Brukinsa™ (zanubrutinib) – New orphan drug approval

- On November 14, 2019, the FDA announced the approval of BeiGene's Brukinsa (zanubrutinib), for the treatment of adult patients with mantle cell lymphoma (MCL) who have received at least one prior therapy.
    - This indication is approved under accelerated approval based on overall response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.
- MCL is a type of non-Hodgkin's lymphoma representing 3% to 10% of all non-Hodgkin's lymphomas in the U.S. By the time it is diagnosed, MCL has usually spread to the lymph nodes, bone marrow and other organs.
- Brukinsa is a small-molecule inhibitor of Bruton's tyrosine kinase (BTK). BTK is a signaling molecule of the B-cell antigen receptor and cytokine receptor pathways. In B-cells, BTK signaling results in activation of pathways necessary for B-cell proliferation, trafficking, chemotaxis, and adhesion.
- The efficacy of Brukinsa was established in an open-label, single-arm study of 86 previously treated patients with MCL who had received at least one prior therapy. Brukinsa was given orally at a dose of 160 mg twice daily until disease progression or unacceptable toxicity. The primary efficacy endpoint was overall response rate (ORR).
    - The ORR was 84% (95% CI: 74, 91). The median duration of response (DOR) was 19.5 months (95% CI: 16.6, not estimable).
- The efficacy of Brukinsa was also assessed in an open-label, dose-escalation, single-arm study of B-cell malignancies including 32 previously treated MCL patients. Brukinsa was given orally at doses of 160 mg twice daily or 320 mg daily. The primary efficacy endpoint was ORR.
    - The ORR was 84% (95% CI: 67, 95). The median DOR was 18.5 months (95% CI: 12.6, not estimable).
- Warnings and precautions for Brukinsa include hemorrhage, infections, cytopenias, second primary malignancies, cardiac arrhythmias, and embryo-fetal toxicity.
- The most common adverse reactions (≥ 20%) with Brukinsa use were decreased neutrophil count, decreased platelet count, upper respiratory tract infection, decreased white blood cell count, decreased hemoglobin, rash, bruising, diarrhea and cough.
- The recommended dose of Brukinsa is 160 mg taken orally twice daily or 320 mg taken orally once daily until disease progression or unacceptable toxicity.
- BeiGene plans to launch Brukinsa in the coming weeks. Brukinsa will be available as a 80 mg capsule.