Medical Information Request: ZUSDURI™ (mitomycin) for intravesical solution and cold cup biopsy.

Thank you for your question regarding ZUSDURI and biopsy procedure and timing during the ENVISION trial.

ZUSDURI™ is indicated for the treatment of adult patients with recurrent low-grade intermediate-risk non-muscle invasive bladder cancer (LG-IR-NMIBC).[1]

Background:

The reverse thermal properties of ZUSDURI allow for local administration of mitomycin as a liquid under chilled conditions, with subsequent conversion to a semisolid gel depot following instillation into the bladder. Following instillation into the bladder, ZUSDURI forms a semisolid gel which dissolves in the urine. ZUSDURI contains mitomycin which is a violet to blue color and is excreted unchanged in the urine. During clinical studies, patients reported visible purple gel in urine for up to 24 hours (median 5 hours) after instillation.[1-5]

Clinical Trial Design:

ENVISION is a Phase 3, single-arm, multinational study evaluating the efficacy and safety of ZUSDURI (UGN-102) as a primary chemoablative therapy in 240 patients with LG-IR-NMIBC across 56 sites in the United States and Europe. Eligible patients had a history of ≥ 1 prior episode of LG-NMIBC requiring treatment with TURBT.[4]

The primary outcome measure of the trial was Complete Response Rate (CRR) at 3 months. Secondary endpoints are Duration of Response (DOR; up to 63 months), Durable Complete Response (DCR), Disease Free Survival (DFS) and Safety/tolerability of intravesical instillations in patients with LG-IR-NMIBC.

- Patients enrolled in ENVISION were eligible to receive six once-weekly intravesical instillations of ZUSDURI.
- The ZUSDURI admixture for intravesical instillations contains 75 mg mitomycin in 56 mL admixture
- All patients returned to the clinic approximately 3 months after the first instillation for determination of response to treatment. Assessment of response was based on visual observation (white light cystoscopy), histopathology of any remaining or new lesions by central pathology lab (if applicable), and interpretation of urine cytology by central pathology lab.
- Patients confirmed to have a complete response (CR) at the 3-month Visit, defined as having no detectable disease (NDD) in the bladder, entered the Follow-up Period of the study. Patients confirmed to have a non-complete response (NCR) underwent Investigator designated standard of care (SOC) treatment of remaining lesions and then entered the Follow-up Period of the study.
- During the Follow-up Period, patients returned to the clinic every 3 months for up to 24 months (i.e., 27 months after the first instillation) for evaluation of response. Patients who remain disease free at the 27-month Visit will continue to return to the clinic every 6 months for up to 36 months (i.e., 63 months after the first instillation) or until disease recurrence, disease progression, death, or the study is closed by the Sponsor, whichever occurs first.
- Patients confirmed to have a disease recurrence during the Follow-up Period or a disease progression at the 3-month Visit or during the Follow-up Period will undergo Investigator designated SOC treatment and have a separate End of Study (EOS) Visit performed. The timing of the EOS Visit will be approximately 3 months after SOC treatment of disease recurrence or progression.

Biopsy times during ENVISION Study

Patient eligibility

As part of the inclusion criteria, LG-NMIBC (Ta) was confirmed by cystoscopy and **cold-cup biopsy** of the visualized tumor (not completely removing the tumor) at screening or within 8 weeks before screening. Over 80% of patients had multifocal disease and would have had no perturbation of residual disease in the nonbiopsied lesion.

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Time between biopsy to first ZUSDURI instillation
In the Phase 3 ENVISION trial, out of 240 patients, the median time between biopsy and first dose of ZUSDURI was 36 days, with the average (range) being 39 (5–85) days.

Patient evaluation
Eligible patients received 6 weekly intravesical instillations of UGN-102 at a dose of 75 mg mitomycin in an ambulatory setting. At 3 months, patients were assessed for CR by cystoscopy, urine cytology, and **for-cause biopsy** to check for bladder cancer.

Complete responders entered follow-up (every 3 months for first 2 years, then every 6 months up to 3 additional years), which included cystoscopy, urine cytology, and **for-cause biopsy** until recurrence, progression, or death.

Biopsy procedure during ENVISION study
Type of cystoscope
The ENVISION study protocol did not specify whether a rigid or flexible cystoscope was used, and this information was not collected in the study database. However, from the sampling of source documentation that we have available for the US, flexible scope seemed to be more commonly used.

Anesthesia during biopsy
Anesthesia was not required for cold cup biopsy, but the use of anesthesia for cold cup biopsy was determined by the site's standard practices, patient's individual needs, regional practices, etc. From the sampling of source documents that we have available for the US, most of the biopsies were not done under general anesthesia.

Multifocal disease
If, in the investigator's assessment, tumors present on cystoscopy were sufficiently heterogenous in presentation such that one biopsy was not adequate, more than one biopsy sample could be taken.

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Please refer to the Full Prescribing Information for ZUSDURI here.

ZUSDURI IMPORTANT SAFETY INFORMATION:

Contraindications

ZUSDURI is contraindicated in patients with perforation of the bladder or in patients with prior hypersensitivity reactions to mitomycin or any component of the product.

Warnings and Precautions

Risks in Patients with Perforated Bladder

ZUSDURI may lead to systemic exposure to mitomycin and severe adverse reactions if administered to patients with a perforated bladder or to those in whom the integrity of the bladder mucosa has been compromised. Evaluate the bladder before the intravesical instillation of ZUSDURI and do not administer to patients with a perforated bladder or mucosal compromise until bladder integrity has been restored.

Embryo-Fetal Toxicity

Based on findings in animals and mechanism of action, ZUSDURI can cause fetal harm when administered to a pregnant woman. In animal reproduction studies, administration of mitomycin resulted in teratogenicity. Advise females of reproductive potential to use effective contraception during treatment with ZUSDURI and for 6 months following the last dose. Advise male patients with female partners of reproductive potential to use effective contraception during treatment with ZUSDURI and for 3 months following the last dose.

Adverse Reactions

Common Adverse Reactions

The most common (≥10%) adverse reactions, including laboratory abnormalities, that occurred in patients treated with ZUSDURI were increased creatinine, increased potassium, dysuria, decreased hemoglobin, increased aspartate aminotransferase, increased alanine aminotransferase, increased eosinophils, decreased lymphocytes, urinary tract infection, decreased neutrophils, and hematuria.

Additional Adverse Reactions Information

Clinically relevant adverse reactions occurring in <10% of patients who received ZUSDURI included increased urinary frequency, fatigue, urinary incontinence, urinary retention, urethral stenosis, genital pain, urinary urgency, genital edema, genital pruritus, genital rash, urethritis, acute kidney injury, balanoposthitis, and nocturia.

Use in Specific Populations

Lactation

Because of the potential for serious adverse reactions in a breastfed child, advise women not to breastfeed during treatment with ZUSDURI and for 1 week following the last dose.

Preparation and Administration Information

ZUSDURI is to be administered by intravesical instillation only. Do not administer ZUSDURI by pyelocalyceal instillation or by any other route.

ZUSDURI must be prepared and administered by a healthcare provider. To ensure proper dosing, it is important to follow the preparation instructions found in the ZUSDURI Instructions for Pharmacy and administration instructions found in the ZUSDURI Instructions for Administration.

ZUSDURI may discolor urine to a violet to blue color following the instillation procedure. Advise patients for at least 24 hours post-instillation to avoid urine contact with skin, to void urine sitting on a toilet, and to flush the toilet several times after use. Advise patients to wash hands, perineum or glans with soap and water after each instillation procedure.

ZUSDURI is a hazardous drug. Follow applicable special handling and disposal procedures.

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You are encouraged to report negative side effects of prescription drugs to the FDA. Visit http://www.fda.gov/medwatch or call 1-800-FDA-1088. You may also report side effects to UroGen Pharma at 1-855-987-6436.

Please see accompanying Full Prescribing Information, Instructions for Pharmacy and Instructions for Administration.

References:

1. ZUSDURI™ (mitomycin) for intravesical solution. Prescribing Information. UroGen Pharma; 2025.
2. ZUSDURI™ (mitomycin) for intravesical solution. Instructions for Pharmacy (IFP)
3. ZUSDURI™ (mitomycin) for intravesical solution. Instructions for Administration (IFA)
4. Prasad SM, Shishkov D, Mihaylov NV, et al. Primary chemoablation of recurrent low-grade intermediate-risk nonmuscle-invasive bladder cancer with UGN-102: A single-arm, open-label phase 3 trial (ENVISION). *J Urol.* 2025;213(2):205-16.
5. Data on file. UroGen Pharma.

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