

Davidson, Mark

From: Davidson, Mark
Sent: Monday, October 02, 2017 6:02 PM
To: 'Rizwana Sproule'
Cc: 'Alex Babayan'; 'Nadia Agopyan'
Subject: BLA 125643 Kite Pharma YESCARTA Risk Evaluation and Mitigation Strategy (REMS) 10.2.17
Attachments: FDA revised Yescarta REMS materials compiled 10.02.17.pdf

Dear Dr. Sproule,

“General Comments for the Applicant: **Please respond by COB Thursday, October 5th 2017.**

All REMS materials must be revised to be consistent with the final labeling and REMS Document and resubmitted for review.

The mechanisms to complete certification (e.g., phone, fax, mail, in-person etc) must be identical in the REMS document and in the REMS materials, including the enrollment form. Harmonize the mechanisms to complete certification throughout the REMS and REMS materials.

Change text that is in all caps in subheadings in all materials to title case. Text in all caps is more difficult to read if used for more than a few words, and especially if text runs over into two lines.

Program Overview:

Remove this piece from the REMS. The information contained in the Program Overview is not needed since the training slides contain a comprehensive explanation of the risks and REMS program requirements.

Yescarta REMS Program Live Training for Hospitals

We have made extensive edits to the training program to remove promotional content, repetitive content and other information that is not directly related to the REMS risks, including slides related to the administration of Yescarta.

We have also reorganized slides and clarified the requirements for hospital certification and the responsibilities of the authorized representative on behalf of the hospital. Risk information is now a separate section of the training. We have also added a slide on patient counseling that includes the signs and symptoms from the Medication Guide as well as instructions for the patient on the wallet card and what to do if a patient has symptoms of CRS or neurologic toxicities.

We have made changes to align the content with the most recent version of the REMS document and prescribing information. Final content of the training program must reflect the final REMS document and prescribing information. In addition, any graphics used to show REMS program materials should be updated as those materials are updated. Because the edits to this training program are significant, we were not able to distinguish between deleted and added text on many of the slides. In addition formatting would have been such so that the new content would have been difficult to read on the cluttered slides.

Please see edited Live Training Program for Hospitals (attached). When resubmitting training program, please submit as a PowerPoint file, as well as a .PDF. Submitting as a PowerPoint file will allow us to format slides (font, spacing) as well as show any changes if needed in the next submission.

Yescarta REMS Knowledge Assessment

The Knowledge Assessment form should include data fields that include the hospital name, address, city, state, zip code, and credentials of representative [(DO, MD, R.Ph, NP/PA, Other (please specify))].

The Knowledge Assessment submitted does not truly assess knowledge of the program as most of the questions can be easily guessed, and other content areas of the REMS program are missing. Replace the true/false questions on the risk information with multiple choice questions that also include foil answers. Add additional multiple choice questions to

test knowledge of signs and symptoms of CRS and neurologic toxicities, time to onset time of CRS and neurologic toxicities after Yescarta treatment. We recommend two vignette type questions to demonstrate knowledge of the management of CRS and neurologic toxicities.

Question 3- Revise the question to read, "A Yescarta Patient Wallet Card must be given to patients who have been infused with Yescarta."

Question 6- Revise the question so the information concerning tocilizumab is specific. For example, "Every certified hospital is required to have a minimum of two doses of tocilizumab on site for each patient and available for administration within 2 hours of Yescarta infusion."

Yescarta REMS Adverse Reaction Management Guide

The guide is too long to be a functional part of management treatment and includes extra information that doesn't directly relate to an adverse reaction and treatment. Include only the tables showing the grading of CRS, Management of CRS and Management of Neurologic events. We have created an example of what the guide could look like as a simple one page tool with information on CRS on the front and neurologic events on the back so that key information is easily and quickly located.

We recommend laminating the guide so it may have repetitive use in in the hospital.

Please see mock-up of management guide (attached).

Yescarta REMS Program Hospital Enrollment Form

We have made significant edits to this form to align the responsibilities of the hospital and authorized representative to what is required in the REMS document.

Revise second sub-heading to "Hospital Responsibilities." Revise the requirements under this sub-heading to state:

As a condition of certification, the certified hospital must:

- Ensure that if the hospital designates a new authorized representative, the new authorized representative must review the Yescarta REMS Training Program, complete the Yescarta REMS Program Knowledge Assessment, complete a new Yescarta REMS Program Hospital Enrollment Form and submit the forms via fax to 1-310-496-0397 or email at YescartaREMS@kitepharma.com.
- Report any adverse events suggestive of CRS, neurological toxicities, or suspected, unexpected serious adverse reactions to FDA at www.fda.gov/medwatch or by calling 1-800-FDA-1088 or Kite Pharma at 1-844-454-KITE.
- Dispense Yescarta 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).
- Maintain documentation of all processes and procedures for the Yescarta RESM Program and provide documentation upon request to Kite Pharma, FDA, or a third party acting on behalf of Kite Pharma or FDA.
- Comply with audits by Kite Pharma, FDA, or a third party acting on behalf of Kite Pharma or FDA Under Authorized Representative Information, include a data field to capture credentials: (DO, MD, R.Ph, NP/PA, Other (specify)
Remove the statement: "By checking this box you indicate you have read and comply with the terms and conditions of the Yescarta REMS Program." The signature ensures that the representative will comply with the REMS Program.

Page 2- replace "Healthcare Facility Agreement" with "Authorized Representative Responsibilities." Include bullets below.

- I must complete the Yescarta REMS Training Program and successfully complete the Yescarta REMS Program Knowledge Assessment.
- I must submit this completed Yescarta REMS Program Hospital Enrollment Form to Kite Pharma via fax to 1-310-496-0397 or email to YescartaREMS@kitepharma.com
- I must submit the Yescarta REMS Program Knowledge Assessment for to Kite Parma via fax to 1-310-496-0397.
- I will oversee implementation and compliance with the Yescarta REMS Program

- I will ensure that my hospital will establish processes and procedures that are subject to monitoring by Kite Pharma, FDA, or a third party acting on behalf of Kite or FDA to help ensure compliance with the requirements of the Yescarta REMS Program, including the following, before administering Yescarta:
 - o Ensuring all relevant staff involved in the prescribing, dispensing, or administering of Yescarta are trained on the REMS Program requirements and successfully complete the Yescarta and maintain records of staff training.
 - o Performing routine re-education of all staff involved in the prescribing, dispensing or administering of Yescarta and maintaining records of training if Yescarta has not been dispensed at least once annually from the date of certification in the Yescarta REMS program.
 - o Put processes and procedures in place to ensure that healthcare providers who prescribe YESCARTA review the YESCARTA Prescribing Information and are aware of the patient monitoring instructions in the YESCARTA Prescribing Information, including hospitalizing the patient for a minimum of 7 days after receiving Yescarta.
 - o Prior to dispensing Yescarta, 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)
 - o Prior to dispensing Yescarta, provide patients/guardians the Patient Wallet Card

Please see edited Hospital Enrollment Form (attached).

Yescarta REMS Patient Wallet Card

The information on the wallet card should contain patient-friendly language consistent with the Medication Guide as appropriate, with bullets, symbols or graphics (e.g., warning symbols) and bold fonts as necessary so that emergency department personnel and other healthcare providers recognize the importance of the information, urgency of action and need to contact the treating oncologist.

The risk of CRS should be clearly laid out for the healthcare providers, along with any actions that should be taken if a patient presents the card in a hospital setting.

We have made edits to card to remove extra information that might take away from the key risk messages for the patients and healthcare providers. We have modified the symptoms to reflect those listed in the Medication Guide. These modifications should allow the card to become shorter in length which will also help emergency personnel and other healthcare providers locate the important information quicker.

Please see mockup of patient wallet card (attached).

Yescarta REMS Website

Presenting the Important Safety Information at the top of the REMS webpage is redundant and not necessary as the Prescribing Information is also included on the page. Remove the ISI from the REMS webpage.

Under What is the Yescarta REMS Program?- Replace second sentence to read: “The FDA has determined that a REMS is necessary to ensure the benefits of Yescarta outweigh the risks of cytokine release syndrome and neurologic events.”

We note that edits must be made to the indication and risk messaging in the bullets under CRS and Neurologic Events to reflect changes made to the label.

We have made edits to clarify the program requirements for the authorized representative when enrolling on behalf of the hospital. The fourth bullet should now read:

- “4. Oversee implementation and compliance with Yescarta REMS Program requirements:
- Ensure all relevant staff involved in the prescribing, dispensing or administering of Yescarta are trained on the REMS program requirements and successfully complete the Yescarta REMS Program Knowledge Assessment
 - Maintain training records of staff.
 - Ensure that the facility has a minimum of two doses of tocilizumab available on site for each patient and are ready for immediate administration (within 2 hours).
 - Prior to dispensing Yescarta, provide patients/caregivers with the Patient Wallet Card.

Put processes and procedures in place to ensure new staff are trained and staff is re-trained if Yescarta has not been dispensed at least once annually from the date of certification in the Yescarta REMS Program.”

Thanks.

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