Indication
TABRECTA™ (capmatinib) tablets is indicated for the treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) whose tumors have a mutation that leads to mesenchymal-epithelial transition (MET) exon 14 skipping as detected by an FDA-approved test.

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.

Important Safety Information
Interstitial Lung Disease (ILD)/Pneumonitis. ILD/pneumonitis, which can be fatal, occurred in patients treated with TABRECTA. ILD/pneumonitis occurred in 4.5% of patients treated with TABRECTA in the GEOMETRY mono-1 study, with 1.8% of patients experiencing grade 3 ILD/pneumonitis and 1 patient experiencing death (0.3%). Eight patients (2.4%) discontinued TABRECTA due to ILD/pneumonitis.

Please see additional Important Safety Information throughout, and click here for full Prescribing Information for TABRECTA.
**METex14 is an oncogenic driver, and patients with METex14 face a poor prognosis**

**Why is METex14 important?**

~70% of patients with mNSCLC have an identifiable oncogenic mutation.5

More than 1 in 4 patients with metastatic NSCLC have an actionable oncogenic mutation.14

METex14 has a prevalence of approximately 3%—similar to that of other genomic mutations.5

There are ~4,000 to 5,000 patients with METex14 in mNSCLC per year in the United States17,18

Patients with METex14 mNSCLC face a poor prognosis5,5

- Many of these patients may have bone, liver, and brain metastases, which are associated with poor outcomes

As many as 148,000 patients are diagnosed with metastatic NSCLC annually and should be considered for METex14 testing7

- ~93,000 are treatment naive and ~55,000 have been treated previously

**Accurate detection of mutations leading to METex14 could facilitate timely intervention**

The complex biological structure of METex14 requires a test that is specifically designed for its detection18,19

- Skipping of exon 14 of MET is due to DNA mutations at splice sites, which flank this exon20
  - DNA mutations leading to METex14 are diverse and can include a variety of substitutions or indels18,20

**How to test for METex14?**

The FoundationOne®CDx is the only FDA-approved test that has been clinically validated to identify patients who are eligible for treatment with TABRECTA™ (capmatinib) tablets1

It is imperative to use a test specifically designed to detect METex14 to identify patients who are eligible for treatment with TABRECTA18

**Important Safety Information (continued)**

Monitor for new or worsening pulmonary symptoms indicative of ILD/pneumonitis (eg, dyspnea, cough, fever). Immediately withhold TABRECTA 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 TABRECTA. Increased alanine aminotransferase [ALT]/aspartate aminotransferase [AST] occurred in 13% of patients treated with TABRECTA in GEOMETRY mono-1. Grade 3 or 4 increased ALT/AST occurred in 6% of patients. Three patients (0.9%) discontinued TABRECTA due to increased ALT/AST.

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FoundationOne®CDx is validated and optimized to detect certain mutations leading to METex14.

Why FoundationOne®CDx?

A companion diagnostic is a medical device used to help determine whether a patient may be an appropriate candidate for a particular therapeutic product.

FoundationOne®CDx is the only FDA-approved companion diagnostic to detect METex14. The ability of FoundationOne®CDx to detect mutations leading to METex14 was demonstrated in a retrospective analysis.

99% Positive percent agreement:
FoundationOne®CDx demonstrated an estimated positive percentage agreement of 99% (72 of 73) with the RNA-based RT-PCR clinical trial assay, which confirmed MET exon 14 skipping for TABRECTA (capmatinib) tablets.*

Mutation testing for METex14 may be integrated into the mNSCLC workup using tissue specimens

- FoundationOne®CDx uses DNA isolated from FFPE tumor tissue specimens.

When feasible, please send:
- FFPE tissue block + 1 H&E slide
- 10 unstained slides (positively charged and unbaked at 4-5 microns thick) + 1 H&E slide†

How to talk to patients about testing

When talking to patients, you may want to explain what you are doing and why.

- Share that genomic testing allows you to look for changes in the DNA that may be promoting tumor growth
- Explain that knowledge of the DNA mutations helps you develop a specific treatment plan

The Centers for Medicare & Medicaid Services (CMS) issued a National Coverage Determination (NCD) for qualifying patients who receive next-generation sequencing (NGS) with FDA-approved tests including FoundationOne®CDx.

Important Safety Information (continued)

Monitor liver function tests (including ALT, AST, and total bilirubin) prior to the start of TABRECTA, 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, reduce dose, or permanently discontinue TABRECTA.

Risk of Photosensitivity. Based on findings from animal studies, there is a potential risk of photosensitivity reactions with TABRECTA. In GEOMETRY mono-1, it was recommended that patients use precautionary measures against ultraviolet exposure, such as use of sunscreen or protective clothing, during treatment with TABRECTA. Advise patients to limit direct ultraviolet exposure during treatment with TABRECTA.

Please see additional Important Safety Information throughout, and click here for full Prescribing Information for TABRECTA.
Indication

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Important Safety Information

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Monitor for new or worsening pulmonary symptoms indicative of ILD/pneumonitis (eg, dyspnea, cough, fever). Immediately withhold TABRECTA 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 TABRECTA. Increased alanine aminotransferase (ALT)/aspartate aminotransferase (AST) occurred in 13% of patients treated with TABRECTA in GEOMETRY mono-1. Grade 3 or 4 increased ALT/AST occurred in 6% of patients. Three patients (0.9%) discontinued TABRECTA due to increased ALT/AST.

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Risk of Photosensitivity. Based on findings from animal studies, there is a potential risk of photosensitivity reactions with TABRECTA. In GEOMETRY mono-1, it was recommended that patients use precautionary measures against ultraviolet exposure, such as use of sunscreen or protective clothing, during treatment with TABRECTA. Advise patients to limit direct ultraviolet exposure during treatment with TABRECTA.

Embryo-Fetal Toxicity. Based on findings from animal studies and its mechanism of action, TABRECTA 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 to use effective contraception during treatment with TABRECTA and for 1 week after the last dose. Advise males with female partners of potential effects on fetal development.

Most Common Adverse Reactions. The most common adverse reactions (≥20%) were peripheral edema (52%), nausea (44%), fatigue (32%), vomiting (28%), dyspnea (24%), and decreased appetite (21%). The most common grade 3 adverse reactions (≥2%) were peripheral edema (9%), fatigue (8%), dyspnea (7%), nausea (2.7%), vomiting (2.4%), and noncardiac chest pain (2.1%).

Important Safety Information (continued)

Clinically Relevant Adverse Reactions. Clinically relevant adverse reactions observed in <10% of patients were pruritus (allergic and generalized), ILD/pneumonitis, cellulitis, acute kidney injury (including renal failure), urticaria, and acute pancreatitis.

Laboratory Abnormalities. Select laboratory abnormalities (≥20%) worsening from baseline in patients who received TABRECTA were decreased hemoglobin (66%), increased creatinine (62%), decreased lymphocytes (44%), increased ALT (37%), increased alkaline phosphatase (32%), increased amylase (31%), increased gamma-glutamyltransferase (29%), increased lipase (26%), increased AST (25%), decreased hemoglobin (24%), decreased leukocytes (23%), decreased sodium (23%), decreased phosphorus (23%), increased potassium (23%), and decreased glucose (21%).

Please click here for full Prescribing Information for TABRECTA.

References:

Knowledge of METex14 status can inform up-front treatment planning¹

Why is METex14 important?

- METex14 is an oncogenic driver with a prevalence of ~3%—similar to that of ALK fusions, BRAF mutations, and ROS1 fusions²,⁹,¹⁶
- Patients with METex14 in mNSCLC face a poor prognosis³⁻⁵
- As many as 148,000 patients are diagnosed with metastatic NSCLC annually and should be considered for METex14 testing¹⁷
  - ~93,000 are treatment naive and ~55,000 have been treated previously

How to test for METex14?

- Exon 14 skipping is due to DNA mutations at splice sites, which flank this exon²⁰
  - DNA mutations leading to METex14 are diverse and can include a variety of substitutions or indels¹⁸,²⁰
- The complex biological structure of METex14 requires a test that is specifically designed for its detection¹⁸,¹⁹

Why FoundationOne® CDx?

- FoundationOne® CDx is the only FDA-approved companion diagnostic to detect METex14

What information will be included in the FoundationOne® CDx report?

- FoundationOne® CDx reports provide information to help develop appropriate treatment plans¹
- FoundationOne® CDx is the only FDA-approved CDx for METex14²³

Learn more at metex14.com

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Highlights of Important Safety Information
TABRECTA has Warnings and Precautions for interstitial lung disease (ILD/pneumonitis), hepatotoxicity, risk of photosensitivity and embryo-fetal toxicity.

The most common adverse reactions (≥20%) are peripheral edema, nausea, fatigue, vomiting, dyspnea, and decreased appetite.

Please see additional Important Safety Information throughout, and click here for full Prescribing Information for TABRECTA.