TEPMETKO® (tepotinib) 225 mg Tablets

SEE ADDITIONAL EXPANDED ANALYSES

ONCE-DAILY DOSING
450 mg

The ONLY approved ONCE-DAILY oral *MET* inhibitor[1]

Recommended dose is 450 mg once daily with food; please see page 12 to learn more.

IT'S METTIME

For all eligible patients with *MET*ex14+ mNSCLC[1]

NCCN PREFERRED

Tepotinib is a National Comprehensive Cancer Network® (NCCN®) preferred treatment in the first-line/subsequent line* setting for patients with *MET*ex14+ mNSCLC (Category 2A)[2†‡§]

*If *MET*ex14+ inhibitors have not previously been given. †Category 2A definition: based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate. ‡See the NCCN Guidelines for detailed recommendations, including other preferred options. §The NCCN Guidelines for NSCLC provide recommendations for certain individual biomarkers that should be tested and recommend testing techniques but do not endorse any specific commercially available biomarker assays or commercial laboratories.[2]

*MET*ex14+=mesenchymal-epithelial transition exon 14 skipping alterations; mNSCLC=metastatic non-small cell lung cancer.

INDICATION

TEPMETKO® (tepotinib) 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.

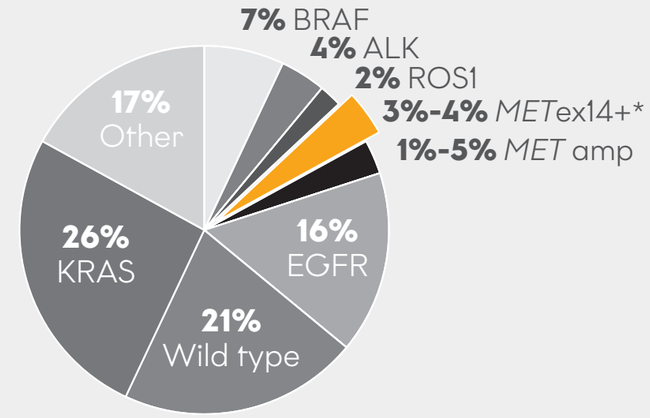
SELECTED IMPORTANT SAFETY INFORMATION

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 2.2% 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 full Prescribing Information enclosed.

Early identification helps inform treatment decisions

*MET*ex14+ should be identified at diagnosis as it plays an important role in NSCLC oncogenesis[3,4]



Prevalence of Oncogenic Drivers in Lung Adenocarcinoma[4-6]

Based on 2023 estimates,
~6,100 to 8,100 patients may be diagnosed with NSCLC harboring *MET*ex14+[7]

3% to 4% of patients may harbor *MET*ex14+[4]

Patients with *MET*ex14+ have been associated with having advanced disease and a poor prognosis.[3]

NCCN

National Comprehensive Cancer Network® (NCCN®) strongly recommends[2]:

- Clinicians obtain molecular testing results for actionable biomarkers in eligible patients with metastatic NSCLC before administering first-line ICI therapy ± chemotherapy, if clinically feasible†
- Targeted therapies for patients with metastatic NSCLC and specific oncogenic drivers independent of PD-L1 levels
- For patients who must immediately start therapy but molecular testing is pending, consider holding immunotherapy for one cycle, unless no driver mutations are confirmed present

**MET*ex14+ is a *MET* gene alteration and its estimated frequency in patients with NSCLC varies between studies. *MET*ex14+ is estimated to occur in 2% of squamous cell carcinomas and 8% to 30% of sarcomatoid carcinomas.[8-10] †The NCCN Guidelines for NSCLC provide recommendations for certain individual biomarkers that should be tested and recommend testing techniques but do not endorse any specific commercially available biomarker assays or commercial laboratories.
ALK=anaplastic lymphoma kinase; BRAF=B-type Raf proto-oncogene; EGFR=epidermal growth factor receptor; ICI=immune checkpoint inhibitor; KRAS=Kirsten rat sarcoma viral oncogene homolog; *MET*=mesenchymal-epithelial transition; *MET* amp=mesenchymal-epithelial transition amplification; *MET*ex14+=mesenchymal-epithelial transition exon 14 skipping alterations; NSCLC=non-small cell lung cancer; PD-L1=programmed death ligand 1; ROS1=c-ros oncogene 1.

Identify *MET*ex14+ at diagnosis

For patients with mNSCLC, *MET*ex14+ identification is critical to help inform treatment decisions[3,4]

All patients with NSCLC should be considered for biomarker testing regardless of:

*MET*ex14+ risk factors

Age[9]
These patients tend to be older than patients with other oncogenic drivers (54 to 65 years of age in ALK, ROS1, EGFR, and KRAS) with an **average age of ~74 years at diagnosis**

Smoking status[3]
Alterations may occur in both smokers (59%) and never smokers (41%)

Sex[11]
Equally likely to be either female (49%) or male (51%)

PD-L1 status[12,13]
~65% may be PD-L1 positive (≥1% expression)

_MET_ex14+ can be detected by an FDA-approved comprehensive biomarker test[14]

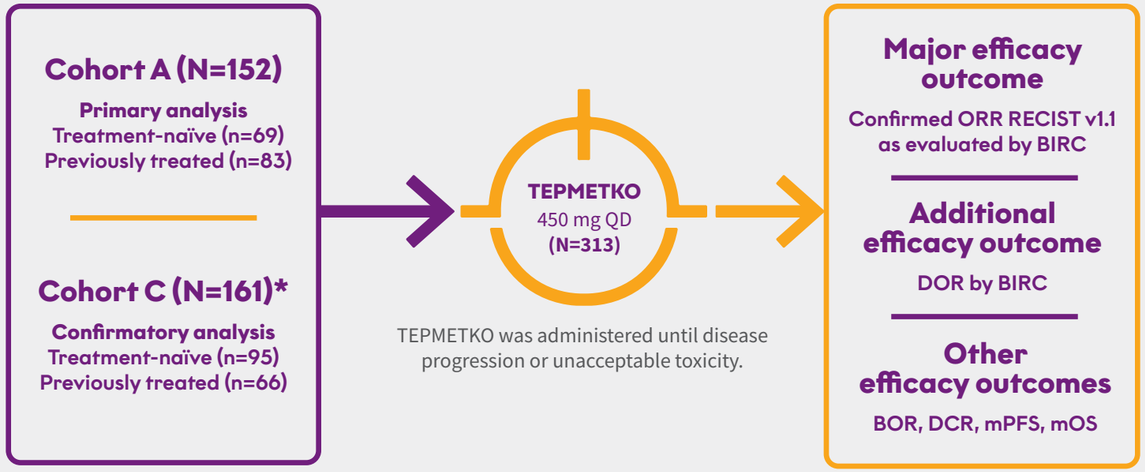
ALK=anaplastic lymphoma kinase; EGFR=epidermal growth factor receptor; KRAS=Kirsten rat sarcoma viral oncogene homolog; *MET*ex14+=mesenchymal-epithelial transition exon 14 skipping alterations; mNSCLC=metastatic non-small cell lung cancer; NSCLC=non-small cell lung cancer; PD-L1=programmed death ligand 1; ROS1=c-ros oncogene 1.

VISION is the largest trial of its kind that led to accelerated approval of TEPMETKO® (tepotinib)[1,14]

Accelerated approval is based on the initial primary analysis of Cohort A

VISION: a single-arm, open-label, multicenter, non-randomized, multicohort, phase 2 trial that studied the efficacy and safety of TEPMETKO in adult patients with metastatic NSCLC harboring *MET*ex14+.

Cohort A studied a total of 255 patients for safety. Of these patients, 152 were evaluated for efficacy.



Eligibility:	Exclusions:
Advanced, metastatic *MET*ex14+ NSCLC†	Symptomatic CNS metastases
EGFR wild-type and ALK-negative status	Clinically significant uncontrolled cardiac disease
≥1 measurable lesion by RECIST v1.1	Prior treatment with any MET or HGF inhibitor
ECOG PS 0-1	
Diagnosed by tissue or liquid biopsy	

*In the pre-planned study design, Cohort A reflects the initial analysis that formed the basis for accelerated FDA approval, total of 255 patients also reflected in the Prescribing Information. Cohort C is a confirmatory analysis for Cohort A, total of 313 patients. Patients were not allowed to enroll in Cohort C until Cohort A was complete. †Identification of *MET*ex14+ was prospectively determined using central laboratories employing either a PCR-based or next-generation sequencing-based clinical trial assay using tissue (58%) and/or plasma (65%) samples. An FDA-approved test for detection of *MET*ex14+ in NSCLC for selecting patients for treatment with TEPMETKO is not available.
ALK=anaplastic lymphoma kinase; BIRC=Blinded Independent Review Committee; BOR=best overall response; CNS=central nervous system; DCR=disease control rate; DOR=duration of response; ECOG PS=Eastern Cooperative Oncology Group Performance Status; EGFR=epidermal growth factor receptor; HGF=hepatocyte growth factor; *MET*=mesenchymal-epithelial transition; *MET*ex14+=mesenchymal-epithelial transition exon 14 skipping alterations; mOS=median overall survival; mPFS=median progression-free survival; NSCLC=non-small cell lung cancer; ORR=overall response rate; PCR=polymerase chain reaction; QD=once daily; RECIST=Response Evaluation Criteria in Solid Tumors.

SELECTED IMPORTANT SAFETY INFORMATION *continued*

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

Please see Important Safety Information throughout and full Prescribing Information enclosed.

Well-studied in a *MET*ex14+ identified population

The primary analysis of Cohort A was designed to include clinically relevant, difficult-to-treat profiles, such as people who smoke, are older, and have brain metastases[1,14]*

Disease characteristics

- **98%** had metastatic disease
- **86%** had adenocarcinoma histology
- **10%** had CNS metastases

Age/ECOG status

- **Median age of 73 years** (range: 41 to 94 years)
  - **82%** were ≥65
- **27%** had ECOG PS 0 and **73%** had ECOG PS 1

Line of therapy

- **45%** first line (n=69)
- **55%** previously treated (n=83)†
  - **89%** prior platinum-based therapy
  - **46%** immune-based therapy

Race and gender

- **71%** White
- **25%** Asian
- **52%** male
- **48%** female

Smoking status

- **43%** never smokers
- **52%** former smokers

The VISION Trial included patients diagnosed by both liquid and tissue biopsies

*MET*ex14+ were identified through either PCR or NGS testing†‡

- **58%** of patients by tissue (RNA-based) testing
- **65%** of patients by plasma (ctDNA-based) testing

*The patient characteristics of those in Cohort C were similar to those studied in Cohort A. †Had progressed on up to 2 lines of prior systemic therapies.[14]
‡Some patients tested positive using both methodologies.[14]
CNS=central nervous system; ctDNA=circulating tumor deoxyribonucleic acid; ECOG PS=Eastern Cooperative Oncology Group Performance Status; *MET*ex14+=mesenchymal-epithelial transition exon 14 skipping alterations; NGS=next-generation sequencing; PRC=polymerase chain reaction.

SELECTED IMPORTANT SAFETY INFORMATION *continued*

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.

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.

TEPMETKO® (tepotinib) 225 mg Tablets

Accelerated approval granted

Based on early and positive efficacy data in Cohort A, the FDA granted TEPMETKO® (tepotinib) accelerated approval status[1,14]

TREATMENT NAÏVE (n=69)

ORR BY BIRC
43%
(95% CI: 32.0, 56.0)

mDOR BY BIRC
10.8 months
(95% CI: 6.9, NE)

Patients with DOR ≥6 months, 67%
Patients with DOR ≥9 months, 30%

The median age of patients in the VISION Trial was 73 years (range: 41 to 94 years).

PREVIOUSLY TREATED (n=83)

ORR BY BIRC
43%
(95% CI: 33.0, 55.0)

mDOR BY BIRC
11.1 months
(95% CI: 9.5, 18.5)

Patients with DOR ≥6 months, 75%
Patients with DOR ≥9 months, 50%

NCCN PREFERRED

Tepotinib is a National Comprehensive Cancer Network® (NCCN®) preferred treatment in the first-line/subsequent line* setting for patients with *MET*ex14+ mNSCLC (Category 2A)[2†‡§]

*If *MET*ex14+ inhibitors have not previously been given. †Category 2A definition: based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate. ‡See the NCCN Guidelines for detailed recommendations, including other preferred options. §The NCCN Guidelines for NSCLC provide recommendations for certain individual biomarkers that should be tested and recommend testing techniques but do not endorse any specific commercially available biomarker assays or commercial laboratories.[2]
BIRC=Blinded Independent Review Committee; DOR=duration of response; mDOR=median duration of response; *MET*ex14+=mesenchymal-epithelial transition exon 14 skipping alterations; NE=not evaluable; ORR=overall response rate (confirmed).

SELECTED IMPORTANT SAFETY INFORMATION *continued*

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.

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%).

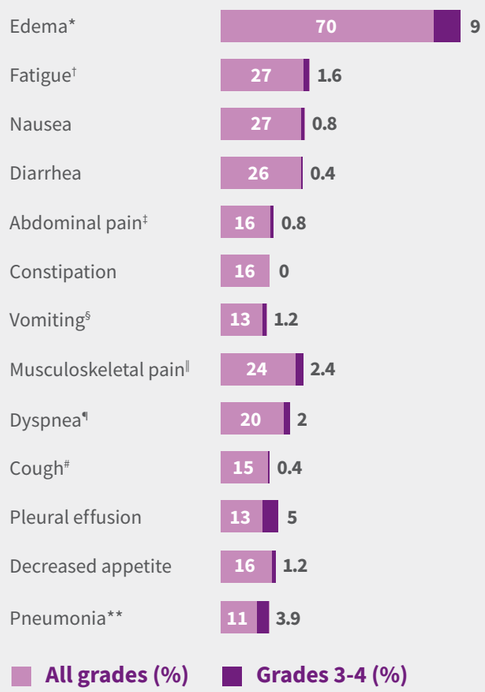
Please see Important Safety Information throughout and full Prescribing Information enclosed.

Manageable safety profile

The safety and tolerability profile of TEPMETKO® (tepotinib) was studied in 255 patients in the VISION Trial[1,14]

- Fatal adverse reactions (ARs) occurred in 1 patient (0.4%) due to pneumonitis, 1 patient (0.4%) due to hepatic failure, and 1 patient (0.4%) due to dyspnea from fluid overload
- Serious ARs occurred in 45% of patients who received TEPMETKO. Serious ARs 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%)

ARs in ≥10% of patients with NSCLC harboring *MET*ex14+[1]



TEPMETKO has no known contraindications.[1]

Due to an AR in patients who received TEPMETKO[1]

- **Permanent discontinuation – 20%**
  - The most frequent ARs (>1%) leading to permanent discontinuations of TEPMETKO were edema (5%), pleural effusion (2%), dyspnea (1.6%), general health deterioration (1.6%), and pneumonitis (1.2%)
- **Dosage interruptions – 44%**
  - ARs that required dosage interruption in >2% of patients who received TEPMETKO included edema (23%), increased blood creatinine (6%), pleural effusion (4.3%), increased ALT (3.1%), and pneumonia (2.4%)
- **Dose reductions – 30%**
  - ARs that required dose reductions in >2% of patients who received TEPMETKO included edema (19%), pleural effusion (2.7%), and increased blood creatinine (2.7%)

Laboratory abnormalities

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

*Edema includes eye edema, face edema, generalized edema, localized edema, edema, genital edema, peripheral edema, periorbital edema, peripheral swelling, and scrotal edema. †Fatigue includes asthenia and fatigue. ‡Abdominal pain includes abdominal discomfort, abdominal pain, abdominal pain lower, abdominal pain upper, gastrointestinal pain, and hepatic pain. §Vomiting includes retching and vomiting. ‖Musculoskeletal pain includes arthralgia, arthritis, back pain, bone pain, musculoskeletal chest pain, musculoskeletal pain, myalgia, non-cardiac chest pain, pain in extremity, and spinal pain. ¶Dyspnea includes dyspnea, dyspnea at rest, and dyspnea exertional. #Cough includes cough, and productive cough. **Pneumonia includes pneumonia, pneumonia aspiration, and pneumonia bacterial.
ALP=alkaline phosphatase; ALT=alanine aminotransferase; AST=aspartate aminotransferase; GGT=gamma-glutamyltransferase; MET=mesenchymal-epithelial transition; *MET*ex14+=mesenchymal-epithelial transition exon 14 skipping alterations; NSCLC=non-small cell lung cancer.

TEPMETKO® (tepotinib) 225 mg Tablets

Intracranial disease control

ADDITIONAL EXPANDED ANALYSES*

Data cutoff as of 2022

Intracranial responses observed with TEPMETKO® (tepotinib) in patients with brain metastases[15]

Across Cohorts A + C, 43 patients with brain metastases were evaluable by RANO-BM[†‡]

INTRACRANIAL ACTIVITY[§] (n=43)

iDCR[‖] 88.4% (95% CI: 74.9, 96.1)

iPFS 20.9 months (95% CI: 5.7, NE)

PATIENTS WITH TARGET BRAIN LESIONS (n=15)

iORR 66.7% (95% CI: 38.4, 88.2)

iDOR NE (95% CI: 0.9, NE)

Due to the single-arm design of the VISION Trial, no formal statistical comparisons were conducted; data were analyzed in a descriptive manner. For analysis of intracranial activity, brain imaging had no mandatory schedule and, as such, data for this retrospective ad hoc analysis were incomplete, and confirmation of response was not required. Impact of prior radiotherapy on this analysis should be considered. Results are subject to change based upon updated analysis. For these reasons, results from these analyses should be interpreted with caution.

*Updated data cutoff as of February 2022. Results are based on an interim analysis, which are subject to change on follow-up. [†]Brain metastases as identified at baseline by IRC or investigator, according to RECIST v1.1. [‡]30 patients (69.8%) received prior brain radiotherapy or surgery. [§]Best overall response per RANO-BM is a composite of radiographic responses, corticosteroid use, and clinical status, giving a more comprehensive overview of the patient compared to RECIST. [‖]Intracranial disease control: defined as CR/PR/SD or non-CR/non-PD.
CR=complete response; iDCR=intracranial disease control rate; iDOR=intracranial duration of response; iORR=intracranial overall response rate; iPFS=intracranial progression-free survival; IRC=independent review committee; NE=not evaluable; PD=progressive disease; PR=partial response; RANO-BM=Response Assessment in Neuro-Oncology Brain Metastases; RECIST=Response Evaluation Criteria in Solid Tumors; SD=stable disease.

SELECTED IMPORTANT SAFETY INFORMATION *continued*

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.

Please see Important Safety Information throughout and full Prescribing Information enclosed.

Additional VISION Trial data*

ADDITIONAL EXPANDED ANALYSES*

Data cutoff as of 2022

Updated efficacy data for Cohorts A† + C‡ (N=313)[15,16]

Due to the single-arm design of the VISION Trial for TEPMETKO® (tepotinib), no formal statistical comparisons were conducted, and data, including PFS and OS, were analyzed in a descriptive manner. For these reasons, results from this analysis should be interpreted with caution.

TREATMENT NAÏVE (n=164)

ORR‖ BY BIRC
56%
(95% CI: 48.1, 63.8)

mDOR BY BIRC
46.4 months
(95% CI: 13.8, NE)

DCR, %
79%
(95% CI: 71.6, 84.7)

mPFS, months
12.6
(95% CI: 9.6, 17.7)

mOS, months
19.1
(95% CI: 13.7, 23.7)

PREVIOUSLY TREATED (n=149)

ORR‖ BY BIRC
45%
(95% CI: 36.8, 53.3)

mDOR BY BIRC
12.4 months
(95% CI: 9.5, 18.5)

DCR, %
74%
(95% CI: 66.0, 80.7)

mPFS, months
11.0
(95% CI: 8.2, 13.7)

mOS, months
19.6
(95% CI: 15.2, 22.3)

The majority of patients taking TEPMETKO responded within approximately 6 weeks.

In treatment-naïve patients who were diagnosed by tissue biopsy, overall response rate in Cohort C (n=69) was 62.3% (95% CI: 49.8, 73.7), in Cohort A (n=42) was 47.6% (95% CI: 32.0, 63.6), and in Cohort A + C (n=111) was 56.8% (95% CI: 47.0, 66.1).

*Updated data cutoff as of February 2022. Results are based on an interim analysis, which are subject to change on follow-up. †The analyses presented here includes all patients enrolled in Cohort A, including 2 patients who were identified as non-responders in the prescribing information, and patients enrolled in Cohort C with 3 months' follow-up. ‡In the pre-planned study design, Cohort C is a confirmatory analysis for Cohort A. Patients were not allowed to enroll in Cohort C until Cohort A was complete. ‖ORR according to RECIST v1.1 as evaluated by a BIRC.
BIRC=Blinded Independent Review Committee; DCR=disease control rate; mDOR=median duration of response; mOS=median overall survival; mPFS=median progression-free survival; NE=not evaluable; ORR=overall response rate; OS=overall survival; PFS=progression-free survival; RECIST=Response Evaluation Criteria in Solid Tumors.

SELECTED IMPORTANT SAFETY INFORMATION *continued*

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%).

Please see Important Safety Information throughout and full Prescribing Information enclosed.

Incidence of treatment-related adverse events

ADDITIONAL EXPANDED ANALYSES*

Data cutoff as of 2022

Updated safety data for Cohorts A† + C‡ (N=313)[15-17]

TRAEs, %		Overall (N=313)
Any grade		91.7
Grade ≥3		34.2
Leading to dose reduction		33.5
Leading to treatment interruption		42.5
Leading to permanent discontinuation		14.7
Occurring in ≥10% of all patients, %	**Any grade**	**Grade ≥3**
Peripheral edema	66.5	10.9
Nausea	23.3	0.6
Hypoalbuminemia	23.0	3.2
Diarrhea	22.4	0.3
Blood creatinine increase	21.7	0.6
ALT increase	13.1	2.2
Decreased appetite	11.2	0.3

Peripheral edema was observed in the VISION trial, yet the mechanism is unknown[17]

Proactive monitoring for peripheral edema is recommended and can be managed with dose reduction of TEPMETKO® (tepotinib) or temporary discontinuation.

Compensatory management of peripheral edema includes:

- Limb elevation
- Compression stockings
- Dietary salt reduction
- Diuretics

*Updated data cutoff as of February 2022. Results are based on an interim analysis, which are subject to change on follow-up. †The analyses presented here includes all patients enrolled in Cohort A, including 2 patients who were identified as non-responders in the prescribing information, and patients enrolled in Cohort C with 3 months' follow-up. ‡In the pre-planned study design, Cohort C is a confirmatory analysis for Cohort A. Patients were not allowed to enroll in Cohort C until Cohort A was complete.
ALT=alanine aminotransferase; TRAE=treatment-related adverse event.

TEPMETKO® (tepotinib) 225 mg Tablets

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

Provide your mNSCLC patients with a convenient and flexible dosing regimen that they can stick with

Convenient once-daily dosing

Recommended Starting Dosage: 450 mg
(Two 225 mg tablets)

Advise patients to:

- Take their dose at approximately the same time every day until disease progression or unacceptable toxicity.
- Swallow tablets whole. Do not chew, crush, or split tablets.
- Never make up a missed dose within 8 hours of the next scheduled dose. If vomiting occurs after taking a dose, take the next dose at the scheduled time.

Flexible dose adjustment

Dose Reduction for the Management of ARs: 225 mg

- Permanently discontinue in patients who are unable to tolerate the 225 mg once-daily dose.
- Management of some ARs may require temporary interruption or permanent discontinuation. See the full Prescribing Information for recommended dose modifications of TEPMETKO® (tepotinib).

One Dose.
Once a Day.

PATIENT SELECTION

Select patients for treatment with TEPMETKO based on the presence of *MET*ex14+ in plasma or tumor specimens. Testing for the presence of *MET*ex14+ 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*ex14+ in NSCLC for selecting patients for treatment with TEPMETKO is not available.

AR=adverse reaction; *MET*=mesenchymal-epithelial transition; *MET*ex14+=mesenchymal-epithelial transition exon 14 skipping alterations; mNSCLC=metastatic non-small cell lung cancer.

SELECTED IMPORTANT SAFETY INFORMATION *continued*

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.

 Please see Important Safety Information throughout and full Prescribing Information enclosed.

Help eligible patients gain appropriate access

ONCOLOGY® navigation center

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® (tepotinib) 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**

The ONC co-pay assistance program is entirely for the benefit of the enrolled patient on TEPMETKO. Full terms and conditions apply.

ONC is available to answer any questions.

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

*Additional program rules and restrictions or conditions may apply. Enrollment Forms and complete program information are available through OncNavigationCenter.com.

TEPMETKO® (tepotinib) 225 mg Tablets

Warnings and precautions[1]

The safety profile of TEPMETKO® (tepotinib) 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 *MET*ex14+ mNSCLC who received TEPMETKO in the VISION Trial.**

Interstitial lung disease (ILD)/pneumonitis

ILD/pneumonitis, which can be fatal, occurred in 2.2% of patients treated with TEPMETKO, with 1 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 1 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 days).

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 TEPMETKO 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 1 week following the final dose.

*MET*ex14+=mesenchymal-epithelial transition exon 14 skipping alterations; mNSCLC=metastatic non-small cell lung cancer.

Actor portrayal

Important Safety Information and Indication[1]

IMPORTANT SAFETY INFORMATION

TEPMETKO® (tepotinib) 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.

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.

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.

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.

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.

See full Prescribing Information in pocket.

References

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 Please see Important Safety Information throughout and full Prescribing Information enclosed.

Notes

Notes

TEPMETKO® (tepotinib) 225 mg Tablets

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

CONSIDER TEPMETKO

TEPMETKO® (tepotinib) 225 mg Tablets

The only once-daily oral *MET* inhibitor

Recommended dose is 450 mg once daily with food; please see page 12 to learn more.

Dosing flexibility

The ONLY approved once-daily oral *MET* inhibitor for all eligible patients with *MET*ex14+ mNSCLC[1]

Treat with confidence

Studied in VISION, the LARGEST trial in patients with *MET*ex14+ mNSCLC and demonstrated robust and lasting efficacy results with a manageable safety profile[1]

–See page 4 for full trial design

CNS activity

Improved intracranial response in patients with brain metastases[15]

CNS=central nervous system; *MET*=mesenchymal-epithelial transition; *MET*ex14+=mesenchymal-epithelial transition exon 14 skipping alterations; mNSCLC=metastatic non-small cell lung cancer.

INDICATION

TEPMETKO® (tepotinib) 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 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 2.2% of patients treated with TEPMETKO, with one patient experiencing a Grade 3 or higher event; this event resulted in death.

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