TEPMETKO®
(tepotinib)

**For ALL eligible *MET*ex14+ mNSCLC patients, consider TEPMETKO® (tepotinib)**

# The ONLY approved once-daily oral *MET* inhibitor[1]*

## *Dosing and Treatment Management Guide*

*Recommended dose is 450 mg once daily with food; please see page 2 to learn more.[1]
mNSCLC=metastatic non-small cell lung cancer.

## 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. This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.

## SELECTED 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 2.2% 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 throughout and on page 7.**
**Click for full Prescribing Information.**

*For all eligible* MET*ex14+ mNSCLC patients, consider*

# TEPMETKO® (tepotinib)—The only approved once-daily oral *MET* inhibitor[1]

## Patient selection[1]

Select patients for treatment with TEPMETKO based on the presence of *MET*ex14 skipping alterations in plasma or tumor specimens. Testing for the presence of *MET*ex14 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.*


## Once-daily dosing[1]

The recommended dosage of TEPMETKO is 450 mg (two 225 mg tablets) orally once daily with food until disease progression or unacceptable toxicity.


## Take TEPMETKO with food[1]

Instruct patients to take their dose 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, advise patients to take the next dose at the scheduled time.

*An FDA-approved test for detection of *MET*ex14 skipping alterations in NSCLC for selecting patients for treatment with TEPMETKO is not available.
mNSCLC=metastatic non-small cell lung cancer.

## SELECTED SAFETY INFORMATION (cont'd)

TEPMETKO can cause **hepatotoxicity**, which can be fatal. Monitor liver function tests (including ALT, 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 alanine aminotransferase (ALT)/increased aspartate aminotransferase (AST) occurred in 13% of patients treated with TEPMETKO. Grade 3 or 4 increased ALT/AST occurred in 4.2% 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 30 days (range 1 to 178).

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 final dose.

## Dose modifications for adverse reactions[1]

The recommended dose reduction is from two 225 mg tablets to one 225 mg tablet orally once daily. Permanently discontinue in patients who are unable to tolerate the 225 mg dose. Management of some adverse reactions may require temporary interruption or permanent discontinuation.

| Adverse reaction | Severity | Dose modification |
|---|---|---|
| Interstitial lung disease (ILD)/Pneumonitis | Any grade | Withhold TEPMETKO® (tepotinib) if ILD is suspected.<br><br>Permanently discontinue TEPMETKO if ILD is confirmed. |
| Increased ALT and/or AST without increased total bilirubin | 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 | 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 | Grade 3 | Withhold TEPMETKO until recovery to baseline bilirubin.<br><br>If recovered to baseline within 7 days, then resume TEPMETKO at a reduced dose; otherwise permanently discontinue. |
| | Grade 4 | Permanently discontinue TEPMETKO. |
| Other adverse reactions | 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. |

mNSCLC=metastatic non-small cell lung cancer.

### SELECTED SAFETY INFORMATION (cont'd)

Avoid concomitant use of TEPMETKO with dual strong **CYP3A inhibitors** and **P-gp inhibitors** and strong **CYP3A inducers**. 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 (0.4%) due to pneumonitis, one patient (0.4%) due to hepatic failure, and one patient (0.4%) due to dyspnea from fluid overload.

# Drug interactions with TEPMETKO® (tepotinib)[1]

## Effects of other drugs on TEPMETKO

### Dual Strong CYP3A inhibitors and P-gp Inhibitors

The effect of strong CYP3A inhibitors or P-gp inhibitors on TEPMETKO has not been studied clinically. However, metabolism and in vitro data suggest concomitant use of drugs that are strong CYP3A inhibitors and P-gp inhibitors may increase tepotinib exposure, which may increase the incidence and severity of adverse reactions of TEPMETKO. Avoid concomitant use of TEPMETKO with dual strong CYP3A inhibitors and P-gp inhibitors.

### Strong CYP3A Inducers

The effect of strong CYP3A inducers on TEPMETKO has not been studied clinically. However, metabolism and in vitro data suggest concomitant use may decrease tepotinib exposure, which may reduce TEPMETKO efficacy. Avoid concomitant use of TEPMETKO with strong CYP3A inducers.

## Effects of TEPMETKO on other drugs

### Certain P-gp Substrates

Tepotinib is a P-gp inhibitor. Concomitant use of TEPMETKO increases the concentration of P-gp substrates, which may increase the incidence and severity of adverse reactions of these substrates. 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.

## SELECTED SAFETY INFORMATION (cont'd)

**Serious adverse reactions** occurred in 45% of patients who received TEPMETKO. Serious adverse reactions in >2% of patients included pleural effusion (7%), pneumonia (5%), edema (3.9%), dyspnea (3.9%), general health deterioration (3.5%), pulmonary embolism (2%), and musculoskeletal pain (2%).

**The most common adverse reactions** (≥20%) in patients who received TEPMETKO were edema, fatigue, nausea, diarrhea, musculoskeletal pain, and dyspnea.

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

**Selected laboratory abnormalities** (≥20%) from baseline in patients receiving TEPMETKO in descending order were: decreased albumin (76%), increased creatinine (55%), increased alkaline phosphatase (ALP) (50%), decreased lymphocytes (48%), increased ALT (44%), increased AST (35%), decreased sodium (31%), decreased hemoglobin (27%), increased potassium (25%), increased gamma-glutamyltransferase (GGT) (24%), increased amylase (23%), and decreased leukocytes (23%).

**The most common Grade 3-4 laboratory abnormalities** (≥2%) in descending order were: decreased lymphocytes (11%), decreased albumin (9%), decreased sodium (8%), increased GGT (5%), increased amylase (4.6%), increased ALT (4.1%), increased AST (2.5%), and decreased hemoglobin (2%).

A **clinically relevant laboratory abnormality** in <20% of patients who received TEPMETKO was increased lipase in 18% of patients, including 3.7% Grades 3 to 4.

# Support for eligible TEPMETKO® (tepotinib) patients

**The EMD Serono Oncology Navigation Center™ (ONC) is a patient access and reimbursement support program available to help eligible patients gain appropriate access to TEPMETKO in the United States.***

- Reimbursement Support
- Bridge Program for New Patients with Insurance Delays
- Co-Pay Assistance for Privately Insured Patients
- Patient Assistance Program/Free Drug Program for Eligible Patients

**Our ONC Access Navigators are committed to helping eligible patients access TEPMETKO.**

ONCOLOGY™ navigation center

**OncNavigationCenter.com**
**Phone:** 1-844-662-3631 (844-ONC-EMD1)
**Fax:** 844-501-0062
**Monday–Friday**: 8:00 AM–8:00 PM Eastern Time

Please contact us if you have any questions or fax a completed ONC Enrollment Form to verify patient-specific coverage or request assistance.

Enrollment Forms and complete program information are available through **OncNavigationCenter.com**.

*Additional program rules and restrictions or conditions may apply.

# TEPMETKO® (tepotinib) Warnings & Precautions[1]

The safety profile of TEPMETKO reflects **exposure to TEPMETKO in 448 patients with various solid tumors**. These patients were enrolled in 5 open-label, single-arm studies, in which they received TEPMETKO as a single agent at a dose of 450 mg once daily. **This included 255 patients with NSCLC positive for *MET*ex14 skipping alterations, who received TEPMETKO in VISION.**

## Interstitial lung disease (ILD)/Pneumonitis

ILD/pneumonitis, which can be fatal, occurred in 2.2% of patients treated with TEPMETKO, with one patient experiencing a Grade 3 or higher event that resulted in death. Four patients (0.9%) discontinued TEPMETKO due to ILD/pneumonitis.

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.

## Hepatotoxicity

Hepatotoxicity occurred in patients treated with TEPMETKO. Increased alanine aminotransferase (ALT)/increased aspartate aminotransferase (AST) occurred in 13% of patients treated with TEPMETKO. Grade 3 or 4 increased ALT/AST occurred in 4.2% of patients. A fatal adverse reaction of hepatic failure occurred in one patient (0.2%). Three patients (0.7%) discontinued TEPMETKO due to increased ALT/AST. The median time-to-onset of Grade 3 or higher increased ALT/AST was 30 days (range: 1 to 178).

Monitor liver function tests (including ALT, 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 bilirubin. Based on the severity of the adverse reaction, withhold, dose reduce, or permanently discontinue TEPMETKO.

## Embryo-fetal toxicity

Based on the mechanism of action and findings in animals, TEPMETKO can cause fetal harm when administered to pregnant women. Oral administration of tepotinib during organogenesis in pregnant rabbits resulted in malformations (teratogenicity) and anomalies starting at exposures less than the human exposure based on area under the curve (AUC) at the 450 mg daily clinical dose. 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 following the final dose.

NSCLC=non-small cell lung cancer.

# IMPORTANT SAFETY INFORMATION and INDICATION

## INDICATION

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**Click for full Prescribing Information.**

**Reference: 1.** TEPMETKO [prescribing information]. EMD Serono, Inc., Rockland, MA; 2021.

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## How supplied/Storage and handling[1]

| NDC number | Size |
|---|---|
| 44087-5000-3 | Box of 30 tablets: 3 blister cards each containing 10 tablets |
| 44087-5000-6 | Box of 60 tablets: 6 blister cards each containing 10 tablets |

TEPMETKO tablets: 225 mg tepotinib, white-pink, oval, biconvex film-coated tablet with embossment “M” on one side and plain on the other side.

The blister cards consist of a child-resistant blister foil.

Store TEPMETKO at 20°C-25°C (68°F-77°F); excursions permitted to 15°C-30°C (59°F-86°F) [see USP-NF Controlled Room Temperature]. Store in original package.

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