CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

216993Orig1s000

REMS

Risk Evaluation and Mitigation Strategy (REMS) Document
VANFLYTA® (quizartinib) REMS

I. Administrative Information

Risk: QT prolongation, Torsades de Pointes, and Cardiac Arrest

Application Number: NDA 216993

Application Holder: Daiichi Sankyo, Inc.

Initial REMS Approval: 07/2023

II. REMS Goals

The goals of the VANFLYTA REMS are to mitigate the serious risks of QT prolongation, Torsades de Pointes, and cardiac arrest by ensuring that:

1. Prescribers are able to identify the unique QT prolonging mechanism of VANFLYTA.
2. Prescribers are able to identify the risk factors that are associated with Torsades de Pointes and cardiac arrest with VANFLYTA.
3. Prescribers are able to identify the importance of providing risk mitigation measures including QTc interval monitoring, electrolyte monitoring and repletion, avoidance of concomitant QTc prolonging medications, and dose modifications/dose interruptions when indicated.

III. REMS Requirements

Daiichi Sankyo, Inc. must ensure that healthcare providers, patients, pharmacies, and wholesalers-distributors comply with the following requirements:

1. Healthcare providers who prescribe VANFLYTA must:	
To become certified to prescribe	1. Review the drug's Prescribing Information. 2. Review the following: Prescriber Training Program. 3. Successfully complete the Knowledge Assessment and submit it to the REMS. 4. Enroll in the REMS by completing and submitting the Prescriber Enrollment Form to the REMS.
Before treatment initiation (first dose)	5. Counsel the patient on how to recognize and respond to signs and symptoms related to QT prolongation, Torsades de Pointes, and cardiac arrest, the need to report any symptoms suggestive of QT prolongation, Torsades de Pointes, and cardiac arrest to their Prescriber or emergency room provider immediately, and the need to carry the Patient Wallet Card at all times.
At discharge	6. Complete the Patient Wallet Card and provide the Patient Wallet Card to the patient.

At all times	7. Report serious adverse events suggestive of QT prolongation, Torsades de Pointes, and cardiac arrest to Daiichi Sankyo, Inc.
2. Patients who are prescribed VANFLYTA:	
Before treatment initiation	1. Receive counseling from the prescriber on how to recognize and respond to signs and symptoms related to QT prolongation, Torsades de Pointes, and cardiac arrest, the need to report any symptoms suggestive of QT prolongation, Torsades de Pointes, and cardiac arrest to your doctor or emergency room provider immediately, and the need to carry the Patient Wallet Card at all times.
At discharge	2. Receive the Patient Wallet Card.
At all times	3. Have the Patient Wallet Card with you and inform other healthcare providers about treatment with VANFLYTA
3. Pharmacies that dispense VANFLYTA must:	
To become certified to dispense	1. Designate an Authorized Representative to carry out the certification process and oversee implementation and compliance with the REMS requirements on behalf of the pharmacy. 2. Have the Authorized Representative enroll in the REMS by completing the Pharmacy Enrollment Form and submitting it to the REMS. 3. Train all relevant staff involved in dispensing on the REMS requirements. 4. Establish processes and procedures to verify the prescriber is certified.
Before dispensing	5. Verify the prescriber is certified through the processes and procedures established as a requirement of the REMS.
To maintain certification to dispense	6. If there is a change in the Authorized Representative, have the new Authorized Representative enroll in the REMS by completing the Pharmacy Enrollment Form.
At all times	7. Report serious adverse events suggestive of QT prolongation, Torsades de Pointes, and cardiac arrest to Daiichi Sankyo, Inc. 8. Do not distribute, transfer, loan, or sell VANFLYTA except to certified pharmacies. 9. Maintain records that processes and procedures are in place and are being followed. 10. Maintain records of all VANFLYTA dispenses and provide data to the REMS. 11. Comply with audits carried out by Daiichi Sankyo, Inc. or a third party acting on behalf of Daiichi Sankyo, Inc to ensure that all training, processes, and procedures are in place and are being followed.

4. Wholesaler-Distributors that distribute VANFLYTA must:	
To be able to distribute	1. Establish processes and procedures to ensure that VANFLYTA is distributed only to certified pharmacies. 2. Train all relevant staff involved in distribution on the REMS requirements.
At all times	3. Distribute only to certified pharmacies. 4. Maintain records that all processes and procedures are in place and are being followed. 5. Maintain records of drug distribution and provide these records on a daily basis to Daiichi Sankyo for submission to the REMS. 6. Comply with audits carried out by Daiichi Sankyo, Inc. or a third party acting on behalf of Daiichi Sankyo, Inc to ensure that all processes and procedures are in place and are being followed.

Daiichi Sankyo, Inc. must provide training to healthcare providers who prescribe VANFLYTA. The training includes the following educational materials: Prescriber Training Program and Knowledge Assessment. The training must be provided online; completed Knowledge Assessment forms may be submitted to the REMS Coordinating Center via fax or e-mail.

To support REMS operations, Daiichi Sankyo, Inc. must:

1. Authorize dispensing based on verifying the Prescriber is certified.
2. Establish and maintain the REMS Website, www.VANFLYTAREMS.com. The REMS Website must include the capability to enroll prescribers and pharmacies; to complete prescriber training online, and an 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 Website. The REMS website must not link back to the promotional product website(s).
3. Make the REMS Website fully operational and all REMS materials available through the website and the REMS Coordinating Center at the time VANFLYTA first becomes commercially available.
4. Establish and maintain a REMS Coordinating Center for REMS participants at 1-855-212-6670.
5. Establish and maintain a validated, secure database of all REMS participants who are enrolled and certified in the VANFLYTA REMS.
6. Ensure prescribers and pharmacies can enroll in the REMS online, by fax, and e-mail.
7. Ensure prescribers can complete the Knowledge Assessment online, by fax, and e-mail.
8. Ensure pharmacies are able to verify the prescriber is certified online and by phone.
9. Notify prescribers and pharmacies within 2 business days after they become certified in the REMS.
10. Provide certified prescribers access to the database of certified pharmacies.
11. Provide certified pharmacies access to the database of certified prescribers.
12. Provide authorized wholesaler-distributors access to a list of certified pharmacies.
13. Report serious QT prolongation, Torsades de Pointes and/or cardiac arrest as soon as possible to the FDA but no later than 15 calendar days from the initial receipt of the information by the Applicant. This requirement does not affect the Applicant's other reporting and follow-up requirements under applicable FDA regulations.

To ensure REMS participants' compliance with the REMS, Daiichi Sankyo, Inc. must:

14. Verify annually that the authorized representative's name and contact information correspond to those of the current designated authorized representative for the pharmacy. If different, the pharmacy must be required to re-certify with a new authorized representative.

15. Maintain adequate records to demonstrate that REMS requirements have been met, including, but not limited to, records of: VANFLYTA distribution and dispensing; certification of prescribers and pharmacies; authorization of wholesalers-distributors; and audits of REMS participants. These records must be readily available for FDA inspections.

16. Monitor healthcare providers, pharmacies, and wholesaler-distributors on an ongoing basis to ensure the requirements of the REMS are being met. Take corrective action if noncompliance is identified, including decertification or deauthorization.

17. Establish and maintain a plan for addressing noncompliance with REMS requirements.

18. Audit all certified pharmacies within 180 calendar days after the pharmacy receives their first shipment of VANFLYTA and annually thereafter to ensure that all REMS processes and procedures are in place, functioning, and support the REMS requirements.

19. Audit wholesaler-distributors that have distributed VANFLYTA within 180 calendar days of being authorized to distribute VANFLYTA and annually thereafter to ensure that all REMS processes and procedures are in place, functioning, and support the REMS requirements. Take corrective action if noncompliance is identified.

20. Take reasonable steps to improve operations of and compliance with the requirements in the VANFLYTA REMS based on monitoring and evaluation of the VANFLYTA REMS.

IV. REMS Assessment Timetable

Daiichi Sankyo, Inc. must submit REMS Assessments to the FDA annually from the date of the initial approval of the REMS **(07/20/2023)**. 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. Daiichi Sankyo, 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 VANFLYTA REMS:

Enrollment Forms

1. Prescriber Enrollment Form
2. Pharmacy Enrollment Form

Training and Educational Materials

Patient:

3. Patient Wallet Card

Prescriber:

4. Prescriber Training Program
5. Knowledge Assessment

Other Materials

6. REMS Website

VI. Statutory Elements

This REMS is required under section 505-1 of the Federal Food, Drug and Cosmetic Act (FD&C Act) (21 U.S.C 355-1) and consists of the following elements:

1. Elements to Assure Safe Use (ETASU)
   - Health care providers who prescribe VANFLYTA are specially certified under 505-1(f)(3)(A).
   - Pharmacies that dispense VANFLYTA are specially certified under 505-1(f)(3)(B).
2. Implementation System
3. Timetable for Submission of Assessments

VANFLYTA® (quizartinib) REMS Prescriber Enrollment Form

VANFLYTA® (quizartinib) is available only through the VANFLYTA REMS (Risk Evaluation and Mitigation Strategy), a restricted distribution program. Only Prescribers and Pharmacies enrolled in the program can prescribe, dispense, and receive VANFLYTA.

INSTRUCTIONS TO BECOME CERTIFIED IN THE REMS

1. Review the ***Prescriber Training Program*** and the VANFLYTA Prescribing Information.
2. Complete and submit the ***Knowledge Assessment*** to the REMS Coordinating Center online at www.VANFLYTAREMS.com, via fax to 1-855-382-6017, or email to enroll@VANFLYTAREMS.com. You will receive a confirmation via email.
3. Complete and submit this ***Prescriber Enrollment Form*** to the REMS Coordinating Center online at www.VANFLYTAREMS.com, or via email to enroll@VANFLYTAREMS.com or fax to 1-855-382-6017. You will receive a confirmation via email.

Complete all mandatory fields on this form to avoid a delay in the enrollment process. Upon completion of these steps, the REMS will notify the Prescriber of successful certification usually within 24 hours but no later than 2 business days.

PRESCRIBER INFORMATION (**indicates required field*)

First Name*:	Last Name*:	National Provider Identifier (NPI #)*:
Credentials* (please select one): ☐ MD ☐ DO ☐ NP ☐ PA ☐ Other, Please specify: _____	Specialty* (please select one): ☐ Oncologist ☐ Hematologist ☐ Other, Please specify: _____	
Office Phone Number*:	Office Fax Number*:	Email Address*:
Practice/Facility Name*:		
Address 1*:		
Address 2:		
City*:	State*:	Zip Code*:

OFFICE CONTACT INFORMATION

First Name:	Last Name:	
Office Phone Number: ☐ Same as above	Office Fax Number: ☐ Same as above	Email Address:

To provide additional Office Contacts, please contact the VANFLYTA REMS Coordinating Center at 1-855-212-6670

Phone: 1-855-212-6670
www.VANFLYTAREMS.com
Fax: 1-855-382-6017
Email: enroll@VANFLYTAREMS.com

VANFLYTA® (quizartinib) tablets

Reference ID: 5212288

PRESCRIBER AGREEMENT

Healthcare providers who prescribe VANFLYTA must:

- Review the drug's Prescribing Information.
- Review the ***Prescriber Training Program***.
- Successfully complete the ***Knowledge Assessment*** and submit it to the REMS.
- Enroll in the VANFLYTA REMS by completing and submitting the ***Prescriber Enrollment Form*** to the VANFLYTA REMS.

Before treatment initiation (first dose), I must:

- Counsel the patient on:
  - how to recognize and respond to signs and symptoms related to QT prolongation, Torsades de Pointes, and cardiac arrest
  - the need to report any symptoms suggestive of QT prolongation, Torsades de Pointes, and cardiac arrest to their prescriber or emergency room provider immediately, and
  - the need to carry the ***Patient Wallet Card*** at all times.

At discharge, I must:

- Complete the ***Patient Wallet Card*** and provide the ***Patient Wallet Card*** to the patient.

At all times, I must:

- Report serious adverse events suggestive of QT prolongation, Torsades de Pointes, and cardiac arrest to Daiichi Sankyo, Inc.

Prescriber Signature*:	Date* (MM/DD/YYYY):

VANFLYTA® (quizartinib) REMS Pharmacy Enrollment Form

Instructions

VANFLYTA® (quizartinib) is only available through the VANFLYTA Risk Evaluation and Mitigation Strategy (REMS). To dispense VANFLYTA, Pharmacies must be certified in the VANFLYTA REMS. Pharmacies must designate an Authorized Representative to:

- Complete the certification process by completing the **Pharmacy Enrollment Form** on behalf of the Pharmacy.
- Oversee implementation and compliance with the VANFLYTA REMS requirements as outlined below.
- Submit this enrollment form to the REMS Coordinating Center online at www.VANFLYTAREMS.com or via fax to 1-855-382-6017 or email to enroll@VANFLYTAREMS.com. You will receive a confirmation via email.

Complete all mandatory fields on this form to avoid a delay in the enrollment process. Upon completion of these steps, the REMS will notify the Authorized Representative of successful certification usually within 24 hours but no later than 2 business days.

If you have any questions, require additional information, or need further copies of any of the VANFLYTA REMS materials, please visit the **REMS Website** at www.VANFLYTAREMS.com or call the VANFLYTA REMS Coordinating Center at 1-855-212-6670.

Pharmacy Information: (*indicates required field)

(Please Check One) ☐ **New Certification** ☐ **Change in Authorized Representative**

Pharmacy Name*:		
Pharmacy Identifier (NPI)#*:	HIN:	DEA#:
Pharmacy Type* Select one: ☐ Inpatient Hospital Pharmacy ☐ Outpatient Hospital Pharmacy ☐ Specialty Pharmacy ☐ Other (please specify) _____		
Address Line 1*:		
Address Line 2:		
City*:	State*:	Zip Code*:
Phone*:	Fax*:	

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Ship To Information:

Ship To Address ☐ **Same as Above**	**Ship To Contact Name*:**	
Address Line 1*:		
Address Line 2:		
City*:	State*:	Zip Code*:
Phone:	Fax:	

Authorized Representative Information (must not be a certified Prescriber)

First Name*:	Last Name*:	
Credentials*: ☐ RPh ☐ PharmD ☐ RN ☐ Other (please specify)		
Phone*:	Fax*:	Email*:
Authorized Representative Signature*:	**Date* (MM/DD/YYYY):**	

Authorized Representative Responsibilities

As the Authorized Representative, I must:

To become certified to dispense:

- Enroll in the VANFLYTA REMS by completing the ***Pharmacy Enrollment Form*** and submitting it to the VANFLYTA REMS.
- Train all relevant staff involved in dispensing on the VANFLYTA REMS requirements.
- Establish processes and procedures to verify the prescriber is certified.

Before Dispensing, all staff must:

- Verify the prescriber is certified through the processes and procedures established as a requirement of the VANFLYTA REMS.

At all times, staff must:

- Report serious adverse events suggestive of QT prolongation, Torsades de Pointes, and cardiac arrest to Daiichi Sankyo, Inc.
- Not distribute, transfer, loan, or sell VANFLYTA except to certified pharmacies.
- Maintain records that processes and procedures are in place and are being followed.
- Maintain records of all VANFLYTA dispenses and provide data to the VANFLYTA REMS.
- Comply with audits carried out by Daiichi Sankyo, Inc. or a third party acting on behalf of Daiichi Sankyo, Inc. to ensure that all training, processes, and procedures are in place and are being followed.
- If there is a change in the Authorized Representative, have the new Authorized Representative enroll in the VANFLYTA REMS by completing the ***Pharmacy Enrollment Form***.

VANFLYTA® (quizartinib) tablets

VANFLYTA (quizartinib) REMS (Risk Evaluation Mitigation Strategy) Prescriber Training Program

Reference ID: 5212288

VANFLYTA Prescriber Training Program

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- This training module provides details related to the VANFLYTA REMS requirements for Prescribers in order to prescribe VANFLYTA.
- Please refer to the Prescribing Information for additional information.

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Training Overview

VANFLYTA® (quizartinib) tablets

- What is a REMS?
- What is VANFLYTA?
  - Indication
  - Boxed Warning
    - **QT Prolongation, Torsades de pointes and cardiac arrest**
  - Clinical Data
- QT Prolongation Mechanism of Action: Inhibition of the Slow Delayed Rectifier Potassium Current, IKs
- What are the Risk Factors for QT Prolongation, Torsades de Pointes and Cardiac Arrest?
- What are the Risk Mitigation Strategies?
  - What do Prescribers Need to Do Before Treatment?
  - What do Prescribers Need to Do During Treatment?
  - Dosing and Administration
  - Dosing Modifications for Adverse Reactions
- How do Prescribers Become Certified in the VANFLYTA REMS?

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What is a REMS?

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- A Risk Evaluation and Mitigation Strategy (REMS) is a program required by the FDA to manage known or potential serious risks associated with a drug product. The FDA has determined that a REMS is necessary to ensure that the benefits of VANFLYTA outweigh its risks.

- The goals of the VANFLYTA REMS are to mitigate the serious risks of QT prolongation, Torsades de Pointes, and cardiac arrest by ensuring that:
  - Prescribers are able to identify the unique QT prolonging mechanism of VANFLYTA.
  - Prescribers are able to identify the risk factors that are associated with Torsades de Pointes and cardiac arrest with VANFLYTA .
  - Prescribers are able to identify the importance of providing risk mitigation measures including QTc interval monitoring, electrolyte monitoring and repletion, avoidance of concomitant QT prolonging medications, and dose modifications/dose interruptions when indicated

Reference ID: 5212288

What is VANFLYTA?

VANFLYTA® (quizartinib) is a kinase inhibitor indicated in combination with standard cytarabine and anthracycline induction and cytarabine consolidation, and as maintenance monotherapy following consolidation chemotherapy, for the treatment of adult patients with newly diagnosed acute myeloid leukemia (AML) that is FLT3 internal tandem duplication (ITD)-positive as detected by an FDA-approved test.

Limitations of Use:

VANFLYTA is not indicated as maintenance monotherapy following allogeneic hematopoietic stem cell transplantation (HSCT); improvement in overall survival with VANFLYTA in this setting has not been demonstrated.

Contraindication:

VANFLYTA is contraindicated in patients with severe hypokalemia, severe hypomagnesemia, long QT syndrome, or in patients with a history of ventricular arrythmias or Torsades de Pointes.

Reference ID: 5212288

Boxed Warning: QT Prolongation, Torsades de Pointes and Cardiac Arrest

VANFLYTA® (quizartinib) tablets

Boxed Warning includes:

- VANFLYTA prolongs the QT interval. Prior to VANFLYTA administration and periodically, perform electrocardiograms (ECGs), monitor for hypokalemia or hypomagnesemia, and correct deficiencies.
- Torsades de pointes and cardiac arrest have occurred in patients receiving VANFLYTA. Do not administer VANFLYTA to patients with severe hypokalemia, severe hypomagnesemia, or long QT syndrome.
- Do not initiate treatment with VANFLYTA or escalate the VANFLYTA dose if **the QT interval corrected by Fridericia's formula (QTcF) is greater than 450 ms.**
- Monitor ECGs more frequently if concomitant use of drugs known to prolong the QT interval is required.
- Reduce the VANFLYTA dose when used concomitantly with strong CYP3A inhibitors, as they may increase quizartinib exposure.

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How Can Prescribers Help Mitigate The Serious Risks?

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Mechanism of Action (IKs inhibition):	Risk Factors:	Mitigation Strategies:
• The mechanism of QT interval prolongation is via inhibition of the slow delayed rectifier potassium current, I_{Ks} • All other medications that prolong the QT interval do so via the rapid delayed rectifier potassium current, $I_{kr.}$ • Inhibition of I_{Ks} and I_{Kr} may leave patients with limited reserve leading to a higher risk of QT prolongation and serious cardiac arrhythmias, including fatal outcomes	• Hypokalemia/hypomagnesemia • Concomitant QT prolonging medications • History of long QT syndrome • Uncontrolled or significant cardiovascular disease, recent myocardial infarction, heart failure, unstable angina, bradyarrhythmias, tachyarrhythmias, uncontrolled hypertension, high degree atrioventricular block, severe aortic stenosis, or uncontrolled hypothyroidism	• Strict QTc interval monitoring • Electrolyte monitoring and repletion • Avoidance of concomitant QT prolonging medications • VANFLYTA Dose interruptions/ dose modifications

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QT Prolongation with Quizartinib: Inhibition of the Slow Delayed Rectifier Potassium Current, IKs

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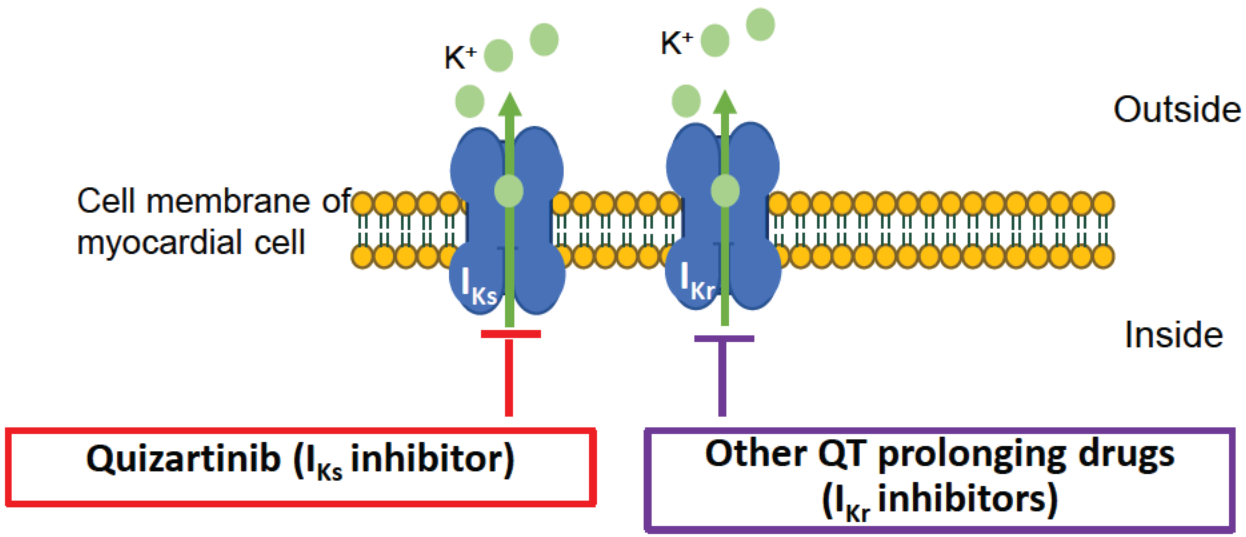
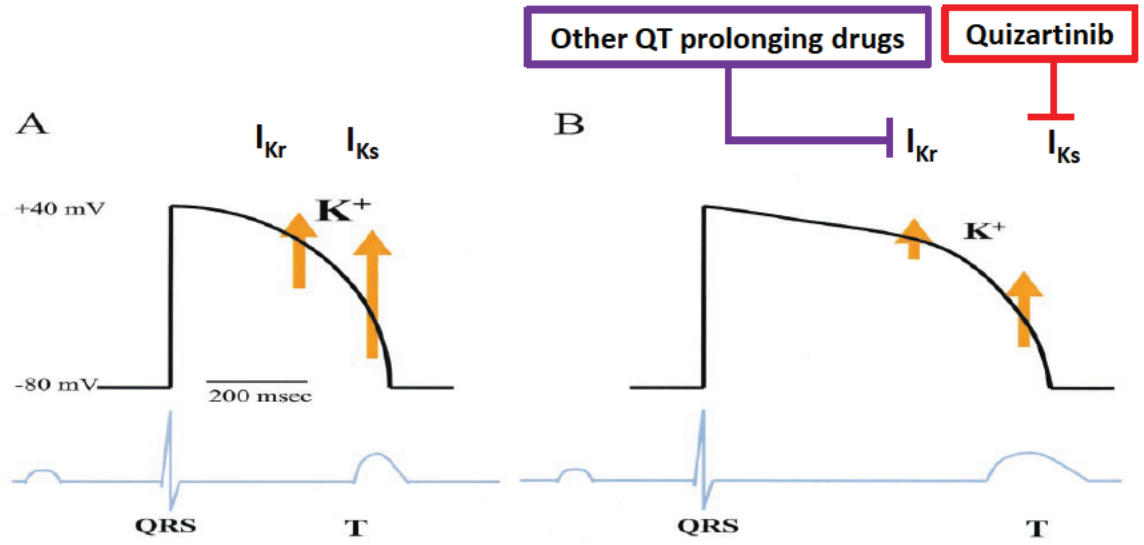
- Ventricular repolarization depends largely on the transmembrane outward transport of potassium ions via rapidly (I_{Kr}) and slowly (I_{Ks}) activating delayed rectifier potassium ion channels
- Second current provides 'repolarization reserve' when one channel is blocked
- A reduction in repolarizing current via I_{Kr} and/or I_{Ks} can prolong the QT interval, resulting in an increased risk of arrythmias





A. Repolarization via I_{Ks} and I_{Kr} in normal conditions

B. Decreased I_{Kr} and/or I_{Ks} repolarizing currents prolong the action potential

1. Adapted with permission from: Tristani-Firouzi M, Chen J, Mitcheson JS, Sanguinetti MC. Molecular biology of K(+) channels and their role in cardiac arrhythmias. Am J Med. 2001 Jan;110(1):50-9..

QT Prolonging Mechanism of Action

VANFLYTA® (quizartinib) tablets

- **Inhibition of the Slow Delayed Rectifier Potassium Current, IKs**
- VANFLYTA prolongs the QT interval in a dose- and concentration-related manner.
  - **The exposure-response analysis predicted a concentration-dependent QTcF interval median prolongation of 18 and 24 ms [upper bound of 2-sided 90% confidence interval (CI): 21 and 27 ms] at the median steady-state Cmax of quizartinib at the 26.5 mg and 53 mg dose level during maintenance therapy**
- The mechanism of QT interval prolongation is via inhibition of the slow delayed rectifier potassium current, I_{Ks}, as compared to all other medications that prolong the QT interval, which is via the rapid delayed rectifier potassium current, I_{Kr}.
  - Therefore, the level of QTc prolongation with VANFLYTA that predicts the risk of cardiac arrhythmias is unclear.
  - Inhibition of IK_s and IK_r may leave patients with limited reserve, leading to a higher risk of QT prolongation and serious cardiac arrhythmia, including fatal outcomes.

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Clinical Studies

- In 1,081 patients with AML treated with VANFLYTA in the clinical trials, Torsades de Pointes occurred in approximately 0.2% of patients, cardiac arrest occurred in 0.6%, including 0.4% with a fatal outcome, and 0.1% of patients experienced ventricular fibrillation. These severe cardiac arrhythmia events occurred predominantly during the induction phase.
- Of 265 patients with newly diagnosed FLT3-ITD-positive AML treated with VANFLYTA in combination with chemotherapy in a clinical trial, 2.3% were found to have a QTcF greater than 500 ms and 10% of patients had an increase from baseline QTcF greater than 60 ms.

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Risk Factors for QT Prolongation, Torsades de Pointes and Cardiac Arrest

VANFLYTA® (quizartinib) tablets

- Induction phase of treatment
- Hypokalemia
- Hypomagnesemia
- Concomitant QT prolonging medications
- History of long QT syndrome
- Uncontrolled or significant cardiovascular disease, recent myocardial infarction, heart failure, unstable angina, bradyarrhythmias, tachyarrhythmias, uncontrolled hypertension, high degree atrioventricular block, severe aortic stenosis, or uncontrolled hypothyroidism

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What do Prescribers Need to do Before Initiating Treatment? (1)

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- **Assess** each Patient for a history of ventricular arrhythmias or Torsades de Pointes, and electrolytes deficiencies
  - Do not use VANFLYTA in patients with severe hypokalemia, severe hypomagnesemia, long QT syndrome or in patients with a history of ventricular arrhythmias or Torsades de Pointes.
- **Perform** an electrocardiogram (ECG).
  - Do not initiate treatment with VANFLYTA if QTcF (QT interval corrected by Fridericia's formula) > 450 ms.
  - During induction and consolidation, perform an ECG prior to initiation and then once weekly during VANFLYTA treatment or more frequently as clinically indicated.
- **Monitor** for hypokalemia and hypomagnesemia and correct deficiencies.
  - Correct electrolyte abnormalities prior to initiation of treatment with VANFLYTA

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What do Prescribers Need to do Before Initiating Treatment? (2)

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- **Screen** for possible drug interactions with other drugs that prolong QT interval or strong CYP3A inhibitors and modify dosing as per the Prescribing Information.
- **Reduce** the VANFLYTA dose when used concomitantly with strong CYP3A inhibitors, as they may increase quizartinib exposure

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What do Prescribers Need to do Before Initiating Treatment? (3)

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Counsel the patient on:

- How to recognize and respond to signs and symptoms related to QT prolongation, Torsades de Pointes, and cardiac arrest.
- The need to report any symptoms suggestive of QT prolongation, Torsades de Pointes, and cardiac arrest to their healthcare provider or emergency room provider immediately
- Carrying the **Patient Wallet Card** at all times and showing to the card to all of their healthcare providers.

Complete the **Patient Wallet Card** and provide to the Patient before discharge.

Reference ID: 5212288

What do Prescribers Need to do During Treatment? (1)

VANFLYTA® (quizartinib) tablets

- During induction and consolidation, **perform** an ECG prior to initiation and then once weekly during VANFLYTA treatment or more frequently as clinically indicated.
- **During maintenance, perform** ECGs once weekly for at least the first month following dose initiation and escalation, and as clinically indicated thereafter. Do not escalate the dose if QTcF is greater than 450 ms.
- Perform ECG monitoring of the QT interval more frequently in patients who are at significant risk of developing QT interval prolongation and torsades de pointes or following dose escalation.
- **Reduce** VANFLYTA if QTcF increases to greater than 480 ms and less than 500 ms. Interrupt and reduce VANFLYTA if QTcF increases to greater than 500 ms.
- **Permanently discontinue** VANFLYTA in patients who develop recurrent QTcF greater than 500 ms or QTc interval prolongation with signs or symptoms of life-threatening arrhythmia

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What do Prescribers Need to do During Treatment? (2)

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- **Monitor** for hypokalemia and hypomagnesemia and correct deficiencies as per the Prescribing Information.
  - Maintain electrolytes in the normal range.
  - Monitor electrolytes and ECGs more frequently in patients who experience diarrhea or vomiting.
- **Screen** for possible drug interactions with other drugs that prolong QT interval or strong CYP3A inhibitors and modify dosing as per the Prescribing Information.
  - **Avoid** concomitant administration of drugs that prolong the QT interval, if possible
  - **Reduce** the VANFLYTA dose when used concomitantly with strong CYP3A inhibitors, as they may increase quizartinib exposure
  - **Monitor** ECGs more frequently if concomitant use of drugs known to prolong the QT interval is required.

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VANFLYTA Dosing and Administration

VANFLYTA® (quizartinib) tablets

VANFLYTA Dose Regimen

VANFLYTA Initiation	Induction*	Consolidation†	Maintenance
	Starting on Day 8 (for 7 + 3 regimen)‡	Starting on Day 6	Starting on Day 1
Dose	35.4 mg orally once daily	35.4 mg orally once daily	• Administer 26.5 mg orally once daily Days 1 through 14 of the first cycle if QTcF is less than or equal to 450 ms. • Increase the dose to 53 mg once daily on Day 15 of the first cycle if QTcF is less than or equal to 450 ms. Maintain the 26.5 mg once daily dose if QTcF greater than 500 ms was observed during induction or consolidation.
Duration (28-day cycles)	Two weeks in each cycle (Days 8 to 21)‡	Two weeks in each cycle (Days 6 to 19)	• Once daily with no break between cycles for up to 36 cycles

*Patients can receive up to 2cycles of induction.
† Patients can receive up to 4cycles of consolidation.
‡ For 5+2 regimen as the second induction cycle, VANFLYTA will be given on Days6 to 19.

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Recommended Dosage Modifications for Adverse Reactions

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Adverse Reaction	Recommended Action
QTcF between 450 ms and 480 ms (Grade 1)	• Continue VANFLYTA dose.
QTcF between 481 ms and 500 ms (Grade 2)	• Reduce the dose of VANFLYTA (see Table 1 on next slide) without interruption. • Resume VANFLYTA at the previous dose in the next cycle if QTcF has decreased to less than 450 ms. Monitor the Patient closely for QT prolongation during the first cycle at the increased dose.
QTcF greater than 500 ms (Grade 3)	• Interrupt VANFLYTA. • Resume VANFLYTA at a reduced dose (see Table 1 on next slide) when QTcF returns to less than 450 ms. • Maintain the 26.5 mg once daily dose during maintenance if QTcF greater than 500 ms was observed during induction or consolidation.
Recurrent QTcF greater than 500 ms (Grade 3)	• Permanently discontinue VANFLYTA if QTcF greater than 500 ms recurs despite appropriate dose reduction and correction/elimination of other risk factors (e.g., serum electrolyte abnormalities, concomitant QT prolonging medications).
Torsades de pointes, polymorphic ventricular tachycardia, signs/symptoms of life-threatening arrhythmia (Grade 4)	• Permanently discontinue VANFLYTA.
Grade 3 or 4 hypokalemia (<3mmol/l) or hypomagnesemia(<0.4 mmol/l or <0.9 mg/dL)	• Interrupt VANFLYTA. • Correct hypokalemia and hypomagnesemia according to institutional guidelines. • VANFLYTA may be restarted at the previous dose when the adverse reaction improves to Grade 2 or less without symptoms.

Grades are in accordance with National Cancer Institute Common Terminology Criteria for Adverse Events version 4.03 (NCI CTCAE v4.03).

VANFLYTA Dosage Modifications

VANFLYTA® (quizartinib) tablets

Table 1 - Recommended Dosage Adjustments for Adverse Reactions

Current Dosage	Modified Dosage
53 mg once daily	35.4 mg once daily
35.4 mg once daily	26.5 mg once daily
26.5 mg once daily	Interrupt
17.7 mg once daily	Interrupt

Reference ID: 5212288

In Summary: How Can Prescribers Help Mitigate The Serious Risks?

VANFLYTA® (quizartinib) tablets

Mechanism of Action (IKs inhibition):	Risk Factors:	**Mitigation Strategies:**
• The mechanism of QT interval prolongation is via inhibition of the slow delayed rectifier potassium current, I_{Ks} • All other medications that prolong the QT interval do so via the rapid delayed rectifier potassium current, $I_{kr.}$ • Inhibition of I_{Ks} and I_{Kr} may leave patients with limited reserve leading to a higher risk of QT prolongation and serious cardiac arrhythmias, including fatal outcomes	• Hypokalemia/hypomagnesemia • Concomitant QT prolonging medications • History of long QT syndrome • Uncontrolled or significant cardiovascular disease, recent myocardial infarction, heart failure, unstable angina, bradyarrhythmias, tachyarrhythmias, uncontrolled hypertension, high degree atrioventricular block, severe aortic stenosis, or uncontrolled hypothyroidism	• Strict QTc interval monitoring • Electrolyte monitoring and repletion • Avoidance of concomitant QT prolonging medications • VANFLYTA Dose interruptions/ dose modifications

Reference ID: 5212288

How do Prescribers Become Certified in the VANFLYTA REMS?

VANFLYTA® (quizartinib) tablets

To become certified, Prescribers must:

- Review this **Prescriber Training Program** and the VANFLYTA Prescribing Information
- Successfully complete and submit the **Knowledge Assessment** to the REMS
- Complete the **Prescriber Enrollment Form** and submit it to the REMS

Note: Pharmacies must also be certified in the REMS. Pharmacies are required to confirm that Prescribers are certified before dispensing VANFLYTA.

Reference ID: 5212288

Adverse Event Reporting

VANFLYTA® (quizartinib) tablets

- To report serious adverse events suggestive of QT prolongation, Torsades de Pointes, and cardiac arrest, or other side effects during the use of VANFLYTA, contact Daiichi Sankyo, Inc. at 1-877-4DS-PROD (1-877-437-7763) and/or to FDA at www.fda.gov/medwatch or call 1-800-FDA-1088.

- For the complete safety profile of VANFLYTA, please see the full US Prescribing Information, available at www.VANFLYTAREMS.com.

VANFLYTA®
(quizartinib) tablets

Additional VANFLYTA REMS Information

For further information, please visit www.VANFLYTAREMS.com or call 1-855-212-6670

VANFLYTA RISK EVALUATION MITIGATION STRATEGY (REMS)

PRESCRIBER KNOWLEDGE ASSESSMENT

Prescriber Information (*indicates required field)		
Prescriber First Name*:	Prescriber Last Name*:	
NPI #*:		
Address Line 1:		
Address Line 2:		
City:	State:	Zip Code:
Credentials*: ☐ MD ☐ DO ☐ NP ☐ PA ☐ Other (please specify)_____		
Phone*:	Fax:	Email*:
Signature*:		**Date (MM/DD/YYYY)*:**

As a condition of certification, the Prescriber must complete the ***Prescriber Knowledge Assessment***. All 10 questions must be answered correctly.

This ***Prescriber Knowledge Assessment*** can be completed online at www.VANFLYTAREMS.com or a completed hard copy can be submitted via fax to 1-855-382-6017 or via Email to enroll@VANFLYTAREMS.com. You must also complete the ***Prescriber Enrollment Form*** at www.VANFLYTAREMS.com or by fax or Email for your certification to be complete.

The VANFLYTA REMS will verify that both the ***Prescriber Knowledge Assessment*** and the ***Prescriber Enrollment Form*** are complete and will provide confirmation of certification via Email after processing.

Please answer the following questions concerning VANFLYTA and the VANFLYTA REMS

1. **The goal of the VANFLYTA REMS is to mitigate the risks of QT prolongation, Torsades de Pointes, and cardiac arrest associated with VANFLYTA.**
   ☐ True ☐ False

2. **Patients with severe hypokalemia, severe hypomagnesemia, long QT syndrome, or a history of ventricular arrhythmias or torsades de pointes must not be treated with VANFLYTA.**
   ☐ True ☐ False

3. **QT prolongation with VANFLYTA is due to inhibition of the slow delayed rectifier potassium current of the IKs as compared to all other medications that prolong the QTc interval which is via the rapid delayed rectifier potassium current Ikr.**
   ☐ True ☐ False

4. **When should ECG monitoring be performed? Select all that apply.**
   ☐ a. Before initiating treatment
   ☐ b. Weekly during induction and consolidation therapy, weekly for at least the first month following initiation or dose escalation in maintenance, and periodically thereafter
   ☐ c. After discontinuing treatment with VANFLYTA
   ☐ d. a and b only
   ☐ e. All of the above

5. **Prescribers need to counsel Patients on which of the following? Select all that apply.**
   ☐ a. How to recognize symptoms related to QT prolongation, Torsades de Pointes, and cardiac arrest
   ☐ b. The need to report symptoms related to QT prolongation or Torsades de Pontes to their Prescriber or seek care at an emergency department
   ☐ c. The need to have ECG monitoring and blood tests for electrolyte monitoring before starting treatment and during treatment as per the direction of their Prescriber
   ☐ d. The risk of drug-drug interactions and the need to tell their Prescriber about all medicines they take
   ☐ e. Carry the ***Patient Wallet Card*** with them at all times and show it to all of their healthcare providers
   ☐ f. All of the above

6. **Risk factors for QT prolongation, Torsades de Pointes, and cardiac arrest associated with VANFLYTA treatment include which of the following? Select all that apply.**
   ☐ a. Treatment during induction chemotherapy
   ☐ b. Severe electrolyte imbalance
   ☐ c. Concomitant QT prolonging medications
   ☐ d. History of long QT syndrome
   ☐ e. All of the above

7. **Coadministration of VANFLYTA with other approved QT prolonging medications may increase the risk of QT prolongation and serious cardiac arrhythmias.**
   ☐ True ☐ False

8. **Monitor and correct hypokalemia and hypomagnesemia prior to and during treatment with VANFLYTA.**
   ☐ True ☐ False

9. **VANFLYTA should be initiated only if the QTcF interval is below 450 ms.**
   ☐ True ☐ False

10. **Interrupt VANFLYTA if QTcF is >500ms and permanently discontinue VANFLYTA if QTcF>500 ms recurs despite appropriate dose reduction and correction/elimination of other risk factors.**
    ☐ True ☐ False

Patient Wallet Card

IMPORTANT SAFETY INFORMATION FOR PATIENTS TAKING VANFLYTA® (quizartinib)

FOR THE PATIENT

(Carry this card at all times and show it to all healthcare providers involved in your care)

VANFLYTA® (quizartinib) tablets

Reference ID: 5212289

IMPORTANT SAFETY INFORMATION YOU SHOULD KNOW:

VANFLYTA treatment has been known to cause QT Prolongation, which may cause Torsades de Pointes and cardiac arrest. If the patient is prescribed other drugs known to prolong the QT interval together with VANFLYTA, monitor ECGs regularly.

If your patient reports any symptoms as referenced on this card, please contact the VANFLYTA Prescriber on this card immediately for further information.

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Version 0.14 XX 2023 XXXXXXXXXX

VANFLYTA can cause serious side effects including changes in the electrical activity of your heart called QT interval prolongation, torsades de pointes, and your heart stopping (cardiac arrest).

QT interval prolongation can cause irregular heartbeats **that can be life-threatening or lead to death**.

If you have **any** of these symptoms, call your healthcare provider **right away**:

- Irregular heartbeat
- Dizziness, lightheadedness, and/or fainting (even for a brief period)
- Chest pain
- Diarrhea or vomiting

You should always ask your healthcare provider about taking other medications while taking VANFLYTA.

IMPORTANT TO REMEMBER: Call your healthcare provider or get emergency medical care right away if you have any of the symptoms! You may need to be treated in a hospital.

FOR HEALTHCARE PROVIDERS: I am taking VANFLYTA® (quizartinib) which is used in combination with certain chemotherapy medicines for the treatment of newly diagnosed acute myeloid leukemia (AML) that is FMS-like tyrosine kinase 3 internal tandem duplication (FLT3-ITD) positive.

_____

Name of VANFLYTA Patient

_____

Name of VANFLYTA Prescriber

_____

Prescriber Telephone Number

Reference ID: 5212288

VANFLYTA® Risk Evaluation and Mitigation Strategy (REMS)

The purpose of the VANFLYTA REMS is to mitigate the serious risks of QT prolongation, Torsades de Pointes, and cardiac arrest by educating prescribers on the optimal risk mitigation strategies including QTc interval monitoring, electrolyte monitoring and repletion, avoidance of concomitant QTc prolonging medications, and dose modifications/dose interruptions when indicated.

Prescribers

Prescribers must be certified in the VANFLYTA REMS to treat patients with VANFLYTA.

Learn More >

Pharmacies

Pharmacies must become certified in the VANFLYTA REMS to dispense VANFLYTA to Patients.

Learn More >

What is the VANFLYTA REMS?

A Risk Evaluation and Mitigation Strategy (REMS) is a program required by the Food and Drug Administration (FDA) to manage known or potential serious risks associated with a drug product. The FDA has determined that a REMS is necessary to ensure that the benefits of VANFLYTA outweigh its risks. The goals of the VANFLYTA REMS are to mitigate the serious risks of QT prolongation, Torsades de Pointes, and cardiac arrest by ensuring that:

1. Prescribers are able to identify the unique QT prolonging mechanism of VANFLYTA.
2. Prescribers are able to identify the risk factors that are associated with Torsades de Pointes and cardiac arrest with VANFLTYA.
3. Prescribers are able to identify the importance of providing risk mitigation measures including QTc interval monitoring, electrolyte monitoring and repletion, avoidance of concomitant QTc prolonging medications, and dose modification/dose interruptions when indicated.

Indication

VANFLYTA® (quizartinib) is a kinase inhibitor indicated in combination with standard cytarabine and anthracycline induction and cytarabine consolidation, and as maintenance monotherapy following consolidation chemotherapy, for the treatment of adult patients with newly diagnosed acute myeloid leukemia (AML) that is FLT3 internal tandem duplication (ITD)-positive as detected by an FDA-approved test.

Limitations of Use:

VANFLYTA is not indicated as maintenance monotherapy following allogeneic hematopoietic stem cell transplantation (HSCT); improvement in overall survival with VANFLYTA in this setting has not been demonstrated.

Contraindications:

VANFLYTA is contraindicated in patients with severe hypokalemia, severe hypomagnesemia, long QT syndrome, or in patients with a history of ventricular arrythmias or Torsades de Pointes

Reporting Adverse Reactions

To report side effects during the use of VANFLYTA, contact Daiichi Sankyo, Inc. at 1-877-4DS-PROD (1-877-437-7763) and/or to FDA at www.fda.gov/medwatch or call 1-800-FDA-1088.

All Patients treated with VANFLYTA should receive a *Patient Wallet Card*. Patients should carry the Wallet Card at all times to remind them of the signs and symptoms related to QT prolongation and Torsades de Pointes, and when to seek immediate medical attention. Patients should share this card with all their healthcare providers to inform them of their VANFLYTA treatment and when to contact the patient's oncologist.

Resources for Prescribers

- *Prescriber Training Program*
- *Knowledge Assessment*
- *Prescriber Enrollment Form*
- *Patient Wallet Card*

Resources for Pharmacies

- *Pharmacy Enrollment Form*

Resources for Patients

- *Patient Wallet Card*

Have Questions?

Contact the VANFLYTA REMS by calling 1-855-212-6670

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Reference ID: 5212288

Prescribers

VANFLYTA REMS Requirements

All Prescribers involved in the prescribing of VANFLYTA must be trained on the VANFLYTA REMS requirements and must successfully complete the ***Knowledge Assessment***.

Prescribers must enroll and become certified in the VANFLYTA REMS to be able to prescribe VANFLYTA.

How does a Prescriber become certified in the VANFLYTA REMS?

step **1** Review the following materials:

- *Prescriber Training Program*
- Prescribing Information

step **2** Successfully complete the *Knowledge Assessment* and submit it to the REMS

step **3** Complete the *Prescriber Enrollment Form* and submit it to the REMS

Resources for Prescribers

- *Prescriber Training Program*
- *Knowledge Assessment*
- *Prescriber Enrollment Form*
- *Patient Wallet Card*

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Pharmacies

VANFLYTA REMS Requirements

All Pharmacies involved in the dispensing of VANFLYTA must become certified in the VANFLYTA REMS.

How does a Pharmacy become certified in the VANFLYTA REMS?

step 1 | Designate an Authorized Representative for the Pharmacy

step 2 | Authorized Representative must complete the *Pharmacy Enrollment Form* and submit it to the REMS

step 3 | Train all relevant staff involved in dispensing VANFLYTA on the REMS requirements

step 4 | Establish processes and procedures to verify the prescriber is certified

Resources for Pharmacies

Pharmacy Enrollment Form

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Reference ID: 5212288

Pharmacies

VANFLYTA® (quizartinib) REMS

Pharmacy Enrollment Form

Instructions

VANFLYTA® (quizartinib) is only available through the VANFLYTA Risk Evaluation and Mitigation Strategy (REMS). To dispense VANFLYTA, Pharmacies must be certified in the VANFLYTA REMS. Pharmacies must designate an Authorized Representative to:

- Complete the certification process by completing the ***Pharmacy Enrollment Form*** on behalf of the Pharmacy.
- Oversee implementation and compliance with the VANFLYTA REMS requirements as outlined below.
- Submit this enrollment form to the REMS Coordinating Center online at www.VANFLYTAREMS.com or via fax to 1-855-382-6017 or email to enroll@VANFLYTAREMS.com. You will receive a confirmation via email.

Complete all mandatory fields on this form to avoid a delay in the enrollment process. Upon completion of these steps, the REMS will notify the Authorized Representative of successful certification usually within 24 hours but no later than 2 business days.

If you have any questions, require additional information, or need further copies of any of the VANFLYTA REMS materials, please visit the ***REMS Website*** at www.VANFLYTAREMS.com or call the VANFLYTA REMS Coordinating Center at 1-855-212-6670.

(* indicates required field)

Pharmacy Information

*Pharmacy NPI#

CONTINUE

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Pharmacies

VANFLYTA® (quizartinib) REMS

Pharmacy Enrollment Form

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Complete all mandatory fields on this form to avoid a delay in the enrollment process. Upon completion of these steps, the REMS will notify the Authorized Representative of successful certification usually within 24 hours but no later than 2 business days.

If you have any questions, require additional information, or need further copies of any of the VANFLYTA REMS materials, please visit the ***REMS Website*** at www.VANFLYTAREMS.com or call the VANFLYTA REMS Coordinating Center at 1-855-212-6670.

(* indicates required field)

Pharmacy Information

*Pharmacy NPI#
1234567890

*Enrollment Type (Please Check One)
○ New Certification ○ Change in Authorized Representative

*Pharmacy Name
University Hospital

Pharmacy Identifier

DEA# HIN

Pharmacy Type (Select one)
○ Inpatient Hospital Pharmacy ○ Outpatient Hospital Pharmacy ○ Specialty Pharmacy
○ Other (please specify)

*Address Line 1 Address Line 2

*City *State -- Please Select -- *Zip Code

*Phone *Fax

Ship To Information

*Ship To Contact Name

☐ Ship To Address - Same as above

*Address Line 1 Address Line 2

*City *State -- Please Select -- *Zip Code

Phone Fax

Authorized Representative Information (must not be a certified Prescriber)

*First Name *Last Name

*Credentials
○ RPh ○ PharmD ○ RN ○ Other (please specify)

*Phone *Fax *Email

Authorized Representative Responsibilities

As the Authorized Representative, I must:

To become certified to dispense:

- Enroll in the VANFLYTA REMS by completing the ***Pharmacy Enrollment Form*** and submitting it to the VANFLYTA REMS.
- Train all relevant staff involved in dispensing on the VANFLYTA REMS requirements.
- Establish processes and procedures to verify the prescriber is certified.

Before Dispensing, all staff must:

- Verify the prescriber is certified through the processes and procedures established as a requirement of the VANFLYTA REMS.

At all times, staff must:

- Report serious adverse events suggestive of QT prolongation, Torsades de Pointes, and cardiac arrest to Daiichi Sankyo, Inc.
- Not distribute, transfer, loan, or sell VANFLYTA except to certified pharmacies.
- Maintain records that processes and procedures are in place and are being followed.
- Maintain records of all VANFLYTA dispenses and provide data to the VANFLYTA REMS.
- Comply with audits carried out by Daiichi Sankyo, Inc. or a third party acting on behalf of Daiichi Sankyo, Inc. to ensure that all training, processes, and procedures are in place and are being followed.
- If there is a change in the Authorized Representative, have the new Authorized Representative enroll in the VANFLYTA REMS by completing the ***Pharmacy Enrollment Form***.

*Authorized Representative Name

Please use your mouse or stylus to sign below

Clear Signature

CLEAR CANCEL SUBMIT

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Pharmacies

VANFLYTA® (quizartinib) REMS

Pharmacy Enrollment Form

Instructions

VANFLYTA® (quizartinib) is only available through the VANFLYTA Risk Evaluation and Mitigation Strategy (REMS). To dispense VANFLYTA, Pharmacies must be certified in the VANFLYTA REMS. Pharmacies must designate an Authorized Representative to:

- Complete the certification process by completing the ***Pharmacy Enrollment Form*** on behalf of the Pharmacy.
- Oversee implementation and compliance with the VANFLYTA REMS requirements as outlined below.
- Submit this enrollment form to the REMS Coordinating Center online at www.VANFLYTAREMS.com or via fax to 1-855-382-6017 or email to enroll@VANFLYTAREMS.com. You will receive a confirmation via email.

Complete all mandatory fields on this form to avoid a delay in the enrollment process. Upon completion of these steps, the REMS will notify the Authorized Representative of successful certification usually within 24 hours but no later than 2 business days.

If you have any questions, require additional information, or need further copies of any of the VANFLYTA REMS materials, please visit the ***REMS Website*** at www.VANFLYTAREMS.com or call the VANFLYTA REMS Coordinating Center at 1-855-212-6670.

(* indicates required field)

Pharmacy Information

*Pharmacy NPI#
1234567890

*Enrollment Type (Please Check One)
○ New Certification ○ Change in Authorized Representative

*Pharmacy Name
University Hospital

Pharmacy Identifier

DEA#

HIN

Pharmacy Type (Select one)
○ Inpatient Hospital Pharmacy ○ Outpatient Hospital Pharmacy ○ Specialty Pharmacy
◉ **Other (please specify)**

*Other Pharmacy Type
Other

*Address Line 1

Address Line 2

*City

*State
-- Please Select --

*Zip Code

*Phone

*Fax

Ship To Information

*Ship To Contact Name

☑ Ship To Address - Same as above

Authorized Representative Information (must not be a certified Prescriber)

*First Name

*Last Name

*Credentials
○ RPh ○ PharmD ○ RN ◉ **Other (please specify)**

*Other Credentials
Please Specify

*Phone

*Fax

*Email

Authorized Representative Responsibilities

As the Authorized Representative, I must:

To become certified to dispense:

- Enroll in the VANFLYTA REMS by completing the ***Pharmacy Enrollment Form*** and submitting it to the VANFLYTA REMS.
- Train all relevant staff involved in dispensing on the VANFLYTA REMS requirements.
- Establish processes and procedures to verify the prescriber is certified.

Before Dispensing, all staff must:

- Verify the prescriber is certified through the processes and procedures established as a requirement of the VANFLYTA REMS.

At all times, staff must:

- Report serious adverse events suggestive of QT prolongation, Torsades de Pointes, and cardiac arrest to Daiichi Sankyo, Inc.
- Not distribute, transfer, loan, or sell VANFLYTA except to certified pharmacies.
- Maintain records that processes and procedures are in place and are being followed.
- Maintain records of all VANFLYTA dispenses and provide data to the VANFLYTA REMS.
- Comply with audits carried out by Daiichi Sankyo, Inc. or a third party acting on behalf of Daiichi Sankyo, Inc. to ensure that all training, processes, and procedures are in place and are being followed.
- If there is a change in the Authorized Representative, have the new Authorized Representative enroll in the VANFLYTA REMS by completing the ***Pharmacy Enrollment Form***.

*Authorized Representative Name

Please use your mouse or stylus to sign below

Clear Signature

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Pharmacies

Thank you for submitting your information to enroll in the VANFLYTA REMS.

A confirmation of this submission has been sent to the email address provided.

You can expect to receive an email with a link to create your online account.

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Reference ID: 5212288

Certified Participant Locator

*Please select a certified participant to locate

○ Prescriber ○ Pharmacy

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Reference ID: 5212288

Certified Participant Locator

*Please select a certified participant to locate

(•) Prescriber ( ) Pharmacy

Please enter a street address, city, state, or Zip Code you would like to search for.

*Find a Prescriber near

*Search Radius

Within 25 miles

SEARCH

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Reference ID: 5212288

Certified Participant Locator

*Please select a certified participant to locate

(•) Prescriber ( ) Pharmacy

Please enter a street address, city, state, or Zip Code you would like to search for.

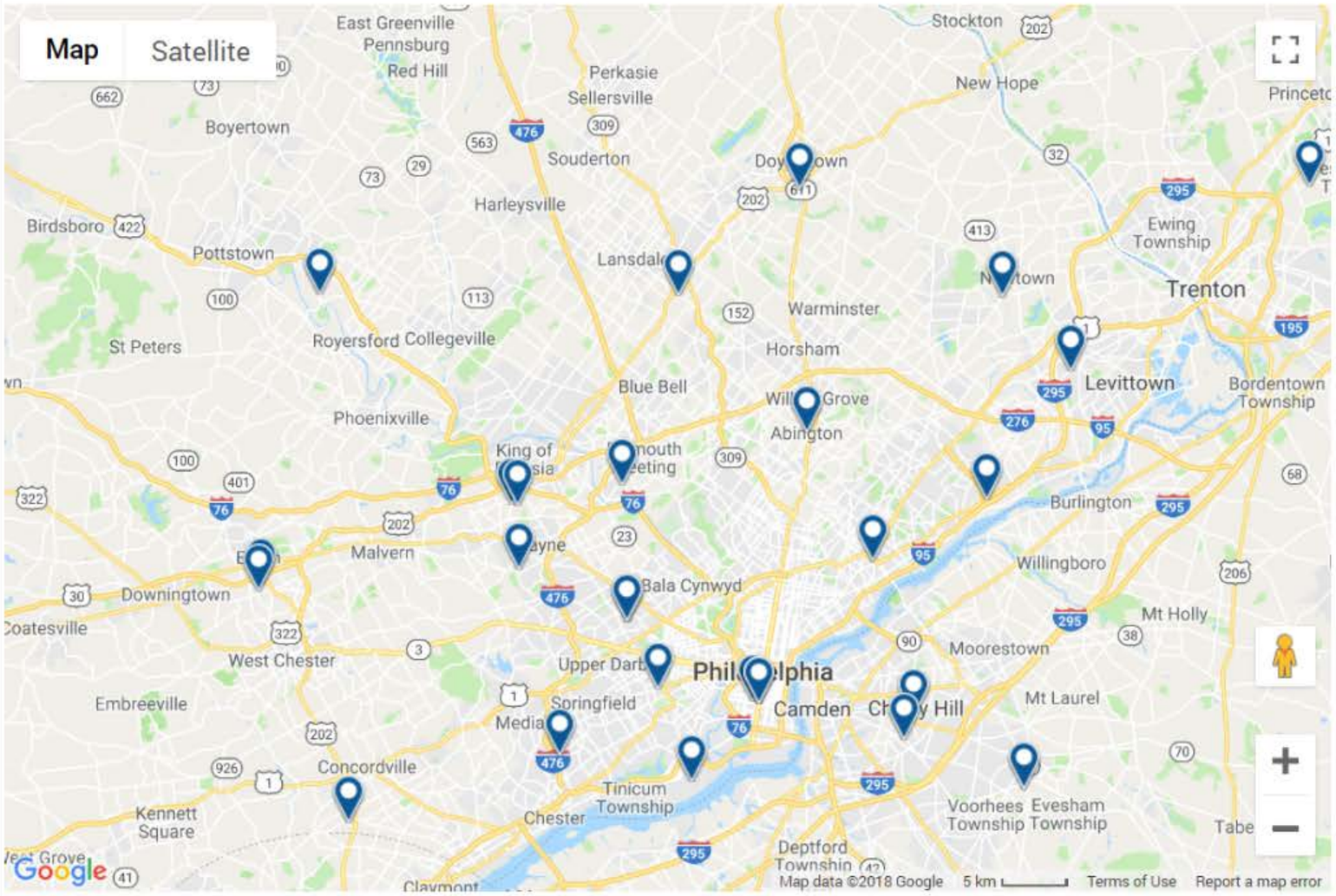
*Find a Prescriber near

12345

*Search Radius

Within 25 miles

SEARCH



PRESCRIBER NAME — 75.1 miles
100 Main St
Blue Bell, PA 19422
555 555-1212
DIRECTIONS

PRESCRIBER NAME — 75.6 miles
100 Main St
Blue Bell, PA 19422
555 555-1212
DIRECTIONS

PRESCRIBER NAME — 75.6 miles
100 Main St
Blue Bell, PA 19422
555 555-1212
DIRECTIONS

PRESCRIBER NAME — 75.6 miles
100 Main St
Blue Bell, PA 19422
555 555-1212
DIRECTIONS

PRESCRIBER NAME — 76.2 miles
100 Main St
Blue Bell, PA 19422
DIRECTIONS

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Reference ID: 5212288

Certified Participant Locator

*Please select a certified participant to locate

○ Prescriber ◉ **Pharmacy**

Pharmacies

Pharmacy Name	Phone Number
ABC Pharmacy	555 555-1212

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Contact Us

Phone

1-855-212-6670

Fax

1-855-382-6017

Hours of Operation

Monday - Friday
8:00 AM—8:00 PM Eastern

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This feature is coming soon.

To enroll in the VANFLYTA REMS, please download the ***Enrollment Form*** from the VANFLYTA REMS website and submit via fax or email.

Please contact the VANFLYTA REMS at 1-855-810-8064 with any questions.

Register

Don't have an online account?

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Online registration is required for Prescribers only.

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*National Provider Identifier (NPI #)

1234567890

Prescriber Information

*First Name

*Last Name

*Credentials (please select one)

○ MD ○ DO ○ NP ○ PA ○ Other, Please specify

*Specialty (please select one)

○ Oncologist ○ Hematologist ○ Other, Please specify

*Office Phone Number

*Office Fax Number

*Email Address

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*Last Name

*Credentials (please select one)

○ MD ○ DO ○ NP ○ PA ◉ **Other, Please specify**

*Credentials Other

Other

*Specialty (please select one)

○ Oncologist ○ Hematologist ◉ **Other, Please specify**

*Specialty Other

Other

*Office Phone Number

*Office Fax Number

*Email Address

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Register

Thank you for submitting your information to create your web account for the VANFLYTA REMS.

A confirmation of this submission has been sent to the Email address provided. You can expect to receive an Email with a link to complete your registration.

If you do not receive the Email within the next few hours, or would like to update your enrollment information at any time, please contact the VANFLYTA REMS at 1-855-212-6670.

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MARC R THEORET
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