Clinical Policy: Nadofaragene Firadenovec-vncg (Adstiladrin)

Reference Number: LA.PHAR.461
Effective Date: 09.29.23
Last Review Date: 06.23.25
Line of Business: Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

****Please note: This policy is for medical benefit****

Description

Nadofaragene firadenovec-vncg (Adstiladrin®) is a gene therapy via a non-replicating adenovirus vector harboring the human interferon alpha2b gene.

FDA Approved Indication(s)

Adstiladrin is indicated for the treatment of adult patients with high-risk, Bacillus Calmette-Guerin (BCG)-unresponsive, non-muscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS) with or without papillary tumors.

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of Louisiana Healthcare Connections® that Adstiladrin is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Non-Muscle Invasive Bladder Cancer (must meet all)**:**

1. Diagnosis of NMIBC characterized as one of the following (a, b, or c) (*see Appendix D*):
   a. CIS only;
   b. Ta/T1 high-grade disease with concomitant CIS;
   c. Ta/T1 high-grade disease without CIS (*off-label*);
2. Prescribed by or in consultation with an oncologist or urologist;
3. Age ≥ 18 years;
4. Member is refractory to BCG* treatment (*see Appendix D)*;
   **Prior authorization may be required for BCG immunotherapy*
5. Members is not a candidate for cystectomy;
6. If request is for a dose increase, request meets one of the following (a or b):*
   a. Dose does not exceed 75 mL (4 vials) of 3 x 10^{11} viral particles (vp)/mL;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).
   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 6 months (1 dose only)

B. Other diagnoses/indications (must meet 1 or 2):
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to LA.PMN.255
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy LA.PMN.53.

II. Continued Therapy

A. Non-Muscle Invasive Bladder Cancer (must meet all)**:**
1. Currently receiving medication via Louisiana Healthcare Connections benefit, or documentation supports that member is currently receiving Adstiladrin for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy as evidenced by freedom from high-grade disease recurrence, as evaluated by cytology, cystoscopy, and/or biopsy;
3. Member has not yet received 4 total lifetime doses of Adstiladrin;
4. If request is for a dose increase, request meets one of the following (a or b):*
   a. New dose does not exceed 75 mL (4 vials) of 3 x 10^{11} vp/mL every 3 months;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 6 months (1 dose only; total of four doses per lifetime)

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to LA.PMN.255
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy LA.PMN.53.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – LA.PMN.53.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

BCG: bacillus Calmette-Guerin
CIS: carcinoma in-situ
FDA: Food and Drug Administration
NMIBC: non-muscle invasive bladder cancer
Ta/T1: description of tumor growth
Ta tumors are "papillary tumors",
T1 tumors have grown into the connective tissue of the bladder wall, but not into the muscle layer

vp: viral particles

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Bacillus Calmette-Guerin vaccine (TICE BCG®)	1 to 8 × 10^8 CFU (a vial) intravesical instillation once per week for 6 weeks	1 to 8 × 10^8 CFU/week

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings
- Contraindication(s): hypersensitivity to interferon alfa or any component of the product
- Boxed warning(s): none

Appendix D: General Information
- Refractory or "BCG unresponsive" is defined as being at least one of the following:
  1. Persistent or recurrent CIS alone or with recurrent Ta/T1 disease within 12 months of completion of adequate BCG therapy, defined as at least one of the following:
     a. At least 5 of 6 doses of an initial induction course plus at least 2 of 3 doses of maintenance therapy;
     b. At least 5 of 6 doses of an initial induction course plus at least 2 of 6 doses of the second induction course;
  2. Recurrent high-grade Ta/T1 disease within 6 months of completion of adequate BCG therapy;
  3. T1 high-grade disease at the first evaluation following an induction BCG course.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
High grade, BCG unresponsive NMIBC	Initial dose: 1 x 10^{11} vp/mL OR 3 x 10^{11} vp/mL Retreatment at months 4, 7, and 10	75 mL (4 vials) of 3 x 10^{11} vp/mL for a total of four doses

VI. Product Availability
Single-use vial: 3 x 10^{11} vp/mL; four single-dose vials per carton

VII. References
1. Adstiladrin Prescribing Information. Kuopio, Finland. Ferring Pharmaceuticals. August 2024. Available at https://www.adstiladrinhcp.com/. Accessed October 27, 2023.
2. Boorjian SA, Alemozaffar M, Bad 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 [published online November 27, 2020]. *Lancet Oncol*. doi: 10.1016/S1470-2045(20)30540-4.
3. National Comprehensive Cancer Network. Bladder Cancer Version 4.2024. Available at https://www.nccn.org/professionals/physician_gls/pdf/bladder.pdf. Accessed August 8, 2024.
4. Shore ND, Boorjian SA, Canter DJ, et al. Intravesical rAD-IFNα/Syn3 for patients with high-grade, Bacillus Calmette-Guerin refractory or relapsed nonmuscle-invasive bladder cancer: a phase II randomized study. *Journal of Clinical Oncology.* August 2017; 35(30): 3410-3416.
5. 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 Jul;212(1):74-86. doi: 10.1097/JU.0000000000004020. Epub 2024 May 5.

Coding Implications
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J9029	Intravesical instillation, nadofaragene firadenovec-vncg, per therapeutic dose

Reviews, Revisions, and Approvals	Date	LDH Approval Date
Policy created	05.01.23	09.29.23
Annual review: removed initial criteria requirement for clinically significant elevated liver or renal function tests per prescribing information; added oncology dosing criteria to allow doses supported by practice guidelines or literature; removed category 2B NCCN recommendation: NMIBC characterized by Ta/T1 high-grade without concomitant CIS per NCCN; removed HCPCS code J3590 and C9399; added HCPCS code J9029; references reviewed and updated	02.07.24	05.10.24
Revised HCPCS code description [J9029]	10.11.24	01.27.25
Annual review: added option for prescribed by or in consultation with a urologist; added off-label indication for Ta/T1 high-grade disease without CIS per NCCN; removed requirement for intravesical chemotherapy per NCCN; added requirement that member is not a candidate for cystectomy; increased approval duration from 3 months to 6 months; references reviewed and updated	06.23.25	

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. LHCC makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable LHCC administrative policies and procedures.

This clinical policy is effective as of the date determined by LHCC. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. LHCC retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom LHCC has no control or right of control. Providers are not agents or employees of LHCC.

representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.