Siklos™ (hydroxyurea) – New orphan drug approval

- The FDA announced the approval Addmedica's Siklos (hydroxyurea), to reduce the frequency of painful crises and to reduce the need for blood transfusions in pediatric patients, 2 years of age and older, with sickle cell anemia with recurrent moderate to severe painful crises.

- Sickle cell disease (SCD) is a genetic blood disorder. The most common form is sickle cell anemia, which results in an abnormal hemoglobin protein in red blood cells.

    - Patients with SCD experience numerous health problem including painful attacks or crises. These crises vary in intensity but may last for a few hours to a few weeks.

- Hydroxyurea is also available generically as a 500 mg capsule and as the branded Droxia® 200 mg, 300 mg and 400 mg capsules.

    - Generic hydroxyurea is indicated in adult patients for the treatment of resistant chronic myeloid leukemia, and locally advanced squamous cell carcinomas of the head and neck (excluding the lip) in combination with chemoradiation.
    - Droxia is approved for the same indication as Siklos, but for adult patients only.

- The efficacy of Siklos was assessed in an open-label single-arm study of 405 pediatric patients with SCD from 2 – 18 years of age.

    - Among pediatric patients not previously treated with hydroxyurea prior to enrollment, the percentage of patients with at least one vaso-occlusive episode, one episode of acute chest syndrome, one hospitalization due to SCD or one blood transfusion decreased after 12 months of Siklos treatment.

- Siklos carries a boxed warning for myelosuppression and malignancies.

- Other warnings and precautions of Siklos include embryo-fetal toxicity, vasculitic toxicities, risks with concomitant use of antiretroviral drugs, risks with concomitant use of live virus vaccine, macrocytosis, and test interference.

- The most common adverse reactions (> 10%) with Siklos use were infections and neutropenia.

- The recommended initial dosage of Siklos is 20 mg/kg orally once daily based on patient's actual or ideal weight, whichever is less.

    - The patient's blood count should be monitored every 2 weeks. If blood counts are in an acceptable range, the dose may be increased by 5 mg/kg/day every 8 weeks or if painful crisis occurs, up to a maximum of 35 mg/kg/day.
    - Doses should be calculated to the nearest 50 mg or 100 mg strength based on clinical judgment.
    - Siklos should be discontinued until hematologic recovery if blood counts are considered toxic. Treatment may be resumed after reducing the dose by 5 mg/kg/day from the dose associated with hematological toxicity.

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- Addmedica’s launch plans for Siklos are pending. Siklos will be available as a 100 mg tablet and a 1,000 mg triple-scored tablet.