Pyrukynd® (mitapivat) – New orphan drug approval

- On February 17, 2022, Agios Pharmaceuticals announced the FDA approval of Pyrukynd (mitapivat), for the treatment of hemolytic anemia in adults with pyruvate kinase (PK) deficiency.

- PK deficiency is a rare, inherited disease that presents as chronic hemolytic anemia. PK deficiency is associated with serious complications, including gallstones, pulmonary hypertension, extramedullary hematopoiesis, osteoporosis, and iron overload.

    — Current management strategies for PK deficiency include red blood cell transfusions and splenectomy.

- Pyrukynd is a first-in-class PK activator that increases PK activity. The red blood cell form of PK (PK-R) is mutated in PK deficiency, which leads to shortened red blood cell lifespan and chronic hemolysis.

- The efficacy of Pyrukynd was established in ACTIVATE, a randomized, double-blind, placebo-controlled study in 80 adults with PK deficiency who were not regularly transfused. Patients were randomized to Pyrukynd or placebo. The primary endpoint was hemoglobin (Hb) response, defined as a ≥ 1.5 g/dL increase in Hb from baseline sustained at 2 or more scheduled assessments (weeks 16, 20, and 24) during the fixed dose period without transfusions.

    — Hb response was achieved in 40% of patients with Pyrukynd vs. 0 patients with placebo (treatment different 39; 95% CI: 24, 55; $p < 0.0001$).

- The efficacy of Pyrukynd was also established in ACTIVATE-T, a single-arm study in 27 adults with PK deficiency who had a minimum of 6 transfusion episodes in the 52-week period prior to informed consent. The primary endpoint was transfusion reduction response, defined as ≥ 33% reduction in the number of red blood cell units transfused during the fixed dose period compared with the patient's historical transfusion burden.

    — Transfusion reduction response was achieved by 33% of patients (95% CI: 17, 54).
    — In addition, 22% (95% CI: 9, 42) of patients were transfusion free during the fixed dose period.

- A warnings and precautions for Pyrukynd is acute hemolysis with abrupt treatment interruption.

- The most common adverse reactions including laboratory abnormalities (≥ 10%) with Pyrukynd use were decreased estrone (males), increased urate, back pain, decreased estradiol (males), and arthralgia.

- The starting dosage for Pyrukynd is 5 mg orally twice daily. To gradually increase Hb, Pyrukynd should be titrated from 5 mg twice daily to 20 mg twice daily, and then to the maximum recommended dose of 50 mg twice daily, with these dose increases occurring every 4 weeks.

    — Hb and transfusion requirement should be assessed before increasing to the next dose level, as some patients may reach and maintain normal Hb at 5 mg twice daily or 20 mg twice daily.

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- Agios Pharmaceuticals plans to launch Pyrukynd in approximately two weeks. Pyrukynd will be available as 5 mg, 20 mg, and 50 mg tablets