Tabrecta (capmatinib)

NEW PRODUCT SLIDESHOW

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Introduction

- **Brand name:** Tabrecta
- **Generic name:** Capmatinib
- **Pharmacologic class:** Kinase inhibitor
- **Strength and Formulation:** 150mg, 200mg; tablets
- **Manufacturer:** Novartis
- **How supplied:** Tabs—56
- **Legal Classification:** Rx

Tabrecta

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Indication

- 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
  - Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s)

Dosage and Administration

- Confirm presence of a mutation that leads to MET exon 14 skipping in tumor specimens
- Swallow whole
- 400mg twice daily
- Recommended dose reductions for adverse reactions:
  - **First**: 300mg twice daily
  - **Second**: 200mg twice daily
  - Permanently discontinue in patients unable to tolerate 200mg twice daily

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Dosage Modifications for Adverse Reactions

- *Interstitial lung disease/pneumonitis*
  - **Any grade**: permanently discontinue
- *Increased ALT and/or AST without increased total bilirubin*
  - **Grade 3**: withhold until recovery to baseline ALT/AST; if recovery to baseline within 7 days, then resume at same dose, otherwise resume at a reduced dose
  - **Grade 4**: permanently discontinue
- *Increased ALT and/or AST with increased total bilirubin in the absence of cholestasis or hemolysis*
  - **ALT and/or AST >3xULN with total bilirubin >2xULN**: permanently discontinue

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Dosage Modifications for Adverse Reactions

- *Increased total bilirubin without concurrent increased ALT and/or AST*
  - **Grade 2**: withhold until recovery to baseline bilirubin; if recovered to baseline within 7 days, then resume at same dose, otherwise resume at reduced dose
  - **Grade 3**: withhold until recovery to baseline bilirubin; if recovered to baseline within 7 days, then resume at reduced dose, otherwise permanently discontinue
  - **Grade 4**: permanently discontinue
- *Other adverse reactions*
  - **Grade 2**: maintain dose level; if intolerable consider withholding until resolved, then resume at reduced dose
  - **Grade 3**: withhold until resolved, then resume at reduced dose
  - **Grade 4**: permanently discontinue

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Considerations for Special Populations

- **Pregnancy:** can cause fetal harm
- **Nursing mothers:** not recommended during and for 1 week after the last dose
- **Pediatric**: not established
- **Geriatrics**: no overall differences observed
- **Renal impairment**: not studied in patients with severe impairment (CrCl 15-29mL/min)

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Warnings and Precautions

- Monitor for pulmonary symptoms indicative of ILD/pneumonitis; withhold immediately if suspected and permanently discontinue if no other causes are identified
- Monitor LFTs prior to initiation, every 2 weeks during 1st 3 months, then once monthly or as clinically indicated; test more frequently if increased AST, ALT or bilirubin develops
- Potential risk of photosensitivity
- Advise patients to limit direct UV exposure
- Advise females of reproductive potential and males (w. female partners) to use effective contraception during and for 1 week after the last dose

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Interactions

- Potentiated by strong CYP3A inhibitors; monitor closely
- Potentiates CYP1A2, P-gp, or BCRP substrates; if unavoidable, decrease substrate dosage
- May potentiate MATE1 or MATE2K substrates; if unavoidable, decrease substrate dosage
- Antagonized by strong or possibly moderate CYP3A inducers; avoid

Adverse Reactions

- **Most common (≥ 20%):** peripheral edema, nausea, fatigue, vomiting, dyspnea, decreased appetite
- **Others**: lab abnormalities, hepatotoxicity

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Mechanism of Action

- Capmatinib is a kinase inhibitor that targets mesenchymal-epithelial transition (MET), including the mutant variant produced by exon 14 skipping
- Capmatinib inhibited cancer cell growth driven by a mutant MET variant lacking exon 14 at clinically achievable concentrations and demonstrated anti-tumor activity in murine tumor xenograft models derived from human lung tumors with either a mutation leading to MET exon 14 skipping or MET amplification

Pharmacokinetics

- Time to peak concentration: ~1-2 hours
- 96% protein bound
- Primarily metabolized by CYP3A4 and aldehyde oxidase
- Effective elimination half-life: 6.5 hours
- Fecal (major), renal excretion

Clinical Trials

- Efficacy evaluated in nonrandomized, open-label study (NCT02414139)
- Eligible patients were required to have NSCLC with a mutation that leads to MET exon 14 skipping, epidermal growth factor receptor (EGFR) wild-type and anaplastic lymphoma kinase (ALK) negative status, and at least 1 measurable lesion
- Out of 78 samples retested with FoundationOne® CDx, 73 were evaluable (20 treatment-naïve and 53 previously treated patients), 72 (20 treatment-naïve and 52 previously treated patients) of which were confirmed to have a mutation that leads to MET exon 14 skipping

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Clinical Trials

- Efficacy population included 28 treatment-naïve patients and 69 previously treated patients
- Median age: 71 years; 60% female; 75% White
- 24% had Eastern Cooperative Oncology Group Performance Status (ECOG PS) 0 and 75% had ECOG PS 1
- 60% never smoked
- 80% had adenocarcinoma
- 12% had CNS metastases
- Among previously treated patients, 88% received prior platinum-based chemotherapy

Clinical Trials

- Patients received capmatinib 400mg orally twice daily until disease progression or unacceptable toxicity
- Major efficacy outcome measure: overall response rate (ORR)
- An additional efficacy outcome measure was duration of response (DoR)

Clinical Trials

- Results showed a confirmed ORR of 68% (95% CI, 48-84) among 28 treatment-naive patients and 41% (95% CI, 29-53) among 69 previously treated patients
- A median DoR of 12.6 months (95% CI, 5.5–25.3) was observed among treatment-naive patients (19 responders) and 9.7 months (95% CI, 5.5-13.0) among previously treated patients (28 responders)

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New Product Monograph

- For more information view the product monograph available at:

  https://www.empr.com/drug/tabrecta/