Instructions for General Electronic Health Record (EHR) Systems to Update or Create Order Sets With TEPMETKO®

INDICATION

TEPMETKO is indicated for the treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) harboring mesenchymal-epithelial transition (*MET*) exon 14 skipping alterations.

SELECT IMPORTANT SAFETY INFORMATION

TEPMETKO can cause **interstitial lung disease (ILD)/pneumonitis**, which can be fatal. Monitor patients for new or worsening pulmonary symptoms indicative of ILD/pneumonitis (eg, dyspnea, cough, fever). Immediately withhold TEPMETKO in patients with suspected ILD/pneumonitis and permanently discontinue if no other potential causes of ILD/pneumonitis are identified. ILD/pneumonitis occurred in 2% of patients treated with TEPMETKO, with one patient experiencing a Grade 3 or higher event; this event resulted in death.

Please see Important Safety Information on page 8.
Click for full Prescribing Information.

TEPMETKO® (tepotinib) 225 mg Tablets

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1. Background

This document is intended to provide medical groups with instructions to update metastatic non-small cell lung cancer (NSCLC) order sets with TEPMETKO® within the approved indication and consistent with the Prescribing Information. This document is not intended to provide any clinical advice or clinical recommendations, which are solely the responsibility of the healthcare professionals.

These instructions are specific to metastatic NSCLC and for general EHR systems and are not appropriate for other conditions, treatments, or therapeutic areas.

2. Considerations

The process outlined below is variable and not all steps will apply to every medical group. Any steps or settings below that are not part of a medical group's standard process should be excluded or modified accordingly. Any questions should be directed to the appropriate service provider. The medical group is solely responsible for implementing, testing, monitoring, and the ongoing operation of any EHR tools.

Please consult the most recent version of the TEPMETKO package insert for full medication details. The most recent version can be found at **https://www.emdserono.com/us-en/pi/tepmetko-pi.pdf**.

A new order set will be available once the optimization process is complete. If the original order set used to update or create the new order set includes TEPMETKO, confirm the original order set is retired or removed from the EHR production system according to the medical group's EHR governing principles.

3. General EHR Instructions

Order sets are commonly used in the management of oncology patients. After initial release, order sets may benefit from a clinical update. The optimization of order sets is a common process and provides an opportunity to incorporate treatment updates. Order sets are typically modified at the system level to help reduce practice variation.

Typically, a medical group will conduct a clinical review process to confirm and approve the suggested optimization. Various stakeholders may participate in reviewing order set optimization requests prior to implementation.

Regimen Name:	*TEPMETKO for metastatic NSCLC with METex14 skipping alterations*
Regimen Description:	*TEPMETKO for metastatic NSCLC with METex14 skipping alterations*
Indication/Disease:	*Metastatic NSCLC with METex14 skipping alterations*
References:	TEPMETKO Prescribing Information: *TEPMETKO dosing and administration information (https://www.emdserono.com/us-en/pi/tepmetko-pi.pdf)* TEPMETKO Resources for Healthcare Providers (HCPs) and Patients: *See URL for additional TEPMETKO Resources for Healthcare Providers (HCPs) and Patients such as a Treatment Guide, Patient Brochure, and Patient Savings Offers (https://www.tepmetko.com/us-en/home.html)*
Regimen Keywords:	Metastatic NSCLC (non-small cell lung cancer)
Treatment Conditions:	**Patient Selection for *MET*ex14 Skipping Alterations** • Select patients for treatment with TEPMETKO based on the presence of *MET* exon 14 skipping alterations in plasma or tumor specimens. Testing for the presence of *MET* exon 14 skipping alterations in plasma specimens is recommended only in patients for whom a tumor biopsy cannot be obtained. If an alteration is not detected in a plasma specimen, reevaluate the feasibility of biopsy for tumor tissue testing. An FDA-approved test for detection of *MET* exon 14 skipping alterations in NSCLC for selecting patients for treatment with TEPMETKO is not available.

FDA=US Food and Drug Administration.

3. General EHR Instructions (cont'd)

Treatment Conditions (cont'd):

Recommended Dosage

- The recommended dosage of TEPMETKO is 450 mg orally once daily with food until disease progression or unacceptable toxicity.
- Instruct patients to take their dose of TEPMETKO at approximately the same time every day and to swallow tablets whole. Do not chew, crush, or split tablets.
- Advise patients not to make up a missed dose within 8 hours of the next scheduled dose.
- If vomiting occurs after taking a dose of TEPMETKO, advise patients to take the next dose at the scheduled time.

Dose Modifications for Adverse Reactions

- The recommended dose reduction of TEPMETKO for the management of adverse reactions is 225 mg orally once daily. Permanently discontinue TEPMETKO in patients who are unable to tolerate 225 mg orally once daily.
- The recommended dosage modifications of TEPMETKO for adverse reactions are provided in Table 1.

Administration to Patients Who Have Difficulty Swallowing Solids

- Place TEPMETKO tablet(s) in a glass containing 30 mL (1 ounce) of non-carbonated water. No other liquids should be used or added. Stir, without crushing, until the tablet(s) is dispersed into small pieces (tablets will not completely dissolve) and drink immediately or within 1 hour. Swallow the tablet dispersion. Do not chew pieces of the tablet. Rinse the glass with an additional 30 mL and drink immediately ensuring no residue remains in the glass and the full dose is administered.
- If an administration via a naso-gastric tube (with at least 8 French gauge) is required, disperse the tablet(s) in 30 mL of non-carbonated water as described above. Administer the 30 mL of liquid immediately or within 1 hour as per naso-gastric tube manufacturer's instructions. Immediately rinse twice with 30 mL each time to ensure that no residue remains in the glass or syringe and the full dose is administered.

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Table 1: Recommended TEPMETKO Dosage Modifications for Adverse Reactions

Adverse Reaction	Severity	Dose Modification
Interstitial lung disease (ILD)/ pneumonitis *[see Warnings and Precautions (5.1)]*	Any grade	Withhold TEPMETKO if ILD is suspected. Permanently discontinue TEPMETKO if ILD is confirmed.
Increased ALT and/or AST without increased total bilirubin *[see Warnings and Precautions (5.2)]*	Grade 3	Withhold TEPMETKO until recovery to baseline ALT/AST. If recovered to baseline within 7 days, then resume TEPMETKO at the same dose; otherwise resume TEPMETKO at a reduced dose.
	Grade 4	Permanently discontinue TEPMETKO.
Increased ALT and/or AST with increased total bilirubin in the absence of cholestasis or hemolysis *[see Warnings and Precautions (5.2)]*	ALT and/or AST greater than 3 times ULN with total bilirubin greater than 2 times ULN	Permanently discontinue TEPMETKO.
Increased total bilirubin without concurrent increased ALT and/or AST *[see Warnings and Precautions (5.2)]*	Grade 3	Withhold TEPMETKO until recovery to baseline bilirubin. If recovered to baseline within 7 days, then resume TEPMETKO at a reduced dose; otherwise permanently discontinue.
	Grade 4	Permanently discontinue TEPMETKO.
Increased lipase or amylase *[see Warnings and Precautions (5.3)]*	Grade 3	Withhold TEPMETKO until ≤ Grade 2 or baseline. If recovered to baseline or ≤ Grade 2 within 14 days, resume TEPMETKO at a reduced dose; otherwise permanently discontinue TEPMETKO.
	Grade 4	Permanently discontinue TEPMETKO.
Pancreatitis *[see Warnings and Precautions (5.3)]*	Grade 3 or 4	Permanently discontinue TEPMETKO.
Other adverse reactions *[see Adverse Reactions (6.1)]*	Grade 2	Maintain dose level. If intolerable, consider withholding TEPMETKO until resolved, then resume TEPMETKO at a reduced dose.
	Grade 3	Withhold TEPMETKO until resolved, then resume TEPMETKO at a reduced dose.
	Grade 4	Permanently discontinue TEPMETKO.

Safety Information: Refer to section 5 and section 6 of the Prescribing Information

Warnings: Refer to section 5 of the Prescribing Information:

- Warnings and Precautions & Adverse Reactions
  See section 5 of the TEPMETKO Prescribing Information for detailed information
  - Interstitial lung disease (ILD)/pneumonitis
  - Hepatotoxicity
  - Pancreatic toxicity
  - Embryo-fetal toxicity

TEPMETKO schedule:

- 450 mg orally once daily with food
- Continue treatment until disease progression or unacceptable toxicity

ALT=alanine aminotransferase; AST=aspartate aminotransferase; ULN=upper limit of normal.

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The medical groups shall be solely responsible for implementation, testing, and monitoring of the instructions to ensure proper orientation in each medical group's EHR system.

After completing the TEPMETKO order set optimization process, a new TEPMETKO order set will be available. If the original order set used to update or create the new TEPMETKO order set included TEPMETKO, confirm the original order set is retired or removed from the EHR production system according to the medical group's EHR governing principles.

Capabilities, functionality, and setup (customization) for each individual EHR system vary. EMD Serono is not responsible for revising the implementation instructions it provides to any medical group.

While EMD Serono tests its implementation instructions on multiple EHR systems, the instructions are not guaranteed to work for all available EHR systems, and EMD Serono shall have no liability therefor.

While EHRs may assist healthcare providers in identifying appropriate patients for consideration of assessment and treatment, the decision and action should ultimately be made by a healthcare provider in consultation with the patient after a review of the patient's records to determine eligibility.

These instructions have not been designed and are not tools and/or solutions for meeting Advancing Care Information, and/or any other quality/accreditation requirement.

Reference to these EHRs is not intended to imply affiliation with or sponsorship of the EHR manufacturer and/or its affiliates.

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TEPMETKO can cause **hepatotoxicity**, which can be fatal. Monitor liver function tests (including alanine aminotransferase [ALT], aspartate aminotransferase [AST], and total bilirubin) prior to the start of TEPMETKO, every 2 weeks during the first 3 months of treatment, then once a month or as clinically indicated, with more frequent testing in patients who develop increased transaminases or total bilirubin. Based on the severity of the adverse reaction, withhold, dose reduce, or permanently discontinue TEPMETKO. Increased ALT/ increased AST occurred in 18% of patients treated with TEPMETKO. Grade 3 or 4 increased ALT/AST occurred in 4.7% of patients. A fatal adverse reaction of hepatic failure occurred in one patient (0.2%). The median time-to-onset of Grade 3 or higher increased ALT/AST was 47 days (range 1 to 262).

TEPMETKO can cause **pancreatic toxicity** in the form of elevations in amylase and lipase levels. Increased amylase and/or lipase occurred in 13% of patients, with Grade 3 and 4 increases occurring in 5% and 1.2% of patients, respectively. Monitor amylase and lipase levels at baseline and regularly during treatment with TEPMETKO and temporarily withhold, dose reduce, or permanently discontinue based on severity of the adverse event.

TEPMETKO can cause **embryo-fetal toxicity**. Based on findings in animal studies and its mechanism of action, TEPMETKO can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential or males with female partners of reproductive potential to use effective contraception during treatment with TEPMETKO and for one week after the last dose.

Avoid concomitant use of TEPMETKO with certain **P-gp substrates** where minimal concentration changes may lead to serious or life-threatening toxicities. If concomitant use is unavoidable, reduce the P-gp substrate dosage if recommended in its approved product labeling.

Fatal adverse reactions occurred in one patient (0.3%) due to pneumonitis, one patient (0.3%) due to hepatic failure, one patient (0.3%) due to dyspnea from fluid overload, one patient (0.3%) due to pneumonia, one patient (0.3%) due to sepsis, and one patient (0.3%) from unknown cause.

Serious adverse reactions occurred in 51% of patients who received TEPMETKO. Serious adverse reactions in >2% of patients included pleural effusion (6%), pneumonia (6%), edema (5%), general health deterioration (3.8%), dyspnea (3.5%), musculoskeletal pain (2.9%), and pulmonary embolism (2.2%).

The most common adverse reactions (≥20%) in patients who received TEPMETKO were edema (81%), nausea (31%), fatigue (30%), musculoskeletal pain (30%), diarrhea (29%), dyspnea (24%), rash (21%), and decreased appetite (21%).

Clinically relevant adverse reactions in <10% of patients who received TEPMETKO included ILD/pneumonitis, fever, dizziness, pruritus, and headache.

Selected laboratory abnormalities (≥20%) from baseline in patients receiving TEPMETKO in descending order were: decreased albumin (81%), increased creatinine (60%), decreased lymphocytes (57%), increased alkaline phosphatase (ALP) (52%), increased ALT (50%), increased AST (40%), decreased sodium (36%), decreased hemoglobin (31%), increased gamma-glutamyltransferase (GGT) (29%), increased potassium (26%), increased amylase (25%), decreased leukocytes (25%), decreased platelets (24%), and increased lipase (21%).

The most common Grade 3-4 laboratory abnormalities (≥2%) in descending order were: decreased lymphocytes (15%), decreased albumin (9%), decreased sodium (9%), increased GGT (6%), increased amylase (5%), increased lipase (5%), increased ALT (4.9%), increased AST (3.6%), and decreased hemoglobin (3.6%).

Please see the full Prescribing Information for TEPMETKO.

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