CLINICAL SUMMARY

ADSTILADRIN®
(nadofaragene firadenovec-vncg)
suspension, for intravesical use / 3×10^{11} viral particles/mL

Your FIRST choice for patients with high-risk NMIBC after BCG

GENERATE THE FIGHT WITHIN

The **FIRST** and **ONLY** FDA-approved intravesical non-replicating gene therapy for high-risk NMIBC

INDICATION: ADSTILADRIN® (nadofaragene firadenovec-vncg) is a non-replicating adenoviral vector-based gene therapy indicated for the treatment of adult patients with high-risk Bacillus Calmette-Guérin (BCG)-unresponsive non-muscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS) with or without papillary tumors.

Please see Important Safety Information on page 4 and full Prescribing Information at adstiladrinHCP.com.

There Is a Need for a Well-Tolerated Localized Treatment for Patients With NMIBC

>50%

of patients with high-risk non–muscle-invasive bladder cancer (NMIBC) experience disease recurrence within 1 year of currently available intravesical therapy[1]

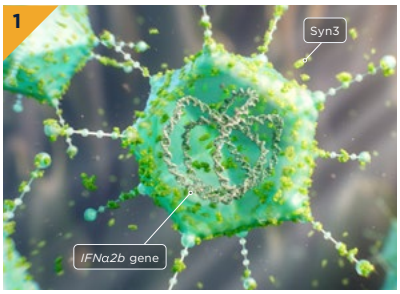
≈50%

of patients become unresponsive to Bacillus Calmette-Guérin (BCG) therapy[2]

ADSTILADRIN is an outpatient option that can be administered when patients **first become BCG unresponsive,** allowing them to remain in the care of their urologist

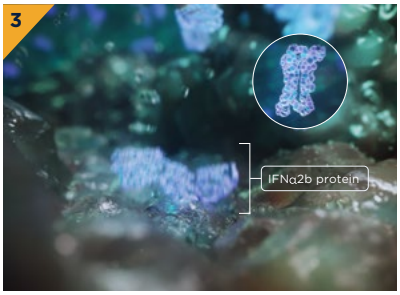
ADSTILADRIN is a unique monotherapy to treat NMIBC

A gene therapy harnessing the body's own immune system to fight cancer



ADSTILADRIN is a **non-replicating adenoviral vector–based gene-mediated immunotherapy** that delivers the human interferon alpha 2B (*IFNα2b*) gene and excipient synapsin III (Syn3) to bladder urothelial cells.[3,4]

Once inside the bladder, ADSTILADRIN penetrates the bladder urothelial cells with help from Syn3 and travels to the cell nucleus to deliver the *IFNα2b* gene.[3,4]



Both normal urothelial and tumor cells in the bladder that have taken up ADSTILADRIN begin to produce and secrete high and transient local levels of IFNα2b, a cytokine that the body uses to fight certain infections and cancers.[3,4]

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ADSTILADRIN Is the FIRST and ONLY FDA-Approved Intravesical Non-Replicating Gene Therapy for High-Risk NMIBC

LOCALLY

Localized, non-replicating gene therapy, offering a **well-tolerated safety profile**[3,5,6]

- **75%** of adverse reactions (ARs) were mild (grades 1 and 2) and resolved within 2 days
  - Serious ARs occurred in 11% of patients who received ADSTILADRIN
  - 0 grade 3 or 4 reactions
- **2%** of patients discontinued treatment due to ARs
- **No new safety signals** out to 5 years

QUARTERLY

Intravesical instillation **once every 3 months**[3]

- **No BCG** coadministration required
- **Seamless integration** into your existing management of NMIBC, reducing the treatment burden

CONFIDENTLY

Proven and durable complete responses (CRs) and **ongoing bladder preservation**[1,3,6]

- **51%** of the carcinoma in situ (CIS) cohort achieved CR by month 3 (after only 1 instillation)
- **≈1/2 of participants** in the CIS cohort had **bladder preservation out to 5 years***

Confirmed coverage and reimbursement[7†]

Study design

The safety and effectiveness of ADSTILADRIN were evaluated in CS-003, a phase 3, open-label, multicenter, single-arm study of 103 patients with high-risk BCG-unresponsive NMIBC, 98 of whom had BCG-unresponsive CIS with or without papillary tumors and could be evaluated for response. **The primary endpoint was CR in CIS ± high-grade Ta/T1** at any time within 12 months after the first dose.[3]

In the study, patients were not reinduced if they did not see a CR

A Guideline-Recommended Treatment

Nadofaragene firadenovec-vncg (ADSTILADRIN) is a recommended treatment option in the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®)‡ and the AUA/SUO Guidelines[8]

*The Kaplan-Meier estimated cystectomy-free survival rate for the CIS cohort was 43% at 5 years.[6]

†ADSTILADRIN has confirmed 99% coverage for commercial and government-insured patients.[7]

‡Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Bladder Cancer V.4.2024. © National Comprehensive Cancer Network, Inc. 2024. All rights reserved. Accessed June 1, 2024. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.

Abbreviations: AUA, American Urological Association; SUO, Society of Urologic Oncology. NCCN, National Comprehensive Cancer Network® (NCCN®).

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Indication and Important Safety Information

INDICATION

ADSTILADRIN is a non-replicating adenoviral vector-based gene therapy indicated for the treatment of adult patients with high-risk Bacillus Calmette-Guérin (BCG)-unresponsive non-muscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS) with or without papillary tumors.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS: ADSTILADRIN is contraindicated in patients with prior hypersensitivity reactions to interferon alfa or to any component of the product.

WARNINGS AND PRECAUTIONS:

- ***Risk with delayed cystectomy:*** Delaying cystectomy in patients with BCG-unresponsive CIS could lead to development of muscle invasive or metastatic bladder cancer, which can be lethal. If patients with CIS do not have a complete response to treatment after 3 months or if CIS recurs, consider cystectomy.
- ***Risk of disseminated adenovirus infection:*** Persons who are immunocompromised or immunodeficient may be at risk for disseminated infection from ADSTILADRIN due to low levels of replication-competent adenovirus. Avoid ADSTILADRIN exposure to immunocompromised or immunodeficient individuals.

DOSAGE AND ADMINISTRATION: Administer ADSTILADRIN by intravesical instillation only. ADSTILADRIN is not for intravenous use, topical use, or oral administration.

USE IN SPECIFIC POPULATIONS: Advise females of reproductive potential to use effective contraception during ADSTILADRIN treatment and for 6 months after the last dose. Advise male patients with female partners of reproductive potential to use effective contraception during ADSTILADRIN treatment and for 3 months after the last dose.

ADVERSE REACTIONS: The most common (>10%) adverse reactions, including laboratory abnormalities (>15%), were glucose increased, instillation site discharge, triglycerides increased, fatigue, bladder spasm, micturition (urination urgency), creatinine increased, hematuria (blood in urine), phosphate decreased, chills, pyrexia (fever), and dysuria (painful urination).

You are encouraged to report negative side effects of prescription drugs to FDA. Visit **www.FDA.gov/medwatch** or call 1-800-332-1088. You may also contact Ferring Pharmaceuticals at 1-888-FERRING.

Please see full Prescribing Information at adstiladrinHCP.com.

References: 1. Boorjian SA, Alemozaffar M, Konety BR, et al. Intravesical nadofaragene firadenovec gene therapy for BCG-unresponsive non-muscle-invasive bladder cancer: a single-arm, open-label, repeat-dose clinical trial. *Lancet Oncol.* 2021;22(1):107-117. doi:10.1016/S1470-2045(20)30540-4 **2.** Kamat AM, Lerner SP, O'Donnell M, et al. Evidence-based assessment of current and emerging bladder-sparing therapies for non–muscle-invasive bladder cancer after Bacillus Calmette-Guerin Therapy: a systematic review and meta-analysis. *Eur Urol Onc.* 2020;3(3):318-340. doi:10.1016/j.euo.2020.02.006 **3.** ADSTILADRIN. Package insert. Ferring Pharmaceuticals, Inc; May 2024. **4.** Narayan VM, Meeks JJ, Jakobsen JS, Shore ND, Sant GR, Konety BR. Mechanism of action of nadofaragene firadenovec-vncg. *Front Oncol.* 2024;14:1359725. doi:10.3389/fonc.2024.1359725 **5.** Data on file. ADSTILADRIN CSR, Ferring Pharmaceuticals, Inc. Parsippany, NJ. **6.** Narayan VM, Boorjian SA, Alemozaffar M, et al. Efficacy of intravesical nadofaragene firadenovec for patients with Bacillus Calmette-Guérin-unresponsive nonmuscle-invasive bladder cancer: 5-year follow-up from a phase 3 trial. *J Urol.* 2024;212(1):1-12. doi:10.1097/JU.0000000000004020 **7.** Ferring Access Support benefits investigations for commercial and government-insured patients through March 15, 2024. **8.** Holzbeierlein J, Bixler BR, Buckley DI, et al. Diagnosis and treatment of non-muscle invasive bladder cancer: AUA/SUO guideline: 2024 amendment. *J Urol.* 2024;211(4):533-538. doi:10.1097/JU.0000000000003846

FERRING PHARMACEUTICALS

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