Evolent Clinical Guideline 3002 for Adstiladrin™ (nadofaragene firadenovec-vncg)

Guideline Number:	Applicable Codes	
Evolent_CG_3002		
"Evolent" refers to Evolent Health LLC and Evolent Specialty Services, Inc. *© 2023 - 2025 Evolent. All rights Reserved.*		
Original Date: February 2023	**Last Revised Date:** February 2025	**Implementation Date:** February 2025

TABLE OF CONTENTS

STATEMENT

Purpose

To define and describe the accepted indications for Adstiladrin (nadofaragene firadenovec-vncg) usage in the treatment of cancer, including FDA approved indications, and off-label indications.

Evolent is responsible for processing all medication requests from network ordering providers. Medications not authorized by Evolent may be deemed as not approvable and therefore not reimbursable.

The use of this drug must be supported by one of the following: FDA approved product labeling, CMS-approved compendia, National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO) clinical guidelines, or peer-reviewed literature that meets the requirements of the CMS Medicare Benefit Policy Manual Chapter 15.

INDICATIONS

Continuation requests for a not-approvable medication shall be exempt from this Evolent policy provided

- The member has not experienced disease progression on the requested medication AND
- The requested medication was used within the last year without a lapse of more than 30 days of having an active authorization AND
- Additional medication(s) are not being added to the continuation request.

Non-Muscle Invasive Bladder Cancer

- The member has high-risk BCG unresponsive non-muscle invasive bladder cancer with carcinoma in situ (CIS), with or without papillary tumors, and Adstiladrin (nadofaragene firadenovec-vncg) will be used as monotherapy for intravesical instillation in members who are refractory to local (intravesical) therapy with Bacillus Calmette-Guérin (BCG) AND
- BCG-Refractory carcinoma in situ (CIS) is defined as one of the following:
    - Persistent or recurrent CIS (+/-recurrent Ta/T1 disease) within 12 months of receiving adequate BCG (at least 5 of 6 doses of an initial induction course plus either at least 2 of 3 doses of maintenance therapy or at least 2 of 6 doses of a second induction course)
    - Recurrent high-grade Ta/T1 disease within 6 months of completion of adequate BCG (at least 5 of 6 doses of an initial induction course plus either at least 2 of 3 doses of maintenance therapy or at least 2 of 6 doses of a second induction course)
    - T1 high-grade disease at the first evaluation following an induction BCG course alone (at least 5 of 6 doses of an initial induction course).

CONTRAINDICATIONS/WARNINGS

- Contraindications
  - Adstiladrin (nadofaragene firadenovec-vncg) is contraindicated in patients with hypersensitivity to interferon alfa or any component of the product.

EXCLUSION CRITERIA

- Disease progression while taking Adstiladrin (nadofaragene firadenovec-vncg) or prior treatment with adenovirus-based drugs.
- Members with extra-vesical (i.e., urethra, ureter, or renal pelvis), muscle invasive (T2-T4), or metastatic urothelial carcinoma.
- Dosing exceeds single dose limit of Adstiladrin (nadofaragene firadenovec-vncg) 75 mL at a concentration of 3×10^{11} viral particles (vp)/mL.
- Treatment exceeds the maximum months duration limit of 12 months or 4 doses (if the patient achieved a complete response).
- Investigational use of Adstiladrin (nadofaragene firadenovec-vncg) with an off-label indication that is not sufficient in evidence or is not generally accepted by the medical community. Sufficient evidence that is not supported by CMS recognized compendia or acceptable peer reviewed literature is defined as any of the following:
  - Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.
  - Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.
  - Whether the reported study outcomes represent clinically meaningful outcomes experienced by patients. Generally, the definitions of Clinically Meaningful outcomes are those recommended by ASCO, e.g., Hazard Ratio of less than 0.80 and the recommended survival benefit for OS and PFS should be at least 3 months.
  - Whether the experimental design, considering the drugs and conditions under investigation, is appropriate to address the investigative question. (For example, in some clinical studies, it may be unnecessary or not feasible to use randomization, double blind trials, placebos, or crossover).
  - That non-randomized clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of drugs.
  - That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
  - That abstracts (including meeting abstracts) without the full article from the approved peer-reviewed journals lack supporting clinical evidence for determining accepted uses of drugs.

CODING AND STANDARDS

Codes

- J9029 - Intravesical instillation, nadofaragene firadenovec-vncg, per therapeutic dose

Applicable Lines of Business

☐	CHIP (Children's Health Insurance Program)
☒	Commercial
☒	Exchange/Marketplace
☒	Medicaid
☐	Medicare Advantage

POLICY HISTORY

Date	Summary
February 2025	• Converted to new Evolent guideline template • This guideline replaces UM ONC_1472 Adstiladrin (nadofaragene firadenovec-vncg) • Updated references
February 2024	• Updated NCH verbiage to Evolent • Updated "continuation request" verbiage

LEGAL AND COMPLIANCE

Guideline Approval

Committee

Reviewed / Approved by Evolent Specialty Clinical Guideline Review Committee

Disclaimer

Evolent Clinical Guidelines do not constitute medical advice. Treating health care professionals are solely responsible for diagnosis, treatment, and medical advice. Evolent uses Clinical Guidelines in accordance with its contractual obligations to provide utilization management. Coverage for services varies for individual members according to the terms of their health care coverage or government program. Individual members' health care coverage may not utilize some Evolent Clinical Guidelines. A list of procedure codes,

services or drugs may not be all inclusive and does not imply that a service or drug is a covered or non-covered service or drug. Evolent reserves the right to review and update this Clinical Guideline in its sole discretion. Notice of any changes shall be provided as required by applicable provider agreements and laws or regulations. Members should contact their Plan customer service representative for specific coverage information.

REFERENCES

1. Boorjian SA, 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 Jan;22(1):107-117. doi: 10.1016/S1470-2045(20)30540-4.
2. Suderman J, et al. Re: IL-15 Superagonist NAI in BCG-Unresponsive Non-muscle-invasive Bladder Cancer. *Eur Urol*. 2023 Jun;83(6):581. doi: 10.1016/j.eururo.2023.01.009.
3. Adstiladrin prescribing information. Ferring Pharmaceuticals, Denmark 2024.
4. Clinical Pharmacology Elsevier Gold Standard 2025.
5. Micromedex® Healthcare Series: Micromedex Drugdex Ann Arbor, Michigan 2025.
6. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium 2025.
7. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD 2025.
8. Ellis LM, et al. American Society of Clinical Oncology perspective: Raising the bar for clinical trials by defining clinically meaningful outcomes. *J Clin Oncol*. 2014 Apr 20;32(12):1277-80.
9. Medicare Benefit Policy Manual Chapter 15 Covered Medical and Other Health Services: https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/bp102c15.pdf.
10. Current and Resolved Drug Shortages and Discontinuations Reported to the FDA: http://www.accessdata.fda.gov/scripts/drugshortages/default.cfm.