AN INTRODUCTION TO

ADSTILADRIN®

(nadofaragene firadenovec-vncg)

suspension, for intravesical use / 3×10^{11} viral particles/mL

The first and only FDA-approved intravesical gene therapy for high-risk non–muscle-invasive bladder cancer

Clinical overview

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.

SELECT IMPORTANT SAFETY INFORMATION

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

Please see additional Important Safety Information on the next page.

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SELECT IMPORTANT SAFETY INFORMATION

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 additional Important Safety Information on the previous page and full Prescribing Information for ADSTILADRIN.

There is a high unmet need in treating patients with NMIBC

More than 1/2 of patients with high-risk non–muscle-invasive bladder cancer (NMIBC) experience disease recurrence within 1 year of currently available intravesical therapy.[1]

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

of patients with NMIBC will progress to muscle-invasive bladder cancer (MIBC)[3]

There is a need for a well-tolerated localized treatment that allows patients to remain in the care of their urologist.

The bladder is an ideal organ for gene therapy

Gene therapy helps fight cancer by:

- Bolstering an immune response[4,5]
- Protecting healthy cells from the side effects of these treatments[5]

Key reasons the bladder is ideal for this type of therapy:

- Direct contact between the gene vector and tumor cells[6,7]
- Local administration limiting systemic exposure[7]
- Easy access to monitor effects of therapy[5]

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The safety and efficacy of ADSTILADRIN were evaluated in CS-003, a phase 3, open-label, multicenter, single-arm clinical study[8]

PATIENT POPULATION	END POINTS
N=98 **High-risk BCG-unresponsive NMIBC** **Cohort:** carcinoma in situ (CIS) ± Ta/T1	**Primary** Complete response (CR) in patients with CIS ± Ta/T1 at any time after the first instillation

ADSTILADRIN delivers on its innovation with proven CRs

51% **of the CIS cohort achieved CR, all by 3 months[8]**

Duration of response[8]*

Median in months

9.7

% with duration ≥12 months

46%

ADSTILADRIN demonstrates durability at 1 year

During the 12-month study period

95% of patients did not progress to MIBC[9]

74% of patients were cystectomy free[9]

0 deaths were reported due to treatment-emergent adverse events[8]

ADSTILADRIN helped patients remain free of high-grade recurrence for up to 2 years

In a post hoc analysis,

36% of the CIS cohort **remained free of high-grade recurrence at 24 months[10]***

ADSTILADRIN is targeted, offering a manageable safety profile

75%
of adverse reactions (ARs) were mild (grade 1 and 2) and resolved within 2 days[11]
Serious ARs occurred in 11% of patients who received ADSTILADRIN[8]

The majority of drug-related ARs were transient and local in nature, with a median duration of
<2 DAYS[11†]

2%
of patients discontinued treatment due to ARs (n=3)[8]
Dosage interruptions of ADSTILADRIN due to an AR occurred in 34% of patients (n=54)[8]

The most common (>10%) ARs, 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, dysuria, and pyrexia (fever).[8]

*Based on patients (n=50) who achieved a CR; reflects period from the time CR was achieved.[8]
†With the exception of fatigue.[11]

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ADSTILADRIN is an intravesical instillation given once every 3 months

ADSTILADRIN is a ready-to-use formulation[8]

ADSTILADRIN is provided in a carton containing 4 vials with an extractable volume of 20 mL each. All vials have a nominal concentration of 3 x 10^{11} viral particles (vp)/mL.

A dose of 75 mL of ADSTILADRIN is administered through a urinary catheter. Premedication with an anticholinergic prior to each instillation is recommended.

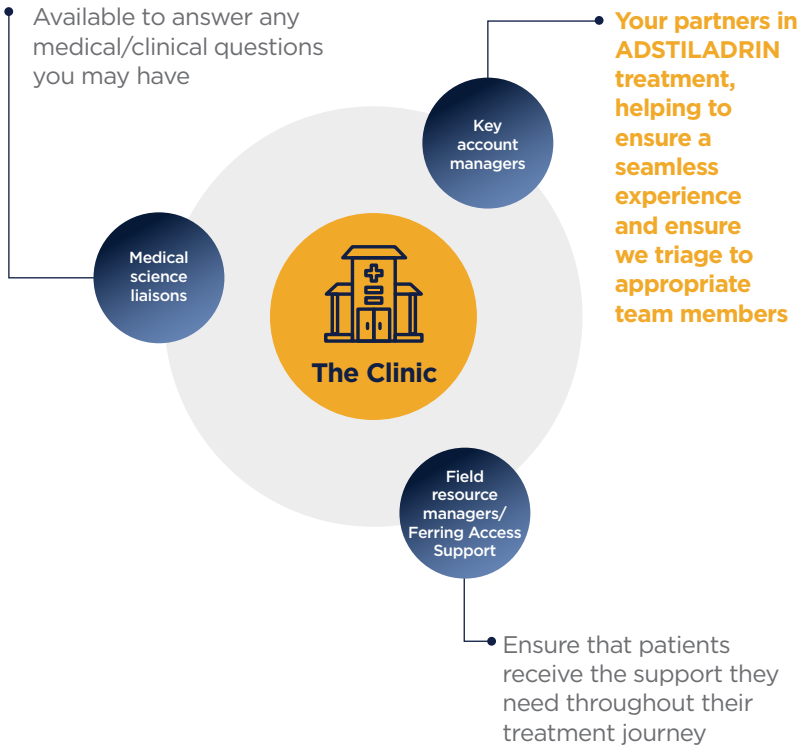
No reconstitution is necessary, and no hood is required for handling.

Allow ADSTILADRIN to be left in the bladder for 1 hour following instillation.

Patient should reposition approximately every 15 minutes from left to right, back, and abdomen to maximize bladder surface exposure.

ADSTILADRIN can be administered to patients in a urology office
Instillation procedure fits into urologists' existing treatment and management of NMIBC.

Ferring is here to support your clinic throughout the treatment process



Ferring is your dedicated partner,
offering a comprehensive package that includes education, implementation, and ongoing support across your practices.

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ADSTILADRIN at a glance

Proven and durable CRs[8]

- **51%** of the CIS cohort achieved CR, all by 3 months
- Of these patients, **46%** remained free of high-grade recurrence at **12 months**

Manageable tolerability profile[8]

- **75%** of ARs were mild (grade 1 and 2) and resolved within 2 days[10]
- **2%** of patients discontinued treatment due to ARs[8]

Ready-to-use formulation[2]

- Intravesical administration once **every 3 months**
- Fits into urologists' existing treatment and management of NMIBC

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