Risk Evaluation and Mitigation Strategy (REMS) Document
CARVYKTI™ (ciltaclabtagene autoleucel) REMS Program

I. Administrative Information
Application Number: BLA 125746
Application Holder: Janssen Biotech, Inc.
Initial REMS Approval: 02/2022

II. REMS Goals
The goals of the CARVYKTI 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 CARVYKTI are specially certified and have on-site, immediate access to tocilizumab.
2. Ensuring that those who prescribe, dispense, or administer CARVYKTI are aware of how to manage the risks of CRS and neurological toxicities.

III. REMS Requirements
Janssen Biotech, Inc. must ensure that hospitals and their associated clinics, and patients comply with the following requirements:

1. Hospitals and their associated clinics that dispense CARVYKTI must:

   a. To become certified to dispense

   b. Have a minimum two doses of tocilizumab available on-site for each patient for immediate administration (within 2 hours).

   c. Designate an Authorized Representative to carry out the certification process and oversee implementation and compliance with the REMS Program requirements on behalf of the hospital and associated clinic(s).

   d. Have the authorized representative complete the Training Program and Adverse Reaction Management Guide provided by the REMS Program.

   e. Have the Authorized Representative successfully complete the Knowledge Assessment and submit it to the REMS Program.

   f. Have the Authorized Representative enroll in the REMS Program by completing the Hospital Enrollment Form and submitting it to the REMS Program.

   g. Train all relevant staff involved in prescribing, dispensing, or administering of CARVYKTI on the REMS Program requirements using the Training Program and the Adverse Reaction Management Guide.

   h. Have all relevant staff involved in prescribing, dispensing, or administering of CARVYKTI successfully complete the Knowledge Assessment and submit it to the REMS Program.
8. Establish processes and procedures to ensure relevant new staff involved in the prescribing, dispensing, or administration of CARVYKTI are trained and complete the Knowledge Assessment and submit it to the REMS Program.

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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<thead>
<tr>
<th>Step</th>
<th>Details</th>
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<tbody>
<tr>
<td>Before infusion</td>
<td>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.</td>
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<td>Before discharge</td>
<td>12. Provide the patient with the Patient Wallet Card through the processes and procedures established as a requirement of the REMS Program.</td>
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<td>To maintain certification to dispense if there is a change in the authorized representative</td>
<td>13. Have a new Authorized Representative enroll in the REMS Program by completing the Hospital Enrollment Form.</td>
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<td>To maintain certification to dispense, if CARVYKTI has not been infused at least once annually from the date of certification in the REMS Program</td>
<td>14. Train all relevant staff involved in prescribing, dispensing, or administering CARVYKTI on the REMS Program requirements using the Training Program and the Adverse Reaction Management Guide.</td>
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<td>15. Have all relevant staff involved in prescribing, dispensing, or administering CARVYKTI successfully complete the Knowledge Assessment.</td>
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<td>At all times</td>
<td>16. Report any serious' adverse events suggestive of CRS or neurological toxicities to the REMS Program.</td>
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<td>17. Maintain records of staff training.</td>
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<td>18. Maintain records that processes and procedures are in place and are being followed.</td>
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<td>19. Comply with audits carried out by Janssen Biotech, Inc. or a third party acting on behalf of Janssen Biotech, Inc. to ensure that all training, processes, and procedures are in place and are being followed.</td>
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2. Patients who are prescribed CARVYKTI:

Before discharge 1. Receive the Patient Wallet Card.

Janssen Biotech, Inc. must provide training to relevant staff who prescribe, dispense, or administer CARVYKTI.

The training includes the following educational materials: Training Program, Adverse Reaction Management Guide, and Knowledge Assessment. The training must be provided in-person, via live webcast, or online.

To support REMS Program operations, Janssen Biotech, Inc. must:

1. Ensure CARVYKTI is distributed only to certified hospitals or their associated clinics.
2. Establish and maintain the REMS Program Website, www.CARVYKTIREMS.com. The REMS Program Website must include the capability to enroll, complete training online, maintain records of that training, and option to print the Prescribing Information (PI), Medication Guide, and REMS materials. All 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 website and the REMS Program Coordinating Center.
4. Establish and maintain a REMS Program Coordinating Center for REMS participants at 1-844-672-0067.
5. Establish and maintain a validated, secure database of all REMS participants who are enrolled and/or have been certified in the REMS Program.
6. Ensure hospitals and their associated clinics are able to enroll in the REMS Program online, through fax and by e-mail.
7. Notify hospitals and their associated clinics within 7 calendar days after they become certified in the REMS Program.

To ensure REMS participants’ compliance with the REMS Program, Janssen Biotech, Inc. must:

8. Verify annually that the designated authorized representative for certified hospitals and their associated clinics 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: CARVYKTI 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 are being met. Take corrective action if non-compliance is identified, including de-certification.
11. Maintain an ongoing annual audit plan of hospitals and their associated clinics.
12. Audit all certified hospitals and their associated clinics no later than 180 calendar days after the hospital places its first order of CARVYKTI to ensure that all REMS processes and procedures are in place, functioning, and support the REMS Program requirements. Certified hospitals and their associated clinics must also be included in Janssen Biotech, Inc.’s ongoing annual audit plan.
13. Take reasonable steps to improve implementation of and compliance with the requirements in the CARVYKTI REMS Program based on monitoring and evaluation of the CARVYKTI REMS Program.

IV. REMS Assessment Timetable

Janssen Biotech, 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 (02/2022). 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 calendar days before the submission date for that assessment. Janssen Biotech, 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 CARVYKTI REMS:

**Enrollment Forms**

Healthcare Facility:

1. Hospital Enrollment Form

**Training and Educational Materials**

Patient:

2. Patient Wallet Card

Healthcare setting:

3. Training Program

4. Adverse Reaction Management Guide

5. Knowledge Assessment

**Other Materials**

6. REMS Program Website

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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.