Revuforj® (revumenib) – New orphan drug approval

- On November 15, 2024, Syndax announced the FDA approval of Revuforj (revumenib), for the treatment of relapsed or refractory acute leukemia with a lysine methyltransferase 2A gene (KMT2A) translocation in adult and pediatric patients 1 year and older.

- Rearrangements of the KMT2A gene (KMT2Ar) give rise to an aggressive form of acute leukemia that is associated with a very poor prognosis and high relapse rates. It is estimated that more than 95% of patients with KMT2Ar acute leukemia have a KMT2A translocation.

- Revuforj is a first-in-class menin inhibitor and works by blocking the interaction of both wild-type KMT2A and KMT2A fusion proteins with menin.

- The efficacy of Revuforj was established in a single-arm cohort of an open-label study in 104 adult and pediatric patients at least 30 days old with relapsed or refractory acute leukemia with a KMT2A translocation. Efficacy was established based on the rate of complete remission (CR) plus CR with partial hematologic recovery (CRh), the duration of CR+CRh, and the rate of conversion from transfusion dependence to transfusion independence.

    — The CR+CRh rate was 21.2% (95% CI: 13.8, 30.3). Of the 22 patients who achieved a CR or CRh, the median time to CR or CRh was 1.9 months (range: 0.9, 5.6 months).
    — Among the 83 patients who were dependent on red blood cell (RBC) and/or platelet transfusions at baseline, 14% became independent of RBC and platelet transfusions during any 56-day postbaseline period. Of the 21 patients who were independent of both RBC and platelet transfusions at baseline, 48% remained transfusion independent during any 56-day post-baseline period.

- Revuforj carries a boxed warning for differentiation syndrome.

- Additional warnings and precautions for Revuforj include QTc interval prolongation and embryo-fetal toxicity.

- The most common adverse reactions (≥ 20%), including laboratory abnormalities, with Revuforj use were hemorrhage, nausea, increased phosphate, musculoskeletal pain, infection, increased aspartate aminotransferase, febrile neutropenia, increased alanine aminotransferase, increased parathyroid hormone intact, bacterial infection, diarrhea, differentiation syndrome, electrocardiogram QT prolonged, decreased phosphate, increased triglycerides, decreased potassium, decreased appetite, constipation, edema, viral infection, fatigue, and increased alkaline phosphatase.

- The recommended oral dose of Revuforj varies by patient weight and concomitant use of strong CYP3A4 inhibitors. Refer to the Revuforj drug label for complete dosing and administration recommendations.

    — Revuforj should be continued until disease progression or unacceptable toxicity. For patients without disease progression or unacceptable toxicity, treat for a minimum of 6 months to allow time for clinical response.

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- Syndax expects that the 110 mg and 160 mg tablets of Revuforj will be available in November. Syndax expects that the 25 mg tablets, which may be used to treat patients who weigh less than 40 kg, will be commercially available in late first quarter or early second quarter of 2025.