Turalio™ (pexidartinib) – New orphan drug approval

- On August 2, 2019, the FDA announced the approval of Daiichi Sankyo's Turalio (pexidartinib), for the treatment of adult patients with symptomatic tenosynovial giant cell tumor (TGCT) associated with severe morbidity or functional limitations and not amenable to improvement with surgery.

    — Turalio is available only through a restricted program called the Turalio Risk Evaluation and Mitigation Strategy (REMS) Program, because of the risk of hepatotoxicity.

- TGCT is a rare tumor that affects the synovium and tendon sheaths. The tumor is rarely malignant but causes the synovium and tendon sheaths to thicken and overgrow, causing damage to surrounding tissue. TGCT can cause debilitating symptoms for patients such as pain, stiffness and limitation of movement.

    — While the exact incidence of TGCT is not known, it is estimated that the incidence of TGCT is 11 to 50 cases per million person-years, based on studies from three countries.
    — Surgery is the primary treatment option, but some patients are not eligible for surgery or have recurrent tumors even after a procedure.

- Turalio inhibits colony stimulating factor-1 receptor, which is a primary growth driver of abnormal cells in the synovium that cause TGCT.

    — Turalio is the first FDA-approved therapy to treat TGCT.

- The efficacy of Turalio was established in a double-blind study (ENLIVEN) in 120 patients with symptomatic TGCT for whom surgical removal of the tumor would be associated with worsening functional limitation or severe morbidity. Patients were randomized to placebo or Turalio and treatment continued until unacceptable toxicity or disease progression. The major efficacy outcome measure was overall response rate (ORR). An additional efficacy outcome measure was mean change from baseline in range of motion of the affected joint at week 25.

    — The ORR was 38% (95% CI: 27, 50) and 0% (95% CI: 0, 6) for Turalio and placebo, respectively ($p < 0.0001$). The duration of response range for Turalio was 6.9+ to 24.9+ months.
    — The analysis of mean change from baseline in range of motion at week 25 also demonstrated a statistically significant improvement in patients randomized to Turalio vs. placebo.

- Turalio carries a boxed warning for hepatotoxicity.

- An additional warning and precaution for Turalio is embryo-fetal toxicity.

- The most common adverse reactions (> 20%) with Turalio use were increased lactate dehydrogenase, increased aspartate aminotransferase, hair color changes, fatigue, increased alanine aminotransferase, decreased neutrophils, increased cholesterol, increased alkaline phosphatase, decreased lymphocytes, eye edema, decreased hemoglobin, rash, dysgeusia, and decreased phosphate.

- The recommended dosage of Turalio is 400 mg taken orally twice daily until disease progression or unacceptable toxicity.

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    - Turalio should be administered on an empty stomach, at least one hour before or two hours after a meal or snack.

- Daiichi Sankyo plans to launch Turalio immediately. Turalio will be available as a 200 mg capsule.