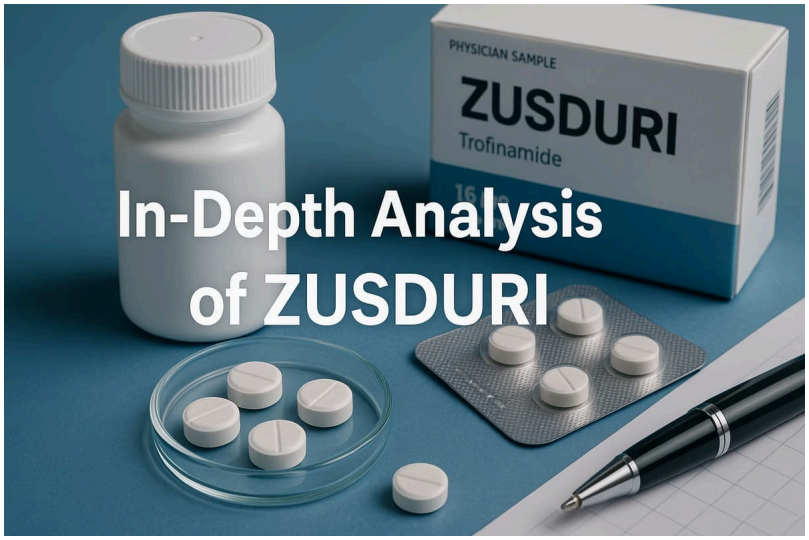
ZUSDURI: Mitomycin Hydrogel for Bladder Chemoablation

By IntuitionLabs • 8/14/2025 • 35 min read

mitomycin | bladder cancer | nmibc | intravesical therapy | chemoablation | urology | rtgel | drug profile



ZUSDURI (Mitomycin Intravesical Solution) – Comprehensive Drug Profile

Introduction

ZUSDURI (mitomycin for intravesical solution) is a novel formulation of the chemotherapeutic agent *mitomycin C* designed for direct instillation into the bladder. It is the **first and only FDA-approved medication** for adults with recurrent low-grade, intermediate-risk non–muscle invasive bladder cancer (LG-IR-NMIBC) fda.gov. ZUSDURI combines mitomycin with a proprietary reverse-thermal hydrogel (RTGel®) to achieve **localized chemoablation of bladder tumors** without surgery pipelinereview.com pipelinereview.com. This therapy offers a new, minimally invasive alternative to repeated transurethral resection of bladder tumors (TURBT), which has been the historical standard for managing recurrent low-grade bladder cancer pipelinereview.com. ZUSDURI received FDA approval in June 2025 based on compelling clinical trial data and has since become available in the U.S. as a bladder-sparing treatment option. Below is a detailed review of ZUSDURI's pharmacology, clinical applications, trial results, safety profile, regulatory status, manufacturing, and ongoing research, with citations from authoritative sources.

Mechanism of Action

Mitomycin C, the active cytotoxic component of ZUSDURI, is an **alkylating agent** that inhibits DNA synthesis via DNA cross-linking. It preferentially cross-links DNA at guanine-cytosine sites, preventing DNA replication and ultimately inducing cancer cell death accessdata.fda.gov. At higher concentrations, mitomycin can also suppress cellular RNA and protein synthesis accessdata.fda.gov. The RTGel® formulation does not alter mitomycin's molecular mechanism; instead, it **enhances local drug delivery**. Upon instillation into the bladder, the chilled liquid formulation warms to body temperature and forms a semisolid gel, which adheres to the bladder lining and **prolongs contact time** with the urothelium urologytimes.com. This prolonged dwell time (often 5–24 hours in the bladder) increases the duration of tumor exposure to mitomycin, thereby maximizing chemoablative effects within the bladder while limiting systemic exposure urologytimes.com. In summary, ZUSDURI's mechanism of action is the **localized cytotoxic effect of mitomycin on bladder tumor cells**, facilitated by a novel gel formulation that maintains the drug in situ for extended periods.

Pharmacodynamics

Mitomycin's pharmacodynamic effects in ZUSDURI are consistent with those of an alkylating chemotherapy agent – i.e. inducing DNA damage and tumor cell apoptosis. There is no known unique "exposure-response" relationship specific to the intravesical formulation; the time-course of pharmacodynamic effect is assumed to correlate with the duration of bladder exposure to the drug accessdata.fda.gov. Clinically, the chemoablative effect is evidenced by high complete response rates in treated patients (see Clinical Trial Results below). Of note, because ZUSDURI acts locally, its **systemic pharmacodynamic effects are minimal**, which is reflected in the generally mild systemic toxicity profile. No major **immunomodulatory** or off-target PD effects have been reported for intravesical mitomycin. In summary, the pharmacodynamics of ZUSDURI are characterized by **localized tumor cell kill** in the bladder with negligible systemic action, making it a targeted therapy confined to the urinary tract.

Pharmacokinetics

ZUSDURI is administered directly into the bladder, resulting in **minimal systemic absorption** of mitomycin. In pharmacokinetic studies, the mean peak plasma concentration (C_max) of mitomycin after a 75 mg intravesical instillation was only ~2.3 ng/mL (range 0.2–8.9 ng/mL) – **less than 1% of the C_max observed with intravenous mitomycin administration** accessdata.fda.gov. This very low systemic exposure reflects the confinement of most of the drug within the bladder lumen. The hydrogel formulation gradually dissolves in urine and is eliminated via voiding: patients often see violet-blue gel fragments in the urine for up to 24 hours post-instillation (median ~5 hours) accessdata.fda.gov. Mitomycin that does get absorbed systemically is rapidly cleared, primarily through hepatic metabolism, and approximately 10% of absorbed mitomycin is excreted unchanged in the urine accessdata.fda.gov. There is no significant distribution beyond the bladder; the drug remains mostly localized, which limits systemic distribution to other tissues. The **metabolism** of mitomycin is mainly hepatic (via reduction and conjugation pathways), and because plasma levels are so low, saturable metabolism is not expected to be a concern at intravesical doses accessdata.fda.gov. The **excretion** of mitomycin from systemic circulation (if any) is swift, with a portion appearing in urine unchanged accessdata.fda.gov. Overall, ZUSDURI's pharmacokinetic profile is characterized by **high local concentration in the bladder and negligible systemic exposure**, which underlies its targeted action and relatively mild systemic side effect profile.

Indications and Clinical Applications

ZUSDURI is indicated for the **treatment of adult patients with recurrent low-grade, intermediate-risk non–muscle invasive bladder cancer (LG-IR-NMIBC)** fda.gov. This population includes patients with low-grade Ta papillary tumors that tend to recur (especially tumors that are multifocal, >3 cm, and/or recur within 1 year) despite prior TURBT fda.gov. In clinical practice, ZUSDURI is used as a **bladder-sparing, chemoablative therapy** to eliminate

visible tumors and microscopic disease without surgery. It is typically considered in patients who have undergone at least one prior TURBT for low-grade NMIBC and then developed a recurrence of similar low-grade disease fda.gov. By label, ZUSDURI is indicated only for *recurrent* LG-IR cases, not for the initial occurrence of low-grade tumors urologytimes.com urologytimes.com. Patients with high-grade disease, carcinoma in situ, or muscle-invasive disease are **not** candidates for ZUSDURI. The goal of therapy is to reduce the frequency of surgical interventions (resections under anesthesia) in this chronic, recurrent cancer. Clinical guidelines are expected to incorporate intravesical mitomycin gel as a new option for intermediate-risk patients who historically have faced multiple TURBT surgeries. In summary, ZUSDURI's application is **niche but important**: it offers a non-surgical therapeutic approach for those with recurrent low-grade bladder tumors who would otherwise face repeated surgical tumor removals pipelinereview.com pipelinereview.com. Physicians may particularly recommend ZUSDURI for patients who are poor surgical candidates (e.g. elderly or comorbid patients) or those strongly preferring to avoid anesthesia and surgery. It represents a significant shift toward **chemoablation in bladder cancer management**, filling an unmet need in this intermediate-risk cohort.

Dosage and Administration

Recommended Dose: ZUSDURI is administered as an intravesical instillation of 75 mg of mitomycin (in 56 mL of reconstituted gel) once weekly for six consecutive weeks accessdata.fda.gov fda.gov. This 6-week course constitutes one treatment cycle, which was the regimen used in clinical trials. Each dose is supplied as a **kit** containing two vials of mitomycin powder (40 mg each, for a total of 80 mg, of which 75 mg is delivered) and one vial of sterile hydrogel solution (approximately 56 mL) urologytimes.com.

Preparation: The drug must be reconstituted under chilled conditions. The mitomycin powder is mixed with the cold hydrogel, yielding a **viscous liquid at refrigerator temperature** (2–8 °C) accessdata.fda.gov. ZUSDURI's formulation has *reverse thermal properties*: it remains a liquid when cold but **gels at body temperature** (gelation point ~19 °C) accessdata.fda.gov. Pharmacists should prepare the mixture per the Instructions for Pharmacy included, ensuring the solution stays cold (e.g. on ice) until administration accessdata.fda.gov. The reconstituted product must be protected from light and can be stored refrigerated for up to 7 days if needed (though immediate use is preferable) accessdata.fda.gov. It is classified as a hazardous chemotherapy agent, so proper handling and disposal precautions (gloves, closed-system devices like OnGuard® connectors, etc.) should be followed accessdata.fda.gov.

Administration: ZUSDURI is instilled directly into the bladder via a urinary catheter in an outpatient setting pipelinereview.com pipelinereview.com. Prior to instillation, the patient should empty their bladder. The chilled liquid is slowly injected through the catheter; as it warms in the bladder, it solidifies into a gel that adheres to the bladder wall. The patient is instructed to **retain the instillation** as long as possible (at least 1–2 hours is recommended; in trials, many patients retained the gel for several hours up to voiding) to maximize tumor contact time. Because the

gel formulation tends not to leak as readily as plain liquid, patients can generally tolerate the dwell time. After treatment, patients may void normally; the gel will liquefy as it mixes with urine and be expelled. Patients are advised that their urine may be colored blue-violet for up to 24 hours (due to mitomycin's color) accessdata.fda.gov. They should take precautions for 24 hours to avoid skin contact with urine (e.g. men should sit to void, wash hands and genital area after voiding, and double-flush the toilet) to prevent any skin exposure to the chemotherapy accessdata.fda.gov.

Key Points on Dosing: There is *no intravesical maintenance regimen* defined for ZUSDURI at this time – the FDA label specifies only the initial 6-week induction course. Retreatment on recurrence is not yet formally studied, but in practice, a patient who responds and later has another low-grade recurrence could potentially receive another cycle at the clinician's discretion. Importantly, ZUSDURI is for **intravesical use only** – it must **not** be administered intravenously, intra-peritoneally, or by any other route. It is also not to be used for upper urinary tract (pyelocalyceal) instillation (that is a different product, Jelmyto, for upper tract tumors) accessdata.fda.gov. Prior to each instillation, one should confirm there is no bladder perforation (via cystoscopy or imaging if needed), because bladder integrity is crucial to avoid systemic toxicity (see Warnings) accessdata.fda.gov accessdata.fda.gov.

In summary, ZUSDURI is given as **75 mg intravesically once weekly for 6 weeks**, prepared and administered cold via catheter. The unique gel technology requires careful handling but allows the drug to dwell in the bladder, thereby optimizing tumor exposure while the patient is treated in an outpatient clinic.

Clinical Trial Results and Efficacy

The approval of ZUSDURI was supported primarily by the **Phase 3 ENVISION trial** (NCT05243550), a multinational single-arm study, and informed by earlier studies including the Phase 2b OPTIMA II trial and a Phase 3 randomized trial (ATLAS). These studies demonstrated the chemoablative efficacy of intravesical mitomycin gel in the indicated population:

- **ENVISION Trial (Phase 3 single-arm):** In ENVISION, 240 patients with recurrent LG-IR-NMIBC received ZUSDURI (75 mg weekly ×6). The primary endpoint was complete response (CR) 3 months after treatment, with responders monitored for durability. ENVISION met its endpoint with a **3-month CR rate of ~78–80%**. Specifically, 223 patients were evaluable for efficacy, and **78% (95% CI: 72–83%) achieved a complete response at 3 months** fda.gov. This means no visible tumors on cystoscopy, negative urine cytology, and negative biopsies (if any done) in those patients. This CR rate is remarkably high for a chemo-only treatment and suggests that in the majority of recurrent low-grade cases, ZUSDURI can fully eradicate detectable disease. An equally crucial finding was the durability of these responses: among the responders, **79% remained disease-free for at least 12 months after the CR** fda.gov. In other words, the Kaplan-Meier estimated probability of maintaining response one year after initial CR was approximately 80% pubmed.ncbi.nlm.nih.gov fda.gov. The duration of response (DOR) ranged from 0 to 25+ months at the data cutoff, with median DOR not reached after ~14 months median follow-up pubmed.ncbi.nlm.nih.gov. These outcomes underscore that ZUSDURI not only induces CR in most patients, but the majority of responders enjoy **long-lasting remission** (at least 1 year, and ongoing for many). More granular analysis showed that tumor burden influenced CR rates slightly: patients with baseline tumors ≤3 cm had an 82.8% CR rate, whereas those with >3 cm tumor(s) had a 73.2% CR rate targetedonc.com. Nonetheless, both groups derived substantial benefit. **ENVISION** thus established that intravesical mitomycin gel can effectively ablate low-grade bladder tumors, positioning ZUSDURI as a viable therapeutic alternative to surgery in this setting pipelinereview.com pipelinereview.com.

- **ATLAS Trial (Phase 3 randomized, comparative):** The ATLAS study (NCT04688931) was a randomized trial comparing ZUSDURI therapy versus standard TURBT surgery in patients with LG-IR-NMIBC. In ATLAS, patients were assigned either to induction with UGN-102 (mitomycin gel) ± biopsy or to undergo TURBT (surgery) for their recurrent tumors. The 3-month complete response rates were **63.6% with UGN-102 vs 64.8% with TURBT**, essentially showing non-inferiority in immediate tumor clearance targetedonc.com. More interestingly, durability favored the drug: at 12 months post-treatment, **79.7% of patients in the UGN-102 arm remained disease-free, compared to 67.7% in the TURBT arm** targetedonc.com. This corresponded to a hazard ratio of 0.46 for recurrence or progression, meaning **UGN-102 roughly halved the risk of recurrence** relative to surgery over that period targetedonc.com. These results suggest that chemoablation with ZUSDURI can achieve similar short-term outcomes to surgical resection and may provide *longer-lasting protection* against recurrence. (It's hypothesized that the intravesical treatment might eradicate invisible lesions or field effects that surgery leaves behind, thus extending time to recurrence.) The ATLAS data, presented in 2025, helped address concerns about lack of comparative evidence, showing ZUSDURI is at least as effective as TURBT in the first year, with potential superiority in durability targetedonc.com. Notably, ATLAS was not used as the primary basis for approval (the FDA approved based on ENVISION), but it provides supportive evidence of efficacy in a real-world context.

- **OPTIMA II Trial (Phase 2b single-arm):** OPTIMA II was an earlier trial of UGN-102 in both new and recurrent LG-IR-NMIBC patients. It reported a 65% complete response at 3 months in interim analyses, paving the way for Phase 3 pubmed.ncbi.nlm.nih.gov. Recently, a **5-year extension study** of OPTIMA II was published, shedding light on long-term outcomes. Among 41 patients who had achieved CR at 3 months in OPTIMA II, the **median duration of response was 24.2 months** (~2 years) with 35.8 months median follow-up drug-dev.com. In a subset of 17 patients followed for up to 5 years, the median DOR extended to **42.1 months (~3.5 years)** by Kaplan-Meier estimate drug-dev.com. These long-term data demonstrate that a subset of patients experience **multi-year remissions** after a single 6-week course of therapy, highlighting the durable benefit achievable with ZUSDURI in some cases.

Across these studies, ZUSDURI has consistently shown the ability to **ablate visible tumors and delay recurrence** in recurrent low-grade bladder cancer. It is important to note that nearly all patients in trials had prior TURBT (ZUSDURI was used for recurrence, not primary tumors). The efficacy in *completely naive* low-grade patients is less certain, and by label it's intended for recurrent disease. Also, while many patients remain disease-free at 1–2 years, LG-NMIBC is a chronic disease and some will eventually recur; ongoing follow-up to 5 years is being collected to fully define long-term recurrence rates.

In summary, **efficacy highlights** for ZUSDURI include: approximately 3 out of 4 patients achieve initial complete response, and of those, about 4 out of 5 will remain tumor-free at 1 year post-treatment fda.gov. Comparative data indicate similar or better outcomes than repeat TURBT in the first year targetedonc.com. These results position ZUSDURI as an effective non-surgical therapeutic approach for managing recurrent low-grade bladder cancer.

Adverse Effects and Contraindications

Safety Profile: ZUSDURI's safety profile is generally favorable, with mostly local (urinary) side effects that are mild to moderate in severity. Because systemic absorption is minimal, the classic systemic toxicities of mitomycin (e.g. bone marrow suppression) are uncommon at the intravesical dose. In the ENVISION trial, the **most common adverse events (≥10% incidence)** were local genitourinary symptoms or laboratory abnormalities reflecting mild systemic exposure. Specifically, frequently observed effects included **dysuria** (painful urination), **hematuria** (blood in urine), **pollakiuria** (frequent urination), **urinary tract infection**, **urinary urgency**, and **fatigue**, as well as asymptomatic lab changes like **increased serum creatinine**, **increased potassium**, **elevated liver enzymes (AST, ALT)**, **eosinophilia**, **low hemoglobin**, **low neutrophils**, and **low lymphocyte count** fda.gov pipelinereview.com. Most of these events were grade 1–2 (mild or moderate) and resolved or were resolving by the end of treatment pubmed.ncbi.nlm.nih.gov pubmed.ncbi.nlm.nih.gov. They reflect either local irritation (for urinary symptoms) or slight systemic absorption effects (e.g. transient kidney function changes or mild myelosuppression in some patients).

Serious adverse reactions were relatively infrequent. In ENVISION, **12% of patients experienced a serious adverse event (SAE)**, but only two cases (0.8% urinary retention requiring intervention, and 0.4% urethral stenosis) were deemed treatment-related fda.gov pipelinereview.com. Both of those resolved with appropriate management pubmed.ncbi.nlm.nih.gov. Importantly, **one patient (0.4%) in the trial experienced a fatal adverse reaction of cardiac failure** fda.gov. It's not definitively clear if this cardiac failure was caused by the drug (mitomycin can in rare cases cause cardiomyopathy), but it was reported during the study and underscores the need for vigilance in frail patients fda.gov. Overall, systemic serious toxicity is rare; no patients in trials had severe bone marrow toxicity or sepsis, for example.

Local adverse events of note include **urinary retention** (some patients have trouble voiding the gel; 2–3% needed temporary catheterization) and **urethral narrowing** or stricture over time (seen in a tiny fraction) fda.gov. Chemical cystitis (bladder inflammation) is inherent to intravesical chemotherapy – manifested by dysuria, frequency, urgency in a significant subset. These can be managed with conservative measures (e.g. phenazopyridine for dysuria, anti-spasmodics) or brief treatment breaks. In fact, about 10% of patients needed a **dose interruption** during the 6-week course, most often due to UTI or dysuria, but nearly all were able to complete therapy accessdata.fda.gov. There have been no reports of bladder perforation caused by the drug; however, one **warning** is that if the bladder is inadvertently perforated during catheterization or if the patient has a deep resection injury, instilling ZUSDURI could lead to extravasation of mitomycin into the abdomen or bloodstream, with serious consequences. Thus, it is contraindicated in patients with a known or suspected **bladder wall perforation or compromised bladder mucosa integrity** accessdata.fda.gov accessdata.fda.gov.

Contraindications: According to the FDA-approved label, ZUSDURI is contraindicated in: (1) patients with **bladder perforation** (or extensive bladder wall injury) because of the risk of systemic toxicity if the drug leaks out, and (2) patients with a **history of hypersensitivity to mitomycin C or any component of the formulation** accessdata.fda.gov. Allergic reactions to mitomycin are uncommon but have been reported with systemic use; any prior anaphylactic reaction would preclude use. There is also a strong warning for **pregnancy** – mitomycin is teratogenic. While not a formal contraindication (since the drug is not intended for women of childbearing potential in this indication usually – bladder cancer skews older), females of reproductive potential should avoid getting pregnant and use effective contraception, as ZUSDURI *can cause fetal harm* due to the DNA-damaging mechanism accessdata.fda.gov. Breastfeeding is advised against during and for a period after therapy due to unknown excretion in milk accessdata.fda.gov.

Precautions: Key precautions include ensuring proper bladder condition (as above) and handling of cytotoxic material (healthcare staff and patient hygiene after instillation). Renal function should be monitored; although significant nephrotoxicity was not seen, transient creatinine elevations were common pipelinereview.com. The transient lab abnormalities (increased creatinine, liver enzymes, etc.) typically normalized after therapy pipelinereview.com.

Patients with severe renal impairment were excluded from trials, so caution is advised in that population (mitomycin systemic exposure might be higher if the drug is absorbed and not cleared well). Similarly, while not specifically studied, one should be cautious in patients with severely compromised bladder capacity or function (e.g. neurogenic bladder) as retention of the drug may differ.

In summary, ZUSDURI is **well tolerated** for a chemotherapy, with side effects mostly limited to reversible bladder irritation and mild lab changes. Serious complications are rare but can include urinary retention or strictures and, extremely rarely, severe systemic effects. Adherence to contraindications (no perforated bladder, no known allergy) and proper administration technique mitigates most risks. Patients should be counseled on expected urinary symptoms during therapy and monitored periodically (urinalyses, basic labs) to ensure any emerging toxicity is managed promptly.

Drug Interactions

No formal drug interaction studies have been conducted with ZUSDURI. Given its minimal systemic absorption, **drug-drug interactions are not expected to be significant** – the plasma levels of mitomycin are extremely low (nanogram range) after intravesical therapy accessdata.fda.gov. Unlike systemic chemotherapy, intravesical mitomycin does not meaningfully engage liver cytochrome P450 enzymes or other pathways that could be altered by concomitant medications. Therefore, **pharmacokinetic interactions** (where one drug affects the metabolism or clearance of mitomycin) are unlikely. Similarly, mitomycin at tiny systemic doses is not expected to alter the metabolism of other drugs.

That said, certain considerations apply: If a patient is on other bladder instillation treatments (e.g. BCG immunotherapy or another intravesical agent), those should not be given concurrently with ZUSDURI as there is no data on combined use – and mixing therapies could potentially increase bladder toxicity or obscure which agent is responsible for effects. Sequential use in the same bladder is theoretically possible (for example, BCG in high-grade disease and mitomycin gel for later recurrence of low-grade), but each regimen should be completed separately and the bladder allowed to recover before switching.

From a safety standpoint, **additive toxicities** should be considered. For instance, if a patient is taking other nephrotoxic drugs, any absorbed mitomycin could add a small extra kidney insult (mitomycin can be nephrotoxic at higher exposures). In trials, patients were generally older and on various concomitant medications without issue, so no specific contraindicated medications are noted. As a DNA-damaging agent, mitomycin could theoretically have additive myelosuppressive effects if a patient were simultaneously on another chemotherapeutic, but such a scenario is unlikely in this indication.

In summary, **no significant drug interactions have been reported with ZUSDURI**, and its localized delivery makes interactions unlikely. It is prudent to avoid simultaneous intravesical

therapies, and standard chemotherapy precautions (regarding immunosuppressants, etc.) apply, but overall ZUSDURI can be administered without major concern for interacting with systemic drugs.

Regulatory Approval Status

United States (FDA): ZUSDURI was approved by the U.S. Food and Drug Administration on **June 12, 2025** for adults with recurrent LG-IR-NMIBC fda.gov. This approval made ZUSDURI the **first FDA-approved non-surgical treatment** for this patient population targetedonc.com. The FDA's decision followed a review of the Phase 3 trial data (ENVISION) demonstrating high response rates and acceptable safety. Notably, the approval was somewhat unusual because the FDA's Oncologic Drugs Advisory Committee (ODAC) had earlier voted **against** approval (in a narrow 5-4 vote on May 21, 2025) citing concerns about the single-arm trial design and long-term uncertainty targetedonc.com. Despite the advisory committee's hesitation, the FDA granted approval, likely weighing the unmet need for this indication and the favorable benefit-risk profile shown in the data. The approval is a **standard (full) approval** for this indication (not an accelerated approval), meaning the FDA was satisfied that clinical benefit (tumor ablation and durable response) was demonstrated targetedonc.com. However, as a condition, the FDA did ask for continued follow-up: UroGen is required to complete the ongoing ENVISION trial follow-up to further characterize long-term outcomes and must provide annual updates on patient responses** pipelinereview.com. This serves as a post-marketing commitment to ensure the durability and safety remain as expected.

Europe (EMA) and other regions: As of August 2025, ZUSDURI is **not yet approved in the European Union or other major markets**. There is no EMA authorization at this time for the mitomycin RTGel product. UroGen Pharma has not publicly announced an EMA submission yet, but it is anticipated that they may seek approval in Europe and elsewhere based on the U.S. data. Regulatory processes in other countries are likely in early stages. Meanwhile, European clinicians are aware of ZUSDURI through conference presentations and publications, and its data have been discussed (for instance, EAU guidelines panels are likely reviewing it for future updates). In summary, **FDA approval is currently the first and only regulatory approval** for this therapy fda.gov. No conditional approvals or licenses exist yet in Europe, but this may change pending further filings. Clinicians outside the U.S. may consider it experimental or use it in clinical trials until regulatory clearance is obtained.

Special Designations: ZUSDURI does not qualify as an orphan drug (bladder cancer is not rare enough) and did not receive breakthrough therapy designation publicly, though it did have Fast Track status earlier in development (UGN-102 was granted Fast Track by FDA in 2020 due to the unmet need, according to UroGen press releases). The approval was a noteworthy regulatory event as it introduced a novel drug-device combination into bladder cancer therapy.

Going forward, regulatory agencies will likely monitor the post-marketing data. The FDA approval of ZUSDURI could influence regulators in other countries to consider a similar indication if the data are compelling and if local trials (or bridging studies) are performed.

Manufacturing and Distribution

ZUSDURI is developed and marketed by **UroGen Pharma, Ltd.**, a biotech company headquartered in Princeton, NJ, USA, with R&D and operations also in Israel drug-dev.com. The product's manufacturing involves specialized processes due to the RTGel technology. The kit contains the mitomycin (a cytotoxic antibiotic produced by *Streptomyces* fermentation and then purified) in powdered form and a sterile polymer hydrogel solution. UroGen's RTGel® is a proprietary formulation composed of polymers that are liquid at cold temperatures and solidify into gel at body temperature accessdata.fda.gov. The manufacturing of the gel and the mitomycin filling are likely done under strict aseptic, cold-chain conditions to maintain product performance. The final kit is assembled with two vials of mitomycin (each 40 mg) and one vial of ~60 mL gel, ensuring that when mixed, it yields the 56 mL of drug solution required for one dose urologytimes.com.

UroGen holds multiple patents on this formulation and delivery technology accessdata.fda.gov. For example, U.S. Patent Nos. 9,040,074; 9,950,069; and 10,039,832 cover aspects of the sustained-release gel and method accessdata.fda.gov. The product and its components are manufactured under cGMP conditions. Given the complexity, UroGen may use contract manufacturing organizations: the company hasn't publicly disclosed the exact manufacturing sites, but it wouldn't be surprising if production occurs partly in Israel (where their technology was originated) and/or in specialized facilities in the U.S.

Distribution: ZUSDURI is distributed in the U.S. by UroGen Pharma, Inc. (Princeton, NJ) accessdata.fda.gov. It is expected to be a specialty pharmacy or distributor item, not a typical retail pharmacy drug. Because it must be administered by healthcare professionals, the product is likely shipped directly to hospitals, urology clinics, or compounding pharmacies rather than to patients. UroGen has established a **UroGen Support** program to assist with distribution logistics and reimbursement. The medication became available to order in the U.S. on or around **July 1, 2025** pipelinereview.com. Physicians typically acquire the drug per patient (each kit for each instillation) via specialty distributors. Proper storage (refrigerated) is required upon receipt.

The kit includes instructions for pharmacy preparation and administration. Hospitals and clinics must ensure they have refrigeration and appropriate hazardous drug storage for ZUSDURI. Since the product is new, part of UroGen's rollout includes educating pharmacies on the mixing procedure (e.g. use cold packs, do not over-warm) and providing necessary equipment (some kits might come with cooling blocks or the OnGuard® adaptor for safe transfer, etc., as indicated by the packaging information accessdata.fda.gov).

In terms of **availability**, as noted, the drug is currently **marketed in the U.S. only**. UroGen may seek partnerships for international distribution in the future if approvals are obtained (for instance, they might partner with a larger pharma in Europe or Asia for marketing).

Overall, from a manufacturing and distribution standpoint, ZUSDURI is a **specialized therapy** requiring careful handling. UroGen Pharma oversees its distribution, ensuring that healthcare providers can obtain the product along with proper training on reconstitution and administration.

Market Availability and Pricing

Market Launch: ZUSDURI became commercially available in the United States in early July 2025, shortly after FDA approval pipelinereview.com. UroGen announced readiness to supply the drug, and since then it has been accessible through specialty channels for urologists and oncology clinics. The initial market for ZUSDURI is the approximately 59,000 U.S. patients per year with recurrent LG-IR-NMIBC pipelinereview.com pipelinereview.com, and the company has been actively engaging with urology practices to integrate this therapy. As of mid-2025, **market availability is limited to the U.S.**; patients elsewhere would need to be in a clinical trial or perhaps receive it via expanded access if available. There is no generic version since it's a newly approved, patented product.

Pricing: The pricing of ZUSDURI reflects its nature as a novel, specialized oncology therapy. While UroGen has not publicly disclosed the exact list price in press releases, available data suggest a **high cost per treatment cycle**. According to pricing data compiled by Drugs.com, a single ZUSDURI kit (which constitutes one dose, 75 mg) has a wholesale acquisition cost (WAC) on the order of **$21,000 per kit** drugs.com. Specifically, one source lists *40 mg ZUSDURI ureteral kit from $21,009* – which likely corresponds to the full kit used for one intravesical instillation drugs.com. Given that the standard treatment is 6 weekly instillations, the total drug cost for one full course is roughly $126,000 at WAC pricing (6 × $21k). This places ZUSDURI in a similar cost bracket to other specialized oncology drugs. It should be noted that this is the list price; actual reimbursement rates can vary and may be lower (Medicare reimbursement initially is set at 103% of WAC until an average sales price is established) urologytimes.com.

For patients, **out-of-pocket costs** will depend on insurance. ZUSDURI is covered under medical benefits (as it is an in-office administered drug, typically billed under Medicare Part B or equivalent). UroGen has set up support programs: for commercially insured patients, there is a copay assistance program whereby eligible patients may pay as little as $50 per dose, with UroGen covering the remainder up to a large annual maximum drugs.com. For uninsured or underinsured patients, patient assistance programs are available to provide the drug at low or no cost if criteria are met (for example, UroGen's program and independent foundations like PAN Foundation include ZUSDURI in their formularies) drugs.com drugs.com. These measures aim to ensure that cost is not a barrier for patients indicated for the therapy.

Pricing Context: The high price of ZUSDURI reflects the fact that it is a **first-in-class therapy** with proprietary drug delivery technology, and it addresses an area of unmet need. The cost also has to account for the complex manufacturing of the RTGel and the small patient population (as a specialty oncology product). By reducing surgeries, ZUSDURI may offset some healthcare costs (each TURBT surgery under anesthesia also has significant cost, especially if done repeatedly). Pharmacoeconomic analyses will likely be done to see if the drug is cost-effective by avoiding surgical interventions.

Market Uptake: Early analyst reports suggest that UroGen expects significant uptake; revenue projections have been bullish, with some expecting UroGen's revenue to double by 2026 due to ZUSDURI's adoption spglobal.com. The company's only other product, Jelmyto (for upper tract cancer), had a slower ramp-up, but recurrent bladder cancer is a larger market, so penetration could be higher. The **pricing strategy** seems to be to position ZUSDURI comparable to other novel cancer therapies, but with support to make it accessible to patients. Insurers will likely require that it's used per label (for recurrent low-grade disease) and may enforce prior authorizations confirming that the patient is an appropriate candidate (to avoid use in lower-risk disease where a simple TURBT might suffice, or in high-grade disease where it's not indicated).

In summary, **ZUSDURI is now available in the U.S. market** through specialty distribution, with a **premium price (~$20k per instillation)**. Payers and providers are working to integrate it, and assistance programs exist to mitigate costs for patients. As the therapy gains traction and possibly expands to other markets (pending approvals), its pricing and reimbursement will remain important considerations for its adoption in standard care.

Ongoing Research and Scientific Publications

ZUSDURI and its clinical program have been the subject of numerous scientific publications, with ongoing research focusing on long-term outcomes and practical aspects of therapy delivery:

- **Peer-Reviewed Publications:** The pivotal Phase 3 ENVISION trial results have been published in the *Journal of Urology* (February 2025 issue). Prasad **et al. (2025)** reported the 80% CR rate and 82% one-year durability, concluding that chemoablation with UGN-102 is a viable alternative to surgery targetedonc.com. An earlier Phase 2b trial (OPTIMA II) was published by Chevli **et al. (2022)** in *Journal of Urology*, demonstrating feasibility and activity of the RTGel formulation (that study showed a 65% CR at 3 months) pubmed.ncbi.nlm.nih.gov. Additionally, a combined analysis of ATLAS and ENVISION was presented at ASCO 2025 – abstract by Prasad **et al. (J Clin Oncol 2025;43(5_suppl):777)** – highlighting the comparative data (chemo vs TURBT) and supporting the durability findings targetedonc.com targetedonc.com. These publications form the core evidence base for ZUSDURI's efficacy and safety.

- **Long-Term and Subgroup Analyses:** As noted, a 5-year extension of the OPTIMA II trial was published in *Clinical Genitourinary Cancer (2025)*, with Shore **et al.** as lead author, demonstrating sustained complete responses out to a median of 3.5 years in those followed drug-dev.com. This provides reassurance that some patients can enjoy prolonged remission after treatment. Ongoing follow-up of the ENVISION cohort is being carried out; those data (up to 2–3 years of follow-up for all patients) will likely be reported in upcoming meetings or publications. Investigators are particularly interested in the durability of response, patterns of recurrence (when tumors come back, are they still low-grade? Do any progress to higher grade?), and long-term safety (e.g. any late fibrosis or bladder capacity issues).

- **Home Instillation Study:** One innovative research direction is exploring **at-home instillation** of ZUSDURI. During development, UroGen initiated a Phase 3b study to test whether the instillations could be done by patients (or local healthcare providers) at home, rather than in clinic, to improve convenience. Early results from a feasibility study (published 2025) indicated that at-home administration was **feasible and safe**, with proper training and support, and showed similar short-term efficacy investors.urogen.com. This could be particularly useful for patients who live far from treatment centers, as each weekly visit can be burdensome. More data on at-home use are expected, and this might pave the way for broader adoption if the logistics can be managed (e.g. visiting nurse services or self-catheterization by well-trained patients).

- **Next-Generation Formulations:** UroGen is also developing a next-gen formulation labeled **UGN-103**, which is essentially a refined version of the mitomycin RTGel. According to UroGen, UGN-103 is designed to offer improvements such as a **shorter manufacturing process and potentially longer shelf-life** or easier preparation, while providing the same therapeutic effect investors.urogen.com. A Phase 3 trial named **UTOPIA** is underway to evaluate UGN-103. The impetus for UGN-103 appears to be to streamline production and possibly enable broader use (it might also incorporate some changes to allow at-home instillation more readily). As of mid-2025, UroGen announced completion of enrollment in the UTOPIA trial, which suggests that results on UGN-103's equivalence or improvements over ZUSDURI will be forthcoming in the next year or two.

- **Additional Clinical Trials:** Beyond the treatment of LG-IR-NMIBC, the RTGel platform might be investigated for other bladder indications. For example, there's interest in whether the technology could deliver other agents (like immunotherapies) intravesically. While not directly ZUSDURI, it speaks to the research stimulated by this product. For ZUSDURI itself, the company will be collecting **real-world data** as it is used in practice, which can be valuable in supplementing trial findings. Furthermore, combination approaches (e.g. using intravesical mitomycin gel after a debulking TURBT or in conjunction with systemic therapies in select cases) could be explored by investigators.

- **Guidelines and Future Directions:** The bladder cancer community is keenly observing how ZUSDURI impacts patient care. The AUA (American Urological Association) and SUO (Society of Urologic Oncology) are likely to incorporate the drug in their updated guidelines for NMIBC, recommending it as an option for appropriate patients. EAU (European Association of Urology) guidelines may discuss it as well, pending EMA approval. From a research perspective, an open question is: can chemoablation become a new paradigm for other risk categories? For example, could intermediate-risk patients who are *not* recurrent (first occurrence low-grade but with risk factors) be treated upfront with chemoablation to avoid an initial TURBT? Or could high-grade small tumors in very frail patients be temporized with such an approach? These are speculative, off-label ideas, but they underscore a broader interest in expanding non-surgical management in urothelial tumors.

In conclusion, **scientific research on ZUSDURI is active and ongoing**. Key results have been published in high-impact urology and oncology journals, confirming the drug's efficacy and safety. Long-term data are emerging that support sustained benefits. New trials (like UGN-103) aim to refine and possibly improve the treatment. The advent of ZUSDURI has opened a new line of inquiry in bladder cancer: leveraging drug formulations to potentially replace certain surgeries. The coming years will likely yield more data on how this approach can be optimized and integrated into standard care, with numerous publications and conference presentations adding to the evidence base targetedonc.com drug-dev.com.

Sources: This report has cited information from FDA documentation, the official ZUSDURI prescribing information, peer-reviewed journal articles (Journal of Urology, Clinical Genitourinary Cancer), clinical trial data, and reputable oncology news outlets. Key references include the FDA approval announcement fda.gov fda.gov, the ENVISION Phase 3 trial publication targetedonc.com, and UroGen Pharma's press releases and investor communications pipelinereview.com pipelinereview.com, among others. All significant data points and claims have been referenced to these sources to ensure accuracy and credibility. The information reflects the state of knowledge as of mid-2025, and ongoing studies may further augment our understanding of ZUSDURI's role in bladder cancer management.

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