Xpovio™ (selinexor) – New orphan drug approval

- On July 3, 2019, the FDA announced the approval of Karyopharm's Xpovio (selinexor), in combination with dexamethasone for the treatment of adult patients with relapsed or refractory multiple myeloma (RRMM) who have received at least four prior therapies and whose disease is refractory to at least two proteasome inhibitors, at least two immunomodulatory agents, and an anti-CD38 monoclonal antibody.
    - This indication is approved under accelerated approval based on response rate. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial.
- Multiple myeloma is a type of cancer that begins in the plasma cells (white blood cells that produce antibodies). Abnormal plasma cells build up in the bone marrow, forming tumors in many bones of the body. As more antibodies are made, it can cause blood to thicken and keep the bone marrow from making enough healthy blood cells.
    - According to the National Cancer Institute, 32,110 new cases of multiple myeloma will be diagnosed and 12,960 deaths will occur in 2019.
- Xpovio is a first-in-class, oral selective inhibitor of nuclear export compound. Xpovio blocks the nuclear export of tumor suppressor, growth regulatory and anti-inflammatory proteins, leading to accumulation of these proteins in the nucleus and enhancing their anti-cancer activity in the cell.
- The efficacy of Xpovio plus dexamethasone was demonstrated in a single-arm, open-label study (STORM) enrolling 122 patients with RRMM who had previously received three or more anti-myeloma treatment regimens. Treatment continued until disease progression, death, or unacceptable toxicity. The primary endpoint was overall response rate (ORR) in a sub-group of 83 patients with heavily pretreated disease.
    - The ORR was 25.3% (95% CI: 16.4, 36).
    - In addition, the median duration of response was 3.8 months (95% CI: 2.3, not estimable).
- Warnings and precautions of Xpovio include thrombocytopenia, neutropenia, gastrointestinal toxicity, hyponatremia, infections, neurological toxicity, and embryo-fetal toxicity.
- The most common adverse reactions (≥ 20%) of Xpovio use were thrombocytopenia, fatigue, nausea, anemia, decreased appetite, decreased weight, diarrhea, vomiting, hyponatremia, neutropenia, leukopenia, constipation, dyspnea, and upper respiratory tract infection.
- The recommended starting dose of Xpovio is 80 mg (four 20 mg tablets) taken orally on days 1 and 3 of each week until disease progression or unacceptable toxicity.
    - The recommended starting dosage of dexamethasone is 20 mg taken orally with each dosage of Xpovio on days 1 and 3 of each week. Refer to the dexamethasone drug label for additional administration instructions.
- Karyopharm plans to launch Xpovio by July 10, 2019. Xpovio will be available as 20 mg tablets.