Braftovi® (encorafenib) – New indication

- On December 20, 2024, Pfizer announced the FDA approval of Braftovi (encorafenib), in combination with Erbitux® (cetuximab) and mFOLFOX6 (fluorouracil, leucovorin, and oxaliplatin), for the **treatment of patients with metastatic colorectal cancer (mCRC) with a *BRAF V600E* mutation**, as detected by an FDA-approved test.
    - This indication is **approved under accelerated approval** based on response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).
- Braftovi is also approved in combination with Erbitux for the treatment of adult patients with mCRC with a *BRAF V600E* mutation, as detected by an FDA-approved test, after prior therapy.
- In addition to mCRC, Braftovi is approved for *BRAF V600E* or *V600K* mutation-positive unresectable or metastatic melanoma and *BRAF V600E* mutation-positive metastatic non-small cell lung cancer (NSCLC).
- The approval of Braftovi for the new indication was based on BREAKWATER, a randomized, active-controlled, open-label study in patients with *BRAF V600E* mutation-positive mCRC. Patients were randomized to receive Braftovi in combination with Erbitux (discontinued after randomization of 158 patients), Braftovi in combination with Erbitux and mFOLFOX6 (n = 236), or mFOLFOX6, FOLFOXIRI, or CAPOX (different chemotherapy regimens) each with or without bevacizumab (n = 243). The major outcome measure was confirmed objective response rate (ORR) and was evaluated in the first 110 participants randomized in each arm.
    - Braftovi in combination with Erbitux and mFOLFOX6 demonstrated a statistically significant improvement in ORR compared to the active comparator (p = 0.008). **The ORR was 61% with Braftovi plus Erbitux and mFOLFOX6 vs. 40% with chemotherapy with or without bevacizumab.**
- The most common adverse reactions (≥ 25%) with Braftovi use in combination with Erbitux and mFOLFOX6, were peripheral neuropathy, nausea, fatigue, rash, diarrhea, decreased appetite, vomiting, hemorrhage, abdominal pain, and pyrexia.
- The recommended dosage of Braftovi is **300 mg (four 75 mg capsules) orally once daily** in combination with biweekly Erbitux and mFOLFOX6 until disease progression or unacceptable toxicity.
    - Refer to the Braftovi drug label for dosing for its other indications.