Alimta® (pemetrexed) – Updated indication

- On January 31, 2019, Eli Lilly announced the FDA approval of Alimta (pemetrexed), in combination with Keytruda® (pembrolizumab) and platinum chemotherapy, for the initial treatment of patients with metastatic, nonsquamous, non-small cell lung cancer (NSCLC), with no EGFR or ALK genomic tumor aberrations.
    - Alimta in combination with Keytruda and carboplatin was first approved in June 2018 under the FDA's accelerated approval process for the first-line treatment of patients with metastatic NSCLC, based on tumor response rates and progression-free survival (PFS) data.
    - In accordance with the accelerated approval process, continued approval was contingent upon verification and description of clinical benefit, which has now been demonstrated and has resulted in the FDA converting the accelerated approval to full (regular) approval.

- Alimta is also approved:
    - In combination with cisplatin for the initial treatment of patients with locally advanced or metastatic, nonsquamous, NSCLC;
    - As a single agent for the maintenance treatment of patients with locally advanced or metastatic, nonsquamous NSCLC whose disease has not progressed after four cycles of platinum-based first-line chemotherapy;
    - As a single agent for the treatment of patients with recurrent, metastatic nonsquamous, NSCLC after prior chemotherapy;
    - In combination with cisplatin, for the initial treatment of patients with malignant pleural mesothelioma whose disease is unresectable or who are otherwise not candidates for curative surgery;
    - Alimta is not indicated for the treatment of patients with squamous cell, non-small cell lung cancer.

- Lung cancer is the leading cause of cancer death in the U.S. NSCLC is much more common than other types of lung cancer and accounts for about 80 to 85% of all lung cancer cases. For those people afflicted with NSCLC, about 70% have nonsquamous cell carcinoma, while about 30% have squamous cell carcinoma.

- The approval of Alimta's expanded indication was based on KEYNOTE-189, a study in 616 patients with metastatic nonsquamous NSCLC, regardless of PD-L1 tumor expression status, who had not previously received systemic therapy for metastatic disease and in whom there were no EGFR or ALK genomic tumor aberrations. Patients were randomized to placebo or Keytruda. All patients received Alimta plus investigator's choice of cisplatin or carboplatin (platinum chemotherapy). The main efficacy outcome measures were overall survival (OS) and PFS. Additional efficacy outcome measures were overall response rate (ORR) and duration of response (DOR).
    - Median OS was not reached for Alimta + Keytruda + platinum chemotherapy vs. 11.3 months (95% CI: 8.7, 15.1) for placebo + Alimta + platinum chemotherapy (HR 0.49, 95% CI: 0.38, 0.64; $p < 0.0001$).
    - Median PFS was 8.8 (95% CI: 7.6, 9.2) for Alimta + Keytruda + platinum chemotherapy vs. 4.9 (95% CI: 4.7, 5.5) for placebo + Alimta + platinum chemotherapy (HR 0.52, 95% CI: 0.43, 0.64; $p < 0.0001$).
    - ORR was 48% (95% CI: 43, 53) for Alimta + Keytruda + platinum chemotherapy vs. 19% (95% CI: 14, 25) for placebo + Alimta + platinum chemotherapy ($p < 0.0001$).

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    - Median DOR was 11.2 months (range: 1.1+, 18.0+) for Alimta + Keytruda + platinum chemotherapy vs. 7.8 months for placebo + Alimta + platinum chemotherapy (range: 2.1+, 16.4+).

- The recommended dose of Alimta when administered with Keytruda and platinum chemotherapy for the initial treatment of metastatic nonsquamous NSCLC is 500 mg/m^2 as an intravenous infusion.

    - Alimta should be administered after Keytruda and prior to carboplatin or cisplatin on day 1 of each 21-day cycle for 4 cycles.
    - Following completion of platinum-based therapy, treatment with Alimta with or without Keytruda is administered until disease progression or unacceptable toxicity.
    - Refer to the drug labels for Keytruda and for carboplatin or cisplatin for additional dosing details.

- Refer to the Alimta drug label for dosing recommendations for all other indications.