Adzynma (ADAMTS13, recombinant-krhn) – New orphan drug approval

- On November 9, 2023, the FDA announced the approval of Takeda's Adzynma (ADAMTS13, recombinant-krhn), for prophylactic or on demand enzyme replacement therapy (ERT) in adult and pediatric patients with congenital thrombotic thrombocytopenic purpura (cTTP).

- cTTP is an ultra-rare blood clotting disorder caused by a disease-causing mutation in the ADAMTS13 gene, which is responsible for making an enzyme, also named ADAMTS13, that regulates blood clotting. A deficiency in this enzyme causes blood clots to form in the small blood vessels throughout the body. Individuals with cTTP may experience severe bleeding episodes, strokes, and damage to vital organs.

    - If left untreated, the disease can be fatal. Treatment for cTTP typically involves prophylactic plasma-based therapy for individuals with chronic disease to reduce the risk of clotting/bleeding by replenishing the absent/low ADAMTS13 enzyme.
    - It is estimated that cTTP affects fewer than 1,000 in the U.S.

- Adzynma is the first approved treatment for cTTP. Adzynma is a purified recombinant form of the ADAMTS13 enzyme that works by providing a replacement for the low levels of the deficient enzyme in patients with cTTP.

- The efficacy of Adzynma was established in a randomized, active-controlled, open-label, two-period crossover study followed by a single arm continuation period (Study 1) evaluating the efficacy and safety of the prophylactic and on demand ERT with Adzynma compared to plasma-based therapies in patients with cTTP.

- The efficacy of Adzynma in the prophylactic treatment of patients with cTTP was evaluated in Study 1, in 46 patients who were randomized to receive 6 months of treatment with either Adzynma or plasma-based therapies (Period 1), then crossed over to the other treatment for 6 months (Period 2). Thirty-five patients have entered the 6-month single arm period with Adzynma (Period 3). Efficacy was established based on the incidence of acute and subacute TTP events and TTP manifestations as well as the incidence of supplemental doses prompted by subacute TTP events over a 6-month time period.

    - No patients receiving Adzynma had an acute TTP event throughout the study, including Period 3. One acute TTP event occurred in a patient receiving plasma-based therapies (FFP) prophylactically during Period 1.
    - No subacute TTP events were reported in patients receiving Adzynma during Periods 1 and 2. In Period 3, two patients receiving Adzynma prophylaxis had two subacute events of which one was treated with four supplemental doses, 2 of FFP and 2 of Adzynma. Four patients receiving plasma-based therapies had five subacute TTP events in Periods 1 and 2. A total of seven supplemental doses, 2 of FVIII-VWF concentrate, 1 of FFP and 4 of Adzynma were given to three of these patients.

- The efficacy of the on demand (OD) ERT was evaluated based on the proportion of acute TTP events responding to Adzynma in both the Prophylactic and the OD cohorts throughout the duration of the study. An acute TTP event responding to Adzynma was defined as a resolved TTP event when platelet count was ≥ 150,000/μL or platelet count was within 25% of baseline, whichever occurs first, and lactate dehydrogenase (LDH) ≤ 1.5 x baseline or ≤ 1.5 x upper limit normal (ULN), without requiring the use of another ADAMTS13-containing agent.

Continued . . .

    - Five adult patients enrolled in the OD cohort and had a total of six acute TTP events. Of these five patients, two patients were randomized to receive on-demand treatment with Adzynma, and three patients were randomized to receive plasma-based therapies.
    - All 6 acute TTP events resolved after treatment with either Adzynma or plasma-based therapies.

- Warnings and precautions for Adzynma include hypersensitivity and immunogenicity.

- The most common adverse reactions (> 5%) with Adzynma use were headache, diarrhea, migraine, abdominal pain, nausea, upper respiratory tract infection, dizziness, and vomiting.

- The recommended intravenous (IV) prophylactic dose of Adzynma is 40 IU/kg body weight once every other week. The prophylactic dosing frequency may be adjusted to 40 IU/kg body weight once weekly based on prior prophylactic dosing regimen or clinical response.

- The recommended IV dosing of Adzynma for on demand treatment of an acute event is as follows:

    - Treatment day 1: 40 IU/kg
    - Treatment day 2: 20 IU/kg
    - Treatment day 3 and beyond: 15 IU/kg once daily until two days after the acute event is resolved.

- Takeda's launch plans for Adzynma are pending. Adzynma will be available as a lyophilized powder in single-dose vials containing nominally 500 or 1500 IU.

Optum