Clinical Policy: Nadofaragene Firadenovec-vncg (Adstiladrin)

Reference Number: PA.CP.PHAR.461
Effective Date: 08/2023
Last Review Date: 10/2024

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 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. Member is not candidate for cystectomy;
6. Dose does not exceed one of the following (a or b):
   a. Dose does not exceed 75 mL (4 vials) of 3×10^{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: 6 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.PHARM.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: 6 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.PHARM.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 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

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 August 27, 2024.
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	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
4Q 2024 annual review: added option for prescribed by or in consultation with an urologist; 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	10/2024