Pepaxto® (melphalan flufenamide) – Safety update

- On July 28, 2021, the FDA alerted patients and health care professionals that a clinical trial (OCEAN, Study OP-103) evaluating Pepaxto (melphalan flufenamide) with dexamethasone to treat patients with multiple myeloma showed an increased risk of death.

- The trial compared Pepaxto with low-dose dexamethasone to Pomalyst® (pomalidomide) with low-dose dexamethasone in patients with relapsed or refractory (resistant) multiple myeloma following 2-4 lines of prior therapy and in patients who were resistant to Revlimid® (lenalidomide) in the last line of therapy.

    — There were 495 randomized patients included in the efficacy analysis.
    — For overall survival (OS), there were 117/246 (48%) deaths in the Pepaxto investigational arm and 108/249 (43%) deaths in the Pomalyst control arm.
    — The hazard ratio of the Pepaxto arm vs. Pomalyst arm was 1.104 (95% CI: 0.846, 1.441) indicating a detriment in survival with Pepaxto vs. Pomalyst.
    — The median OS with Pepaxto was 19.7 months (95% CI: 15.1, 25.6) vs. 25.0 months (95% CI: 18.1, 31.9) with Pomalyst. The median follow-up for survival was 19.1 months.

- The FDA encourages health care professionals to review patients' progress on Pepaxto and discuss the risks of continued administration with each patient in the context of other treatments. Patients currently receiving Pepaxto should also discuss with their health care professional the risks and benefits of receiving Pepaxto.

- In February 2021, the FDA approved Pepaxto under accelerated approval for use in combination with dexamethasone to treat adult patients with relapsed or refractory multiple myeloma who have received at least four prior lines of therapy and whose disease was refractory to at least one proteasome inhibitor, one immunomodulatory agent, and one CD38-directed monoclonal antibody. The manufacturer, Oncopeptides AB, was required to conduct the OCEAN trial as a post-approval requirement under the accelerated approval program.

- Due to the detrimental effect on OS in the OCEAN trial, the FDA is requiring the manufacturer suspend enrollment in the trial. The FDA has also suspended enrollment in other ongoing Pepaxto clinical trials. Patients receiving clinical benefit from Pepaxto may continue treatment in the OCEAN trial provided they are informed of the risks and sign a revised written informed consent.

- The FDA continues to evaluate the OCEAN trial results and may hold a future public meeting to discuss these safety findings and explore the continued marketing of Pepaxto. The agency will update patients and health care professionals when new information is available.