RISK EVALUATION AND MITIGATION STRATEGY (REMS) DOCUMENT

YESCARTA (Axicabtagene Ciloleucel) REMS Program

I. Administrative Information

Application Number: BLA 125643
Application Holder: Kite Pharma, Inc.
Initial REMS Approval: 10/2017
Most Recent REMS Update: 11/2019

II. REMS Goal

The goals of the YESCARTA 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 are specially certified and have on-site, immediate access to tocilizumab.

2. Ensuring those who prescribe, dispense, or administer YESCARTA 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 must:**

<table>
<thead>
<tr>
<th>To become certified to dispense</th>
<th>1. Have a minimum of two doses of tocilizumab available on-site for each patient for immediate administration (within 2 hours).</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>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.</td>
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<td>3. Have the authorized representative enroll in the REMS by completing the <a href="#">Hospital Enrollment Form</a> and submitting it to the REMS Program.</td>
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<td>4. Have the authorized representative complete the <a href="#">Live Training</a>.</td>
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<td></td>
<td>5. Have the authorized representative successfully complete a <a href="#">Knowledge Assessment</a> and submit it to the REMS Program.</td>
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<td>6. Train all relevant staff involved in prescribing, dispensing, or administering of YESCARTA on the REMS Program requirements using the <a href="#">Live Training</a> and <a href="#">Adverse Reaction Management Guide</a>.</td>
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<tr>
<td></td>
<td>7. Have all relevant staff involved in prescribing, dispensing, or administering of YESCARTA successfully complete the <a href="#">Knowledge Assessment</a>.</td>
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<tr>
<td></td>
<td>8. Establish processes and procedures to ensure relevant new staff involved in prescribing, dispensing, or administering of YESCARTA are trained and complete the <a href="#">Knowledge Assessment</a>.</td>
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<td></td>
<td>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).</td>
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<tr>
<td></td>
<td>10. Establish processes and procedures to provide patients with the <a href="#">Patient Wallet Card</a>.</td>
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<thead>
<tr>
<th>Before infusion</th>
<th>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.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before discharge</td>
<td>12. Provide the patient with the <a href="#">Patient Wallet Card</a> through the processes and procedures established as a requirement of the REMS Program.</td>
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</tbody>
</table>
1. Hospitals and their associated clinics that dispense YESCARTA must:

<table>
<thead>
<tr>
<th>To maintain certification to dispense</th>
<th>13. Have the new authorized representative enroll in the REMS Program by completing the Hospital Enrollment Form.</th>
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</thead>
</table>
| To maintain certification to dispense, if YESCARTA 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 of YESCARTA on the REMS Program requirements using the Live Training.  
15. Have all relevant staff involved in prescribing, dispensing, or administering of YESCARTA successfully complete the Knowledge Assessment. |
| At all times | 16. Report any serious adverse events 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:

| Before discharge | 1. Receive the Patient Wallet Card. |

Kite Pharma, Inc. must provide training to relevant staff who prescribe, dispense, or administer Yescarta.

The training includes the following educational material: Live Training. The Training must be provided in-person or live webcast.

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

1. Ensure that YESCARTA is distributed only to certified hospitals and their associated clinics.
2. Establish and maintain a REMS Program Website (www.YESCARTArem.com). The REMS Program Website must include the option to print the Prescribing Information, Medication Guide, 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.
5. Establish and maintain a validated, secure database of hospitals and their associated clinics that are certified to administer Yescarta in the YESCARTA 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 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 after the hospital places its first order for YESCARTA to ensure that all processes and procedures are in place and functioning to support the requirements of the YESCARTA 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 REMS Program based on the monitoring and evaluation of the YESCARTA 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 REMS (10/18/2017). 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 REMS:

**Enrollment Forms**

Prescriber:

1. Hospital Enrollment Form

**Training and Educational Materials**

Patient:

2. Patient Wallet Card

Healthcare Setting:

3. Live Training
4. Knowledge Assessment
5. Adverse Reaction Management Guide

**Other Materials**

6. REMS Program website