Gemcitabine Implant (INLEXZO) in BCG Unresponsive, Non–muscle Invasive Bladder Cancer

National Drug Mini-Monograph

May 2026

VA Pharmacy Benefits Management Services and National Formulary Committee

The purpose of VA PBM Services drug monographs is to provide a focused drug review for making formulary decisions. The Product Information or other resources should be consulted for detailed and most current drug information.

Abbreviations: NMIBC, non-muscle invasive bladder cancer; BCG, Bacillus Calmette-Guérin; CIS, carcinoma in situ; TURBT, transurethral resection of bladder tumor; UTI, urinary tract infection

FDA PRESCRIBING INFORMATION[1]	
Description / MOA	A pyrimidine antimetabolite that inhibits DNA synthesis and blocks the progression of cells through the G1/S-phase of the cell cycle.
Indication Under Review	BCG Unresponsive, Non–muscle Invasive Bladder Cancer with carcinoma in situ (CIS) with or without papillary tumors
Dosage Regimen	Intravesical instillation: 225 mg once every 3 weeks for up to 8 doses (6 months), followed by 225 mg once every 12 weeks for up to 6 doses (18 months), or until persistent or recurrent non–muscle invasive bladder cancer, disease progression, or unacceptable toxicity
Dosage Forms Under Review	Implant (Inlexzo Intravesical): 225 mg of gemcitabine • Insert into the bladder via provided urinary catheter and stylet and remove after 3 weeks with cystoscope
Treatment Monitoring	• Verify pregnancy status prior to treatment initiation. • Evaluate bladder mucosal integrity prior to intravesical instillation. • Monitor for progression of bladder cancer. • Monitor for signs/symptoms of urinary tract infection.

EFFICACY CONSIDERATIONS	
Trial	**Gemcitabine intravesical system (aka TAR-200) for Bacillus Calmette-Guérin-Unresponsive High-Risk Non-Muscle-Invasive Bladder Cancer: Results from the Phase IIb SunRISe-1 (NCT04640623)**
Design	Phase IIb parallel cohort study
Population	Cohort 2 BCG-unresponsive CIS with or without papillary disease (high-grade Ta, any T1) or Cohort 4 papillary disease-only NMIBC (high-grade Ta any T1 and absence of CIS) within 12 months of last dose of BCG • Median age = 71 yo • Male = 80% • 87.1% white • 27.1% of patients were from America • 58.8% were former nicotine users • 91.8% were ECOG performance status 0 • 67.1% were CIS only • Median total doses of previous BCG was 12 Primary endpoints: • Complete response • Disease free survival
Intervention	TAR-200
Comparator	TAR-200 plus Cetrelimab or Cetrelimab monotherapy (Cetrelimab cohorts closed and TAR-200 cohorts prioritized)
Results	

Outcome	TAR-200	Cetrelimab
Overall complete response rate	**82.4% (95% CI 72.6-89.8)**	**46.4% (95% CI 27.5-66.1)**
3-month complete response rate	78.8% (95% CI 68.6-86.9)	
12-month complete response rate	45.9% (95% CI 35.0-57.0)	
12 month duration of response rate	56.2% (95% CI 43.4-67.1)	38.5% (95% CI 14.1-62.8)
Median duration of response	25.8 months (95% CI 8.3 to NE)	8.6 months
12 month disease-free survival in patients with high-risk papillary disease only (Cohort 4)	**70.2% (95%CI 51.6-82.8)**	

Sources: Daneshmand S, Van der Heijden MS, Jacob JM, et al. TAR-200 for Bacillus Calmette-Guérin-Unresponsive High-Risk Non-Muscle-Invasive Bladder Cancer: Results From the Phase IIb SunRISe-1 Study. J Clin Oncol. 2025;43(33):3578-3588. doi:10.1200/JCO-25-01651

Authors' Conclusions	TAR-200 monotherapy is the first intravesical drug-releasing system with demonstrated efficacy and safety in the treatment of localized bladder cancer. TAR-200 is a novel bladder-sparing treatment option for patients with BCG-unresponsive high-risk non-muscle invasive bladder cancer.

SAFETY CONSIDERATIONS	
Boxed Warnings	None
Contraindications	Hypersensitivity (including anaphylaxis) to gemcitabine or any component of the formulation; perforation of the bladder.
Other Warnings	• Delaying cystectomy in patients with Bacillus Calmette-Guérin unresponsive carcinoma in situ (CIS) could lead to the development of muscle-invasive or metastatic bladder cancer • Precaution: use with MRI; gemcitabine for injection and gemcitabine intravesical are not interchangeable
Top 5 AEs	Urinary frequency (48%), urinary tract infection (44%), dysuria (26-42%), urinary urgency (34%), decreased hemoglobin (31%)
Drug Interactions	No known significant interactions
Pregnancy	Verify pregnancy status prior to treatment initiation in patients who could become pregnant. Patients who could become pregnant should use effective contraception during treatment and for 6 months after the final gemcitabine removal from the bladder. Patients with partners who could become pregnant should use effective contraception during treatment and for 3 months after the final gemcitabine removal.
Lactation	It is not known if gemcitabine is present in human milk. Breastfeeding is not recommended during treatment and for at least 1 week after gemcitabine removal from the bladder.
Trial Safety Results	Any grade: pollakiuria (43.5%), dysuria (40%), micturition urgency (24.7%), UTI (21.2%), hematuria (16.5%) Grade 3+: urinary tract pain (4.7%), bladder pain (2.4%), UTI (1.2%), urinary retention (1.2%), cystitis (1.2%)

OTHER CONSIDERATIONS	
AUA/ASCO/ASTRO/SUO Guidelines 2017 (addendum 2024)	• Recommends radical cystectomy +/- neoadjuvant chemotherapy • Bladder preserving options: maximal TURBT, partial cystectomy with lymphadenectomy, primary radiation therapy, and multi-modal therapy
VA clinical pathways February 2026-V2.2026	• Recommends radical cystectomy, intravesical gemcitabine/docetaxel, pembrolizumab, or nadofaragene firadenovec for high risk non-muscle invasive bladder cancer

THERAPEUTIC ALTERNATIVES AND THEIR PLACE IN THERAPY

DRUG	VANF	CFU	FDA	GUIDELINES
Pembrolizumab (systemic) • Significant ≥grade 3 toxicities in 13% of patients • Modest durable complete responses	PA-F	Yes	FDA Approved 1/8/2020	• **VA Bladder Cancer Oncology Pathway:** Recommends for BCG unresponsive patients to used shared decision making with pembrolizumab being one option • **NCCN Bladder Cancer Guidelines V3.2025:** Recommends as one option pembrolizumab
Gemcitabine/Docetaxel (intravesical) • Only retrospective data to support use	PA-F	No		• **VA Bladder Cancer Oncology Pathway:** Recommends for BCG unresponsive patients to used shared decision making with gemcitabine/docetaxel being one option
Nadofaragene firadenovec (intravesical) • Requires storage at ≤-60°C (≤-76°F) • In a freezer -25°C to -15°C up to 3 months without exceeding expiration • Store up to 24 hours at room temperature or refrigerated once removed from freezer • Protect vials from light	PA-F	Yes	FDA Approved 12/16/2022	• **VA Bladder Cancer Oncology Pathway:** Recommends for BCG unresponsive patients to used shared decision making with Nadofaragene firadenovec being one option • **NCCN Bladder Cancer Guidelines V3.2025:** Recommends Nadofaragene firadenovec as one option
Nogapadekin alfa + BCG (intravesical) • Must be stored under refrigeration at 2°C to 8°C (36°F-46°F) • Do not freeze	NF	Yes	FDA Approved 4/22/2024	• **NCCN Bladder Cancer Guidelines V3.2025:** Recommends Nogapadekin alfa + BCG as one option

POTENTIAL PLACE IN THERAPY OF TAR-200

TAR-200 is one option for BCG unresponsive high risk non-muscle invasive bladder cancer in patients desiring bladder sparing therapy or who are unable to undergo radical cystectomy.

- Based on the phase IIb SunRISe-1 study TAR-200 showed efficacy with a complete response rate of 82.4% and 12 month disease free survival in patients with high risk papillary disease of 70.2%.
- Side effects include pollakiuria, dysuria, micturition urgency, UTI, and hematuria.
- Limitations to its use include cost, administration requirements, as well as removal after a 3 week indwelling period.
- Alternative options include pembrolizumab (limitation: systemic side effects), gemcitabine/docetaxel (limitation: no prospective data), Nadofaragene firadenovec (limitation: storage requirements), Nogapadekin alfa + BCG (limitation: requires administration with BCG). However, selection of agents cannot be based on cross trial comparison.

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References

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2. Daneshmand S, Van der Heijden MS, Jacob JM, et al. TAR-200 for Bacillus Calmette-Guérin-Unresponsive High-Risk Non-Muscle-Invasive Bladder Cancer: Results From the Phase IIb SunRISe-1 Study. *J Clin Oncol*. 2025;43(33):3578-3588. doi:10.1200/JCO-25-01651

3. NCCN Guidelines Version 1.2026. Bladder Cancer. https://www.nccn.org/professionals/physician_gls/pdf/bladder.pdf Accessed March 29, 2026

4. VHA Oncology Bladder Cancer V2.2026 Bladder Cancer - Non-Muscle Invasive High Risk Accessed March 29, 2026

5. Holzbeierlein J, Bixler BR, Buckley DI, et al. Treatment of non-metastatic muscle-invasive bladder cancer: AUA/ASCO/SUO guideline (2017; amended 2020, 2024). J Urol. Published online April 25, 2024. doi:10.1097/JU.0000000000003981 https://www.auajournals.org/doi/10.1097/JU.0000000000003981