Medical Information Request: ZUSDURI™ (mitomycin) for intravesical solution and Home Instillation

Thank you for your question regarding home instillation of ZUSDURI.

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

Background

Utilizing UroGen's proprietary sterile hydrogel technology, ZUSDURI is a hydrogel-based formulation designed to enable longer exposure of bladder tissue to mitomycin. Based on patient-reported visibility of gel in urine post-treatment, ZUSDURI has a median dwell time of 5 hours with reports up to 24 hours. 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.

The efficacy and safety of ZUSDURI for primary chemoablation of LG-IR-NMIBC was initially assessed in two phase 3 trials, ATLAS and ENVISION. Subsequently, a phase 3 study examined the feasibility of home instillation of ZUSDURI in this same population.

Study Design

Home instillation of ZUSDURI for recurrent LG-IR-NMIBC was examined in a single-arm, open-label, phase 3B trial (NCT05136898) which enrolled a limited number of patients (n = 8). The primary endpoint of this study was **feasibility**, assessed as safety, discontinuation rate, and questionnaire feedback. The secondary study endpoint was **complete response (CR)** at 3 months, determined by endoscopic evaluation, urine cytology, and for-cause biopsy.

ZUSDURI was administered intravesically weekly for 6 weeks. The first instillation of ZUSDURI was administered at the respective investigative site, with all five subsequent instillations administered at the participant's home by a trained home health professional (HHP).

Study Participants

Inclusion Criteria	Exclusion Criteria

• ≥18 years of age
• Newly diagnosed or historic LG-IR-NMIBC (Ta) histologically confirmed by cold cup biopsy at screening or within 8 weeks before screening
• IR disease was defined as 1 or 2 of the following:
  ○ The presence of multiple tumors
  ○ A solitary tumor of >3 cm
  ○ Recurrence (≥ 1 occurrence of LG-NMIBC within 1 year of the current diagnosis at the initial screening visit)
• Negative voiding cytology for HG disease within 6 weeks before screening
	• Bacillus Calmette-Guérin (BCG) treatment for urothelial carcinoma within the previous 1 year
	• A history of high-grade bladder cancer (papillary or carcinoma in situ) in the past 2 years
	• Known allergy or sensitivity to mitomycin that in the investigator's opinion could not be readily managed

Results

Patients highly rated their home instillation experience for each domain of the patient questionnaire. The median patient questionnaire scores remained the same throughout the treatment period:

- Median **comfort** domain score 12.0 (range: 10 to 12)
- Median **safety** domain score 4.0 (range: 3 to 4)
- Median **communication** domain score 8.0 (range: 6 to 8)
- Median **preference** domain score 4.0 (range: 2 to 4)

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- Median **overall experience** score 4.0 (range: 3 to 4)
- Median **composite score** was 32.0 (range: 26 to 32)

Visiting home health professionals reported ZUSDURI home instillation as feasible. At each instillation visit, most available HCP responses were in favor of home instillation, with the majority of HCPs reporting no difficulty in performing ZUSDURI instillation in the patient's home.

At the 3-month visit, 6/8 participants achieved a complete response. Two patients discontinued treatment (after 5 and 4 doses, respectively) due to adverse events unrelated to study treatment. These two patients were counted as non-responders.

An end of study survey was also administered, with the following pertinent findings:

- 6/8 patients completed all 6 instillations of ZUSDURI; 2 discontinued due to an adverse event
- 5/6 patients recommend ZUSDURI over transurethral resection of bladder tumor (TURBT)
- 3/4 investigators considered at-home treatment "not different" from in-office treatment

Safety

All 8 patients experienced treatment emergent adverse events, with 4/8 (50%) deemed treatment-related. Most patients had mild-to-moderate adverse events. Serious adverse events occurred in 3/8 patients, but none were considered treatment related.

Treatment emergent adverse events occurring in ≥ 2 patients:

- Dysuria 25% (2/8); 2 deemed treatment-related
- Fatigue 25% (2/8); 2 deemed treatment-related
- Hypertonic bladder 25% (2/8); 1 deemed treatment-related
- Urinary tract infection 25% (2/8); 1 deemed treatment-related

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,

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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.

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. Morris D, Kramolowsky II EV, Bivins VM, et al. Home instillation of UGN-102 for primary chemoablation of recurrent low-grade intermediate-risk non-muscle-invasive bladder cancer: a single-arm, open-label, phase 3B trial. Poster presented at: 25th Annual Meeting of the Society of Urologic Oncology; December 4-6, 2024; Dallas, TX.
5. Data on file. UroGen Pharma

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