Clinical Management of Gem-iDRS in Bladder Cancer

See INLEXZO Indication and Safety Information Summary on page 4

Baseline Assessment and Prophylactic Measures to Consider

What are lower urinary tract symptoms (LUTS)?[1–3]

LUTS are commonly implicated with bladder cancer and its treatment and can cause discomfort for patients. They can be...

Storage
- Increased frequency
- Urgency
- Nocturia
- Urinary incontinence

Voiding
- Weak stream
- Hesitancy
- Intermittency
- Straining

Post-micturition
- Feeling of incomplete emptying

Pain

Why treat LUTS and/or underlying conditions prior to gem-iDRS? [3–7]

- LUTS are **symptom-defined and multifactorial,** which can impact adherence
- LUTS may be **exacerbated during treatment**

Baseline screening and assessment[3,4,7]

1	**Symptom screening**	Use validated tool (IPSS/AUA-SI) to assess **storage, voiding, and post-void symptoms**
2	**Baseline clinical evaluation**	• **Previous intravesical therapy history** and experience (symptom duration/severity) • **Physical exam**, including a focused urologic exam • **Urinalysis** to rule out UTI/hematuria
3	**Reassessment**	**Track symptom progression and response**

Manage underlying conditions

Additionally, consider the management of the following underlying conditions:

- Screen patients with BPH and based on treatment guidelines, consider treatment with alpha blockers (tamsulosin, alfuzosin) and/or 5-alpha reductase inhibitors (finasteride, dutasteride)[4]
- In patients with underlying OAB, consider treatment per guidelines with beta agonists or anticholinergics; or consider referral to an OAB specialist[8]
- For post-menopausal females with underlying GU syndrome, treat appropriately per guidelines[9]

Patient education and prophylactic measures throughout gem-iDRS treatment

In the **SunRISe-1 study**, investigators were instructed to administer **at least 1 dose of prophylactic periprocedural antibiotics** for any gem-iDRS insertion or removal[10]

Advise patients to **consume at least 1500 mL (~6.5 cups) of liquid** each day during the dosing period[10,11]

In the **SunRISe-1 study**, investigators were instructed to consider use of **prophylactic administration of anticholinergics, NSAIDS, and bladder analgesics**[10]

- **Educate patients on potential LUTS** prior to initiation and throughout treatment[11]
- Consider counseling patients to **avoid bladder irritants (e.g., spicy foods, caffeine, alcohol, drinks containing artificial sweeteners)**[12,13]

Select concomitant medications used in SunRISe-1 Cohort 2[14]

The following table lists commonly used (≥10%) concomitant antibiotics, analgesics, and urologic medications in SunRISe-1 Cohort 2. Selection and use of individual medications were not specified in the protocol and were at investigator discretion. The effectiveness of these medications in the context of gem-iDRS has not been established.

Antibiotics		Analgesics	
Ciprofloxacin	44.7%	Acetaminophen	40%
Fosfomycin	31.8%	Acetylsalicylic acid	29.4%
Combinations of sulfonamides and trimethoprim	29.4%	Ibuprofen	15.3%
Amoxicillin and clavulanate	21.2%	Tramadol	13.6%
Cefazolin	18.8%	**Urologics**	
Nitrofurantoin	17.6%	Mirabegron	27.1%
Levofloxacin	16.5%	Oxybutynin	24.7%
Cefalexin	14.1%	Tamsulosin	24.7%
Cefuroxime	12.9%	Solifenacin	22.3%
Cefixime	11.8%	Phenazopyridine	12.9%
		Festoterodine	10.6%

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Ongoing Monitoring and Adverse Event Management During Treatment

Safety of gem-iDRS in SunRISe-1 study[15]

See INLEXZO Indication and Safety Information Summary on page 4

Gem-iDRS was studied in adults with BCG-unresponsive NMIBC with CIS, with or without papillary tumors, in Cohort 2 of the SunRISe-1 study (safety population N=85)

- The **most common adverse reactions (>15%)** with gem-iDRS were urinary frequency, UTI, dysuria, micturition urgency, urinary tract pain, hematuria, and bladder irritation. Most adverse reactions were Grade 1–2
- **Dosage interruptions*** of gem-iDRS occurred in **41% of patients** and **permanent discontinuation** of gem-iDRS occurred in **7% of patients**

Gemcitabine and dFdU are excreted in urine throughout the indwelling period for gem-iDRS. Of the total gemcitabine dose, **77% was excreted by Day 7** and **99% was excreted by Day 21** in urine as gemcitabine and dFdU

Symptom-driven management[11]

Information provided below was developed based on expert urologic experiences. There are no available studies or analyses on the effectiveness of these recommendations. These recommendations are not included in any iDRS USPI or IFU (see page 4 for more information). These recommendations should not override the HCPs' decision-making, which should consider clinical judgement, patient history, AE experience, and institutional guidelines where applicable for symptom and side effect management of iDRS use.

An **international (US, Europe, China, and Japan) expert panel (n=17)** was convened to develop consensus recommendations on the management of side effects associated with iDRS treatment

- **7** Urologists and urologic oncologists with iDRS experience the sponsor's (Johnson & Johnson) clinical trials
- **2** Functional urologists
- **8** Physicians and clinical scientist affiliates of the sponsor (Johnson & Johnson)

LUTS

Dysuria in the absence of UTI

1. Consider continuing iDRS treatment while initiating symptom management
2. If no clinical improvement, consider removing/delaying insertion of new iDRS after removal
3. After complete resolution, iDRS treatment may be resumed

OAB†

Steps 1–3 may be followed as listed for dysuria

1. If OAB symptoms persist despite symptom management, consider cystoscopy to evaluate the degree of mucosal irritation‡

Bladder pain associated with OAB

Steps 1–3 may be followed as listed for dysuria

1. Consider the WHO three-step analgesic ladder, with the potential addition of antispasmodics and/or phenazopyridine§

UTI

UTIs

1. Initiate appropriate antibiotics based on urinalysis and urine culture results
2. Consider leaving iDRS in the bladder through antimicrobial treatment to avoid instrumentation and risks of seeding infection
3. If signs and symptoms worsen after treatment for 48–72 hours, clinical judgement should be used regarding whether the iDRS should be removed

Urosepsis

1. Remove iDRS as soon as patient is clinically stable following initiation of broad-spectrum antibiotics
2. After complete resolution of the infection, iDRS treatment may be resumed based on clinical judgement

Hematuria

Macroscopic‖

1. Consider continuing iDRS treatment, while initiating therapy to target cause
2. If no clinical improvement, consider removal/ delaying insertion
3. If persistent, consider cystoscopy to evaluate presence/recurrence of bladder tumor

Complicated¶

1. Consider removing iDRS
2. Consider management of other symptoms (i.e., anemia, obstruction) as clinically indicated, including invasive intervention
3. After complete resolution, iDRS treatment may be resumed based on clinical judgement

*During the SunRISe-1 study, gem-iDRS treatment interruption was defined as removal of gem-iDRS.[7] †OAB symptoms include micturition urgency, pollakiuria, urge incontinence, and/or nocturia. ‡To treat mucosal irritation, HCPs could consider a short course of corticosteroids. §Step 1 initially and step 2 for persistent pain. ‖Defined as with no clots, no signs of retention, and negative urine culture. ¶Defined as with clots leading to retention, and/or dysuria or hematuria with anemia.

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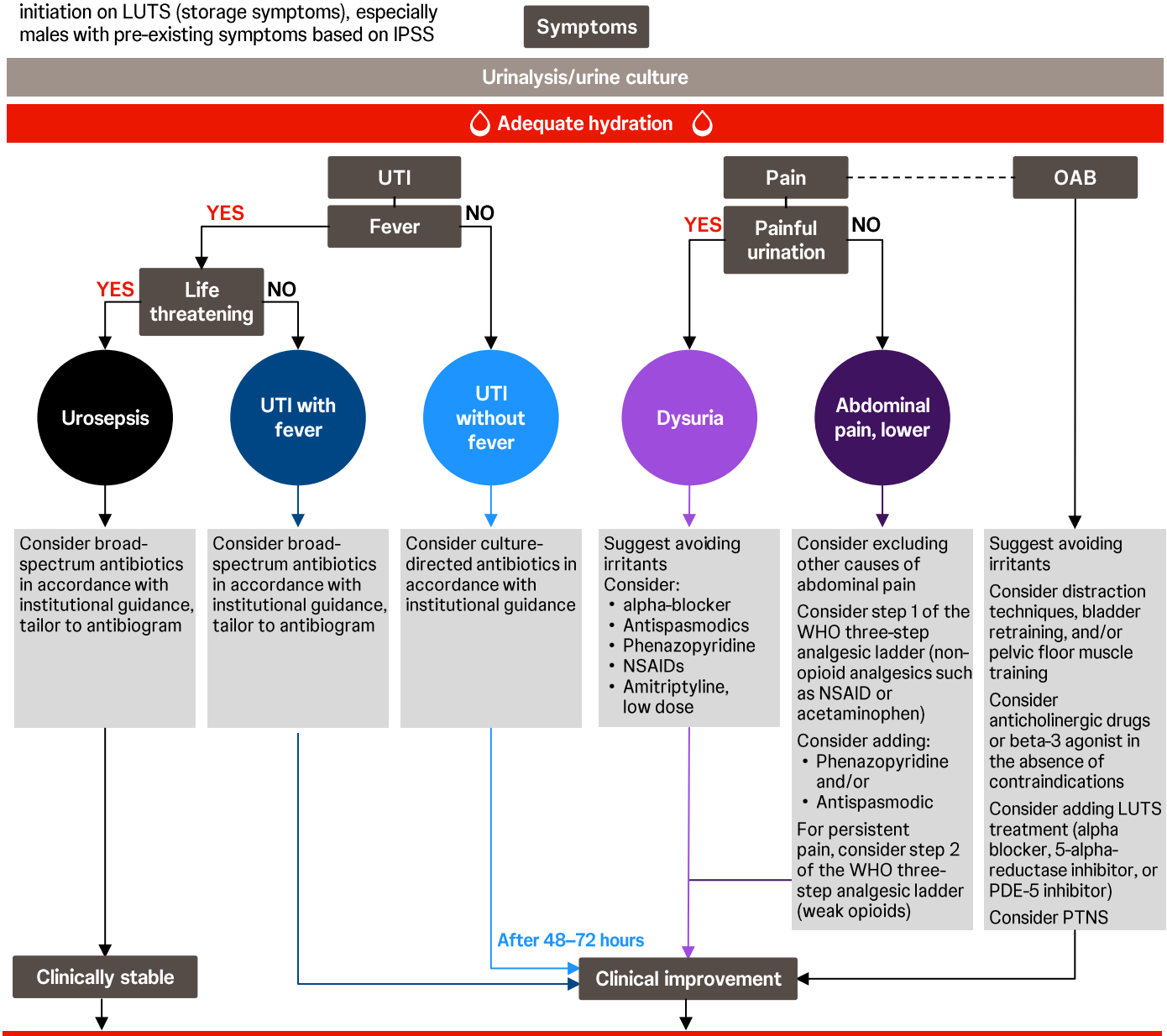
Considerations for iDRS Clinical Management Based on Expert Panel Recommendations[11]

Information provided below was developed based on expert urologic experiences (urologists/urologic oncologists from iDRS clinical trials, functional urologists, physicians, and clinical scientists). There are no available studies or analyses on the effectiveness of these recommendations. These recommendations are not included in any iDRS USPI or IFU (see page 4 for more information). These recommendations should not override the HCPs' decision-making, which should consider clinical judgement, patient history, AE experience, and institutional guidelines where applicable for symptom and side effect management of iDRS use.

Consider counseling patients from treatment initiation on LUTS (storage symptoms), especially males with pre-existing symptoms based on IPSS



When deciding whether to remove or continue iDRS, HCPs are advised to apply their clinical judgment with each case. Please refer to Pradere et al. (2025) for additional information from this expert panel, including iDRS management.

Adapted with permission from Pradere B, et al. *Curr Opin Urol.* 2025. doi:10.1097/MOU.0000000000001350.

Scan QR code or go to tago.ca/pradere2025 for more information. See the full manuscript: Pradere B, Schuit M, Guerrero-Ramos F, et al. Side effect management and procedural best practices with indwelling intravesical drug releasing systems in the treatment of bladder cancer: recommendations from expert panels. *Curr Opin Urol.* 2025. doi:10.1097/MOU.0000000000001350.

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See INLEXZO Indication and Safety Information Summary on page 4

INLEXZO™ (gemcitabine intravesical system) INDICATION AND SAFETY INFORMATION SUMMARY

Indication

INLEXZO™ (gemcitabine intravesical system) is indicated for the treatment of adult patients with Bacillus Calmette-Guérin (BCG)-unresponsive, non-muscle invasive bladder cancer (NMIBC) with carcinoma *in situ* (CIS), with or without papillary tumors. Prior hypersensitivity reactions to gemcitabine or any component of the product.

Contraindications

INLEXZO™ is contraindicated in patients with:

- Perforation of the bladder.
- Prior hypersensitivity reactions to gemcitabine or any component of the product.

Adverse Reactions

Serious adverse reactions occurred in 24% of patients receiving INLEXZO™. Serious adverse reactions that occurred in >2% of patients included urinary tract infection, hematuria, pneumonia, and urinary tract pain. Fatal adverse reactions occurred in 1.2% of patients who received INLEXZO™, including cognitive disorder. The most common (>15%) adverse reactions, including laboratory abnormalities, were urinary frequency, urinary tract infection, dysuria, micturition urgency, decreased hemoglobin, increased lipase, urinary tract pain, decreased lymphocytes, hematuria, increased creatinine, increased potassium, increased AST, decreased sodium, bladder irritation, and increased ALT.

Warnings and Precautions

Risks in Patients with Perforated Bladder

INLEXZO™ may lead to systemic exposure to gemcitabine and to 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 administration of INLEXZO™ and do not administer to patients with a perforated bladder or mucosal compromise until bladder integrity has been restored.

Risk of Metastatic Bladder Cancer

Delaying cystectomy in patients with BCG-unresponsive CIS could lead to development of muscle invasive or metastatic bladder cancer, which can be lethal. The risk of developing muscle invasive or metastatic bladder cancer increases the longer cystectomy is delayed in the presence of persisting CIS.

Of the 83 evaluable patients with BCG-unresponsive CIS treated with INLEXZO™ in Cohort 2 of SunRISe-1, 7 patients (8%) progressed to muscle invasive (T2 or greater) bladder cancer. Three patients (3.5%) had progression determined at the time of cystectomy. The median time between determination of persistent or recurrent CIS or T1 and progression to muscle invasive disease was 94 days.

Magnetic Resonance Imaging (MRI) Safety

INLEXZO™ can only be safely scanned with MRI under certain conditions. Refer to section 5.3 of the USPI for details on conditions.

Embryo-Fetal Toxicity

Based on animal data and its mechanism of action, INLEXZO™ can cause fetal harm when administered to a pregnant woman if systemic exposure occurs. In animal reproduction studies, systemic administration of gemcitabine was teratogenic, embryotoxic, and fetotoxic in mice and rabbits.

Advise pregnant women and females of reproductive potential of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment and for 6 months after final removal of INLEXZO™. Advise male patients with female partners of reproductive potential to use effective contraception during treatment and for 3 months after final removal of INLEXZO™.

Use in Specific Populations

Pregnancy

There are no available data on the use of INLEXZO™ in pregnant women to inform a drug-associated risk. Please see Embryo-Fetal Toxicity for risk information related to pregnancy.

Lactation

Because of the potential for serious adverse reactions in breastfed infants, advise women not to breastfeed during treatment and for 1 week after final removal of INLEXZO™.

Females and Males of Reproductive Potential

- **Pregnancy Testing** - Verify pregnancy status in females of reproductive potential prior to initiating INLEXZO™.
- **Contraception** - Please see Embryo-Fetal Toxicity for information regarding contraception.
- **Infertility (Males)** - Based on animal studies, INLEXZO™ may impair fertility in males of reproductive potential. It is not known whether these effects on fertility are reversible.

Geriatric Use

Of the patients given INLEXZO™ monotherapy in Cohort 2 of SunRISe-1, 72% were 65 years of age or older and 34% were 75 years or older. There were insufficient numbers of patients <65 years of age to determine if these patients respond differently to patients 65 years of age and older.

Scan QR code or click here to read the full Prescribing Information for INLEXZO™

Scan QR code or click here to read the Instruction for Use for INLEXZO™

AE, adverse event; AUA-SI, American Urological Association Symptom Index; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BCG, Bacillus Calmette-Guérin; BPH, benign prostatic hyperplasia; CIS, carcinoma in situ; dFDU, days to first deterioration; GU, genitourinary; HCP, healthcare professional;iDRS, intravesical drug-releasing system; IFU, Instructions for Use; IPSS, International Prostate System Score; LUTS, lower urinary tract symptoms; NMIBC, non-muscle invasive bladder cancer; NSAIDs, nonsteroidal anti-inflammatory drugs; OAB, overactive bladder; PDE-5, phosphodiesterase-5; PTNS, percutaneous tibial nerve stimulation; USPI, United States Prescribing Information; UTI, urinary tract infection; WHO, World Health Organization.

1. Albakr A, et al. *Transl Androl Urol.* 2025;14(10):3402–3412. 2. D'Ancona C, et al. *Neurourol Urodyn.* 2019;38(2):433–477. 3. European Association of Urology. EAU Guidelines on Non-neurogenic Male Lower Urinary Tract Symptoms (LUTS). 2026. 4. GoueliR, et al. Management of Lower Urinary Tract Symptoms Attributed to Benign Prostatic Hyperplasia: AUA Guideline (2026) *J Urol. 2026*;0(0). 5. BourlotosG, et al. *Front Neurosci.* 2024;17:1327053. 6. American Cancer Society. Bladder Incontinence (Urine Leakage); 2024. Available at: https://www.cancer.org/cancer/managing-cancer/side-effects/stool-or-urine-changes/bladder-incontinence.html (Accessed June 26, 2026). 7. European Association of Urology. EAU guidelines on Management of Non-Neurogenic Female Lower Urinary Tract Symptoms. 2026. 8. Cameron AP, et al. *J Urol.* The AUA/SUFU Guideline on the Diagnosis and Treatment of Idiopathic Overactive Bladder. 2024;212(1):11–20. 9. Kaufman MR, et al. *J Urol.* Genitourinary Syndrome of Menopause: AUA/SUFU/AUGS Guideline. 2025;0(0). 10. Janssen Research & Development. SunRISe-1 Protocol 17000139BLC2001, Version 5; 2 July 2024. 11. PradereB, et al. *Curr Opin Urol.* 2025. doi:10.1097/MOU.0000000000001350. 12. National Cancer Institute. Urination Changes During Cancer Treatment. National Institutes of Health; 2022. Available at: https://www.cancer.gov/about-cancer/treatment/side-effects/urination-changes (Accessed June 17, 2026). 13. National Institute of Diabetes and Digestive and Kidney Diseases. Prevention of Bladder Control Problems (Urinary Incontinence) & Bladder Health. National Institutes of Health; 2021. Available at: https://www.niddk.nih.gov/health-information/urologic-diseases/bladder-control-problems/prevention (Accessed June 17, 2026). 14. Data on File. Johnson & Johnson. 2026.
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