Rybrevant™ (amivantamab-vmjw) – New drug approval

- On May 21, 2021, Johnson & Johnson announced the FDA approval of Rybrevant (amivantamab-vmjw), for the treatment of adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR) exon 20 insertion mutations, as detected by an FDA-approved test, whose disease has progressed on or after platinum-based chemotherapy.
    - 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 the confirmatory trials.
- Lung cancer is one of the most common cancers, and NSCLC makes up 80 to 85% of all lung cancers. Among the most common driver mutations in NSCLC are alterations in EGFR, which is a receptor tyrosine kinase supporting cell growth and division.
    - EGFR mutations are present in 10 to 15%. EGFR exon 20 insertion mutations are the third most prevalent activating EGFR mutation.
- Rybrevant is a bispecific antibody that targets EGFR exon 20 insertion mutations. It is the first targeted therapy for this specific population.
- The efficacy of Rybrevant was established in CHRYSALIS, an open-label, multi-cohort clinical study in 81 patients with locally advanced or metastatic NSCLC with EGFR exon 20 insertion mutation. Patients received Rybrevant once weekly for 4 weeks, then every 2 weeks thereafter until disease progression or unacceptable toxicity. The major efficacy outcome measure was overall response rate (ORR). An additional efficacy outcome measure was duration of response (DOR).
    - The ORR was 40% (95% CI: 29, 51).
    - The median DOR was 11.1 months (95% CI: 6.9, not estimable).
- Warnings and precautions for Rybrevant include infusion-related reactions, interstitial lung disease/pneumonitis, dermatologic adverse reactions, ocular toxicity, and embryo-fetal toxicity.
- The most common adverse reactions (≥ 20%) with Rybrevant use were rash, infusion-related reactions, paronychia, musculoskeletal pain, dyspnea, nausea, fatigue, edema, stomatitis, cough, constipation, and vomiting.
- The most common Grade 3 or 4 laboratory abnormalities (≥ 2%) with Rybrevant use were decreased lymphocytes, decreased albumin, decreased phosphate, decreased potassium, increased alkaline phosphatase, increased glucose, increased gamma-glutamyl transferase, and decreased sodium.
- The recommended dose of Rybrevant is based on baseline body weight. In patients weighing < 80 kg, the recommended dose is 1,050 mg. In patients weighing ≥ 80 kg, the recommended dose is 1,400 mg. Rybrevant should be administered weekly for 4 weeks, with the initial dose as a split infusion in week 1 on day 1 and day 2, then administer every 2 weeks thereafter until disease progression or unacceptable toxicity.

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    - Prior to initial infusion of Rybrevant (week 1, days 1 and 2), premedications should be administered to reduce the risk of infusion-related reaction.

- Johnson & Johnson's launch plans for Rybrevant are pending. Rybrevant will be available as a 350 mg/7 mL (50 mg/mL) solution in a single-dose vial.