Clinical Policy Title:	tepotinib
Policy Number:	RxA.681
Drug(s) Applied:	Tepmetko®
Original Policy Date:	06/15/2021
Last Review Date:	04/18/2022
Line of Business Policy Applies to:	All lines of business

Background

Tepotinib is a kinase inhibitor indicated for the treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) harbouring mesenchymal-epithelial transition (MET) exon 14 skipping alterations. Tepotinib inhibits hepatocyte growth factor (HGF) dependent and independent MET phosphorylation and subsequently MET-dependent downstream signaling pathways.

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.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
tepotinib (Tepmetko®)	Metastatic non-small cell lung cancer (NSCLC) harboring mesenchymal-epithelial transition (MET) exon 14 skipping alterations.	450 mg orally once daily with food until disease progression or unacceptable toxicity.	450 mg once daily

Dosage Forms

- Tablet: 225 mg

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

A. Non-Small Cell Lung Cancer (must see all):

1. Diagnosis of advanced NSCLC with MET exon 14 skipping alterations;
2. Prescribed by or in consultation with an oncologist;
3. Member is 18 years of age or older;
4. Tepotinib is prescribed as monotherapy;

5. Request meets one of the following (a or b): *
   a. Dose does not exceed 450 mg orally once daily;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).
   *Prescribed regimen must be FDA-approved or recommended by NCCN.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

A. Non-Small Cell Lung Cancer (must see all):

1. Member is currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
2. Member is responding positively to the therapy (i.e., absence of tumor progression);
3. If request is for a dose increase, request meets one of the following (a or b): **
   a. New dose does not exceed 450 mg orally once daily;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).
   **Prescribed regimen must be FDA-approved or recommended by NCCN.

Approval Duration
Commercial: 12 months
Medicaid: 12 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
NSCLC: Non-Small Cell Lung Cancer
FDA: Food and Drug Administration
MET: Mesenchymal-epithelial transition
ILD: Interstitial Lung Disease
METex14: Mesenchymal-epithelial transition exon 14
NCCN: National Comprehensive Cancer Network
HGF: hepatocyte growth factor

APPENDIX B: Therapeutic Alternatives
Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Maximum Dose
Tabrecta™	400 mg orally twice daily with or without food	400 mg orally twice daily

Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand, Brand name® when the drug is available by brand only and generic name when the drug is available by generic only.

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - None reported.

- Boxed Warning(s):

- None reported.

APPENDIX D: General Information

- Interstitial lung disease (ILD)/pneumonitis: ILD/pneumonitis, which can be fatal, occurred in 2.2% of patients treated tepotinib. One patient experienced a grade 3 or higher event that resulted in death. Four patients (0.9%) discontinued therapy due to ILD/pneumonitis. Monitor for new or worsening pulmonary symptoms that would be indicative of ILD/pneumonitis. Immediately withhold tepotinib in patients with suspected ILD/pneumonitis. Permanently discontinue tepotinib in patients diagnosed with ILD/pneumonitis of any severity.
- Hepatotoxicity: Increased ALT/AST occurred in 13% of the patients treated with tepotinib. Grade 3 or 4 increases occurred in 4.2% of patients. One patient (0.2%) experienced a fatal adverse reaction of hepatic failure. Three patients (0.7%) discontinued due to increases in ALT/AST. Median time-to-onset of grade 3 or higher increased ALT/AST was approximately 30 days (range 1 to 178). Monitor liver function tests prior to the start of therapy and every two (2) weeks during the first three (3) months of therapy, then once a month or as clinically indicated. Withhold, dose reduce, or permanently discontinue tepotinib based on severity of the adverse reaction.
- Embryo-fetal toxicity: Tepotinib can cause fetal harm when administered to a pregnant woman based on animal studies and its mechanism of action. 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 tepotinib and one week after the final dose.

References

1. Tepmetko® Prescribing Information. Rockland, MA: EMD Serono Inc; February 2021. Available at: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=80a0f1b9-071a-47f5-9e67-32d638a669dc&type=display#section-4. Accessed February 1, 2022.
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3. Clinical Pharmacology [database online] powered by ClinicalKey. Tampa, FL: Elsevier, 2022. Available at: https://www.clinicalkey.com/pharmacology/ . Accessed February 1, 2022.
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5. NCCN Guidelines. Non-small Cell Lung Cancer. Version 1.2022; Available at: https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf . Accessed February 1, 2022.
6. Paik PK, Felip E, Veillon R, et al. Tepotinib in Non-Small-Cell Lung Cancer with MET Exon 14 Skipping Mutations. N Engl J Med 2020; 3838: 931-943. Available at: https://pubmed.ncbi.nlm.nih.gov/32469185/. Accessed February 1, 2022.
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Review/Revision History	Review/Revision Date	P&T Approval Date
Policy was established.	04/12/2021	06/10/2021
Policy was reviewed: 1. Initial Approval Criteria, IA5: Updated dosing criteria from	02/01/2022	04/18/2022

Dose does not exceed 450 mg orally once daily to Request meets one of the following (a or b): a. Dose does not exceed 450 mg orally once daily; b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence). *Prescribed regimen must be FDA-approved or recommended by NCCN. 2. Continued Therapy Approval Crtieria, IIA3: Updated dosing criteria from Dose does not exceed 450 mg orally once daily to If request is for a dose increase, request meets one of the following (a or b): a. New dose does not exceed 450 mg orally once daily; b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence). *Prescribed regimen must be FDA-approved or recommended by NCCN. 3. Appendix A: Updated to include abbreviations for National Comprehensive Cancer Network, hepatocyte growth factor. 4. Appendix B, Drug Name: Updated to remove unavailable generic therapeutic alternative capmatinib. 5. Statement about drug listing		

format in Appendix B is rephrased to "Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand; Brand name® when the drug is available by brand only and generic name when the drug is available by generic only". 6. References were reviewed and updated.		