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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 1 prior anti-CD20-based regimen**

FL **Relapsed or refractory follicular lymphoma (FL) who have received at least 3 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 AND FL PATIENT POPULATIONS IN THE CLINICAL TRIAL

	PATIENT TYPE	PRIOR TREATMENT	PRIOR LINES
MZL	R/R MZL (SPLENIC, NODAL, OR EXTRANODAL); 97% OF PATIENTS HAD A BASELINE ECOG PERFORMANCE STATUS OF 0 OR 1	PROGRESSED AFTER ≥1 PRIOR THERAPY, INCLUDING AN ANTI-CD20 REGIMEN	A MEDIAN OF 2 PRIOR LINES OF THERAPY (RANGE 1-6), WITH 26% REFRACTORY TO THE LAST THERAPY
FL	R/R FL; 97% OF PATIENTS HAD A BASELINE ECOG PERFORMANCE STATUS OF 0 OR 1	PROGRESSED AFTER ≥2 PRIOR THERAPIES, INCLUDING AN ANTI-CD20 MONOCLONAL ANTIBODY AND ALKYLATING AGENT	A MEDIAN OF 3 PRIOR LINES OF THERAPY (RANGE 1-10), WITH 36% REFRACTORY TO THE LAST THERAPY

ECOG=Eastern Cooperative Oncology Group.

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. 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.

Please see additional Important Safety Information throughout and full Prescribing Information.

VISIT **UKONIQ.COM** TO LEARN MORE.

UKONIQ ADVERSE REACTIONS (ALL CAUSE) IN ≥10% OF PATIENTS WITH MZL AND FL FROM A POOLED SAFETY POPULATION (N=221)

	UKONIQ N=221		
Adverse reactions	**All Grades (%)**	**Grade 3 (%)**	**Grade 4 (%)**
Gastrointestinal disorders			
Diarrhea	58	10	0
Nausea	38	<1	0
Vomiting	21	<1	0
Abdominal pain[a]	19	3	0
General disorders and administration site conditions			
Fatigue[b]	41	3	0
Edema[c]	14	<1	0
Pyrexia	10	0	0
Musculoskeletal and connective tissue disorders			
Musculoskeletal pain[d]	27	2	0
Infections			
Upper respiratory tract infection[e]	21	<1	0
Metabolism and nutrition disorders			
Decreased appetite	19	2	0
Skin and subcutaneous tissue disorders			
Rash[f]	18	3	0
Psychiatric disorders			
Insomnia	14	<1	0

- 14% of patients permanently discontinued UKONIQ due to an adverse reaction. The most common reasons for discontinuation (in ≥5% of patients) included diarrhea or colitis (6%) and transaminase elevations (5%)
- 43% of patients had dose interruptions due to an adverse reaction. The most common reason for dose interruptions (in ≥5% of patients) included diarrhea or colitis (18%), transaminase elevation (7%), neutropenia (5%), vomiting (5%), and upper respiratory tract infection (5%)
- 11% of patients received a dose reduction due to an adverse reaction. The most common reason for dose reduction (in ≥4% of patients) included diarrhea or colitis (4%)

[a]Abdominal pain includes abdominal pain, abdominal pain upper, abdominal pain lower, abdominal discomfort.
[b]Fatigue includes fatigue, asthenia, lethargy.
[c]Edema includes edema peripheral, face edema, pulmonary edema, fluid overload, generalized edema.
[d]Musculoskeletal pain includes back pain, myalgia, pain in extremity, musculoskeletal pain, neck pain, spinal pain, musculoskeletal chest pain, musculoskeletal discomfort.
[e]Upper respiratory tract infection includes upper respiratory tract infection, sinusitis, nasopharyngitis, rhinitis.
[f]Rash includes rash, rash maculopapular, rash erythematous, rash pruritic, rash macular, exfoliative dermatitis.

- Clinically relevant adverse reactions in <10% of patients who received UKONIQ included urinary tract infection (9%), dyspnea (7%), pneumonia (6%), sepsis (3%), colitis (2%), pneumonitis (<1%), and exfoliative dermatitis (<1%)
- The pooled safety data reflect 221 patients with MZL and FL who received UKONIQ 800 mg orally once daily in 3 single-arm, open-label trials and 1 open-label extension trial

IMPORTANT SAFETY INFORMATION (CONT'D)

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.

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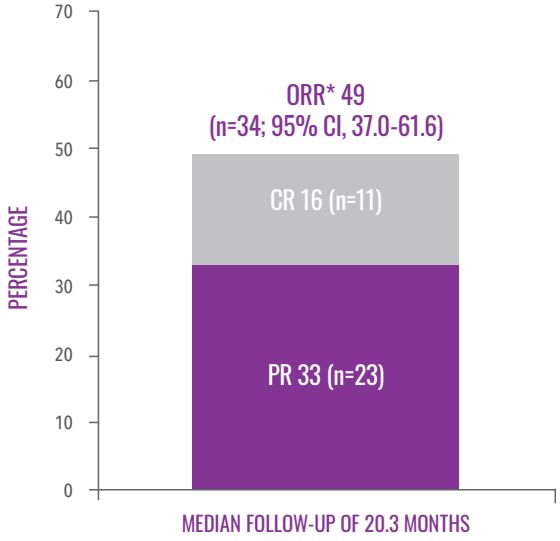
Here are some key data highlighting UKONIQ response rates in MZL/FL:

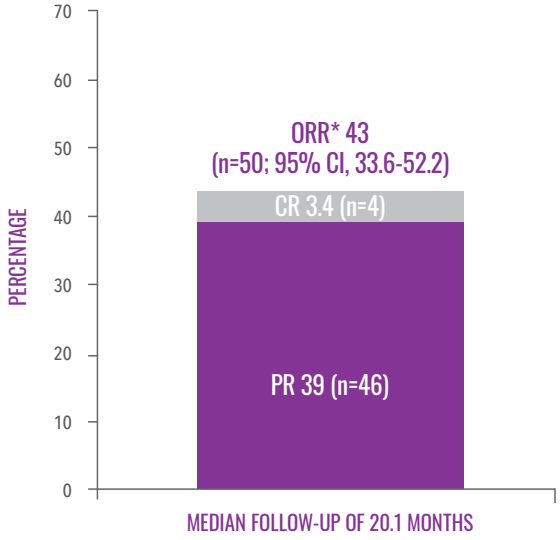
MZL 49% OF PATIENTS WITH R/R MZL RESPONDED TO UKONIQ



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)‡

UKONIQ was evaluated in a single-arm cohort of 69 patients with MZL who received at least 1 prior therapy, including an anti-CD20 regimen, in UNITY-NHL, an open-label, multicenter, multi-cohort trial. The trial excluded patients with prior exposure to a PI3K inhibitor.

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



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 a single-arm cohort of 117 patients with FL who received at least 2 prior systemic therapies in UNITY-NHL, an open-label, multicenter, multi-cohort trial. The trial excluded patients with Grade 3b FL, large-cell transformation, prior allogeneic transplant, history of CNS lymphoma, and prior exposure to a PI3K inhibitor.

CI=confidence interval; CR=complete response; mDOR=median duration of response; NE=not evaluable; PR=partial response.
*Responses were assessed by an International 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 (CONT'D)

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 additional Important Safety Information throughout and full Prescribing Information.

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HOW TO ACCESS UKONIQ

UKONIQ may be dispensed through an in-office dispensing pharmacy or through our specialty pharmacy partner, Onco360. **For more information, visit UKONIQ.com/patientsupport.**

TG PatientSupport™

TG Patient Support is a comprehensive program that provides information and support to help patients navigate the reimbursement process and understand their treatment with UKONIQ.

Services include:

- Insurance support, including verifying the patient's insurance coverage for UKONIQ and co-pay or co-insurance responsibility
- Information about financial assistance options,* including:
  - Commercial co-pay assistance
  - Quick Start and Bridge programs
  - Patient Assistance Program
  - Independent charitable organization support
- Educational support to help patients understand their prescription for UKONIQ

*For additional information on eligibility criteria and full terms and conditions, **please visit UKONIQ.com/patientsupport**.

Visit **UKONIQ.com/patientsupport** to download the enrollment form.

If your patients have questions, they can call **1-877-TGTXPSP (1-877-848-9777)** to speak with a program case manager for more information.

Translation services are available.

Please see Important Safety Information throughout and full Prescribing Information.

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TG Therapeutics