Tepmetko® (tepotinib) – New drug approval

- On February 3, 2021, EMD Serono announced the FDA approval of Tepmetko (tepotinib), 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 trial(s).

- In the U.S. in 2020, there were an estimated 228,820 new cases of lung cancer and more than 135,000 deaths from lung cancer. Alterations of the MET signaling pathway, including *MET* exon 14 (*MET*ex14) skipping alterations, are estimated to occur in 3% to 4% of NSCLC cases.

- Tepmetko is a MET inhibitor that inhibits the oncogenic MET receptor signaling caused by *MET* (gene) alterations.

- The efficacy of Tepmetko was established in a single-arm, open-label, non-randomized, multicohort study in 152 patients with advanced or metastatic NSCLC with *MET* exon 14 skipping alterations. Patients received Tepmetko once daily until disease progression or unacceptable toxicity. The major efficacy outcome measure was confirmed overall response rate (ORR). An additional efficacy outcome measure was duration of response (DOR).

    — In treatment-naïve patients, the ORR was 43% (95% CI: 32, 56) and the median DOR was 10.8 months (95% CI: 6.9, not estimable).
    — In previously treated patients, the ORR was 43% (95% CI: 33, 55) and the median DOR was 11.1 months (95% CI: 9.5, 18.5).

- Warnings and precautions for Tepmetko include interstitial lung disease/pneumonitis, hepatotoxicity, and embryo-fetal toxicity.

- The most common adverse reactions (≥ 20%) with Tepmetko use were edema, fatigue, nausea, diarrhea, musculoskeletal pain, and dyspnea.

- The most common grade 3 to 4 laboratory abnormalities (≥ 2%) were decreased lymphocytes, decreased albumin, decreased sodium, increased gamma-glutamyltransferase, increased amylase, increased ALT, increased AST, and decreased hemoglobin.

- The recommended dosage of Tepmetko is 450 mg orally once daily with food until disease progression or unacceptable toxicity.

    — Patients should be selected for treatment 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, re-evaluate 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.

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- EMD Serono’s launch plans for Tepmetko are pending. Tepmetko will be available as a 225 mg tablet

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