Side Effect Management with Indwelling Intravesical Drug-Releasing Systems in the Treatment of Bladder Cancer: Recommendations from Expert Panels

Johnson&Johnson

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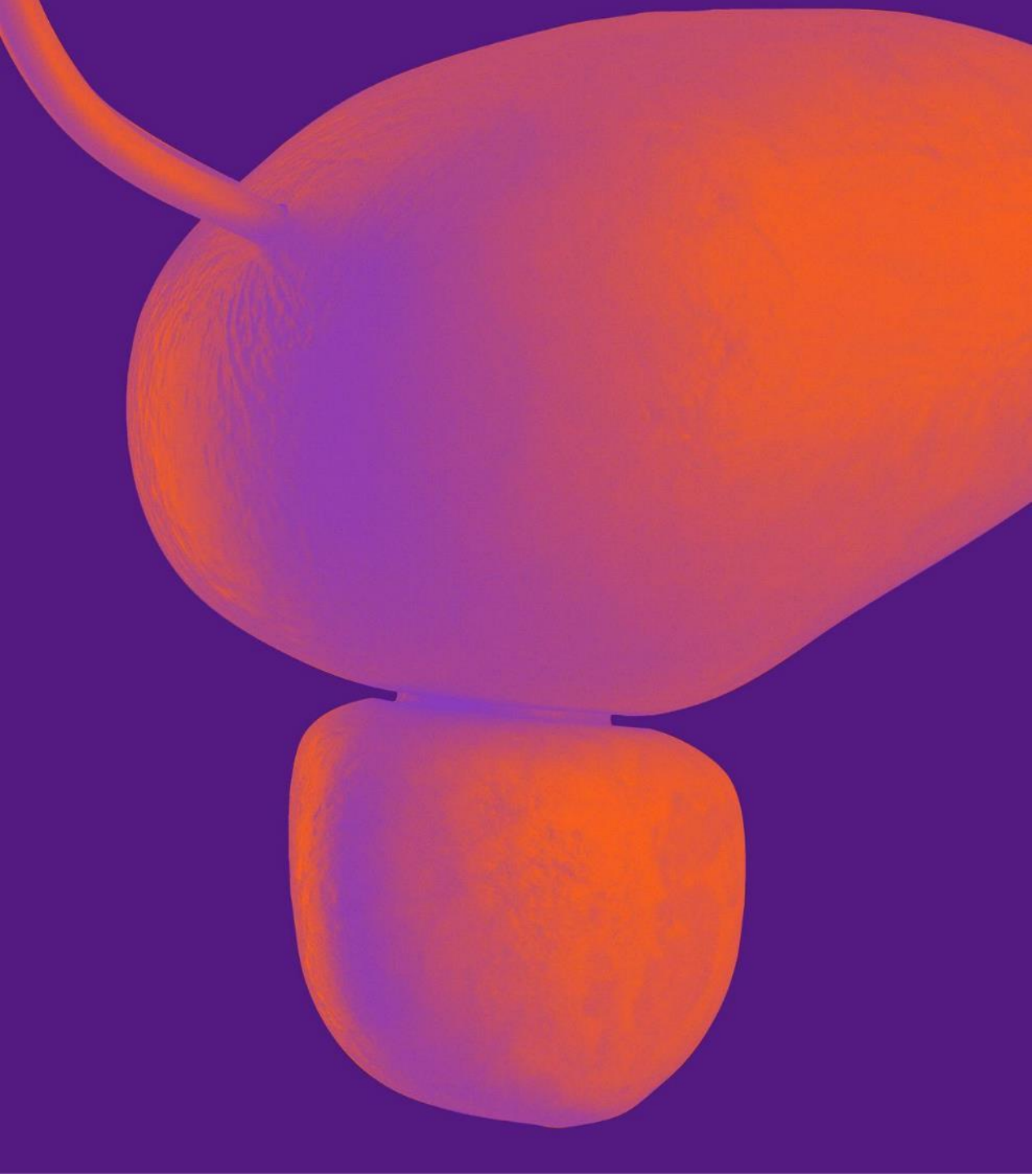
Provided in response to a medical information request. All MIR responses will meet standards required by the Medical Affairs SOP on Response to Unsolicited Questions. Responses should be fair, balanced, factual, objective, and nonpromotional for any MIR response, as well as specific to the HCP question and not beyond.

The guidance provided in this presentation is based on the expert opinion of leading urologists and oncologists with clinical trial experience in the SunRISe and MoonRISe programs. It is intended to provide recommendations on how to optimize the management of commonly experienced side effects, including when to remove and resume iDRS treatment.

Treatment decisions should reflect HCP clinical judgement and local, national, and institutional guidelines. The availability of medications presented for symptom management may vary based on local regulatory approvals, and their use should be tailored to individual patient needs, considering any patient-specific contraindications.

Information provided below was developed based on expert clinical experience. There is no data to support the effectiveness of the recommendations below. Prescribing HCPs should use their clinical judgement when treating patients with intravesical drug releasing systems.



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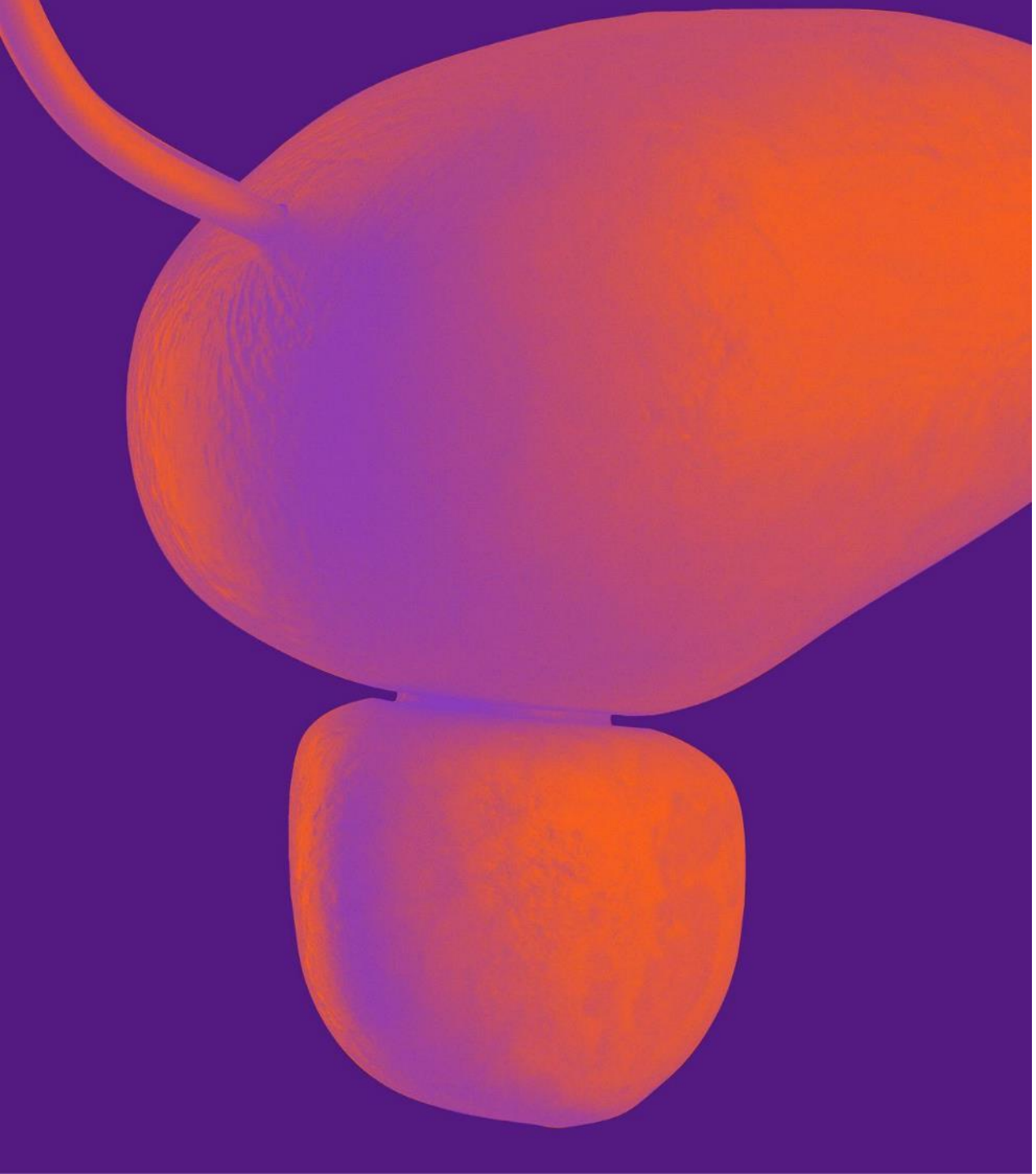

Introduction

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Introduction

Intravesical therapies are a mainstay for the treatment of localized bladder cancer

Lower urinary tract symptoms (LUTS), including dysuria, pollakiuria, and micturition urgency, urinary tract infection (UTI), and hematuria are frequent side effects associated with all intravesical therapies[1–5]

Notably, these events may be related to concurrent urinary tract conditions, urinary catheterization, or recent surgery, many patients exhibit urinary tract signs and symptoms before initiating any intravesical therapy[6]

1. TICE® BCG [package insert]. Roseland, NJ: Organon USA Inc.; 2009; 2. KEYTRUDA® (pembrolizumab) injection, for intravenous use [prescribing information]. 374 Merck & Co., Inc., Rahway NJ, USA; 2024 (initial US approval, 2014). 3. ANKTIVA® (nogapendekin alfa inbakicept-pmln) solution for intravesical use [package insert]. Culver City, CA: Altor Bioscience, LLC, an indirect wholly-owned subsidiary of Immunity Bio, Inc.; 2024; 4. Koch GE,et al.. *Urology.* 2021;149:11–20; 5. Mathes J and Todenhofer T. *Eur Urol Focus.* 2018;4:464–467; 6. Gontero P, et al. *European Urology.* 2024;86:531–549.

Introduction cont'd

Gemcitabine intravesical system (previously TAR-200) and TAR-210 are intravesical drug-releasing systems (iDRS)designed to provide sustained local delivery of therapy within the bladder over several weeks or months[1,2]

Gemcitabine intravesical system is the first iDRS with regulatory approval, **recently approved in the United States to treat patients with BCG unresponsive high-risk non-muscle–invasive bladder cancer (NMIBC) with carcinoma in situ with or without papillary disease**, and it is under investigation in ongoing phase 2/3 trials in NMIBC and muscle-invasive bladder cancer (MIBC) populations[2–5]

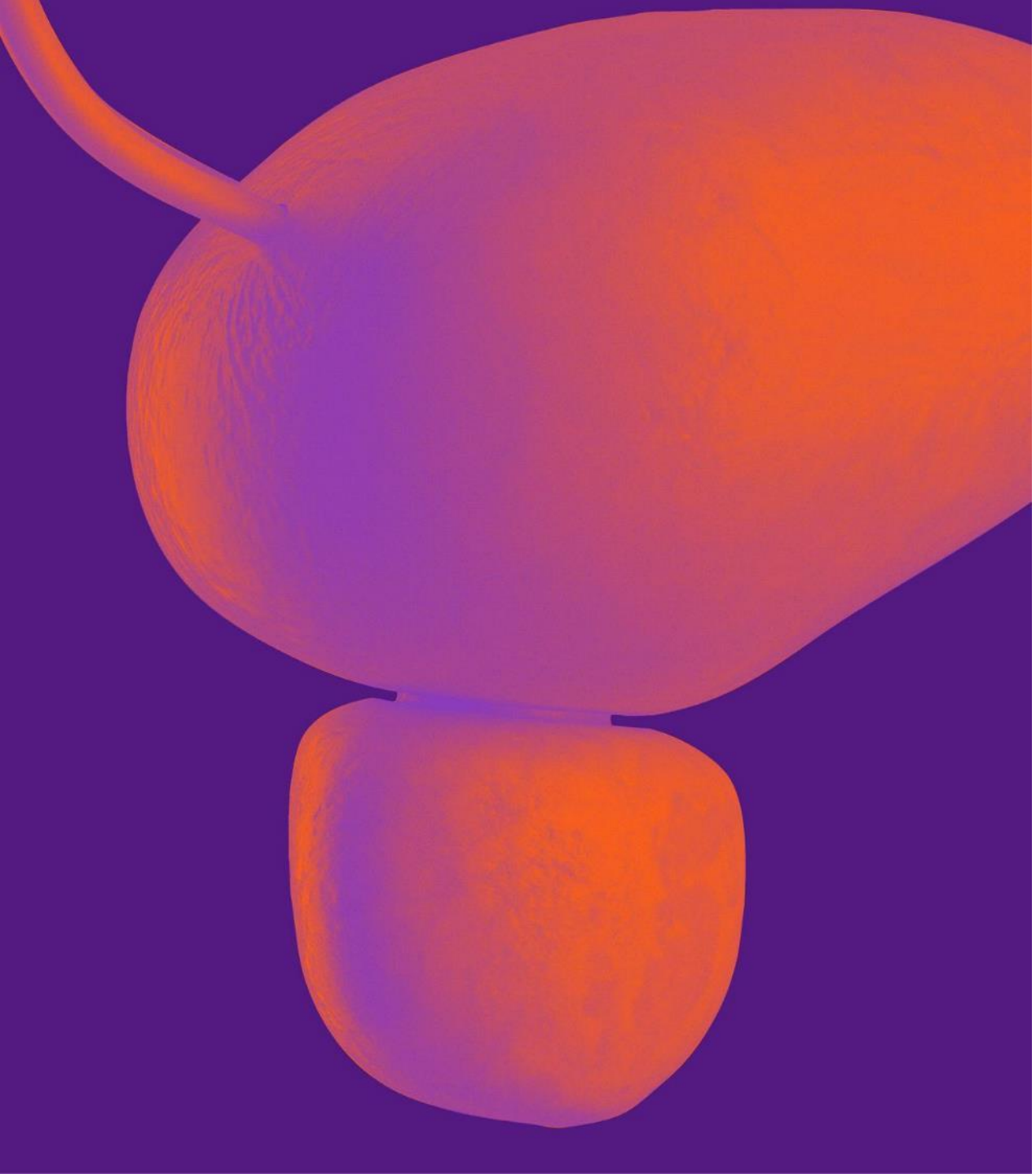
Additionally, TAR-210, an iDRS designed to provide sustained, local delivery of erdafitinib, is also under investigation in biomarker-selected NMIBC populations in an ongoing phase 1 study and ongoing phase 2/3 studies[1,6,7]

The toxicity profile of iDRS as reported in published clinical trials is characterized by dysuria, UTI, overactive bladder (OAB) symptoms, and hematuria (generally low grade)[1,3,4,8]

Appropriate management of side effects associated with iDRS treatment is critical to ensure minimal impact on patient's way of life, mitigate treatment interruption, and improve adherence and outcomes.

HCP, healthcare professional; UTI, urinary tract infection.

1. Vilaseca A, et al. *J Urol.* 2024;211(5S):e987; 2. Daneshmand S, et al.. *Urol Oncol.* 2025;286–296; 3. Daneshmand S, et al. *J Clin Oncol.* 2025:10.1200/JCO-25-01651. 4. Necchi A, et al. *Lancet Oncol.* 2025; 26(10):1312-1322. 5. INLEXZO™ (gemcitabine intravesical system) [prescribing information]. Janssen Products, LP, Horsham PA, USA; 2025. 6. Li R, et al. *J Urol.* 2025;213(5S2):e15. 7. Shore ND, et al. *J Urol.* 2025;213(5S2):e15. 8. Daneshmand S, et al. *Urol Oncol.* 2025;43(3_suppl):55.



Methods

Introduction

Methods

Expert panel recommendations

Recommendations flow-chart

Methods

An international panel convened to provide recommendations on the management of side effects associated with iDRS treatment

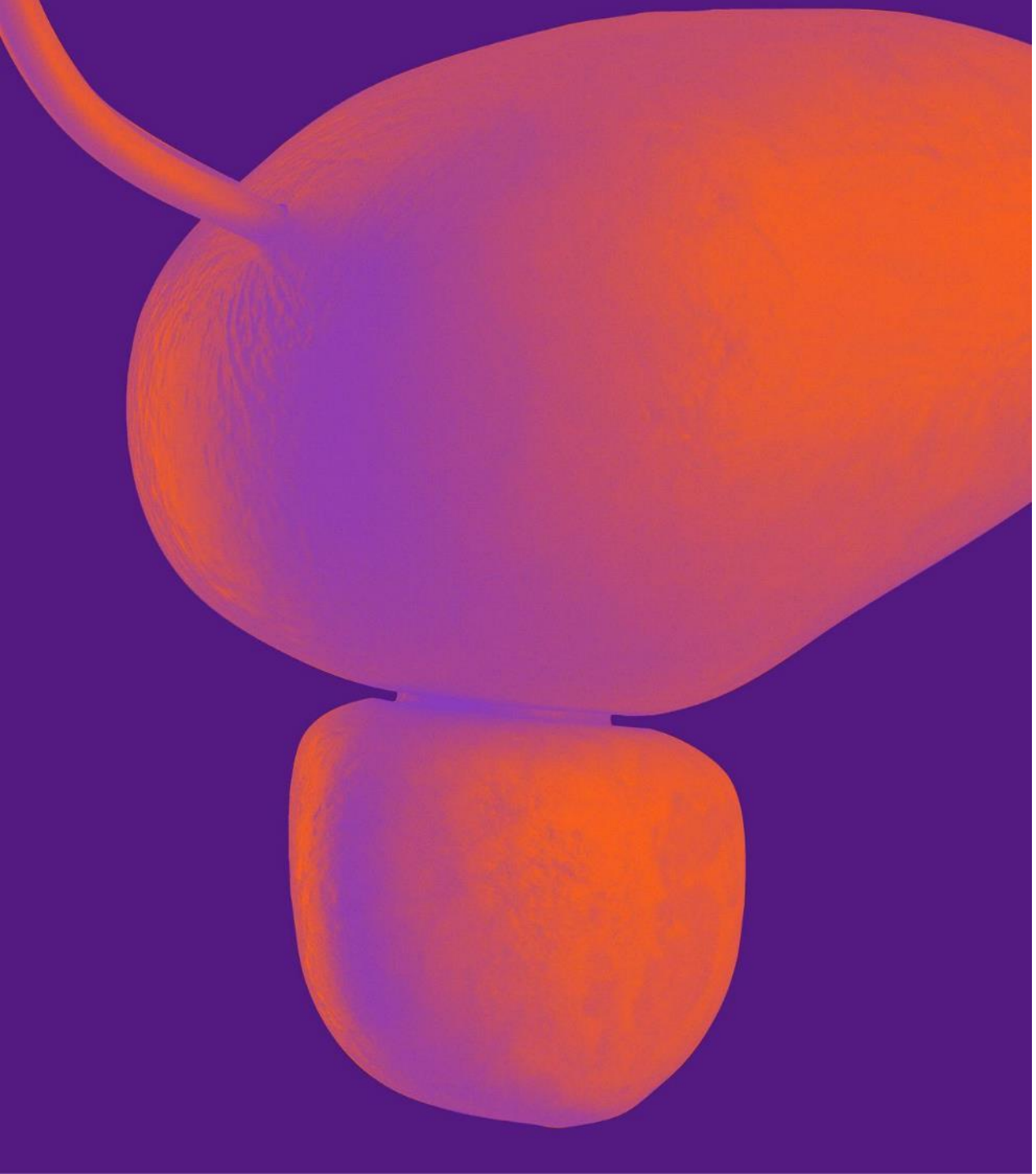
- **7** Urologic oncologists with experience with iDRS in clinical trials
- **2** Functional urologists
- **8** Physicians and clinical scientist affiliates of the sponsor (Johnson & Johnson)

From US, Europe, China & Japan

Discussed management strategies of side effects associated with iDRS treatment → Drafted consensus clinical recommendations → Reviewed and revised side effect management recommendations based on final input from the functional urologists

iDRS, intravesical drug-releasing systems; US, United States.

Pradere B, et al. *Curr Opin Urol*. 2025. In Press.



Expert panel recommendations

General principles and prophylactic measures

General recommendations for managing iDRS-associated side effects include:

Counsel on potential LUTS prior to initiation and throughout the treatment course, and **screen** for **pre-existing LUTS***

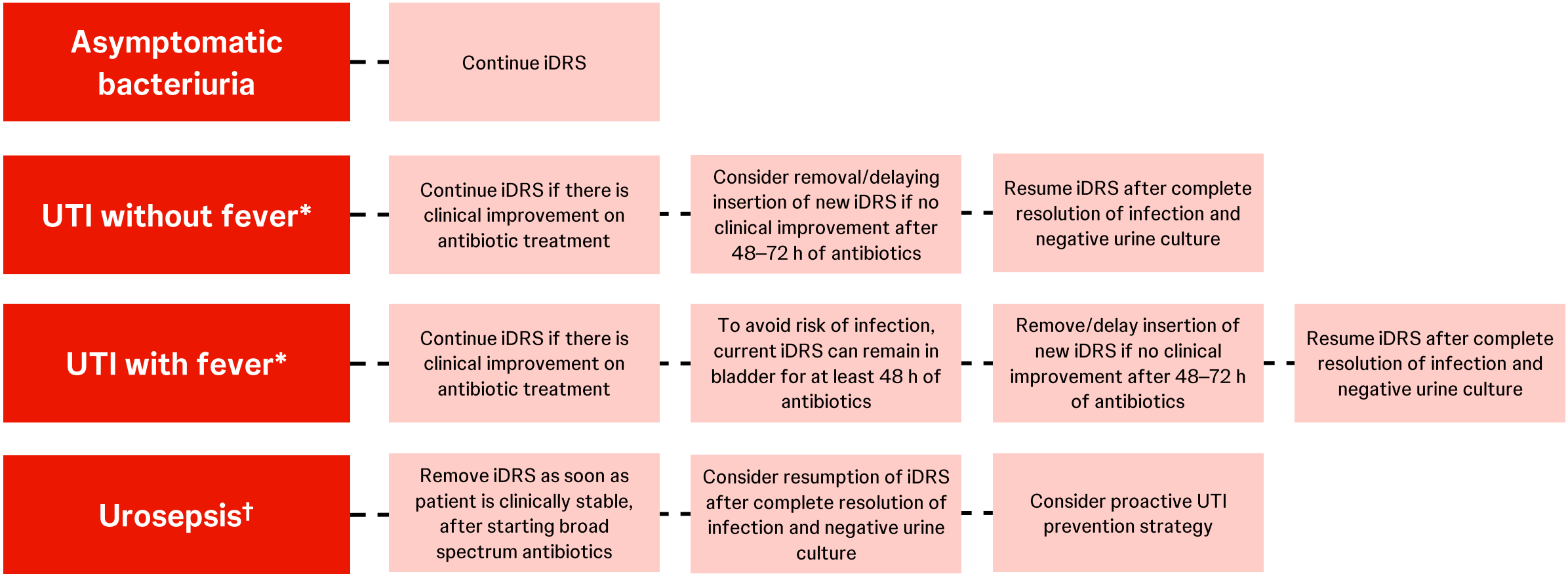
Consume **≥1500 mL** of non-alcoholic, non-caffeinated **liquid** each day during the iDRS dosing period

Avoid bladder irritants (spicy foods, citrus fruits) if patient has ongoing LUTS or history of LUTS prior to treatment†

*Especially in male patients with storage symptoms based on International Prostate Symptom Score which may worsen during iDRS treatment. †If LUTS occur, urinalysis and urine culture should be conducted, and, if UTI is present, treatment should be tailored to standard practice.
iDRS, intravesical drug-releasing systems; LUTS, lower urinary tract symptoms; UTI, urinary tract infection.
Pradere B, et al. *Curr Opin Urol.* 2025. In Press.

Management of UTI and bacteriuria

iDRS management



*UTI is defined as a symptomatic infection with a positive urine culture with a bacterial count of $\geq 10^5$ colony forming units (CFU)/mL in urine voided from women or $>10^4$ CFU/mL in urine voided from men, or in straight-catheter urine from women that cannot be cleared with antibiotic therapy; †Urosepsis is defined as life threatening organ dysfunction caused by dysregulated host response to infection originating from the urinary tract and/or male genital organs.

h, hour; iDRS, intravesical drug-releasing systems; UTI, urinary tract infection.

Pradere B, et al. *Curr Opin Urol.* 2025. In Press.

Management of UTI and bacteriuria

Symptom management

	Asymptomatic bacteriuria	UTI without fever*	UTI with fever*	Urosepsis†
	Encourage adequate hydration			**Urgent management, hospitalization, adequate hydration**
		Collect urinalysis and urine culture	Collect urinalysis and urine culture, and consider blood culture	Urine culture and blood culture
	Consider tailored antibiotic treatment based on antibiogram results if symptoms develop‡	Start culture-directed oral antibiotics in accordance with institutional guidance	Start broad spectrum antibiotics in accordance with institutional guidance, tailor to antibiogram	Start broad spectrum antibiotics in accordance with institutional guidance, tailor to antibiogram

*UTI is defined as a symptomatic infection with a positive urine culture with a bacterial count of $\geq 10^5$ colony forming units (CFU)/mL in urine voided from women or $>10^4$ CFU/mL in urine voided from men, or in straight-catheter urine from women that cannot be cleared with antibiotic therapy; †Urosepsis is defined as life threatening organ dysfunction caused by dysregulated host response to infection originating from the urinary tract and/or male genital organs; ‡In accordance with institutional guidance.

UTI, urinary tract infection.

Pradere B, et al. *Curr Opin Urol.* 2025. In Press.

Management of dysuria (in the absence of UTI)

Definition

Painful or burning sensation during urination

iDRS management

Continue iDRS and initiate symptom management

If no clinical improvement with symptom management, (next slide) remove iDRS or delay insertion

When symptoms resolve, iDRS treatment can be resumed

iDRS, intravesical drug-releasing systems; UTI, urinary tract infection.

Pradere B, et al. *Curr Opin Urol*. 2025. In Press.

Management of dysuria (in the absence of UTI)

Symptom management

- Encourage adequate hydration
- Collect urinalysis and urine culture
- Avoid irritants (caffeine, alcohol, spicy food)
- Review recommendations for management of OAB symptoms

Medication*

Consider:

- Alpha-blockers (e.g., tamsulosin, alfuzosin, silodosin)
- Antispasmodics (dicyclomine, hyoscyamine, scopolamine)
- Phenazopyridine, if available per local regulation
- NSAIDs
- Amitryptyline (at low dose)

+ Click here for OAB symptom management

*Select examples are listed on the slide. List is not meant to be exhaustive. Use as directed per clinician judgement, guidelines, and availability per local regulations.
NSAID, non-steroidal anti-inflammatory drugs; OAB, overactive bladder; UTI, urinary tract infection.
Pradere B, et al. *Curr Opin Urol.* 2025. In Press.

Management of OAB symptoms and bladder pain

Definition

Increase in micturition urgency, micturition frequency (pollakiuria), urge incontinence, nocturia, or pain

iDRS management

Continue iDRS and initiate symptom management

If no clinical improvement with symptom management (next slide) remove iDRS or delay insertion

When symptoms improve, iDRS treatment can be resumed

iDRS, intravesical drug-releasing systems; OAB, overactive bladder.

Pradere B, et al. *Curr Opin Urol.* 2025. In Press.

Management of OAB symptoms (1/2)

Symptom management

OAB management

- Start anticholinergic drugs (oxybutynin, trospium, solifenacin, fesoterodine)* or beta-3 agonist (mirabegron, vibegron)* in absence of contraindications
- After initiating anticholinergics consider checking PVR and bowel function (constipation)
- Consider adding LUTS treatment (alpha-blocker, e.g. tamsulosin, alfuzosin, silodosin*)
- In male patients with outlet obstruction, consider adding 5-alpha reductase inhibitor (e.g., finasteride) or PDE-5 inhibitor (e.g., tadalafil)*
- If urine culture is negative and OAB symptoms persist, consider cystoscopy to evaluate mucosal irritation. A short course of corticosteroids can be considered

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*Select examples are listed on the slide. List is not meant to be exhaustive. Use as directed per clinician judgement, guidelines, and availability per local regulations.
LUTS, lower urinary tract symptoms; OAB, overactive bladder; PDE, phosphodiesterase; PVR, post-void residual.
Pradere B, et al. *Curr Opin Urol.* 2025. In Press.

Management of OAB symptoms and bladder pain (2/2)

Symptom management

Conservative measures

Encourage adequate hydration

Collect urinalysis and urine culture

Avoid irritants (caffeine, alcohol, spicy food)

Consider distraction techniques, bladder retraining, and/or pelvic floor muscle training

Pain management*

WHO Step 1

For mild pain: Consider step 1 of the WHO three-step ladder - non-opioid analgesics (e.g., NSAIDs or acetaminophen)

For persistent pain: Despite non-opioid analgesics, consider adding phenazopyridine and/or antispasmodics (e.g., dicyclomine, hyoscyamine, scopolamine)

WHO Step 2

For persistent pain: Despite above measures, consider step 2 of the WHO three-step ladder. *For moderate pain: W*eak opioids (hydrocodone, codeine, tramadol) with or without non-opioid analgesics

*Select examples are listed on the slide. List is not meant to be exhaustive. Use as directed per clinician judgement, guidelines, and availability per local regulations.
NSAID, non-steroidal anti-inflammatory drugs; OAB, overactive bladder; WHO, World Health Organization.
Pradere B, et al. *Curr Opin Urol.* 2025. In Press.

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Management of hematuria

Definition

Macroscopic hematuria: no clots, with no signs of retention, and negative urine culture

Complicated hematuria: clots leading to retention and/or dysuria or hematuria with anemia

iDRS management

Macroscopic hematuria – – – Continue iDRS

Complicated hematuria – – – Remove/delay insertion of iDRS in case of refractory or recurrent hematuria, leading to blood transfusions or requiring hospital admissions – – – After complete resolution of hematuria, iDRS treatment can be resumed

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iDRS, intravesical drug-releasing systems.

Pradere B, et al. *Curr Opin Urol.* 2025. In Press.

Management of hematuria

Symptom management

Macroscopic hematuria

- Encourage adequate hydration
- Collect urinalysis and urine culture
- If hematuria persists, perform cystoscopy to evaluate presence/recurrence of bladder tumor

Complicated hematuria

- Encourage adequate hydration
- Collect urinalysis, urine culture, and blood count
- Urinary catheter placement or (continuous) bladder irrigation indicated
- Consider performing ultrasound to rule out bladder clots
- Consider invasive intervention as clinically indicated
- Treat anemia, when clinically indicated, in accordance with institutional guidance
- In case of obstruction, urgent intervention is needed (eg, clot evacuation)

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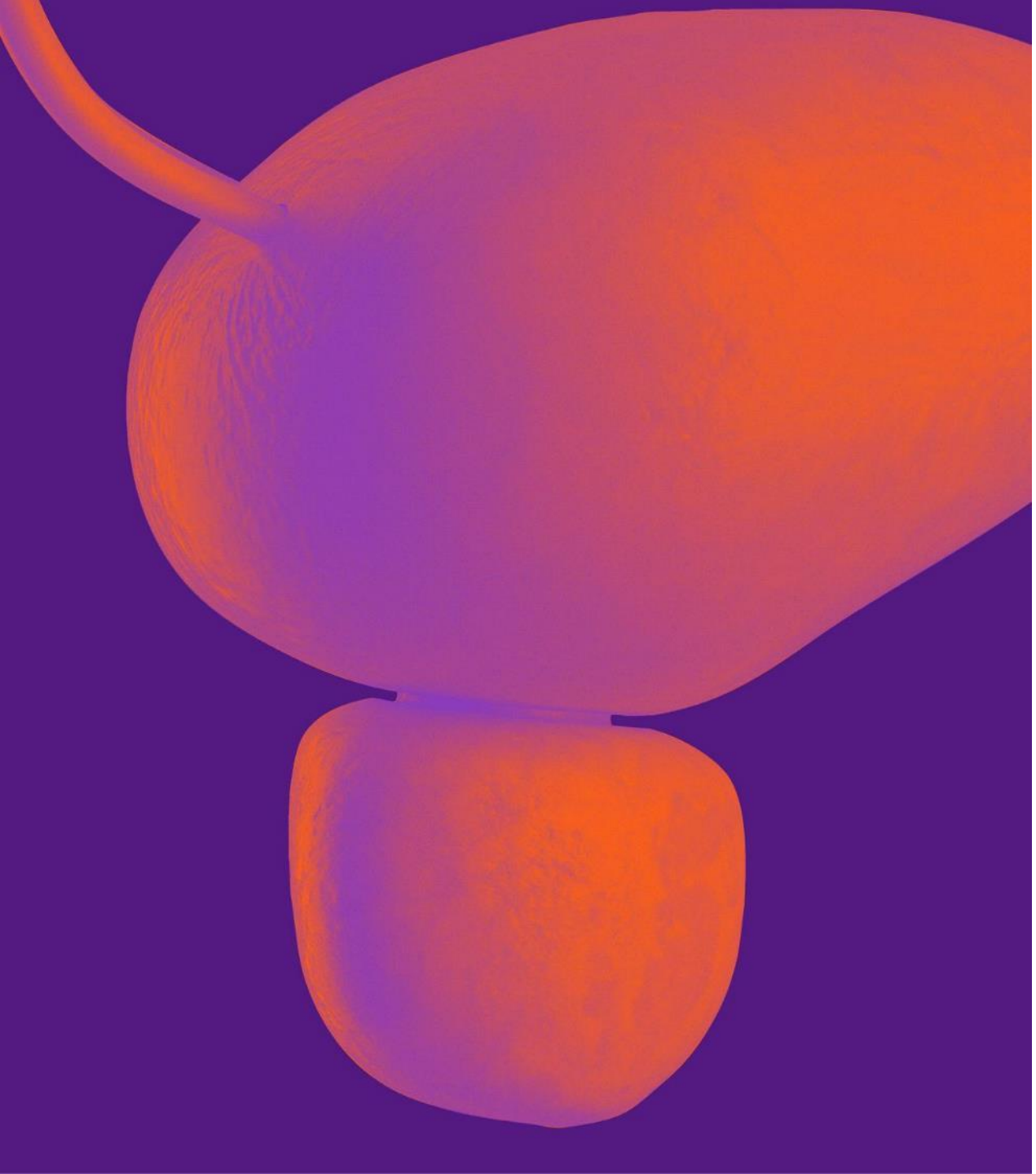
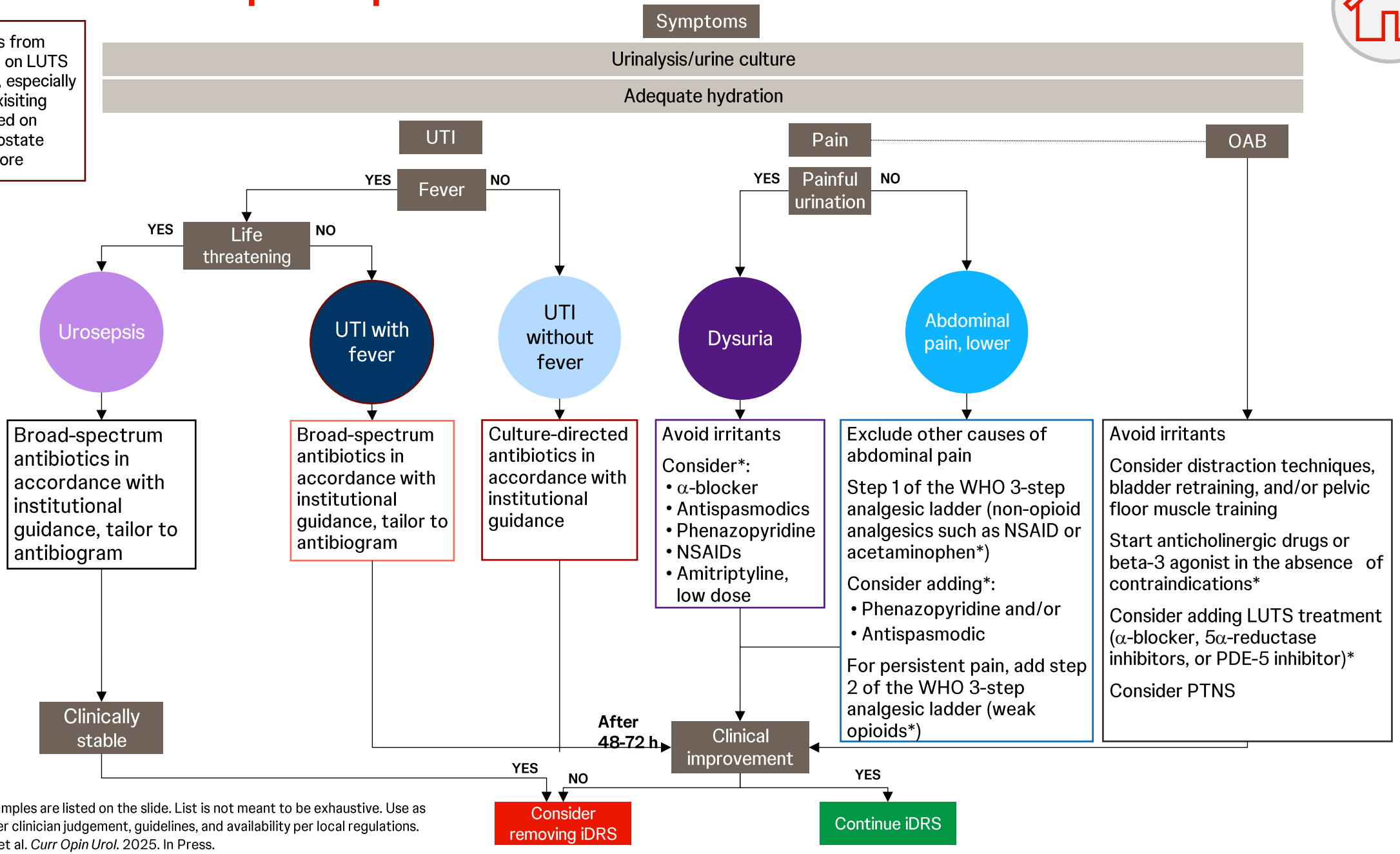


Recommendations flow-chart

Flowchart of expert panel recommendations

Counsel patients from treatment initiation on LUTS (storage symptoms), especially males with preexisiting symptoms based on International Prostate Symptom Score



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