# UKONIQ®
## umbralisib 200 mg tablets

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

TG Therapeutics is proud to share important and helpful information about 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.[1-4]

### MZL AND FL PATIENT POPULATIONS IN THE CLINICAL TRIAL[1]

| | PATIENT TYPE | PRIOR TREATMENT | PRIOR LINES |
|---|---|---|---|
| MZL | R/R MZL (SPLENIC, NODAL, OR EXTRANODAL) WITH ECOG PERFORMANCE STATUS ≤2* | 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 WITH ECOG PERFORMANCE STATUS ≤2* | PROGRESSED AFTER ≥2 PRIOR SYSTEMIC THERAPIES, INCLUDING AN ANTI-CD20 MONOCLONAL ANTIBODY AND AN ALKYLATING AGENT | A MEDIAN OF 3 PRIOR LINES OF THERAPY (RANGE 1-10), WITH 36% REFRACTORY TO THE LAST THERAPY |

*97% of patients had a baseline ECOG performance status of 0 or 1.
ECOG=Eastern Cooperative Oncology Group; R/R=relapsed or refractory.

**See UKONIQ safety information on next page.**

## 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.

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

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## UKONIQ ADVERSE REACTIONS (ALL CAUSE) IN ≥10% OF PATIENTS WITH MZL AND FL FROM A POOLED SAFETY POPULATION (N=221)[1,5]

| | 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 |

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.

[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.

- Serious adverse reactions occurred in 18% of 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%)

**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 dosage 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%)

## IMPORTANT SAFETY INFORMATION (CONT'D)

**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.

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## ADDITIONAL CLINICALLY RELEVANT ADVERSE EVENTS IN PATIENTS WHO RECEIVED UKONIQ[1,5]

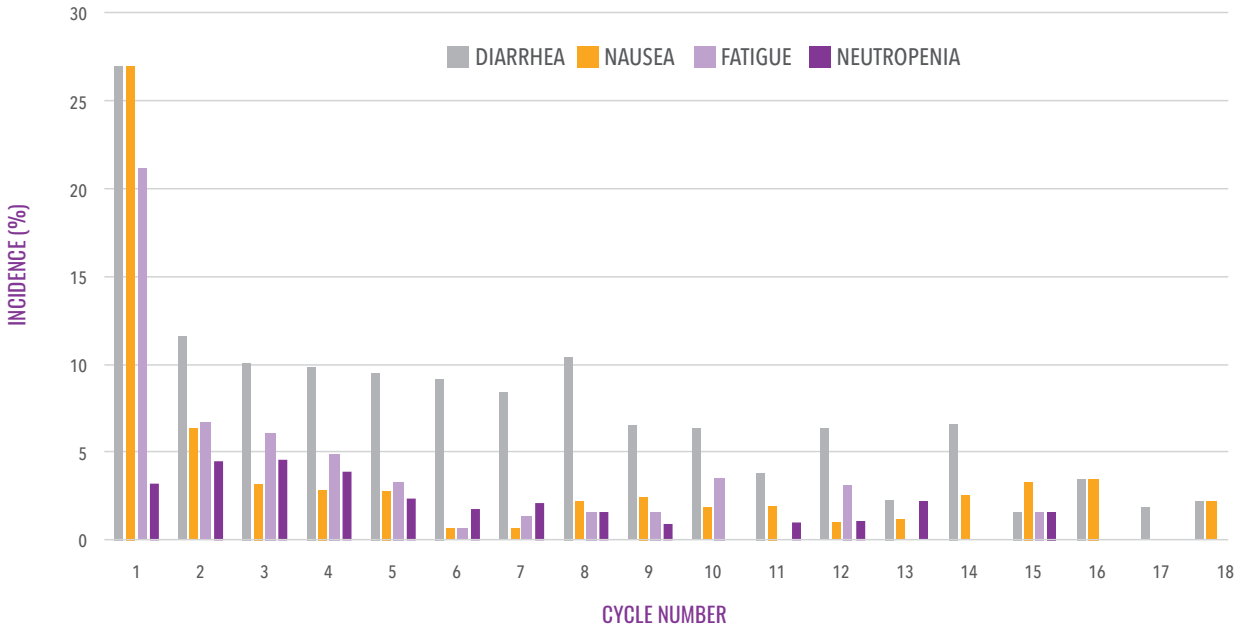
| Adverse reactions | All Grades (%) | Grade 3 (%) | Grade 4 (%) |
|---|---|---|---|
| Colitis | 2.4 | <1 | 0 |
| AST increased | 32 | 7 | 0 |
| ALT increased | 33 | 5.4 | 1.4 |
| Pneumonitis | <1 | 0 | 0 |

ALT=alanine aminotransferase; AST=aspartate aminotransferase.

Other laboratory abnormalities that worsened from baseline in ≥20% of patients included decreased neutrophils (all grades=33%; Grade 3 or 4=16%); decreased hemoglobin (all grades=27%; Grade 3 or 4=3%); decreased platelets (all grades=26%; Grade 3 or 4=4%); creatinine increased (all grades=79%; Grade 3 or 4=0%); potassium decreased (all grades=21%; Grade 3 or 4=4%).

Additional clinically relevant adverse reactions in <10% of patients who received UKONIQ included urinary tract infection (9%), dyspnea (7%), pneumonia (6%), sepsis (3%), and exfoliative dermatitis (<1%).

## DIARRHEA, NAUSEA, FATIGUE, AND NEUTROPENIA (ALL GRADES) PRIMARILY OCCUR WITHIN THE FIRST 2 CYCLES (N=221)[5]




- The median time to onset for any grade diarrhea was 1.2 months (range, 0.03–22.8), with 75% of cases occurring by 3.0 months
- The median time to onset for any grade nausea was 0.3 months (range, 0.03–15.6), with 75% of cases occurring by 1.5 months
- The median time to onset for any grade fatigue was 1.0 months (range, 0.03–49.7), with 75% of cases occurring by 2.8 months
- The median time to onset for any grade neutropenia was 2.8 months (range, 0.03–14.6), with 75% of cases occurring by 4.6 months

## IMPORTANT SAFETY INFORMATION (CONT'D)

**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.

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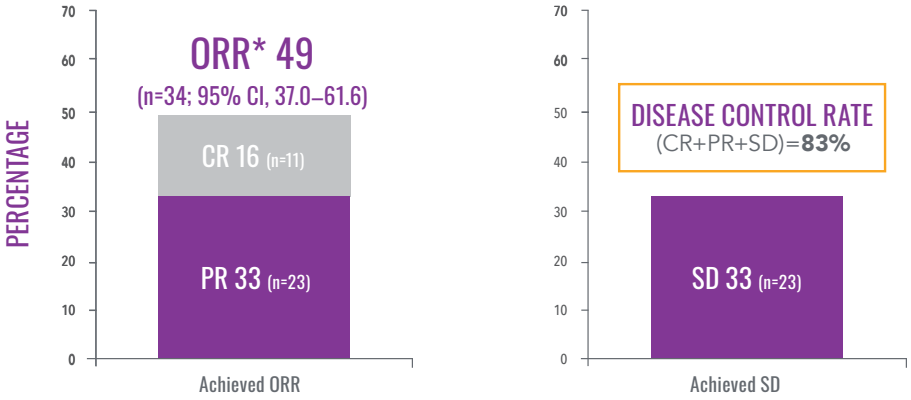
# MZL

**Here are some key efficacy data for UKONIQ in MZL:**

UKONIQ was evaluated in a single-arm cohort of 69 patients with MZL who received at least 1 prior therapy, including an anti-CD20-containing regimen, in UNITY-NHL, an open-label, multicenter, multi-cohort trial. The trial excluded patients with prior exposure to a PI3K inhibitor. Efficacy was based on ORR as assessed by an IRC using criteria adopted from the IWG for malignant lymphoma.[1]

Limitations: The study was not powered to determine efficacy based on disease control rate. It is not possible to determine if stable disease is experienced as a result of the natural progression of disease or treatment with UKONIQ.

## POWERFUL EFFICACY WITH ~50% OF PATIENTS RESPONDING TO SINGLE-AGENT UKONIQ[1,5]

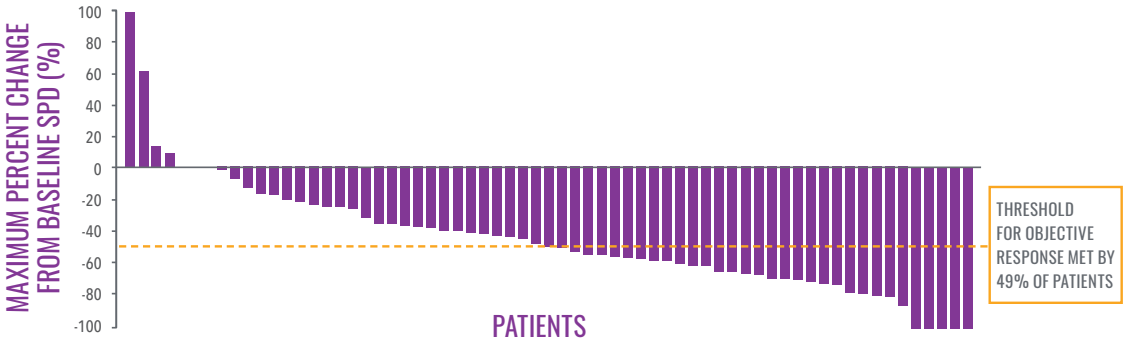



## DURABLE RESPONSES IN R/R MZL[1,5]

- **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)[1‡]**

CI=confidence interval; CR=complete response; mDOR=median duration of response; NE=not evaluable; ORR=overall response rate; PR=partial response; SD=stable disease.

## PERCENT CHANGE OF TARGET LESIONS[5§]




Limitations:

- The clinical meaningfulness of a change in target lesions not meeting the threshold for an objective response (SPD <50% from baseline) is unclear
- The change in target lesion size may not reflect confirmed responses and may not account for new lesions

*Responses were assessed by IRC using criteria adopted from the IWG criteria for malignant lymphoma.
†Denotes censored observation.
‡Based on Kaplan-Meier estimation. DOR rates were determined from non-parametric estimation of the Kaplan-Meier analysis at 6 and 12 months, respectively.
§Percent change in target lesions was determined by 2007 IWG criteria. Patients with a change in target lesions not meeting the threshold for an objective response (SPD <50% from baseline) were classified as having stable disease or progressive disease depending on the percent change in target lesions and other factors including the presence of new lesions.
DOR=duration of response; IRC=independent review committee; IWG=International Working Group; SPD=sum of the product of the diameters.

## IMPORTANT SAFETY INFORMATION (CONT'D)

**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.

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

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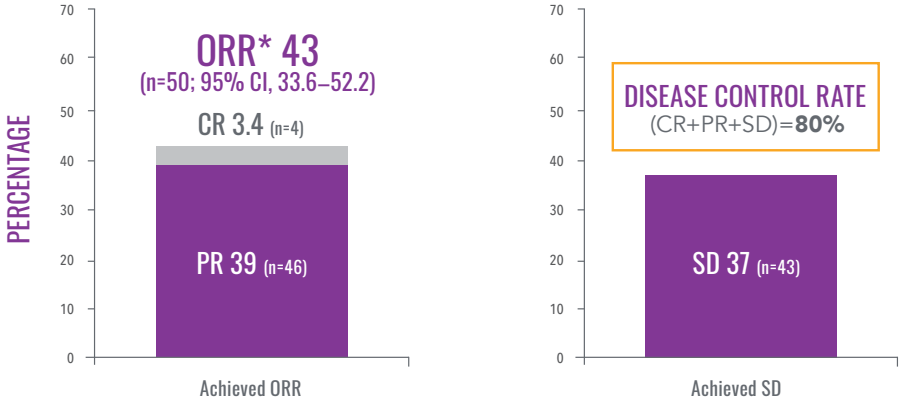
# FL

**Here are some key efficacy data for UKONIQ in FL:**

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. Efficacy was based on ORR as assessed by an IRC using criteria adopted from the IWG for malignant lymphoma.[1]

Limitations: The study was not powered to determine efficacy based on disease control rate. It is not possible to determine if stable disease is experienced as a result of the natural progression of disease or treatment with UKONIQ.

## POWERFUL EFFICACY WITH 43% OF PATIENTS ACHIEVING PR/CR[1,5]

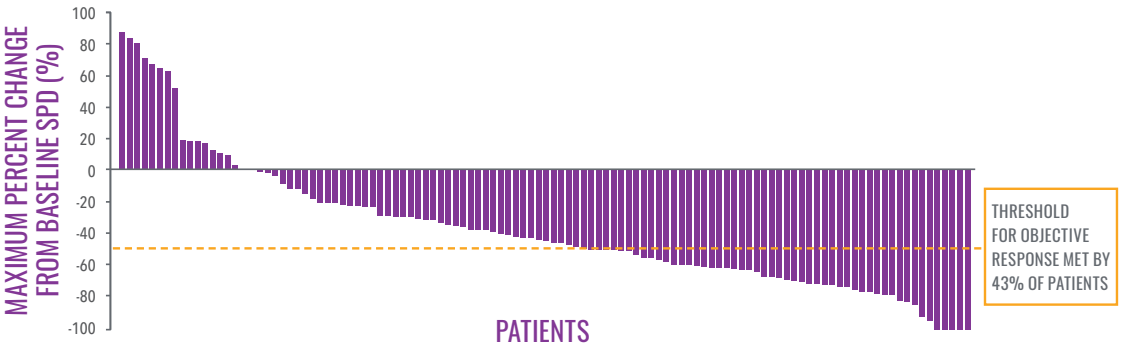



MEDIAN FOLLOW-UP OF 20.1 MONTHS

## NEARLY 50% OF RESPONDERS WITH R/R FL WERE STILL RESPONDING AT 1 YEAR[5]

- **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)[1‡]**

## PERCENT CHANGE OF TARGET LESIONS[5§]




Limitations:

- The clinical meaningfulness of a change in target lesions not meeting the threshold for an objective response (SPD <50% from baseline) is unclear
- The change in target lesion size may not reflect confirmed responses and may not account for new lesions

*Responses were assessed by IRC using criteria adopted from the IWG criteria for malignant lymphoma.
†Denotes censored observation.
‡Based on Kaplan-Meier estimation. DOR rates were determined from non-parametric estimation of the Kaplan-Meier analysis at 6 and 12 months, respectively.
§Percent change in target lesions was determined by 2007 IWG criteria. Patients with a change in target lesions not meeting the threshold for an objective response (SPD <50% from baseline) were classified as having stable disease or progressive disease depending on the percent change in target lesions and other factors including the presence of new lesions.
CNS=central nervous system.

## IMPORTANT SAFETY INFORMATION (CONT'D)

**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. **Support services include:**

### INSURANCE SUPPORT

including verifying the patient's insurance coverage for UKONIQ and co-pay or co-insurance responsibility

### FINANCIAL ASSISTANCE PROGRAMS

- Commercial co-pay assistance
- Quick Start and Bridge programs
- Patient Assistance Program*
- Information about independent charitable organization support

### EDUCATIONAL SUPPORT

to help patients understand their prescription for UKONIQ

*Patients must meet certain eligibility criteria to qualify for the Patient Assistance Program. Eligible patients must be uninsured or underinsured with an annual family gross income equal to or less than 600% of the current federal poverty level.

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 additional Important Safety Information throughout and full Prescribing Information.**

**References: 1.** UKONIQ [prescribing information]. New York, NY: TG Therapeutics; 2021. **2.** Ortiz-Maldonado V, et al. *Ther Adv Hematol.* 2015;6(1):25-36. **3.** Curigliano G, et al. *Drug Saf.* 2019;42(2):247-262. **4.** Durand CA, et al. *J Immunol.* 2009;183(9):5673-5684. **5.** TG Therapeutics, Inc. data on file.


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TG Therapeutics