

RISK EVALUATION AND MITIGATION STRATEGY (REMS) Document

YESCARTA (axicabtagene ciloleucel) and TECARTUS (brexucabtagene autoleucel) REMS Program

I. Administrative Information

Application Number: BLA 125643 and BLA 125703

Application Holder: Kite Pharma, Inc.

Initial REMS Approval: 10/2017

Most Recent REMS Update: XX/XXXX

II. REMS Goals

The goals of the YESCARTA and TECARTUS REMS are to mitigate the risks of cytokine release syndrome (CRS) and neurological toxicities by:

1. Ensuring that hospitals and their associated clinics that dispense YESCARTA and/or TECARTUS are specially certified and have on-site, immediate access to tocilizumab.
2. Ensuring those who prescribe, dispense, or administer YESCARTA and/or TECARTUS are aware of how to manage the risks of CRS and neurological toxicities.

III. REMS Requirements

Kite Pharma, Inc. must ensure that hospitals and their associated clinics, and patients comply with the following requirements:

1. Hospitals and their associated clinics that dispense YESCARTA and/or TECARTUS must:

To become certified to dispense

1. Have a minimum of two doses of tocilizumab available on-site for each patient for immediate administration (within 2 hours).
 2. Designate an authorized representative to complete the certification process and oversee implementation and compliance with the REMS Program requirements on behalf of the hospital and their associated clinics.
 3. Have the authorized representative enroll in the REMS by completing the [Hospital Enrollment Form](#) and submitting it to the REMS Program.
 4. Have the authorized representative complete the [Program Training](#).
 5. Have the authorized representative successfully complete a [Knowledge Assessment](#) and submit it to the REMS Program.
 6. Train all relevant staff involved in prescribing, dispensing, or administering of YESCARTA and/or TECARTUS on the REMS Program requirements using the [Program Training](#) and [Adverse Reaction Management Guide](#).
 7. Have all relevant staff involved in prescribing, dispensing, or administering YESCARTA and/or TECARTUS successfully complete the [Knowledge Assessment](#).
 8. Establish processes and procedures to ensure relevant new staff involved in prescribing, dispensing, or administering YESCARTA and/or TECARTUS are trained and complete the [Knowledge Assessment](#).
 9. Establish processes and procedures to verify that a minimum of two doses of tocilizumab are available on-site for each patient and are ready for immediate administration (within 2 hours).
 10. Establish processes and procedures to provide patients with the [Patient Wallet Card](#).
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Before infusion

11. Verify that a minimum of two doses of tocilizumab are available on-site for each patient and are ready for immediate administration (within 2 hours) through the processes and procedures established as a requirement of the REMS Program.
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1. Hospitals and their associated clinics that dispense YESCARTA and/or TECARTUS must:

Before discharge 12. Provide the patient with the [Patient Wallet Card](#) through the processes and procedures established as a requirement of the REMS Program.

To maintain certification to dispense, if there is a change in authorized representative 13. Have the new authorized representative enroll in the REMS Program by completing the [Hospital Enrollment Form](#).

To maintain certification to dispense, if YESCARTA or TECARTUS has not been dispensed at least once annually from the date of initial certification in the REMS Program 14. Train all relevant staff involved in prescribing, dispensing, or administering YESCARTA and/or TECARTUS on the REMS Program requirements using the [Program Training](#).
15. Have all relevant staff involved in prescribing, dispensing, or administering YESCARTA and/or TECARTUS successfully complete the [Knowledge Assessment](#).

At all times 16. Report any serious adverse events¹ suggestive of cytokine release syndrome or neurological toxicities to the REMS Program.
17. Maintain records of staff training.
18. Maintain documentation that all processes and procedures are in place and are being followed.
19. Comply with audits by Kite Pharma, Inc. or a third party acting on behalf of Kite Pharma, Inc. to ensure that all training, processes, and procedures are in place and are being followed.

2. Patients who are dispensed YESCARTA or TECARTUS:

Before discharge 1. Receive the [Patient Wallet Card](#).

¹ For the purpose of this REMS, serious adverse event is defined as any adverse experience occurring at any dose that results in any of the following outcomes: death, a life-threatening adverse experience, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant disability/incapacity, or a congenital anomaly/birth defect.

Kite Pharma, Inc. must provide training to relevant staff who prescribe, dispense, or administer YESCARTA and/or TECARTUS.

The training includes the following educational material: [Program Training](#). The Training must be provided in-person, live webcast, or on-line.

To support REMS Program operations, Kite Pharma, Inc. must:

1. Ensure that YESCARTA and TECARTUS are distributed only to certified hospitals and their associated clinics.
2. Establish and maintain a [REMS Program website](#) (www.YescartaTecartusREMS.com). The REMS Program website must include the capability to complete training online, maintain records of that training, and the option to print the Prescribing Information, Medication Guides, and REMS materials. The product websites for consumers and healthcare providers must include prominent REMS-specific links to the REMS Program website.
3. Make the REMS Program website fully operational and all REMS materials available through the website and call center.
4. Establish and maintain a REMS Program call center for REMS participants at 1-844-454-KITE (5483).
5. Establish and maintain a validated, secure database of all REMS participants who are enrolled and/or certified in the REMS Program.
6. Ensure that hospitals and their associated clinics are able to enroll in the REMS Program in-person, via email, and fax.
7. Notify hospitals and their associated clinics within 7 calendar days after they become certified by the REMS Program.

To ensure REMS participants' compliance with the REMS Program, Kite Pharma, Inc. must:

8. Verify annually that the designated authorized representative remains the same. If different, the hospital and their associated clinics must re-certify with a new authorized representative.
9. Maintain adequate records to demonstrate that REMS requirements have been met, including, but not limited to records of: YESCARTA and/or TECARTUS distribution and dispensing, certification of hospitals and their associated clinics, and audits of REMS participants. These records must be readily available for FDA inspections.
10. Monitor hospitals and their associated clinics on an ongoing basis to ensure the requirements of the REMS Program are being met. Take corrective action if noncompliance is identified, including decertification.
11. Maintain an ongoing annual audit plan of hospitals and their associated clinics.
12. Audit all certified hospitals within 180 calendar days from the first order of YESCARTA and/or TECARTUS for the first patient to ensure that all processes and procedures are in place and functioning to support the requirements of the YESCARTA and TECARTUS REMS Program. Certified hospitals and their associated clinics must also be included in the Kite Pharma, Inc. ongoing annual audit plan.
13. Take reasonable steps to improve implementation of and compliance with the requirements in the YESCARTA and TECARTUS REMS Program based on the monitoring and evaluation of the YESCARTA and TECARTUS REMS program.

IV. REMS Assessment Timetable

Kite Pharma, Inc. must submit REMS Assessments to the FDA at 6 months, 12 months, and annually thereafter from the date of the initial approval of the YESCARTA and TECARTUS REMS (XX/XX/XXXX). To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment should conclude no earlier than 60 days before the submission date for that assessment. Kite Pharma, Inc. must submit each assessment so that it will be received by the FDA on or before the due date.

V. REMS Materials

The following materials are part of the YESCARTA and TECARTUS REMS:

Enrollment Forms

Prescriber:

1. [Hospital Enrollment Form](#)

Training and Educational Materials

Patient:

2. [Patient Wallet Card](#)

Healthcare Setting:

3. [Program Training](#)
4. [Knowledge Assessment](#)
5. [Adverse Reaction Management Guide](#)

Other Materials

6. [REMS Program website](#)

YESCARTA and TECARTUS REMS Program Hospital Enrollment Form

YESCARTA and TECARTUS REMS Program Hospital Enrollment

YESCARTA[®] and TECARTUS[™] are available only through the YESCARTA and TECARTUS REMS Program. Only hospitals and their associated clinics certified in the YESCARTA and TECARTUS REMS Program are permitted to dispense YESCARTA and TECARTUS.

YESCARTA and TECARTUS REMS Hospital Attestations

As a condition of certification, the certified hospital and its associated clinics must:

- Ensure that if the hospital and its associated clinics designate a new authorized representative, the new authorized representative must review the YESCARTA and TECARTUS REMS Program Training , complete the YESCARTA and TECARTUS REMS Program Knowledge Assessment, complete a new YESCARTA and TECARTUS REMS Program Hospital Enrollment Form, and submit the forms via fax to 1-310-496-0397 or email at YTREMS@kitepharma.com.
- Report any serious adverse events suggestive of CRS or neurological toxicities.
- Report suspected serious adverse events associated with either YESCARTA or TECARTUS by contacting Kite at 1-844-454-KITE (5483) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.
- Dispense YESCARTA or TECARTUS to patients only after verifying that a minimum of 2 doses of tocilizumab are available on-site for each patient and are ready for immediate administration (within 2 hours).
- Provide the patient with the Patient Wallet Card.
- Maintain documentation of all processes and procedures for the YESCARTA and TECARTUS REMS Program and provide documentation upon request to Kite, or a third party acting on behalf of Kite.
- Comply with audits by Kite, or a third party acting on behalf of Kite.

YESCARTA and TECARTUS REMS Program Hospital Registration Form

Please email the completed form to YTREMS@kitepharma.com or fax to **1-310-496-0397**.

Important Notice: Completion of the enrollment form and knowledge assessment does not guarantee that your hospital and its associated clinics will be certified to administer YESCARTA or TECARTUS. Please contact 1-844-454-KITE or visit the YESCARTA and TECARTUS REMS Program website at www.YescartaTecartusREMS.com for more information.

YESCARTA and TECARTUS REMS Program Hospital Enrollment Form

To finalize your registration in the YESCARTA and TECARTUS REMS Program, please complete the form below in its entirety.

New Certification

Recertification

Change in Authorized Representative

Authorized Representative Information:

First Name: _____ Last Name: _____

Title: _____ Credentials: DO MD RPh RN/NP PA Other: _____

Phone Number: _____ Fax Number: _____

Email Address: _____

Hospital/ Associated Clinic Contact Information:

Hospital/ Associated Clinic Name: _____

Street Address: _____

City: _____ State: _____ ZIP Code: _____

YESCARTA and TECARTUS REMS Authorized Representative Attestations

- **I am the authorized representative designated by my hospital and its associated clinics to coordinate the activities of the YESCARTA and TECARTUS REMS Program.**
- **By signing this form, I attest that I understand and agree to comply with the following REMS Program requirements:**
- I must complete the YESCARTA and TECARTUS REMS Program Training and successfully complete the YESCARTA and TECARTUS REMS Program Knowledge Assessment.
- I must submit this completed YESCARTA and TECARTUS REMS Program Hospital Enrollment Form to Kite via fax at 1-310-496-0397 or email to YTREMS@kitepharma.com.
- I must submit the YESCARTA and TECARTUS REMS Program Knowledge Assessment training online on the REMS Program website or send to Kite via fax at 1-310-496-0397 or email to YTREMS@kitepharma.com.
- I will oversee implementation and compliance with the YESCARTA and TECARTUS REMS Program.
- I will ensure that my hospital and its associated clinics establishes processes and procedures that are subject to monitoring by Kite or a third party acting on behalf of Kite to help ensure compliance with the requirements of the YESCARTA and TECARTUS REMS Program, including the following, before administering YESCARTA or TECARTUS:

- Ensure that all relevant staff involved in the prescribing, dispensing, or administering of YESCARTA or TECARTUS are trained on the YESCARTA and TECARTUS REMS Program requirements as described in the training materials, successfully complete the YESCARTA and TECARTUS REMS Program Knowledge Assessment, and maintain training records for all staff.
- Put processes and procedures in place to ensure that relevant staff involved in the prescribing, dispensing, or administering of YESCARTA or TECARTUS are retrained if YESCARTA or TECARTUS have not been dispensed at least once annually from the date of certification in the YESCARTA and TECARTUS REMS Program.
- Prior to dispensing YESCARTA or TECARTUS, put processes and procedures in place to verify a minimum of 2 doses of tocilizumab are available on-site for each patient and are ready for immediate administration (within 2 hours).
- Prior to discharge, provide patients/caregivers with the Patient Wallet Card and instruct patient to remain within close proximity (within 2 hours) of the certified administering hospital and its associated clinics for at least 4 weeks following YESCARTA or TECARTUS infusion.

Authorized Representative Name

Title

Signature

Date

YESCARTA (*axicabtagene ciloleucel*) and TECARTUS (*brexucabtagene autoleucel*) Adverse Reaction Management Guide

This follow-up guidance is supplemental to the YESCARTA® US Prescribing Information (USPI).

Guidance on Managing Cytokine Release Syndrome (CRS)

Patients should be monitored for signs and symptoms of CRS. Diagnosis of CRS requires ruling out alternate causes of systemic inflammatory response, including concurrent infections. Treatment algorithms have been developed to ameliorate some of the CRS symptoms experienced by patients on YESCARTA®. This includes the use of tocilizumab or tocilizumab and corticosteroids for moderate, severe, or life-threatening CRS.

CRS Grading and Management Guidance

CRS Grade*	Tocilizumab	Corticosteroids
Grade 1 Symptoms require symptomatic treatment only (eg, fever, nausea, fatigue, headache, myalgia, malaise)	N/A	N/A
Grade 2 Symptoms require and respond to moderate intervention Oxygen requirement less than 40% FiO ₂ or hypotension responsive to fluids or low dose of one vasopressor or Grade 2 organ toxicity†	Administer tocilizumab‡ 8 mg/kg intravenous 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	Manage per Grade 3 if no improvement within 24 hours after starting tocilizumab
Grade 3 Symptoms require and respond to aggressive intervention Oxygen requirement greater than or equal to 40% FiO ₂ or hypotension requiring high-dose or multiple vasopressors or Grade 3 organ toxicity or Grade 4 transaminitis	Per Grade 2	Administer methylprednisolone 1 mg/kg intravenous twice daily or equivalent dexamethasone (eg, 10 mg intravenous every 6 hours) Continue corticosteroids use until the event is Grade 1 or less, then taper over 3 days
Grade 4 Life-threatening symptoms Requirements for ventilator support, CVVHD, or Grade 4 organ toxicity (excluding transaminitis)	Per Grade 2	Administer methylprednisolone 1000 mg intravenous per day for 3 days; if improves, then manage as above

Abbreviation: CVVHD, continuous veno-venous hemodialysis.

*Lee DW, Gardner R, Porter DL, et al. Current concepts in the diagnosis and management of cytokine release syndrome. *Blood*. 2014;124(2):188-195.

†Refer to page 2 on the back for management of neurologic toxicity.

‡Refer to tocilizumab Prescribing Information for details.

Guidance on Managing Neurologic Toxicity

Monitor patients for signs and symptoms of neurologic toxicities. Treatment algorithms have been developed to ameliorate the neurologic toxicities experienced by patients on YESCARTA®. This includes the use of corticosteroids or corticosteroids and tocilizumab for moderate, severe, or life-threatening neurologic toxicities.

NEUROLOGIC TOXICITY GRADING AND MANAGEMENT GUIDANCE

Neurologic Event (Grading Assessment CTCAE 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	Supportive care	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 the table on the other side for management of Grade 2 CRS If no improvement within 24 hours after starting tocilizumab, administer dexamethasone 10 mg intravenous every 6 hours if not already taking other corticosteroids Continue dexamethasone use until the event is Grade 1 or less, then taper over 3 days Consider nonsedating, antiseizure medicines (eg, levetiracetam) for seizure prophylaxis	Administer dexamethasone 10 mg intravenous every 6 hours Continue dexamethasone use until the event is Grade 1 or less, then taper over 3 days Consider nonsedating, antiseizure medicines (eg, levetiracetam) for seizure prophylaxis
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 the table on the other side for management of Grade 2 CRS In addition, administer dexamethasone 10 mg intravenous 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 over 3 days Consider nonsedating, antiseizure medicines (eg, levetiracetam) for seizure prophylaxis	Administer dexamethasone 10 mg intravenous every 6 hours Continue dexamethasone use until the event is Grade 1 or less, then taper over 3 days Consider nonsedating, antiseizure medicines (eg, levetiracetam) for seizure prophylaxis
Grade 4 Life-threatening consequences Urgent intervention indicated Requirement for mechanical ventilation Consider cerebral edema	Administer tocilizumab per the table on the other side for management of Grade 2 CRS Administer methylprednisolone 1000 mg intravenous per day with first dose of tocilizumab and continue methylprednisolone 1000 mg intravenous per day for 2 more days; if improves, then manage as above Consider nonsedating, antiseizure medicines (eg, levetiracetam) for seizure prophylaxis	Administer methylprednisolone 1000 mg intravenous per day for 3 days; if improves, then manage as above Consider nonsedating, antiseizure medicines (eg, levetiracetam) for seizure prophylaxis

Abbreviation: ADLs, activities of daily living.

*National Institutes of Health, National Cancer Institute. *Common Terminology Criteria for Adverse Events (CTCAE)*. Version 4.03. Bethesda, MD: National Institutes of Health; 2009. Revised June 2010. NIH publication 09-5410.



YESCARTA and TECARTUS Adverse Reaction Management Guide

This follow-up guidance is supplemental to the TECARTUS™ US Prescribing Information (USPI).

Guidance on Managing Cytokine Release Syndrome (CRS)

Patients should be monitored for signs and symptoms of CRS. Diagnosis of CRS requires ruling out alternate causes of systemic inflammatory response, including concurrent infections. Treatment algorithms have been developed to ameliorate some of the CRS symptoms experienced by patients on TECARTUS™.

CRS GRADING AND MANAGEMENT GUIDANCE

CRS Grade*	Tocilizumab	Corticosteroids
<p>Grade 1 Symptoms require symptomatic treatment only (eg, fever, nausea, fatigue, headache, myalgia, malaise)</p>	<p>If not improving after 24 hours, administer tocilizumab 8 mg/kg IV over 1 hour (not to exceed 800 mg)</p>	<p>N/A</p>
<p>Grade 2 Symptoms require and respond to moderate intervention Oxygen requirement less than 40% FiO₂ or hypotension responsive to fluids or low dose of one vasopressor or Grade 2 organ toxicity†</p>	<p>Administer tocilizumab‡ 8 mg/kg intravenously over 1 hour (not to exceed 800 mg)</p> <p>Repeat tocilizumab every 8 hours as needed if not responsive to intravenous 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</p> <p>If improving, discontinue tocilizumab</p>	<p>Manage per Grade 3 if no improvement within 24 hours after starting tocilizumab</p> <p>If improving, taper corticosteroids, and manage as Grade 1</p>

CRS Grade*	Tocilizumab	Corticosteroids
<p>Grade 3 Symptoms require and respond to aggressive intervention Oxygen requirement greater than or equal to 40% FiO₂ or hypotension requiring high-dose or multiple vasopressors or Grade 3 organ toxicity or Grade 4 transaminitis</p>	<p>Per Grade 2 If improving, discontinue tocilizumab</p>	<p>Administer methylprednisolone 1 mg/kg intravenously twice daily or equivalent dexamethasone (e.g., 10 mg intravenously every 6 hours) until Grade 1, then taper corticosteroids</p> <p>If improving, manage as Grade 2</p> <p>If not improving, manage as Grade 4</p>
<p>Grade 4 Life-threatening symptoms Requirements for ventilator support, CVVHD, or Grade 4 organ toxicity (excluding transaminitis)</p>	<p>Per Grade 2 If improving, discontinue tocilizumab</p>	<p>Administer methylprednisolone 1000 mg intravenously per day for 3 days</p> <p>If improving, taper corticosteroids, and manage as Grade 3</p> <p>If not improving, consider alternate immunosuppressants</p>

Abbreviation: CVVHD, continuous veno-venous hemodialysis.

*Lee DW, Gardner R, Porter DL, et al. Current concepts in the diagnosis and management of cytokine release syndrome. *Blood*. 2014;124(2):188-195.

†Refer to page 4 on the back for management of neurologic toxicity.

‡Refer to tocilizumab Prescribing Information for details.

Guidance on Managing Neurologic Toxicity

Monitor patients for signs and symptoms of neurologic toxicities. Treatment algorithms have been developed to ameliorate the neurologic toxicities experienced by patients on TECARTUS™.

NEUROLOGIC TOXICITY GRADING AND MANAGEMENT GUIDANCE

Neurologic Event*	Concurrent CRS	No Concurrent CRS
<p>Grade 1 Examples include: Somnolence—mild drowsiness or sleepiness Confusion—mild disorientation Encephalopathy—mild limiting of ADLs Dysphasia—not impairing ability to communicate</p>	<p>Administer tocilizumab per the table on the other side for management of Grade 1 CRS</p>	<p>Supportive care</p>
<p>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)</p>	<p>Administer tocilizumab per the table on the other side for management of Grade 2 CRS</p> <p>If not improving within 24 hours after starting tocilizumab, administer dexamethasone 10 mg intravenously every 6 hours until the event is Grade 1 or less, then taper corticosteroids</p> <p>If improving, discontinue tocilizumab</p> <p>If still not improving, manage as Grade 3</p>	<p>Administer dexamethasone 10 mg intravenously every 6 hours until the event is Grade 1 or less</p> <p>If improving, taper corticosteroids</p>
	<p>Consider non-sedating, antiseizure medicines (eg, levetiracetam) for seizure prophylaxis</p>	

Neurologic Event*	Concurrent CRS	No Concurrent CRS
<p>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</p>	<p>Administer tocilizumab per the table on the other side for management of Grade 2 CRS</p> <p>In addition, administer dexamethasone 10 mg intravenously 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</p> <p>If improving, discontinue tocilizumab and manage as Grade 2</p> <p>If still not improving, manage as Grade 4</p>	<p>Administer dexamethasone 10 mg intravenously every 6 hours</p> <p>Continue dexamethasone use until the event is Grade 1 or less, then taper corticosteroids</p> <p>If not improving, manage as Grade 4</p>
	<p>Consider nonsedating, antiseizure medicines (eg, levetiracetam) for seizure prophylaxis</p>	
<p>Grade 4 Life-threatening consequences Urgent intervention indicated Requirement for mechanical ventilation Consider cerebral edema</p>	<p>Administer tocilizumab per the table on the other side for management of Grade 2 CRS</p> <p>Administer methylprednisolone 1000 mg intravenously per day with first dose of tocilizumab and continue methylprednisolone 1000 mg intravenously per day for 2 more days</p> <p>If improving, then manage as Grade 3</p> <p>If not improving, consider</p>	<p>Administer methylprednisolone 1000 mg intravenously per day for 3 days</p> <p>If improving, then manage as Grade 3</p> <p>If not improving, consider alternate immunosuppressants</p>

Neurologic Event*	Concurrent CRS	No Concurrent CRS
	alternate immunosuppressants	
	Consider nonsedating, antiseizure medicines (eg, levetiracetam) for seizure prophylaxis	

Abbreviation: ADLs, activities of daily living.

*National Institutes of Health, National Cancer Institute.

Common Terminology Criteria for Adverse Events (CTCAE).

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YESCARTA and TECARTUS REMS Program
REMS Program Training Program – Table
Month Year

		Slide Number (new)	Proposed Content (new)
		1	YESCARTA® and TECARTUS™ Risk Evaluation and Mitigation Strategy (REMS) Program Training
		2	The educational module contains information on adverse reactions associated with YESCARTA and TECARTUS, including cytokine release syndrome and neurologic toxicities. These are not all of the adverse reactions associated with YESCARTA and TECARTUS.
		3	<p>Indication - YESCARTA® YESCARTA® is a CD19-directed genetically modified autologous T cell immunotherapy indicated for the treatment of adult patients with relapsed or refractory large B-cell lymphoma 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.</p> <p><u>Limitation of Use:</u> YESCARTA® is not indicated for the treatment of patients with primary central nervous system lymphoma.</p> <p>Please see full Prescribing Information, including BOXED WARNING and Medication Guide.</p>
		4	<p>Indication – TECARTUS™ 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)</p>

		Slide Number (new)	Proposed Content (new)
			Please see full Prescribing Information, including BOXED WARNING and Medication Guide.
		5	YESCARTA and TECARTUS REMS Program Overview
		6	<p>What is the YESCARTA and TECARTUS REMS (Risk Evaluation and Mitigation Strategy) Program?</p> <p>A REMS Program is a strategy to manage known or potential risks associated with a drug and is required by the United States (US) Food and Drug Administration (FDA) to ensure that the benefits of the drug outweigh its risks. YESCARTA and TECARTUS are available only under a program called the YESCARTA and TECARTUS REMS Program because of the serious risks of cytokine release syndrome (CRS) and neurologic toxicities.</p> <p>The goals of the YESCARTA and TECARTUS REMS Program are to mitigate the risks of CRS and neurologic toxicities by:</p> <ul style="list-style-type: none"> • Ensuring that hospitals and their associated clinics that dispense YESCARTA and/or TECARTUS are specially certified and have on-site, immediate access to a minimum of 2 doses of tocilizumab • Ensuring that those relevant individuals who prescribe, dispense, or administer YESCARTA and/or TECARTUS are aware of how to manage the risks of CRS and neurologic toxicities
		7	<p>Hospital Certification</p> <p>To become certified to dispense YESCARTA and/or TECARTUS, hospitals and their associated clinics must:</p> <ol style="list-style-type: none"> 1. Designate an authorized representative to complete the training program by completing and submitting the YESCARTA and TECARTUS REMS Program Hospital Enrollment Form on behalf of the hospital and its associated clinics 2. Ensure that the authorized representative oversees implementation and compliance with the YESCARTA and TECARTUS REMS Program requirements

		Slide Number (new)	Proposed Content (new)
			<p>3. Dispense YESCARTA and/or TECARTUS only after verifying that a minimum of 2 doses of tocilizumab are available on-site for each patient and ready for administration within 2 hours</p> <p>4. Recertify in the YESCARTA and TECARTUS REMS Program if a new authorized representative is designated</p>
		8	<p>Hospital Certification (continued)</p> <p>5. Maintain documentation that all processes and procedures are in place and are being followed for the YESCARTA and TECARTUS REMS Program; provide this documentation upon request to Kite, or a third party acting on behalf of Kite or FDA</p> <p>6. Comply with audits by Kite, or a third party acting on behalf of Kite or FDA, to ensure that all training, processes, and procedures are in place and are being followed for the YESCARTA and TECARTUS REMS Program</p> <p>7. Report any serious adverse events* suggestive of CRS or neurologic toxicities</p> <p>* Serious adverse events are defined as any adverse experience occurring at any dose that results in any of the following outcomes: death, a life-threatening adverse experience, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant disability/incapacity, or a congenital anomaly/birth defect</p>
		9	<p>Who Can Be an Authorized Representative?</p> <p>An authorized representative at the hospital and its associated clinics can be a:</p> <ul style="list-style-type: none"> • Physician • Nurse • Any responsible individual assigned by the hospital and its associated clinics <p>One representative (the “authorized representative”) must enroll for each hospital and its associated clinics and attest to the enrollment requirements as stated on the YESCARTA and TECARTUS REMS Program Hospital Enrollment Form.</p>

		Slide Number (new)	Proposed Content (new)
		10	<p>YESCARTA and TECARTUS REMS Authorized Representative Attestations</p> <ul style="list-style-type: none"> • Complete the YESCARTA and TECARTUS REMS Program Training and successfully complete the YESCARTA and TECARTUS REMS Program Knowledge Assessment • Submit the completed YESCARTA and TECARTUS REMS Program Hospital Enrollment Form to Kite via fax at 1-310-496-0397 or email to YTREMS@kitepharma.com • Submit the YESCARTA and TECARTUS REMS Program Knowledge Assessment to Kite via fax at 1-310-496-0397 or email to YTREMS@kitepharma.com • Oversee implementation and compliance with the YESCARTA and TECARTUS REMS Program
		11	<p>YESCARTA and TECARTUS REMS Authorized Representative Attestations (continued)</p> <ul style="list-style-type: none"> • Ensure that the hospital and its associated clinics will establish processes and procedures that are subject to monitoring by Kite or a third party acting on behalf of Kite to help ensure compliance with the requirements of the YESCARTA and TECARTUS REMS Program, including the following, before administering YESCARTA and/or TECARTUS: <ul style="list-style-type: none"> - Ensure that all relevant staff involved in the prescribing, dispensing, or administering of YESCARTA and/or TECARTUS are trained on the REMS Program requirements as described in the training materials, successfully complete the YESCARTA and TECARTUS REMS Program Knowledge Assessment, and maintain training records for all staff

		Slide Number (new)	Proposed Content (new)
			<ul style="list-style-type: none"> ▪ The Authorized Representative will determine relevant staff who require training - Put processes and procedures in place to ensure that staff involved in the prescribing, dispensing, or administering of YESCARTA and/or TECARTUS are retrained if YESCARTA or TECARTUS has not been dispensed at least once annually from the date of certification in the YESCARTA and TECARTUS REMS Program - Prior to dispensing YESCARTA and/or TECARTUS, put processes and procedures in place to verify a minimum of 2 doses of tocilizumab are available on-site for each patient and are ready for immediate administration (within 2 hours) - Prior to patient discharge, provide patients/caregivers with the Patient Wallet Card
		12	Serious Risks of YESCARTA and TECARTUS
		13	<p>Serious Risks Associated With YESCARTA BOXED WARNING: CYTOKINE RELEASE SYNDROME and NEUROLOGIC TOXICITIES</p> <ul style="list-style-type: none"> • Cytokine Release Syndrome (CRS), including fatal or life-threatening reactions, occurred in patients receiving YESCARTA. Do not administer YESCARTA to patients with active infection or inflammatory disorders. Treat severe or life-threatening CRS with tocilizumab or tocilizumab and corticosteroids • Neurologic toxicities, including fatal or life-threatening reactions, occurred in patients receiving YESCARTA, including concurrently with CRS or after CRS resolution. Monitor for neurologic toxicities after treatment with

		Slide Number (new)	Proposed Content (new)
			YESCARTA. Provide supportive care and/or corticosteroids as needed
		14	<p>Serious Risks Associated With TECARTUS BOXED WARNING: CYTOKINE RELEASE SYNDROME and NEUROLOGIC TOXICITIES</p> <ul style="list-style-type: none"> • 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
		15	Management of CRS
		16	<p>Cytokine Release Syndrome - YESCARTA</p> <ul style="list-style-type: none"> • CRS, including fatal or life-threatening reactions, occurred following treatment with YESCARTA • In a Kite clinical trial, CRS occurred in 94% (101/108) of patients receiving YESCARTA, including Grade 3 or higher CRS in 13% (14/108) of patients • The median time to onset was 2 days (range, 1-12 days) • The median duration of CRS was 7 days (range, 2-58 days) • 45% (49/108) of patients received tocilizumab after infusion of YESCARTA • Among patients who died after receiving YESCARTA®, 4 had ongoing CRS events at the time of death

		Slide Number (new)	Proposed Content (new)
		17	<p>Cytokine Release Syndrome – TECARTUS</p> <ul style="list-style-type: none"> • CRS, including life-threatening reactions, occurred following treatment with TECARTUS • In a Kite clinical trial, CRS occurred in 91% (75/82) of patients receiving TECARTUS, including Grade 3 or higher CRS in 18% of patients • The median time to onset was 3 days (range, 1-13 days) • The median duration of CRS was 10 days (range, 1-50 days)
		18	<p>Patient Assessment of CRS Associated with YESCARTA</p> <p>The following are signs and symptoms of CRS with YESCARTA</p> <ul style="list-style-type: none"> Capillary leak syndrome Cardiac arrest Cardiac arrhythmias Cardiac failure Chills Fever Hemophagocytic lymphohistiocytosis/macrophage activation syndrome (HLH/MAS) Hypotension Hypoxia Renal insufficiency Tachycardia

		Slide Number (new)	Proposed Content (new)
		19	<p>Patient Assessment of CRS Associated with TECARTUS</p> <p>The following are signs and symptoms of CRS with TECARTUS</p> <ul style="list-style-type: none"> Alanine aminotransferase increase Aspartate aminotransferase increased Acute kidney injury Chills Diarrhea Fatigue Fever Headache Hypotension Hypoxia Nausea Tachycardia

		Slide Number (new)	Proposed Content (new)
		20	<p>Guidance on Managing CRS for YESCARTA</p> <ul style="list-style-type: none"> • Identify CRS based on clinical presentation • Evaluate for and treat other causes of fever, hypoxia, and hypotension • If CRS is suspected, manage according to the recommendations on slide 21 • Tocilizumab, an interleukin-6 receptor antagonist, is recommended for the management of Grade 2 or higher CRS associated with YESCARTA • Patients who experience Grade 2 or higher CRS (eg, hypotension, not responsive to fluids, or hypoxia requiring supplemental oxygenation) should be monitored with continuous cardiac telemetry and pulse oximetry • For patients experiencing severe CRS, consider performing an echocardiogram to assess cardiac function • For severe or life-threatening CRS, consider intensive care supportive therapy • Monitor patients at least daily for 7 days at the certified hospitals and their associated clinics following infusion for signs and symptoms of CRS • Monitor patients for signs or symptoms of CRS for 4 weeks after infusion
New	New Slide for Guidance on Managing CRS - YESCARTA	21	<p>Guidance on Management of CRS for YESCARTA</p> <p>Grading and Management of YESCARTA-Related CRS</p> <p>[Guidance and Management Table per the YESCARTA and TECARTUS Adverse Reaction Management Guide]</p>

		Slide Number (new)	Proposed Content (new)
	New slide for Guidance on Management of CRS - TECARTUS	22	<p>Guidance on Managing CRS for TECARTUS</p> <ul style="list-style-type: none"> • Identify CRS based on clinical presentation • Evaluate for and treat other causes of fever, hypoxia, and hypotension • If CRS is suspected, manage according to the recommendations on slide 23 • Tocilizumab, an interleukin-6 receptor antagonist, is recommended for the management of Grade 1 or higher CRS associated with TECARTUS • Patients who experience Grade 2 or higher CRS (eg, hypotension, not responsive to fluids, or hypoxia requiring supplemental oxygenation) should be monitored with continuous cardiac telemetry and pulse oximetry • For patients experiencing severe CRS, consider performing an echocardiogram to assess cardiac function • For severe or life-threatening CRS, consider intensive care supportive therapy • Monitor patients at least daily for 7 days at the certified hospitals and their associated clinics following infusion for signs and symptoms of CRS • Monitor patients for signs or symptoms of CRS for 4 weeks after infusion
		23	<p>Guidance on Management of CRS for TECARTUS</p> <p>Grading and Management of TECARTUS-Related CRS</p> <p>[Guidance and Management Table per the YESCARTA and TECARTUS Adverse Reaction Management Guide]</p>

		Slide Number (new)	Proposed Content (new)
		24	Management of Neurologic Toxicities
		25	<p>Neurologic Toxicities - YESCARTA</p> <ul style="list-style-type: none"> • Neurologic toxicities, that were fatal or life-threatening, occurred following treatment with YESCARTA • Neurologic toxicities occurred in 87% of patients, including Grade 3 or higher neurologic toxicities in 31% of patients • 98% of all neurologic toxicities occurred within the first 8 weeks of YESCARTA infusion • The median time to onset was 4 days (range, 1-43 days) following YESCARTA infusion • The median duration was 17 days • Prolonged encephalopathy lasting up to 173 days was noted • Serious events including leukoencephalopathy and seizures occurred with YESCARTA • Fatal and serious cases of cerebral edema have occurred in patients treated with YESCARTA
		26	<p>Neurologic Toxicities - TECARTUS</p> <ul style="list-style-type: none"> • Neurologic events, including those that were life-threatening, occurred following treatment with TECARTUS • Neurologic events occurred in 81% of patients, 37% of whom experienced Grade 3 or higher (severe or life threatening) adverse reactions • 85% of all treated patients experienced the first CRS or neurological event within the first 7 days after TECARTUS infusion • The median time to onset was 6 days (range, 1-32 days) following TECARTUS infusion • The median duration was 21 days (range, 2-454 days) • Serious events including encephalopathy, aphasia, and seizures occurred with TECARTUS
		27	<p>Patient Assessment of Neurologic Toxicities Associated With YESCARTA</p> <p>The following are common signs and symptoms of neurologic toxicities</p>

		Slide Number (new)	Proposed Content (new)
			Anxiety Aphasia Delirium Dizziness Encephalopathy Headache Insomnia Tremor
		28	<p>Patient Assessment of Neurologic Toxicities Associated With TECARTUS</p> <p>The following are common signs and symptoms of neurologic toxicities</p> Aphasia Delirium Encephalopathy Headache Tremor
		29	<p>Guidance on Managing Neurologic Toxicities for YESCARTA and TECARTUS</p> <ul style="list-style-type: none"> • Monitor patients for signs and symptoms of neurologic toxicities • Rule out other causes of neurologic symptoms • Patients who experience Grade 2 or higher neurologic toxicities should be monitored with continuous cardiac telemetry and pulse oximetry • Provide intensive care supportive therapy for severe or life-threatening neurologic toxicities • Consider non-sedating, antiseizure medicines (eg, levetiracetam) for seizure prophylaxis for any Grade 2 or higher neurologic toxicities • Monitor patients at least daily for 7 days at the certified hospitals and their associated clinics 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
		30	<p>Guidance on Managing Neurologic Toxicities for YESCARTA</p>

		Slide Number (new)	Proposed Content (new)
			Grading and Management of YESCARTA-Related Neurologic Toxicities [Grading and Management Table – per the YESCARTA and TECARTUS Adverse Reaction Management Guide for Grade 1 and Grade 2]
		31	Guidance on Managing Neurologic Toxicities for YESCARTA Grading and Management of YESCARTA-Related Neurologic Toxicities (continued) [Grading and Management Table – per the YESCARTA and TECARTUS Adverse Reaction Management Guide for Grade 3 and Grade 4]
New	New slide for Guidance on Management of Neurologic Toxicities - TECARTUS	32	Guidance on Managing Neurologic Toxicities for TECARTUS Grading and Management of TECARTUS-Related Neurologic Toxicities [Grading and Management Table – per the YESCARTA and TECARTUS Adverse Reaction Management Guide for Grade 1 and Grade 2]
New	New Slide for Guidance on Management of Neurologic Toxicities - TECARTUS	33	Guidance on Managing Neurologic Toxicities for TECARTUS Grading and Management of TECARTUS-Related Neurologic Toxicities (continued) [Grading and Management Table – per the YESCARTA and TECARTUS Adverse Reaction Management Guide for Grade 3 and Grade 4]
New	New Slide for Adverse Event Reporting	34	Adverse Event Reporting

		Slide Number (new)	Proposed Content (new)
		35	<p>Adverse Event Reporting</p> <p>Reporting suspected adverse events after administration of therapy is important. It allows continued monitoring of the risk/benefit balance of therapy.</p> <p>Hospitals and its associated clinics must report any serious adverse event* suggestive of CRS or neurologic toxicities to Kite at 1-844-454-KITE (5483) or medinfo@kitepharma.com or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch. Healthcare providers are also encouraged to report any suspected serious adverse events* associated with YESCARTA or TECARTUS as outlined above.</p> <p>* Serious adverse events are defined as any adverse experience occurring at any dose that results in any of the following outcomes: death, a life-threatening adverse experience, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant disability/incapacity, or a congenital anomaly/birth defect</p>
		36	<p>Patient Counseling</p>
		37	<p>Patient Counseling</p> <ul style="list-style-type: none"> • Talk to the patient about the risk of CRS and neurologic toxicities. Tell them to contact their healthcare provider and/or seek immediate care if experiencing the signs and symptoms associated with CRS and neurologic toxicities: <ul style="list-style-type: none"> - Fever (100.4F/38C or higher) - Difficulty breathing - Chills or shaking chills - Confusion - Dizziness or lightheadedness - Severe nausea, vomiting, or diarrhea - Fast or irregular heartbeat - Severe fatigue or weakness • Provide the YESCARTA and TECARTUS REMS Patient Wallet Card to the patient or the patient’s caregiver. Tell the patient to carry the Patient Wallet Card at all times and to share the Patient Wallet Card with

		Slide Number (new)	Proposed Content (new)
			<p>any healthcare provider involved in the patient's treatment.</p> <ul style="list-style-type: none"> • Advise patients to refrain from driving or operating heavy or potentially dangerous machinery until at least 8 weeks after YESCARTA or TECARTUS infusion • Instruct patient to remain within close proximity (within 2 hours) of the certified administering hospital and its associated clinics for at least 4 weeks following YESCARTA or TECARTUS infusion.
		38	<p>YESCARTA and TECARTUS REMS Program Resources</p>
		39	<p>YESCARTA and TECARTUS REMS Program Kit</p> <p>Includes:</p> <ul style="list-style-type: none"> • YESCARTA full Prescribing Information and Medication Guide • TECARTUS full Prescribing Information and Medication Guide • YESCARTA and TECARTUS REMS Program Training • YESCARTA and TECARTUS REMS Program Knowledge Assessment • YESCARTA and TECARTUS REMS Program Hospital Enrollment Form • YESCARTA and TECARTUS Adverse Reaction Management Guide • YESCARTA and TECARTUS Patient Wallet Card
		40	<p>Additional YESCARTA and TECARTUS REMS Program Information and Resources</p> <p>To enroll in the YESCARTA and TECARTUS REMS Program or obtain information regarding enrollment in the program, call 1-844-454-KITE or visit the YESCARTA and TECARTUS REMS Program website at www.YescartaTecartusREMS.com. The REMS Program website contains the most current version of REMS-related materials.</p> <p>YESCARTA, the YESCARTA Logo, TECARTUS, the TECARTUS Logo, KITE, and the KITE Logo are</p>

		Slide Number (new)	Proposed Content (new)
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REMS-CTF-0002 MM/YYYY

YESCARTA and TECARTUS REMS Program Knowledge Assessment

To become an authorized representative for your hospital and its associated clinics in the YESCARTA and TECARTUS REMS Program, you will need to answer all questions below correctly. All other REMS trained staff must also answer all questions correctly.

Responses to the YESCARTA and TECARTUS REMS Program Knowledge Assessment questions and the YESCARTA and TECARTUS REMS Hospital Enrollment Form must be emailed to

YTREMS@kitepharma.com or
faxed to **1-310-496-0397**.

Questions

1. Prior to discharge, a YESCARTA and TECARTUS REMS Patient Wallet Card must be given to patients who have been infused with YESCARTA or TECARTUS.

True_____ False _____

2. Every certified hospital and its associated clinics are required to have immediate access to a minimum of 2 doses of tocilizumab on-site for each patient and available for administration, for treatment of cytokine release syndrome (CRS), within 2 hours of YESCARTA or TECARTUS infusion.

True_____ False _____

3. After YESCARTA or TECARTUS infusion, patients should be advised to:

- A. Refrain from driving or operating heavy or potentially dangerous machinery for at least 8 weeks after YESCARTA or TECARTUS infusion
- B. Remain within close proximity (within 2 hours) of the certified treating hospital and its associated clinics for at least 4 weeks following infusion
- C. Seek immediate attention if they experience signs and symptoms of CRS and/or neurological toxicities
- D. All of the above

4. Which of the following is true regarding the time to onset of CRS following YESCARTA infusion? It typically occurs:

- A. With a median time to onset of 7 days
- B. With a median time to onset of 5 days
- C. With a median time to onset of 2 days
- D. Rarely starts during the first week

5. Which of the following is true regarding the time to onset of CRS following TECARTUS infusion? It typically occurs:

- A. With a median time to onset of 3 days
- B. With a median time to onset of 5 days
- C. With a median time to onset of 10 days
- D. Rarely starts during the first week

6. All of the following regarding neurologic toxicity related to YESCARTA or TECARTUS are correct **except**:

- A. Neurologic toxicity always occurs concurrently with CRS
- B. Continuous cardiac telemetry and pulse oximetry are recommended for Grade 2 or higher neurologic toxicity
- C. The median time to onset of neurologic toxicity is 4 days (YESCARTA) or 6 days (TECARTUS)
- D. The most common signs or symptoms of neurologic toxicity include encephalopathy, headache, tremor, dizziness, aphasia, delirium, insomnia, and anxiety

7. Four days after infusion with YESCARTA, a 49-year-old woman with relapsed diffuse large B-cell lymphoma (DLBCL) fully recovers from a Grade 3 CRS that started the day after infusion of YESCARTA. The next day, she develops a Grade 2 dysphasia. She has no signs or symptoms of CRS. Appropriate management for this patient would include (please select single best answer):

- A. Consider nonsedating, antiseizure medicines (eg, levetiracetam) for seizure prophylaxis
- B. Start tocilizumab 8 mg/kg intravenously over 1 hour (not to exceed 800 mg)
- C. Start dexamethasone 10 mg intravenously every 6 hours
- D. A and C

8. One day after infusion of TECARTUS, a 60-year-old man with mantle cell lymphoma (MCL) develops the following signs and symptoms of CRS: high fever (39-40°C), hypoxia requiring <40% FiO₂, and hypotension requiring intravenous fluids. This patient's CRS grade would be most consistent with:

- A. Grade 1 CRS
- B. Grade 2 CRS
- C. Grade 3 CRS
- D. Grade 4 CRS

Please Complete All Fields Below

Name Title

Credentials _____ DO _____ MD _____ RPh _____ RN/NP _____ PA Other _____

Hospital/Associated Clinic Name

Address

City State ZIP Code

Signature Date

Patient Information

YESCARTA® and TECARTUS™ can cause side effects that can lead to death.

Call or see your oncologist or get emergency help **RIGHT AWAY** if you have any of **these symptoms**:

- Fever (100.4°F/38°C or higher)
- Difficulty breathing
- Chills or shaking chills
- Confusion
- Dizziness or lightheadedness
- Severe nausea, vomiting, or diarrhea
- Fast or irregular heartbeat
- Severe fatigue or weakness

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Important Information for Healthcare Providers

Name of treating oncologist: _____

Office phone: _____

After-hours phone: _____

Kite CAR T product administered:
 YESCARTA® TECARTUS™

Date of Kite CAR T infusion: _____

- This patient has received a CD19-

Patient Wallet Card

Carry this card with you at all times. SHOW THIS CARD if you go to the emergency room or see any physician.

Tell any healthcare provider that sees you that you are being treated with YESCARTA® or TECARTUS™.

Stay within close proximity (within 2 hours) of the location where you received your treatment for at least 4 weeks after getting YESCARTA® or TECARTUS™.

directed genetically modified autologous T-cell immunotherapy (CAR T).

- CAR T therapy can cause cytokine release syndrome (CRS) and neurologic toxicities, which may be fatal or life threatening. CRS may involve any organ system



- Contact the patient's oncologist immediately for further information

YESCARTA Full Prescribing Information and Medication Guide
TECARTUS Full Prescribing Information and Medication Guide

Risk Evaluation and Mitigation Strategy (REMS)

This website is intended for US healthcare professionals only.

What Is the YESCARTA and TECARTUS REMS Program?

A REMS is a program required by the United States (US) Food and Drug Administration (FDA). The FDA has determined that a REMS is necessary to ensure that the benefits of YESCARTA and TECARTUS outweigh the risks of cytokine release syndrome and neurologic toxicities. YESCARTA and TECARTUS are available only through the YESCARTA and TECARTUS REMS Program.

YESCARTA Prescribing Information and Medication Guide
TECARTUS Prescribing Information and Medication Guide

Boxed Warning for YESCARTA

Cytokine Release Syndrome

- Cytokine release syndrome (CRS), including fatal or life-threatening reactions, occurred following treatment with YESCARTA
- CRS occurred in 94% (101/108) of patients receiving YESCARTA including Grade 3 or higher CRS in 13% (114/108) of patients
- Among patients who died after receiving YESCARTA, 4 had ongoing CRS events at the time of death
- The median time to onset was 2 days (range: 1-12 days), and the median duration of CRS was 7 days (range: 2-58 days)
- Key manifestations of CRS include fever (78%), hypotension (41%), tachycardia (28%), hypoxia (22%), and chills (20%)
- Serious events that may be associated with CRS include cardiac arrhythmias (including atrial fibrillation and ventricular tachycardia), cardiac arrest, cardiac failure, renal

insufficiency, capillary leak syndrome, hypotension, hypoxia, and hemophagocytic lymphohistiocytosis/macrophage activation syndrome (HLH/MAS)

Neurologic Toxicities

- Neurologic toxicities, that were fatal or life-threatening, occurred following treatment with YESCARTA
- The median time to onset was 4 days (range: 1-43 days) following YESCARTA infusion
- Neurologic toxicities occurred in 87% of patients with a median duration of 17 days
- 98% of all neurologic toxicities occurred within the first 8 weeks of YESCARTA infusion
- Grade 3 or higher neurologic toxicities occurred in 31% of patients
- The most common neurologic toxicities included encephalopathy (57%), headache (44%), tremor (31%), dizziness (21%), aphasia (18%), delirium (17%), insomnia (9%), and anxiety (9%)
- Prolonged encephalopathy lasting up to 173 days was noted
- Serious events including leukoencephalopathy and seizures occurred with YESCARTA
- Fatal and serious cases of cerebral edema have occurred in patients treated with YESCARTA

Boxed Warning for TECARTUS

Cytokine Release Syndrome

- Cytokine release syndrome (CRS), including life-threatening reactions, occurred following treatment with TECARTUS
- CRS occurred in 91% (75/82) of patients receiving TECARTUS including Grade 3 or higher CRS in 18% of patients
- The median time to onset was 3 days (range: 1-13 days), and the median duration of CRS was 10 days (range: 1-50 days)
- Key manifestations of CRS 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

Neurologic Toxicities

- Neurologic events, including those that were life-threatening, occurred following treatment with TECARTUS
- The median time to onset was 6 days (range: 1-32 days) following TECARTUS infusion
- Neurologic events occurred in 81% of patients, 37% of whom experienced Grade 3 or higher (severe or life threatening) adverse reactions
- Neurologic events resolved for 52 out of 66 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
- Eighty-five percent of all treated patients experienced the first CRS or neurological event within the first 7 days after TECARTUS infusion
- The most common neurologic toxicities included encephalopathy (51%), headache (35%), tremor (38%), aphasia (23%), and delirium (16%)
- Serious events including encephalopathy, aphasia, and seizures occurred after treatment with TECARTUS

YESCARTA and TECARTUS REMS Program Requirements

Hospitals and their associated clinics must be enrolled in the YESCARTA and TECARTUS REMS Program to be able to dispense YESCARTA and/or TECARTUS.

All relevant staff involved in the prescribing, dispensing, or administering of YESCARTA and/or TECARTUS are trained on the YESCARTA and TECARTUS REMS Program requirements, and must successfully complete a YESCARTA and TECARTUS REMS Program Knowledge Assessment.

Hospital Enrollment Instructions

An authorized representative must enroll in the YESCARTA and TECARTUS REMS Program on behalf of the hospital and its associated clinics. To be enrolled in the YESCARTA and TECARTUS REMS Program, the representative must:

1. Complete the training program, which includes review of:
 - YESCARTA and TECARTUS full Prescribing Information
 - YESCARTA and TECARTUS REMS Program Training
 - YESCARTA and TECARTUS Adverse Reaction Management Guide
2. Successfully complete the YESCARTA and TECARTUS REMS Program Knowledge Assessment.
3. Complete the YESCARTA and TECARTUS REMS Program Hospital Enrollment Form.
4. Oversee implementation and compliance with the YESCARTA and TECARTUS REMS Program requirements:
 - Ensure that all relevant staff involved in the prescribing, dispensing, or administering of YESCARTA and/or TECARTUS are trained on the REMS Program requirements and successfully complete the YESCARTA and TECARTUS REMS Program Knowledge Assessment. The authorized representative will determine relevant staff who require training
 - Maintain training records of staff
 - Ensure that the hospital and its associated clinics have a minimum of 2 doses of tocilizumab available on-site for each patient and are ready for immediate administration (within 2 hours)
 - Prior to patient discharge, provide patients/caregivers with the Patient Wallet Card and instruct patient to remain within close proximity (within 2 hours) of the certified administering hospital and its associated clinics for at least 4 weeks following YESCARTA or TECARTUS infusion
 - Put processes and procedures in place to ensure that relevant new staff are trained, and relevant staff are retrained if YESCARTA or TECARTUS has not been dispensed at least once annually from the date of certification in the YESCARTA and TECARTUS REMS Program

Indication

YESCARTA is a CD19-directed genetically modified autologous T cell immunotherapy indicated for the treatment of adult patients with relapsed or refractory large B-cell lymphoma 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.

Limitation of Use: YESCARTA is not indicated for the treatment of patients with primary central nervous system lymphoma.

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).

Where to Find YESCARTA and TECARTUS REMS Program Information and Resources

For more information about the YESCARTA and TECARTUS REMS Program, see the Program Resources or call 1-844-454-KITE (5483).

Reporting Adverse Reactions

You are encouraged to report suspected serious adverse events associated with YESCARTA or TECARTUS by contacting Kite at 1-844-454-KITE or medinfo@kitepharma.com or the FDA at www.fda.gov/medwatch or 1-800-FDA-1088.

Need Help?

If you have questions about the YESCARTA and TECARTUS REMS Program or need help registering, call 1-844-454-KITE.

LEFT HAND CORNER:

Resources for Healthcare Professionals

Download All Resources

YESCARTA and TECARTUS REMS Program Knowledge Assessment

YESCARTA and TECARTUS REMS Program Training

YESCARTA and TECARTUS REMS Program Hospital Enrollment Form

YESCARTA and TECARTUS Adverse Reaction Management Guide

YESCARTA and TECARTUS REMS Training

Log in to the YESCARTA and TECARTUS REMS Gilead Learning Management System here:

<https://gsir.gilead.com>

[When the end user clicks on this hyperlink, an intermediary page loads which states: Contact your institution's Authorized Representative for REMS Training. You are now leaving www.YescartaTecartusREMS.com. Select CANCEL to return or OK to continue.]

Resources for Patients

All patients treated with YESCARTA or TECARTUS receive a Patient Wallet Card listing adverse reactions and other information. Patients should carry the card with them at all times and show it to any healthcare professional who treats them, including in the emergency room.

YESCARTA and TECARTUS REMS Patient Wallet Card

Adobe Reader is required to view PDFs. If you do not have it installed, download it here.

[Terms and Conditions](#) [Privacy Policy](#)

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