The VANFLYTA REMS

A **one-time** training for: Prescribers, Pharmacies, and Wholesalers/Distributors before prescribing, dispensing, or distributing VANFLYTA*

ENROLL TODAY AT **www.VANFLYTAREMS.com**
OR BY CALLING **1-855-212-6670**

*Pharmacies: If the person designated as the Authorized Representative changes, a new representative from your organization must be trained and certified.

VANFLYTA®
quizartinib tablets
26.5 mg | 17.7 mg

Indication

VANFLYTA® (quizartinib) is 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.

Important Safety Information

WARNING: QT PROLONGATION, TORSADES DE POINTES, and CARDIAC ARREST

- **VANFLYTA prolongs the QT interval in a dose- and concentration-related manner. Prior to VANFLYTA administration and periodically, monitor for hypokalemia or hypomagnesemia, and correct deficiencies. Perform electrocardiograms (ECGs) to monitor the QTc at baseline, weekly during induction and consolidation therapy, weekly for at least the first month of maintenance, and periodically thereafter.**
- **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.**
- **Because of the risk of QT prolongation, VANFLYTA is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the VANFLYTA REMS.**

Please see Important Safety Information and Full Prescribing Information, including Boxed WARNINGS, and Medication Guide.

What is the VANFLYTA REMS?

REMS (Risk Evaluation and Mitigation Strategy) is a drug safety program that helps to ensure that the benefits of the medication outweigh its risks. The goals of the VANFLYTA REMS are to mitigate the serious risks of QT prolongation, torsades de pointes, and cardiac arrest through education of optimal risk mitigation strategies, including QTc interval monitoring, monitoring and correction of hypokalemia and hypomagnesemia, dose modification, and screening for drug interactions.

See page 4 for REMS requirements for Wholesalers/Distributors

For Prescribers

Become certified at www.VANFLYTAREMS.com with a one-time enrollment to prescribe VANFLYTA:

1. Review the US Prescribing Information (USPI) for VANFLYTA.
2. Review the REMS Prescriber Training Program.
3. Successfully complete the Prescriber Knowledge Assessment and submit it to the REMS.
4. Enroll by completing the Prescriber Enrollment Form and submitting it to the REMS.

Before treatment initiation (first dose) with VANFLYTA:

1. 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
   - The need to carry the Patient Wallet Card at all times
2. Complete the Patient Wallet Card and provide the Patient Wallet Card to the Patient.

During treatment:

Report serious adverse events suggestive of QT prolongation, torsades de pointes, and cardiac arrest to Daiichi Sankyo, Inc.

Important Safety Information

Contraindications

- VANFLYTA is contraindicated in patients with severe hypokalemia, severe hypomagnesemia, long QT syndrome, or in patients with a history of ventricular arrhythmias or torsades de pointes.

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For Pharmacies

Become certified to dispense at www.VANFLYTAREMS.com:

1. Designate an Authorized Representative to carry out the certification process and oversee implementation and compliance with the VANFLYTA REMS requirements on behalf of the Pharmacy.
2. Have the Authorized Representative enroll by completing the Pharmacy Enrollment Form and submitting it to the REMS at www.VANFLYTAREMS.com.
3. Train all relevant staff involved in dispensing VANFLYTA on the REMS requirements prior to dispensing.
4. Establish processes and procedures to verify the Prescriber is certified.
5. If the Authorized Representative changes, the new Authorized Representative must enroll in the REMS by completing the Pharmacy Enrollment Form.

Before dispensing:

Verify the Prescriber is certified through the processes and procedures established as a requirement of the REMS.

At all times:

1. Report serious adverse events suggestive of QT prolongation, torsades de pointes, and cardiac arrest to Daiichi Sankyo, Inc.
2. Do not distribute, transfer, loan, or sell VANFLYTA except to certified Pharmacies.
3. Maintain records that processes and procedures are in place and are being followed.
4. Maintain records of all VANFLYTA dispenses and provide data to the REMS.
5. Comply with audits to ensure that all training, processes, and procedures are in place and are being followed.

Important Safety Information

Warnings and Precautions

QT Prolongation, Torsades de Pointes, and Cardiac Arrest (See BOXED WARNING)

- VANFLYTA prolongs the QT interval in a dose- and concentration-dependent manner. The mechanism of QTc interval prolongation is via inhibition of the slow delayed rectifier potassium current, I_{Ks}, as compared to all other medications that prolong the QTc interval, which is via the rapid delayed rectifier potassium current, I_{Kr}.

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For Wholesalers/Distributors

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.
3. Distribute VANFLYTA 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 to the REMS at specified intervals.
6. Comply with audits to ensure that all processes and procedures are in place and are being followed.

See pages 2-3 for The REMS requirements for Prescribers and for Pharmacies

Enroll in the REMS today to ensure you can prescribe VANFLYTA

For more information and to enroll, visit **www.VANFLYTAREMS.com** or call the REMS Coordinating Center at **1-855-212-6670**

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- **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.**
- **Because of the risk of QT prolongation, VANFLYTA is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the VANFLYTA REMS.**

To report SUSPECTED ADVERSE REACTIONS, contact Daiichi Sankyo, Inc., at 1-877-437-7763 or the FDA at 1-800-FDA-1088 or fda.gov/medwatch.

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Warnings and Precautions

QT Prolongation, Torsades de Pointes, and Cardiac Arrest (See BOXED WARNING)

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- The level of QTc prolongation with VANFLYTA that predicts the risk of cardiac arrhythmias is unclear. 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. Torsades de pointes, ventricular fibrillation, cardiac arrest, and sudden death have occurred in patients treated with VANFLYTA.
- Among 1,081 VANFLYTA-treated AML patients in clinical trials, severe cardiac arrhythmias occurred primarily during induction and included torsades de pointes (0.2%), cardiac arrest (0.6%, including 0.4% fatal), and ventricular fibrillation (0.1%).

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Important Safety Information (cont.)

Warnings and Precautions (cont.)

QT Prolongation, Torsades de Pointes, and Cardiac Arrest (See BOXED WARNING) (cont.)

- Of the 265 patients who received VANFLYTA in the clinical trial, 2.3% had a QTcF >500 ms and 10% had an increase of >60 ms from baseline. The trial excluded patients with a QTcF ≥450 ms or other factors that increased the risk of QT prolongation or arrhythmic events (eg, NYHA Class III/IV congestive heart failure, hypokalemia, or a family history of long QT interval syndrome).
- Avoid use in patients who are at significant risk of developing torsades de pointes, including uncontrolled or significant cardiac disease, recent myocardial infarction, heart failure, unstable angina, bradyarrhythmias, tachyarrhythmias, uncontrolled hypertension, high-degree atrioventricular block, severe aortic stenosis, or uncontrolled hypothyroidism.
- 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 prior to initiation, once weekly for at least the first month following dose initiation and escalation, and as clinically indicated thereafter.
- 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.
- Monitor and correct hypokalemia and hypomagnesemia prior to and during treatment. Maintain electrolytes in the normal range. Monitor electrolytes and ECGs more frequently in patients who experience diarrhea or vomiting.
- Reduce the VANFLYTA dose if QTc increases to greater than 480 ms and less than 500 ms. Interrupt and reduce the VANFLYTA dose if QTc increases to greater than 500 ms. Permanently discontinue VANFLYTA in patients who develop recurrent QTc greater than 500 ms or QTc interval prolongation with signs or symptoms of life-threatening arrhythmia.

VANFLYTA REMS

- Requirements include:
  - Prescribers must be certified in the VANFLYTA REMS by enrolling and completing training.
  - Prescribers must counsel patients receiving VANFLYTA about the risk of QT prolongation, torsades de pointes, and cardiac arrest, and provide patients with a Patient Wallet Card.
  - Pharmacies that dispense VANFLYTA must be certified with the VANFLYTA REMS and must verify prescribers are certified through the VANFLYTA REMS.
- Further information is available at www.VANFLYTAREMS.com or by telephone at 1-855-212-6670.

Embryo-Fetal Toxicity

- Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with VANFLYTA and for 7 months after the last dose. Advise males with female partners of reproductive potential to use effective contraception during treatment with VANFLYTA and for 4 months after the last dose.

Adverse Reactions

- The most common (>20%) adverse reactions, including laboratory abnormalities, were lymphocytes decreased (60%), potassium decreased (59%), albumin decreased (53%), phosphorus decreased (52%), alkaline phosphatase increased (51%), magnesium decreased (44%), febrile neutropenia (44%), diarrhea (42%), mucositis (38%), nausea (34%), calcium decreased (33%), abdominal pain (30%), sepsis (30%), neutropenia (29%), headache (28%), creatine phosphokinase increased (26%), vomiting (25%), and upper respiratory tract infection (21%).

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Important Safety Information (cont.)

Drug Interactions

- **Strong CYP3A Inhibitors:** Reduce the VANFLYTA dose due to increased quizartinib systemic exposure.
- **Strong or Moderate CYP3A Inducers:** Avoid concomitant use due to decreased quizartinib systemic exposure.
- **QT Interval Prolonging Drugs:** VANFLYTA Prolongs the QT/QTc interval. Monitor patients more frequently with ECG if co-administration with drugs known to prolong the QT interval is required.
- **Breast Cancer Resistant Protein (BCRP) substrates:** Avoid concomitant use as it may increase the risk of BCRP substrate-associated adverse reactions. If concomitant use is unavoidable, monitor patients more frequently for BCRP substrate-associated adverse reactions and decrease the BCRP substrate dosage(s) according to their respective Prescribing Information.

Use in Specific Populations

- Advise women not to breastfeed during treatment with VANFLYTA and for one month after the last dose.

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