitis
Grade 4	Life-threatening symptoms Requirements for ventilator support or CVVHD or Grade 4 organ toxicity (excluding transaminitis)

Abbreviations:
CRS = cytokine release syndrome; CVVHD = continuous veno-venous hemodialysis.
* {Lee 2014}

Table 3. Yescarta: Categories of CRS Severity and Management

CRS Gradea	Tocilizumab	Corticosteroids
Grade 1		
• Symptoms require symptomatic treatment only (e.g., fever, nausea, fatigue, headache, myalgia, malaise).	• If symptoms (e.g., fever) not improving after 24 hours, consider managing as Grade 2.	• If not improving after 3 days, administer one dose of dexamethasone 10 mg IV.
Grade 2		
• Symptoms require and respond to moderate intervention. • Oxygen requirement < 40% FiO2 or hypotension responsive to fluids or low dose of one vasopressor or Grade 2 organ toxicityb.	• Administer Tocilizumabc 8 mg/kg IV over 1 hour (not to exceed 800 mg). • If no clinical improvement in the signs and symptoms of CRS after the first dose, repeat tocilizumab every 8 hours as needed. • Limit to a maximum of 3 doses in a 24-hour period; maximum total of 4 doses. • If improving, discontinue tocilizumab.	• Administer dexamethasone 10 mg IV once daily. • If improving, manage as Grade 1 above and continue corticosteroids until the severity is Grade 1 or less, then quickly taper as clinically appropriate. • If not improving, manage as appropriate grade below.
Grade 3		
• Symptoms require and respond to aggressive intervention. • Oxygen requirement ≥ 40% FiO2 or hypotension requiring high dose or multiple vasopressors or • Grade 3 organ toxicity or Grade 4 transaminitis.	• Per Grade 2. • If improving, manage as appropriate grade above.	• Dexamethasone 10 mg IV 3 times a day. • If improving, manage as appropriate grade above and continue corticosteroids until the severity is Grade 1 or less, then quickly taper as clinically appropriate. • If not improving, manage as Grade 4.
Grade 4		
• Life-threatening symptoms. • Requirements for ventilator support or CVVHD. • Grade 4 organ toxicity (excluding transaminitis).	• Per Grade 2. • If improving, manage as appropriate grade above.	• Administer methylprednisolone 1000 mg IV once per day for 3 days. • If improving, manage as appropriate grade above and continue corticosteroids until the severity is Grade 1 or less, then taper as clinically appropriate. • If not improving, consider methylprednisolone 1000 mg 2 3 times a day or alternate therapy. considermethylprednisolone 1000 mg 2 3 times a day or alternate therapyd.

Abbreviations: CRS = cytokine release syndrome; CVVHD = continuous veno-venous hemodialysis; IV = intravenously

a Lee et al. 2014.

b Refer to Table 6 for management of neurologic toxicity.

c Refer to tocilizumab Prescribing Information for details.

d Alternate therapy includes (but is not limited to): ruxolitinib, cyclophosphamide, intravenous immunoglobulin and anti-thymocyte globulin.

Table 4. Tecartus: Categories of CRS Severity and Management

CRS Gradea	Tocilizumab	Corticosteroids
Grade 1		
• Symptoms require symptomatic treatment only (e.g., fever, nausea, fatigue, headache, myalgia, malaise).	• If not improving after 24 hours, administer tocilizumabc 8 mg/kg IV over 1 hour (do not exceed 800 mg).	• Not appliable.
Grade 2		
• Symptoms require and respond to moderate intervention. • Oxygen requirement < 40% FiO2 or hypotension responsive to fluids or low dose of one vasopressor or Grade 2 organ toxicity[b].	• Administer tocilizumabc 8 mg/kg IV over 1 hour (not to exceed 800 mg). • Repeat tocilizumab ever 8 hours as needed if not responsive to IV fluids or increasing supplemental oxygen. Limit to a maximum of 3 doses in a 24-hour period; maximum total of 4 doses if no clinical improvement in the signs and symptoms of CRS • If improving, discontinue tocilizumab.	• Manager per Grade 3 if no improvement within 24 hours after starting tocilizumab. • If improving, taper corticosteroids.
Grade 3		
• Symptoms require and respond to aggressive intervention. • Oxygen requirement ≥ 40% FiO2 or hypotension requiring high dose or multiple vasopressors or • Grade 3 organ toxicity or Grade 4 transaminitis.	• Per Grade 2. • If improving, discontinue tocilizumab.	• Administer methylprednisolone 1 mg/kg IV twice daily or equivalent dexamethasone (e.g., 10 mg IV every 6 hours) until Grade 1, then taper corticosteroids. • If improving, manage as Grade 2. • If not improving, manage as Grade 4.
Grade 4		
• Life-threatening symptoms. • Requirements for ventilator support or CVVHD. • Grade 4 organ toxicity (excluding transaminitis).	• Per Grade 2. • If improving, discontinue tocilizumab.	• Administer methylprednisolone 1000 mg IV once per day for 3 days. • If improving, taper corticosteroids, and manage as Grade 3. • If not improving, consider alternate immunosuppressants.

Abbreviations: CRS = cytokine release syndrome; CVVHD = continuous veno-venous hemodialysis; IV = intravenously

a Lee et al. 2014.

b Refer to Table 7 for management of neurologic toxicity.

c Refer to tocilizumab Prescribing Information for details.

5. GUIDANCE ON MANAGING NEUROLOGIC ADVERSE REACTIONS

Table 5. Signs and Symptoms Associated With Neurologic Adverse Reactions

NEUROLOGIC ADVERSE REACTIONS	
The following are common signs and symptoms:	
Seizures	Ataxia
Somnolence	Memory impairment
Headache	Mental status changes
Confusion	Hallucinations
Agitation	Depressed level of consciousness
Speech disorders	Delirium
Tremor	Dysmetria
Encephalopathy	

Yescarta

The most common neurologic toxicities (≥ 10%) in all patients combined included encephalopathy, headache, tremor, dizziness, delirium, aphasia, and insomnia. Prolonged encephalopathy lasting up to 173 days was noted. Serious events including aphasia, leukoencephalopathy, dysarthria, lethargy, and seizures occurred. Fatal and serious cases of cerebral edema have occurred in patients treated with Yescarta.

For additional information regarding neurologic adverse reactions, see the product summary of product characteristics.

There is limited experience with Yescarta in patients with lymphomas involving the central nervous system (CNS). Patients with a history of CNS disorders such as seizures or cerebrovascular ischemia may be at increased risk. Patients should be monitored at least daily for 7 days at the certified healthcare facility following infusion for signs and symptoms of neurologic toxicity. After the first 7 days following the infusion, the patient should be monitored at the physician's discretion.

Tecartus

The most common neurologic events (>10%) were similar in MCL and ALL and 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.

For additional information regarding neurologic adverse reactions, see the product summary of product characteristics. Monitor patients daily for at least 7 days for patients with MCL and at least 14 days for patients with ALL at the certified healthcare facility following infusion for signs and symptoms of neurologic toxicities. Monitor patients for signs or symptoms of neurologic toxicities for 4 weeks after infusion and treat promptly.

Yescarta and Tecartus

Treatment algorithms have been developed to ameliorate the neurologic adverse reactions experienced by patients following Yescarta or Tecartus treatment (see Table 6 for Yescarta and Table 7 for Tecartus for more details). Patients should be instructed to remain within proximity of a certified healthcare facility for at least 4 weeks following infusion to monitor for signs and symptoms of neurologic adverse reactions. Counsel patients to seek immediate medical attention should signs or symptoms of neurologic adverse reactions occur at any time.

Table 6. Yescarta: Grading and Management of Neurologic Adverse Reactions/ICANS

Neurologic Adverse Reaction Grading Assessment CTCAEa 4.03)	Concurrent CRS	No concurrent CRS
Grade 1		
Examples include: • Somnolence-mild drowsiness or sleepiness. • Confusion-mild disorientation. • Encephalopathy-mild limiting of ADLs. • Dysphasia-not impairing ability to communicate.	• Administer tocilizumab per Table 3 for management of Grade 1 CRS. • In addition, administer 1 dose of dexamethasone 10 mg IV. • If not improving after 2 days, repeat dexamethasone 10 mg IV. *Consider levetiracetam for seizure prophylaxis.*	• Administer 1 dose of dexamethasone 10 mg IV. • If not improving after 2 days, repeat dexamethasone 10 mg IV.
Grade 2		
Examples include: • Somnolence-moderate, limiting instrumental ADLs. • Confusion-moderate disorientation. • Encephalopathy-limiting instrumental ADLs. • Dysphasia-moderate impairing ability to communicate spontaneously. • Seizure(s)	• Administer tocilizumab per Table 3 for management of Grade 2 CRS. • In addition, administer dexamethasone 10 mg IV 4 times a day. • If improving, continue corticosteroids until the severity is Grade 1 or less, then quickly taper as clinically appropriate. • If not improving, manage as appropriate grade below. *Consider levetiracetam for seizure prophylaxis.*	• Administer dexamethasone 10 mg intravenously 4 times a day. • If improving, continue corticosteroids until the severity is Grade 1 or less, then quickly taper as clinically appropriate. • If not improving, manage as appropriate grade below.
Grade 3		
Examples include: • Somnolence-obtundation or stupor. • Confusion-severe disorientation. • Encephalopathy-limiting self- care ADLs. • Dysphasia-severe receptive or expressive characteristics, impairing ability to read, write, or communicate intelligibly.	• Administer tocilizumab per Table 3 for management of Grade 2 CRS. • In addition, administer methylprednisolone 1000 mg IV once daily. • If improving, manage as appropriate grade above and continue corticosteroids until the severity is Grade 1 or less, then taper as clinically appropriate. • If not improving, manage as Grade 4. *Consider levetiracetam for seizure prophylaxis.*	• Administer methylprednisolone 1000 mg IV once daily. • If improving, manage as appropriate grade above and continue corticosteroids until the severity is Grade 1 or less, then taper as clinically appropriate. • If not improving, manage as Grade 4.

Grade 4			
Examples include: • Life-threatening consequences. • Urgent intervention indicated. • Requirement for mechanical ventilation. • Consider cerebral edema.	• Administer tocilizumab per Table 3 for management of Grade 2 CRS. • In addition, administer methylprednisolone 1000 mg IV twice per day. • If improving, manage as appropriate grade above and continue corticosteroids until the severity is Grade 1 or less, then taper as clinically appropriate. • If not improving, consider 1000 mg of methylprednisolone IV 3 times a day or alternate therapy [b]. *Consider levetiracetam for seizure prophylaxis.*	• Administer methylprednisolone 1000 mg IV twice per day. • If improving, manage as appropriate grade above and continue corticosteroids until the severity is Grade 1 or less, then taper as clinically appropriate. • If not improving, consider 1000 mg of methylprednisolone IV 3 times a day or alternate therapy [b].	

Abbreviations: ADL = activities of daily living; CRS = cytokine release syndrome; CTCAE = Common Terminology Criteria for Adverse Events; EEG = electroencephalogram; IV = intravenously; MRI = magnetic resonance imaging.
a Severity based on Common Terminology Criteria for Adverse Events.
b Alternate therapy includes (but is not limited to): ruxolitinib, cyclophosphamide, intravenous immunoglobulin and anti-thymocyte globulin.

Table 7. Tecartus: Grading and Management of Neurologic Adverse Reactions

Neurologic Adverse Reaction

Neurologic Event[a]	Concurrent CRS	No concurrent CRS
Grade 1		
Examples include: • Somnolence-mild drowsiness or sleepiness. • Confusion-mild disorientation. • Encephalopathy-mild limiting of ADLs. • Dysphasia-not impairing ability to communicate.	• Administer tocilizumab per Table 4 for management of Grade 1 CRS.	• Supportive care.
Grade 2		
Examples include: • Somnolence-moderate, limiting instrumental ADLs. • Confusion-moderate disorientation. • Encephalopathy-limiting instrumental ADLs. • Dysphasia-moderate impairing ability to communicate spontaneously. • Seizure(s)	• Administer tocilizumab per Table 4 for management of Grade 2 CRS. • If not improving within 24 hours after starting tocilizumab, administer dexamethasone 10 mg IV every 6 hours until the event is Grade 1 or less, then taper corticosteroids. • If improving, discontinue tocilizumab. • If still not improving, manage as Grade 3. *Consider non-sedating, anti-seizure medicines (e.g., levetiracetam) for seizure prophylaxis.*	• Administer dexamethasone 10 mg IV every 6 hours until the event is Grade 1 or less. • If improving, taper corticosteroids.
Grade 3		
	• Administer tocilizumab per Table 4 for management of Grade 2 CRS. • In addition, administer dexamethasone 10 mg IV with the first dose of tocilizumab and repeat dose every 6 hours. Continue dexamethasone use until the event is Grade 1 or less, then taper corticosteroids. • If improving, discontinue tocilizumab and manage as Grade 2. • If still not improving, manage as Grade 4. *Consider non-sedating, anti-seizure medicines (e.g., levetiracetam) for seizure prophylaxis.*	• Administer dexamethasone 10 mg IV every 6 hours. Continue dexamethasone use until the event is Grade 1 or less, then taper corticosteroids. • If not improving, manage as Grade 4.

Neurologic Event[a]	Concurrent CRS	No concurrent CRS
Grade 4		
Examples include: • Life-threatening consequences. • Urgent intervention indicated. • Requirement for mechanical ventilation. • Consider cerebral edema.	• Administer tocilizumab per Table 4 for management of Grade 2 CRS. • Administer methylprednisolone 1000 mg IV per day with first dose of tocilizumab and continue methylprednisolone 1000 mg IV per day for 2 more days. • If improving, then manage as Grade 3. • If not improving, consider alternate immunosuppressants. *Consider non-sedating, anti-seizure medicines (e.g., levetiracetam) for seizure prophylaxis.*	• Administer methylprednisolone 1000 mg IV per day for 3 days. • If improving, then manage as Grade 3. • If not improving, consider alternate immunosuppressants.

Abbreviations: ADL = activities of daily living; CRS = cytokine release syndrome; IV = intravenously.
a Severity based on Common Terminology Criteria for Adverse Events.

6. POST YESCARTA AND TECARTUS INFUSION MONITORING

Post Yescarta or Tecartus infusion recommendations:

- Patients should be monitored daily for the first 7 days following infusion of Yescarta or Tecartus and at least 14 days for patients with ALL following infusion of Tecartus for signs and symptoms of potential CRS, neurologic adverse reactions and other toxicities.
- Physicians should consider hospitalization for the first 7 days post infusion or at the first signs or symptoms of CRS and/or neurologic adverse reaction. After the first 7 days following Yescarta or Tecartus infusion, the patient should be monitored at the physician's discretion.
- Patients should be instructed to stay within proximity of the certified healthcare facility for at least 4 weeks so that they can be monitored for signs and symptoms of CRS and neurologic adverse reactions.
- Treating HCPs should make weekly phone calls to assess for any signs or symptoms suggestive of CRS and neurologic adverse reactions.
- If the patients develop any signs or symptoms of CRS or neurologic adverse reaction, they should be instructed to immediately go to the certified healthcare facility (or nearest hospital if travel is deemed unsafe) for evaluation for hospitalization and treatment which includes supportive care and use of tocilizumab and/or corticosteroids.
- Patient should be advised to refrain from driving or operating heavy or potentially dangerous machinery after axicabtagene ciloleucel infusion for at least 8 weeks after infusion.

Below is a checklist of some of the signs and symptoms that the HCP should assess for during weekly calls to the patient. This checklist is not meant to be all-inclusive. Based on the responses below, the decision to bring the patient for evaluation will be at the discretion of the treating physician.

GENERAL	YES	NO
Do you have a fever?		
Do you have any chills?		
Do you have any nausea or vomiting?		
Are you having difficulty sleeping?		
Are you having problems staying awake?		
Are you lightheaded or experiencing dizziness?		
Do you have headaches?		
Do you have loss of balance or coordination?		
Do you have difficulty in speaking or slurred speech?		
Do you have confusion or disorientation?		
Do you have any unusual body movements?		
Do you have dizziness when you stand up?		
Do you have difficulty understanding numbers or doing math?		
Do you have difficulty writing?		
Do you have shortness of breath or rapid breathing?		
Are you having difficulty breathing?		
Do you have palpitations?		
Are you more tired than you were before the Yescarta or Tecartus infusion?		

7. PATIENT COUNSELLING

Talk to the patient about the risk of CRS and neurologic adverse reactions. Early diagnosis and appropriate management of CRS and neurologic adverse reactions are essential to minimize life threatening complications. Remind the patient not to treat their own symptoms. Instruct patients to contact their HCP and/or seek immediate care if they experience any signs and symptoms associated with CRS and/or neurologic adverse reactions, which include:

- Fever (e.g., temperature above 38°C)
- Difficulty breathing
- Chills or shaking chills
- Confusion
- Decreased level of consciousness
- Seizures
- Tremors
- Dizziness or lightheadedness
- Severe nausea, vomiting, or diarrhoea
- Fast or irregular heartbeat
- Severe fatigue or weakness

Provide the product PAC to the patient or the patient’s caregiver. Tell the patient to carry the PAC at all times and to share the PAC with any HCP involved in the patient's treatment.

After Yescarta or Tecartus infusion, advise patients to stay within proximity of a certified healthcare facility for a minimum of 4 weeks to monitor for signs and symptoms of CRS or neurologic adverse reactions.

8. REPORTING OF ADVERSE REACTIONS

Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product.

HCPs are asked to report any suspected adverse reactions associated with axicabtagene ciloleucel or brexucabtagene autoleucel to Gilead or the competent authorities directly.

Please contact the National Pharmacovigilance Center (NPC) – Saudi Food and Drug Authority (SFDA) call center 19999, e-mail: npc.drug@sfda.gov.sa, or website: https://ade.sfda.gov.sa/ or contact the Gilead patient safety department e-mail: DrugSafety.

KSA@Gilead.com.

9. REFERENCES

Lee DW, Gardner R, Porter DL, Louis CU, Ahmed N, Jensen M, et al. Current concepts in the diagnosis and management of cytokine release syndrome. Blood 2014;124 (2):188-95.