Gavreto® (pralsetinib) – New orphan drug approval

- approval of Gavreto (pralsetinib), for the treatment of adult patients with metastatic rearranged during transfection (RET) fusion-positive non-small cell lung cancer (NSCLC) 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 trial(s).

- RET activating fusions and mutations are key disease drivers in many cancer types, including NSCLC. RET fusions are implicated in approximately 1 to 2 percent of patients with NSCLC.

- Gavreto is a kinase inhibitor of wild-type RET and oncogenic RET fusions and mutations. Certain RET fusion proteins and activating point mutations can drive tumorigenic potential through hyperactivation of downstream signaling pathways leading to uncontrolled cell proliferation.

- The efficacy of Gavreto was demonstrated in a non-randomized, open-label study in 114 patients with RET fusion-positive metastatic NSCLC. Patients received Gavreto 400 mg orally once daily until disease progression or unacceptable toxicity. The major efficacy outcome measures were overall response rate (ORR) and duration of response (DOR).

    — In the 87 patients who were previously treated with platinum-based therapy, the ORR was 57% (95% CI: 46, 68) and the median DOR in months was not estimable (NE) (95% CI: 15.2, NE).
    — In the 27 patients who were treatment-naive, the ORR was 70% (95% CI: 50, 86) and the median DOR was 9.0 months (95% CI: 6.3, NE).

- Warnings and precautions for Gavreto include Interstitial lung disease/pneumonitis, hypertension, hepatotoxicity, hemorrhagic events, risk of impaired wound healing, and embryo-fetal toxicity.

- The most common adverse reactions (≥ 25%) with Gavreto use were fatigue, constipation, musculoskeletal pain, and hypertension.

- The most common grade 3 - 4 laboratory abnormalities (≥ 2%) with Gavreto use were decreased lymphocytes, decreased neutrophils, decreased phosphate, decreased hemoglobin, decreased sodium, decreased calcium (corrected), and increased alanine aminotransferase.

- The recommended dose of Gavreto is 400 mg orally once daily on an empty stomach (no food intake for at least 2 hours before and at least 1 hour after taking Gavreto). Treatment should be continued until disease progression or until unacceptable toxicity.

    — Patients should be selected for treatment with Gavreto based on the presence of a RET gene fusion. Information on FDA-approved tests is available at http://www.fda.gov/CompanionDiagnostics.

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- Roche and Blueprint Medicines plan to launch Gavreto within one week. Gavreto will be available as a 100 mg capsule.

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