# Clinical Policy: Nadofaragene Firadenovec-vncg (Adstiladrin)

Reference Number: PA.CP.PHAR.461
Effective Date: 08/2023
Last Review Date: 01/2024

**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 PA Health & Wellness® 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 without concomitant CIS;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Member is refractory to BCG treatment (*see Appendix D)*;
   **Prior authorization may be required for BCG immunotherapy*
5. For members who are not candidates for cystectomy, failure of intravesical chemotherapy, unless contraindicated or clinically significant adverse effects are experienced;
6. Dose does not exceed 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*).

**Approval duration: 3 months (1 dose only)**

**B. Other diagnoses/indications**

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

## II. Continued Therapy

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

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
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. 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*).

**Approval duration: 3 months (1 dose only)**

**B. Other diagnoses/indications** (must meet 1 or 2)**:**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies.
   **Approval duration: Duration of request or 12 months (whichever is less)**; or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.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 policies – PA.CP.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 for all relevant lines of business 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 per week |
| gemcitabine | varies | varies |
| mitomycin | varies | varies |

*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<br>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. September 2023. 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. FKD Therapies Oy. A study to evaluate Instiladrin in patients with high-grade, Bacillus Calmette-Guerin (BCG) unresponsive NMIBC. Available at: https://clinicaltrials.gov/ct2/show/study/NCT02773849. Accessed September 27, 2021.
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. National Comprehensive Cancer Network. Bladder Cancer Version 3.2023. Available at https://www.nccn.org/professionals/physician_gls/pdf/bladder.pdf. Accessed October 27, 2023.

**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 | Injection, nadofaragene firadenovec-vncg, per therapeutic dose |

| Reviews, Revisions, and Approvals | Date |
|---|---|
| Policy created | 07/2023 |
| 1Q 2024 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 4 doses in lifetime; removed HCPCS code J3590 and C9399; references reviewed and updated. | 01/2024 |