NOW APPROVED

UKONIQ™
umbralisib 200 mg tablets

THE **FIRST AND ONLY** TARGETED KINASE INHIBITOR OF **PI3K-DELTA** AND **CK1-EPSILON**

TG Therapeutics is proud to announce the approval of UKONIQ. UKONIQ is indicated for the treatment of adult patients with:

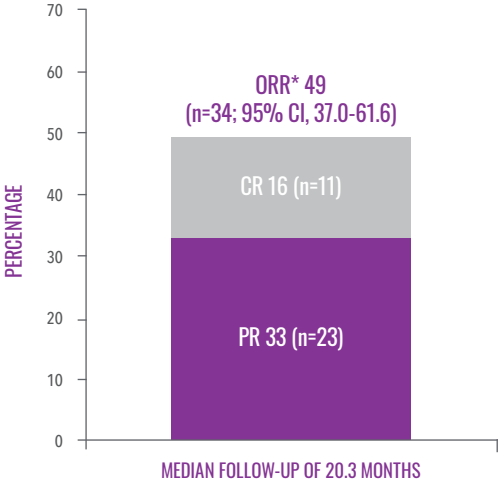
MZL **Relapsed or refractory marginal zone lymphoma (MZL) who have received at least one prior anti-CD20-based regimen**

FL **Relapsed or refractory follicular lymphoma (FL) who have received at least three prior lines of systemic therapy**

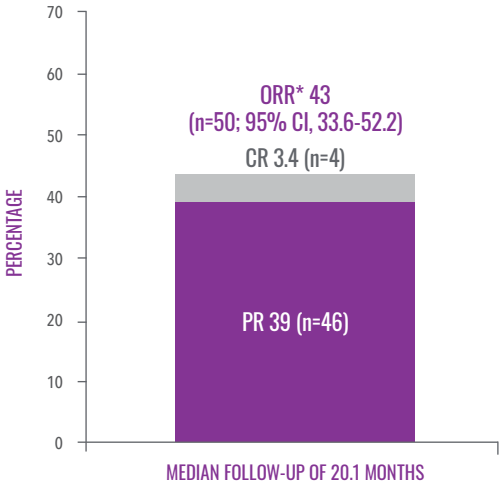
These indications are approved under accelerated approval based on overall response rate. Continued approval for these indications may be contingent upon verification and description of clinical benefit in a confirmatory trial.

UKONIQ is a targeted kinase inhibitor of PI3K-delta and CK1-epsilon. PI3K-delta is expressed in normal and malignant B cells. CK1-epsilon has been implicated in the pathogenesis of cancer cells, including lymphoid malignancies.

MZL 49% OF PATIENTS WITH R/R MZL RESPONDED TO UKONIQ



FL 43% OF PATIENTS WITH R/R FL RESPONDED TO UKONIQ



mDOR NOT REACHED (95% CI, 9.3-NE; RANGE, 0.0†-21.8†) WITH A MEDIAN FOLLOW-UP OF 20.3 MONTHS (RANGE, 15.0-28.7)‡

mDOR 11.1 MONTHS (95% CI, 8.3-16.4; RANGE, 0.0†-20.9†) WITH A MEDIAN FOLLOW-UP OF 20.1 MONTHS (RANGE, 13.5-29.6)‡

UKONIQ was evaluated in an open-label, multi-cohort, single-arm study in 69 patients with MZL who received at least 1 prior therapy (including an anti-CD20 regimen) and 117 patients with FL who received at least 2 prior systemic therapies (including an anti-CD20 monoclonal antibody and an alkylating agent). The primary endpoint was overall response rate.

CI=confidence interval; CR=complete response; mDOR=median duration of response; NE=not evaluable; PR=partial response; R/R=relapsed or refractory.
*Responses were assessed by an Independent Review Committee (IRC) using criteria adopted from the International Working Group (IWG) criteria for malignant lymphoma.
†Denotes censored observation.
‡Based on Kaplan-Meier estimation.

IMPORTANT SAFETY INFORMATION

Infections: Serious, including fatal, infections occurred in patients treated with UKONIQ. Grade 3 or higher infections occurred in 10% of 335 patients, with fatal infections occurring in <1%. The most frequent Grade ≥3 infections included pneumonia, sepsis, and urinary tract infection. Provide prophylaxis for Pneumocystis jirovecii pneumonia (PJP) and consider prophylactic antivirals during treatment with UKONIQ to prevent CMV infection, including CMV reactivation.

Please see additional Important Safety Information on next page and accompanying full Prescribing Information.

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IMPORTANT SAFETY INFORMATION (CONT'D)

Infections (cont'd): Monitor for any new or worsening signs and symptoms of infection, including suspected PJP or CMV, during treatment with UKONIQ. For Grade 3 or 4 infection, withhold UKONIQ until infection has resolved. Resume UKONIQ at the same or a reduced dose. Withhold UKONIQ in patients with suspected PJP of any grade and permanently discontinue in patients with confirmed PJP. For clinical CMV infection or viremia, withhold UKONIQ until infection or viremia resolves. If UKONIQ is resumed, administer the same or reduced dose and monitor patients for CMV reactivation by PCR or antigen test at least monthly.

Neutropenia: Serious neutropenia occurred in patients treated with UKONIQ. Grade 3 neutropenia developed in 9% of 335 patients and Grade 4 neutropenia developed in 9%. Monitor neutrophil counts at least every 2 weeks for the first 2 months of UKONIQ and at least weekly in patients with neutrophil count <1 x 10^9/L (Grade 3-4) neutropenia during treatment with UKONIQ. Consider supportive care as appropriate. Withhold, reduce dose, or discontinue UKONIQ depending on the severity and persistence of neutropenia.

Diarrhea or Non-Infectious Colitis: Serious diarrhea or non-infectious colitis occurred in patients treated with UKONIQ. Any grade diarrhea or colitis occurred in 53% of 335 patients and Grade 3 occurred in 9%. For patients with severe diarrhea (Grade 3, i.e., > 6 stools per day over baseline) or abdominal pain, stool with mucus or blood, change in bowel habits, or peritoneal signs, withhold UKONIQ until resolved and provide supportive care with antidiarrheals or enteric acting steroids as appropriate. Upon resolution, resume UKONIQ at a reduced dose. For recurrent Grade 3 diarrhea or recurrent colitis of any grade, discontinue UKONIQ. Discontinue UKONIQ for life-threatening diarrhea or colitis.

Hepatotoxicity: Serious hepatotoxicity occurred in patients treated with UKONIQ. Grade 3 and 4 transaminase elevations (ALT and/or AST) occurred in 8% and <1%, respectively, in 335 patients. Monitor hepatic function at baseline and during treatment with UKONIQ. For ALT/AST greater than 5 to less than 20 times ULN, withhold UKONIQ until return to less than 3 times ULN, then resume at a reduced dose. For ALT/AST elevation greater than 20 times ULN, discontinue UKONIQ.

Severe Cutaneous Reactions: Severe cutaneous reactions, including a fatal case of exfoliative dermatitis, occurred in patients treated with UKONIQ. Grade 3 cutaneous reactions occurred in 2% of 335 patients and included exfoliative dermatitis, erythema, and rash (primarily maculo-papular). Monitor patients for new or worsening cutaneous reactions. Review all concomitant medications and discontinue any potentially contributing medications. Withhold UKONIQ for severe (Grade 3) cutaneous reactions until resolution. Monitor at least weekly until resolved. Upon resolution, resume UKONIQ at a reduced dose. Discontinue UKONIQ if severe cutaneous reaction does not improve, worsens, or recurs. Discontinue UKONIQ for life-threatening cutaneous reactions or SJS, TEN, or DRESS of any grade. Provide supportive care as appropriate.

Allergic Reactions Due to Inactive Ingredient FD&C Yellow No. 5: UKONIQ contains FD&C Yellow No. 5 (tartrazine), which may cause allergic-type reactions (including bronchial asthma) in certain susceptible persons, frequently in patients who also have aspirin hypersensitivity.

Embryo-fetal Toxicity: Based on findings in animals and its mechanism of action, UKONIQ can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise females and males with female partners of reproductive potential to use effective contraception during treatment and for at least one month after the last dose.

Serious adverse reactions occurred in 18% of 221 patients who received UKONIQ. Serious adverse reactions that occurred in ≥2% of patients were diarrhea-colitis (4%), pneumonia (3%), sepsis (2%), and urinary tract infection (2%). Permanent discontinuation of UKONIQ due to an adverse reaction occurred in 14% of patients. Dose reductions of UKONIQ due to an adverse reaction occurred in 11% of patients. Dosage interruptions of UKONIQ due to an adverse reaction occurred in 43% of patients.

The most common adverse reactions (>15%), including laboratory abnormalities, in 221 patients who received UKONIQ were increased creatinine (79%), diarrhea-colitis (58%, 2%), fatigue (41%), nausea (38%), neutropenia (33%), ALT increase (33%), AST increase (32%), musculoskeletal pain (27%), anemia (27%), thrombocytopenia (26%), upper respiratory tract infection (21%), vomiting (21%), abdominal pain (19%), decreased appetite (19%), and rash (18%).

Lactation: Because of the potential for serious adverse reactions from umbralisib in the breastfed child, advise women not to breastfeed during treatment with UKONIQ and for at least one month after the last dose.

Please see accompanying full Prescribing Information.

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TG Therapeutics