Ukoniq™ (umbralisib) – New orphan drug approval

- On February 5, 2021, TG Therapeutics announced the FDA approval of Ukoniq (umbralisib), for the treatment of adult patients with: (1) relapsed or refractory marginal zone lymphoma (MZL) who have received at least one prior anti-CD20-based regimen or (2) relapsed or refractory follicular lymphoma (FL) who have received at least three prior lines of systemic therapy.
    - These indications were 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(s).
- MZL comprises a group of indolent (slow growing) mature B-cell non-Hodgkin lymphomas (NHLs). MZL is generally considered a chronic and incurable disease. The annual incidence is approximately 8,200 newly diagnosed patients in the U.S.
- FL is typically an indolent form of NHL that arises from B-lymphocytes. FL is also generally not curable and is considered a chronic disease. The annual incidence in the U.S. is approximately 13,200 newly diagnosed patients.
- Ukoniq is an inhibitor of phosphoinositide 3 kinase (PI3K) delta and casein kinase 1 (CK1) epsilon. PI3K-delta is known to play an important role in supporting cell proliferation and survival, cell differentiation, intercellular trafficking and immunity and is expressed in both normal and malignant B-cells. CK1-epsilon is a regulator of oncoprotein translation and has been implicated in the pathogenesis of cancer cells, including lymphoid malignancies.
- The efficacy of Ukoniq was established in Study UTX-TGR-205, an open-label, multi-cohort trial. The MZL cohort included 69 patients. Patients received Ukoniq until disease progression or unacceptable toxicity. Efficacy was based on overall response rate (ORR).
    - The ORR was 49% (95% CI: 37.0, 61.6).
    - The median duration of response (DOR) was not reached (95% CI: 9.3, not evaluable).
- The FL cohort of Study UTX-TGR-205 included 117 patients. Patients received Ukoniq until disease progression or unacceptable toxicity and efficacy was based on ORR.
    - The ORR was 43% (95% CI: 33.6, 52.2).
    - The median DOR was 11.1 months (95% CI: 8.3, 16.4).
- Warnings and precautions for Ukoniq include infections, neutropenia, diarrhea or non-infectious colitis, hepatotoxicity, severe cutaneous reactions, allergic reactions due to inactive ingredient FD&C Yellow No. 5, and embryo-fetal toxicity.
- The most common adverse reactions (≥ 15%), including laboratory abnormalities, with Ukoniq use were increased creatinine, diarrhea-colitis, fatigue, nausea, neutropenia, transaminase elevation, musculoskeletal pain, anemia, thrombocytopenia, upper respiratory tract infection, vomiting, abdominal pain, decreased appetite, and rash.
- The recommended dose of Ukoniq is 800 mg taken orally once daily with food until disease progression or unacceptable toxicity.

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- — Prophylaxis should be provided for *Pneumocystis jirovecii* pneumonia during treatment with Ukoniq.
- — Prophylactic antivirals should be considered during treatment with Ukoniq to prevent cytomegalovirus (CMV) infection, including CMV reactivation.

- TG Therapeutics plans to launch Ukoniq in the next few days. Ukoniq will be available as a 200 mg tablet.