

## Clinical Policy: Nadofaragene Firadenovec (Instiladrin)

Reference Number: CP.PHAR.461

Effective Date: **FDA Approval Date**

Last Review Date: 02.22

Line of Business: Commercial, HIM, Medicaid

[Coding Implications](#)

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

### Description

Nadofaragene firadenovec (Instiladrin<sup>®</sup>) is a gene therapy via a non-replicating adenovirus vector harboring the human interferon alpha2b gene.

### FDA Approved Indication(s) [Pending]

Instiladrin is indicated for the treatment of high grade, bacillus Calmette-Guerin (BCG) unresponsive non-muscle invasive bladder cancer (NMIBC).

Limitation(s) of use: Current or previous evidence of muscle invasive disease

### 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 health plans affiliated with Centene Corporation<sup>®</sup> that Instiladrin is **medically necessary** when the following criteria are met:

#### I. Initial Approval Criteria\*

*\*Criteria will mirror the clinical information from the prescribing information once FDA-approved*

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

1. NMIBC characterized as one of the following (*see Appendix D*) (a, b, or c):\*
  - a. Carcinoma in situ (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  $\geq$  18 years;\*
4. Refractory 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. At the time of request, member does not have clinically significant and unexplained elevated liver or renal function tests;\*
7. Dose does not exceed  $3 \times 10^{11}$  viral particles (vp)/mL.\*

**Approval duration: 3 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 one of the following policies (a or b):
  - a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
  - b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
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 for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

**II. Continued Therapy\***

*\*Criteria will mirror the clinical information from the prescribing information once FDA-approved*

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

1. Member meets one of the following (a or b):
  - a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
  - b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B*);
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 Instiladrin;
4. Dose does not exceed  $3 \times 10^{11}$  viral particles (vp)/mL.\*

**Approval duration: 3 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 one of the following policies (a or b):
  - a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
  - b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

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 for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

**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 – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, or evidence of coverage documents.

**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

*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 <sup>®</sup> )	1 to 8 × 10 <sup>8</sup> CFU (a vial) intravesical instillation once per week for 6 weeks	1 to 8 × 10 <sup>8</sup> CFU per week
valrubicin (Valstar <sup>®</sup> )	800 mg intravesical (retain for 2 hours) once per week for 6 weeks	800 mg per week
gemcitabine	varies	varies
mitomycin	varies	varies

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

*Appendix C: Contraindications/Boxed Warnings [Pending]*

- Contraindication(s): **pending**
- Boxed warning(s): **pending**

*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 [Pending]**

Indication	Dosing Regimen	Maximum Dose
High grade, BCG Unresponsive NMIBC *	Initial dose: 1 x 10 <sup>11</sup> vp/mL OR 3 x 10 <sup>11</sup> vp/mL* Retreatment at Months 4, 7, and 10*	Pending*

**VI. Product Availability [Pending]**

Pending\*

**VII. References**

1. 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.
2. 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.
3. Shore ND, Boorjian SA, Canter DJ, et al. Intravesical rAD-IFN $\alpha$ /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.
4. TICE BCG Prescribing Information. Whitehouse Station, NJ: Merck Sharp and Dohme Corporation; May 2021. Available at: <https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=c9b74876-e665-442b-87ad-b7333bc9a67a>. Accessed September 27, 2021.
5. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: [http://www.nccn.org/professionals/drug\\_compendium](http://www.nccn.org/professionals/drug_compendium). Accessed September 27, 2021.
6. National Comprehensive Cancer Network. Bladder Cancer Version4.2021. Available at [https://www.nccn.org/professionals/physician\\_gls/pdf/bladder.pdf](https://www.nccn.org/professionals/physician_gls/pdf/bladder.pdf). Accessed September 27, 2021.

**Coding Implications [Pending]**

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
Pending	Pending

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	01.21.20	02.20
1Q 2021 annual review: no significant changes as drug is not yet FDA-approved; references to HIM.PHAR.21 revised to HIM.PA.154; references reviewed and updated.	12.02.20	02.21
1Q 2022 annual review: no significant changes as drug is not yet FDA-approved; revised requirement for valrubicin to “intravesical chemotherapy” per NCCN; references reviewed and updated.	09.27.21	02.22
Template changes applied to other diagnoses/indications and continued therapy section.	10.06.22	

**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. The Health Plan 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. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

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 Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. 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. The Health Plan 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 the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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**Note:**

**For Medicaid members**, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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