Medical Information Request: ZUSDURI™ (mitomycin) for intravesical solution and additional administration information

Thank you for your request for additional details regarding the administration 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). Please see the Instructions for Administration (IFA), that accompany the full prescribing information, for complete information on bladder instillation.

Administration Information per the Prescribing Information (PI)/Instructions for Administration (IFA):

Administer ZUSDURI by intravesical instillation only. Do not administer by pyelocalyceal instillation or by any other route.

ZUSDURI must be reconstituted by a healthcare professional prior to instillation. Reconstituted ZUSDURI has reverse thermal properties with a gelation point of approximately 19°C (66°F) and will appear as a viscous liquid under chilled conditions and a semisolid gel at room temperature.[1-4]

ZUSDURI must be chilled at -3°C to 5°C (27°F to 41°F) to convert to a viscous liquid prior to instillation. When instilling ZUSDURI, each syringe must be emptied within thirty (30) seconds to avoid gelation.

Please see the ZUSDURI IFA for information on how to instill ZUSDURI using the ZUSDURI vial and devices listed under Supplies Needed. When you administer ZUSDURI, you will need to use special adaptors for your catheter and syringes. These adaptors will create a closed pathway to protect you and your patient during and after administration. Fluid will only be able to pass between connection points when the adaptors are fully engaged, preventing drips or leaks.[1-5]

The UroGen 16Fr Urinary Catheters and OnGuard®2 CSTD Luer lock adaptor are recommended for the administration of ZUSDURI admixture. The UroGen 16Fr urinary catheters – straight tip and coudé tip – are supplied as part of the Intravesical Administration Kit (IVAK). Only the equipment listed within the ZUSDURI IFA is recommended for use during instillation.[1-5]

Advise patients that 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, to wash hands and genital area with water and soap after each urination, and to flush the toilet several times after use.

Additional Information:

Your institution's use of this "Additional Information" is entirely within your institution's sole discretion. UroGen recommends following the Instructions for Administration (IFA). Please refer to the Full Prescribing Information and the Instructions for Administration (IFA) for ZUSDURI (mitomycin) for intravesical solution for detailed information on the preparation and administration of ZUSDURI. The below "Additional Information" should not be construed as a recommendation, advice to pharmacists, or advice to other healthcare professionals.

Based on ZUSDURI clinical trial experience, below is additional information for the administration process provided by our Clinical Development team and confirmed by our Research and Development team in response to frequently asked questions:

1. ZUSDURI admixture storage conditions: Instill reconstituted ZUSDURI as soon as possible. If not used immediately, store reconstituted ZUSDURI:
    - Under refrigeration at 2℃ to 8℃ (36°F to 46°F) for up to 7 days; or

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- Under refrigeration at 2℃ to 8℃ (36°F to 46°F) for up to 6 days followed by no more than 24 hours at room temperature, 20°C to 25°C (68°F to 77°F).
  - Discard 7 days after reconstitution.
  - Protect from light.
  - Avoid excessive heat over 40°C (104°F).

2. Once the ZUSDURI admixture is removed out of refrigerated conditions and transferred to room temperature - it should not be returned to storage in refrigerated conditions. It may continue to be kept at room temperature for up to 24 hours.
3. The lower the temperature of the room is, the easier it will be to withdraw the admixture.
4. A closed system transfer device (CSTD) should be used for the whole procedure (end-to-end).
5. When using CSTDs, you should disinfect the connections with an alcohol wipe (4-5 seconds of contact) before each use.
6. When cooling the ZUSDURI vial to liquify prior to administration, remember that ZUSDURI must be placed on ice for at least 20 minutes before use. Ensure the ZUSDURI vial is completely immersed in the ice bath (Step A1, A2).
7. Before connecting the adaptors to the administration syringes, draw approximately 5 mL of air into each syringe. Inject the air from each syringe into the vial prior to admixture withdrawal, this prevents a vacuum from forming and facilitates the withdrawal.
8. After connecting the adaptors to the administration syringes, place them in the bag and into the ice bath while also chilling the ZUSDURI vial. The syringes should be kept cold. Remove each syringe from the ice bath prior to use.
9. While withdrawing ZUSDURI into the administration syringe(s), make sure not to hold the vial, syringe, or adaptors with your hand in places where there is ZUSDURI admixture to prevent warming the ZUSDURI admixture, as this may cause it to solidify and not to flow through the adaptors (Step B5).
10. Anytime you withdraw ZUSDURI admixture from the vial ensure that the motion is slow, smooth, and gentle. Note that there might be some foaming in the syringes while withdrawing ZUSDURI (Step B5).
11. If you encounter difficulty withdrawing the necessary volume into the last syringe, place the vial back into the ice bath for approximately 5 minutes in an inverted position. Then, re-attach the syringe and withdraw the leftover admixture from the vial, while holding it upside down. This will allow the admixture to flow toward the vial neck while cold (Step B5). Step 11 may be repeated several times, if necessary.
12. In order to ensure chilling of the admixture in the syringes, remember which order the syringes were filled and preferably use the same order to instill ZUSDURI into the bladder: First in, First out.
13. The catheter that needs to be used for the instillation is a urinary catheter with a fixed Luer lock (provided in IVAK). A fixed Luer lock is required due to the viscosity of ZUSDURI.
14. Prior to each ZUSDURI administration, the urine needs to be drained from the bladder (Step C1).
15. Disconnect only the syringe adaptor from the catheter adaptor at the end of each syringe instillation and not the other adaptors (Step C5, C6).
16. The catheter Luer lock adaptor must stay connected to the catheter during the entire instillation, also when flushing the catheter (Step C7).
17. Work swiftly when injecting and changing syringes to minimize the possibility that the residual gel in the catheter from the previous syringe will get warm and clog the catheter.
18. The injection of the first syringe will always be much easier than the second, third and fourth syringes. In those last 3 syringes the injection requires more force at first to clear the catheter of the remaining gel from the previous syringe which was warmed by the body and became more viscous. After the initial pressure to unclog the catheter, the injection continues with much less effort.

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

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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.

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.

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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. Chilling Block (Model UCB002). Instructions for Use (IFU)
5. Data on file. UroGen Pharma.

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