Evolent Clinical Guideline 3182 for Vanflyta™ (quizartinib)

Guideline Number:	Applicable Codes	
Evolent_CG_3182		
"Evolent" refers to Evolent Health LLC and Evolent Specialty Services, Inc. 		
Original Date:	**Last Revised Date:**	**Implementation Date:**
September 2023	September 2025	September 2025

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STATEMENT

Purpose

To define and describe the accepted indications for Vanflyta (quizartinib) usage in the treatment of cancer, including FDA approved indications, and off-label indications.

Evolent is responsible for processing all medication requests from network ordering providers. Medications not authorized by Evolent may be deemed as not approvable and therefore not reimbursable.

The use of this drug must be supported by one of the following: FDA approved product labeling, CMS-approved compendia, National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO) clinical guidelines, or peer-reviewed literature that meets the requirements of the CMS Medicare Benefit Policy Manual Chapter 15.

INDICATIONS

Continuation requests for a not-approvable medication shall be exempt from this Evolent policy provided

- The member has not experienced disease progression on the requested medication AND
- The requested medication was used within the last year without a lapse of more than 30 days of having an active authorization AND
- Additional medication(s) are not being added to the continuation request.

Acute Myeloid Leukemia (AML)

- Vanflyta (quizartinib) may be used with standard cytarabine and anthracycline induction and cytarabine consolidation, and as maintenance monotherapy following consolidation chemotherapy, for the treatment of adult members with newly diagnosed acute myeloid leukemia (AML) that is FLT3 internal tandem duplication (ITD)-positive, as detected by an FDA-approved test.

CONTRAINDICATIONS/WARNINGS

- Contraindications
  - Severe hypokalemia, severe hypomagnesemia, long QT syndrome, or a history of ventricular arrhythmias or torsades de pointes.
- US Boxed Warning
  - Quizartinib prolongs the QT interval in a dose- and concentration-related manner. Prior to quizartinib administration and periodically, monitor for hypokalemia or hypomagnesemia, and correct deficiencies. Perform 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 quizartinib. Do not administer quizartinib to patients with severe hypokalemia, severe

hypomagnesemia, or long QT syndrome. Do not initiate treatment with quizartinib or escalate the quizartinib dose if the QTcF is >450 msec. Monitor ECGs more frequently if concomitant use of drugs known to prolong the QT interval is required. Reduce the quizartinib dose when used concomitantly with strong CYP3A inhibitors, as they may increase quizartinib exposure.

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

EXCLUSION CRITERIA

- Disease progression while taking Vanflyta (quizartinib).
- Dosing exceeds single dose limit of Vanflyta (quizartinib) 53 mg.
- Treatment exceeds the maximum limit of 28 (17.7 mg) or 56 (26.5 mg) tablets/month.
- Investigational use of Vanflyta (quizartinib) with an off-label indication that is not sufficient in evidence or is not generally accepted by the medical community. Sufficient evidence that is not supported by CMS recognized compendia or acceptable peer reviewed literature is defined as any of the following:
  - Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.
  - Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.
  - Whether the reported study outcomes represent clinically meaningful outcomes experienced by patients. Generally, the definitions of Clinically Meaningful outcomes are those recommended by ASCO, e.g., Hazard Ratio of less than 0.80 and the recommended survival benefit for OS and PFS should be at least 3 months.
  - Whether the experimental design, considering the drugs and conditions under investigation, is appropriate to address the investigative question. (For example, in some clinical studies, it may be unnecessary or not feasible to use randomization, double blind trials, placebos, or crossover).
  - That non-randomized clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of drugs.
  - That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
  - That abstracts (including meeting abstracts) without the full article from the approved peer-reviewed journals lack supporting clinical evidence for determining accepted uses of drugs.

CODING AND STANDARDS

Codes

- J8999 - quizartinib

Applicable Lines of Business

☐	CHIP (Children's Health Insurance Program)
☒	Commercial
☒	Exchange/Marketplace
☒	Medicaid
☐	Medicare Advantage

POLICY HISTORY

Date	Summary
September 2025	• Converted to new Evolent guideline template • This guideline replaces UM ONC_1484 Vanflyta (quizartinib) • Updated indication section • Added maximum dosage form quantities to exclusion criteria • Updated references
September 2024	• Updated exclusion criteria

LEGAL AND COMPLIANCE

Guideline Approval

Committee

Reviewed / Approved by Evolent Specialty Clinical Guideline Review Committee

Disclaimer

Evolent Clinical Guidelines do not constitute medical advice. Treating health care professionals are solely responsible for diagnosis, treatment, and medical advice. Evolent uses Clinical Guidelines in accordance with its contractual obligations to provide utilization management. Coverage for services varies for individual members according to the terms of their health care coverage or government program. Individual members' health care

coverage may not utilize some Evolent Clinical Guidelines. Evolent clinical guidelines contain guidance that requires prior authorization and service limitations. A list of procedure codes, services or drugs may not be all inclusive and does not imply that a service or drug is a covered or non-covered service or drug. Evolent reserves the right to review and update this Clinical Guideline in its sole discretion. Notice of any changes shall be provided as required by applicable provider agreements and laws or regulations. Members should contact their Plan customer service representative for specific coverage information.

REFERENCES

1. Erba HP, et al; QuANTUM-First Study Group. Quizartinib plus chemotherapy in newly diagnosed patients with FLT3-internal-tandem-duplication-positive acute myeloid leukaemia (QuANTUM-First): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet*. 2023 May 13;401(10388):1571-1583. doi: 10.1016/S0140-6736(23)00464-6.
2. Vanflyta prescribing information. Daiichi Sankyo, Inc., Basking Ridge, NJ 2024.
3. Clinical Pharmacology Elsevier Gold Standard 2025.
4. Micromedex® Healthcare Series: Micromedex Drugdex Ann Arbor, Michigan 2025.
5. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium 2025.
6. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD 2025.
7. Ellis LM, et al. American Society of Clinical Oncology perspective: Raising the bar for clinical trials by defining clinically meaningful outcomes. *J Clin Oncol*. 2014 Apr 20;32(12):1277-80.
8. Medicare Benefit Policy Manual Chapter 15 Covered Medical and Other Health Services: **https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/bp102c15.pdf**.
9. Current and Resolved Drug Shortages and Discontinuations Reported to the FDA: **http://www.accessdata.fda.gov/scripts/drugshortages/default.cfm**.