

RISK EVALUATION AND MITIGATION STRATEGY (REMS) DOCUMENT

BREYANZI® (LISOCABTAGENE MARALEUCEL) REMS PROGRAM

I. ADMINISTRATIVE INFORMATION

Application Number: BLA 125714

Application Holder: Juno Therapeutics, Inc., a Bristol-Myers Squibb Company

Initial REMS Approval: XX/2020

II. REMS GOALS

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

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

III. REMS REQUIREMENTS

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

1. Hospitals and their associated clinics that dispense BREYANZI 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 carry out the certification process and oversee implementation and compliance with the REMS Program requirements on behalf of the hospital and associated clinic(s).
 3. Have the authorized representative complete the [Live Training Program](#) provided by the REMS Program
 4. Have the authorized representative successfully complete the [Knowledge Assessment](#) and submit it to the REMS Program.
 5. Have the authorized representative enroll in the REMS Program by completing the [Hospital Enrollment Form](#) and submitting it to the REMS Program.
 6. Train all relevant staff involved in prescribing, dispensing, or administering of BREYANZI on the REMS Program requirements using the [Live Training Program](#).
 7. Have all relevant staff involved in prescribing, dispensing, or administering of BREYANZI 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
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	<p>of BREYANZI are trained and complete the Knowledge Assessment and submit it to the REMS Program.</p> <p>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).</p> <p>10. Establish processes and procedures to provide patients with the Patient Wallet Card.</p>
Before infusion	<p>11. Provide the patient with the Patient Wallet Card</p> <p>12. 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.</p>
To maintain certification to dispense, if there is a change in authorized representative	<p>13. Have a new Authorized Representative enroll in the REMS Program by completing the Hospital Enrollment Form.</p>
To maintain certification to dispense, if BREYANZI has not been dispensed at least once annually from the date of certification in the REMS Program	<p>14. Train all relevant staff involved in prescribing, dispensing, or administering of BREYANZI on the REMS Program requirements using the Live Training Program.</p> <p>15. Have all relevant staff involved in prescribing, dispensing, or administering of BREYANZI successfully complete the Knowledge Assessment.</p>
At all times	<p>16. Report any serious¹ adverse events suggestive of cytokine release syndrome or neurological toxicities to the REMS Program.</p> <p>17. Maintain records of staff training.</p> <p>18. Maintain records that processes and procedures are in place and are being followed.</p> <p>19. Comply with audits carried out by Juno Therapeutics, Inc., or a third party acting on behalf of Juno Therapeutics, Inc., to ensure that all training, processes, and procedures are in place and are being followed.</p>

2. Patients who are prescribed BREYANZI:

Before infusion	<p>1. Receive the Patient Wallet Card.</p>
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¹ For the purpose of this REMS Program, 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.

Juno Therapeutics Inc. must provide training to relevant staff who prescribe, dispense, or administer BREYANZI.

The training includes the following educational materials: [Live Training Program](#) and [Knowledge Assessment](#). The training must be provided in-person or via live webcast.

To support REMS Program operations, Juno Therapeutics, Inc. must:

1. Ensure BREYANZI is distributed only to certified hospitals or their associated clinics.
2. Establish and maintain the [REMS Program website, www.BreyanziREMS.com](#). The REMS Program website must include the 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 call center.
4. Establish and maintain a REMS Program Call Center for REMS participants at 1-888-423-5436.
5. Establish and maintain a validated, secure database of all REMS participants who are enrolled and/or certified in the REMS Program.
6. Ensure hospitals and their associated clinics are able to enroll in the REMS Program in person, online, fax and telephone.
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, Juno Therapeutics, 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: BREYANZI 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 BREYANZI to ensure that all REMS processes and procedures are in place, functioning, and support the BREYANZI REMS Program requirements. Certified hospitals and their associated clinics must also be included in Juno Therapeutics, Inc.'s, ongoing annual audit plan.
13. Take reasonable steps to improve implementation of and compliance with the requirements in the BREYANZI REMS Program based on monitoring and evaluation of the BREYANZI REMS Program.

IV. REMS ASSESSMENT TIMETABLE

Juno Therapeutics, 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 (XX/XX/2020). 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. Juno Therapeutics, 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 BREYANZI REMS:

Enrollment Forms:

Health Care Setting:

1. [Hospital Enrollment Form](#)

Training and Educational Materials:

Patient:

2. [Patient Wallet Card](#)

Health Care Setting:

3. [Live Training Program](#)
4. [Knowledge Assessment](#)

Other Materials:

5. [REMS Program Website](#)