DR.017.A Adstiladrin® (Nadofaragene firadenovec-vncg)

Original Implementation Date : 7/1/2024
Version [A] Date : 7/1/2024
Last Reviewed Date: 06/27/2024

PRODUCT VARIATIONS

This policy applies to Medicaid, CHIP and Medicare product lines.

Gene therapy is a benefit exclusion for Individual and Family (ACA) product lines and therefore, non-covered.

POLICY STATEMENT

We consider Nadofaragene firadenovec-vncg (Adstiladrin®) medically necessary for its FDA approved indications when the prior authorization listed in this policy are met.

FDA INDICATIONS

Gene Therapy is the introduction, removal, or change in the content of a person's genetic code with the goal of treating or curing a disease. It includes therapies such as gene transfer, gene modified cell therapy, and gene editing.

Adstiladrin® is a non-replicating adenoviral vector-based gene therapy indicated for the treatment of adult patients with high-risk Bacillus Calmette-Guérin (BCG)-unresponsive non-muscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS) with or without papillary tumors.

OFF-LABEL USE

N/A

PRIOR AUTHORIZATION CRITERIA

Prior authorization is required for Adstiladrin® (Nadofaragene firadenovec-vncg)

INITIAL CRITERIA

Adstiladrin® (Nadofaragene firadenovec-vncg) may be considered medically necessary when all of the following apply:

1. Individuals must have a documented diagnosis of high-risk Bacillus Calmette-Guérin (BCG)-unresponsive non-muscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS) with or without papillary tumors.

2. Individuals do not have a hypersensitivity to interferon alfa or any component of the product.

3. Has premedication with an anticholinergic before each instillation of the product.

4. FDA approved dosing.

    a. The dose is 75 mL of ADSTILADRIN at a concentration of 3 x 1011 viral particles (vp)/mL, instilled once every three (3) months.

5. Administered for intravesical instillation only.

6. If female, verify pregnancy status in females of reproductive potential prior to initiating product.

7. Individual is complaint with necessary monitoring parameters.

8. Individual is ineligible for or has elected not to undergo a cystrectomy AND
    a. Documentation of Eastern Cooperative Oncology Group (ECOG) performance status of 2 or less.

1-888-991-9023
1101 Market Street, Suite 3000
Philadelphia, PA 19107
JeffersonHealthPlans.com

RENEWAL CRITERIA

1. Individual is 18 years of age or older.

2. Adstiladrin® (Nadofaragene firadenovec-vncg) may be considered medically necessary when initial criteria for use are met and the member shows no signs of intolerance/ adverse effects and remains disease free during the treatment with this drug.

SAFETY AND MONITORING

Risk factors:

1. Metastatic Bladder Cancer with Delayed Cystectomy: delaying cystectomy in patients with BCG- unresponsive CIS could lead to development of muscle-invasive or metastatic bladder cancer.

2. Disseminated adenovirus infection: Patients who are immunocompromised or immunodeficient may be at risk for disseminated infection from Adstiladrin® due to low levels of replication- competent adenovirus. Avoid Adstiladrin® exposure to immunocompromised or immunodeficient individuals.

Monitoring:

1. The most common (>10%) adverse reactions, including laboratory abnormalities (>15%), were glucose increased, instillation site discharge, triglycerides increased, fatigue, bladder spasm, micturition urgency, creatinine increased, hematuria, phosphate decreased, chills, dysuria, and pyrexia.

2. Serious adverse reactions occurring in >1% of patients included coronary artery disease and hematuria.

DOSAGE AND ADMINISTRATION

Adstiladrin® is a suspension for intravesical instillation, supplied as single-use vials. Adstiladrin® is provided in a carton containing four (4) vials. All vials have a nominal concentration of 3 × 1011 viral particles (vp)/mL. Each vial of Adstiladrin® contains an extractable volume of not less than 20 mL.

- Administration: Premedication with an anticholinergic is recommended before each instillation of Adstiladrin®. Administer Adstiladrin® by intravesical instillation only.
- Dose: The dose is 75 mL of Adstiladrin® at a concentration of 3 x 10^{11} viral particles (vp)/mL, instilled once every three (3) months. Allow Adstiladrin® to be left in the bladder for 1 hour following instillation.

BENEFIT APPLICATION

Medical policies do not constitute a description of benefits. This medical necessity policy assists in the administration of the member's benefits which may vary by line of business. Applicable benefit documents govern which services/items are eligible for coverage, subject to benefit limits, or excluded completely from coverage.

This policy is invoked only when the requested service is an eligible benefit as defined in the Member's applicable benefit contract on the date the service was rendered. Services determined by the Plan to be investigational or experimental are excluded from coverage for all lines of business. For Medicaid members under 21 years old, benefits and coverage are always based on medical necessity review.

BACKGROUND

Adstiladrin® (Nadofaragene firadenovec-vncg,) is a non-replicating adenoviral vector-based gene therapy for intravesical instillation. It is a recombinant adenovirus serotype 5 vector containing a transgene encoding the human interferon alfa-2b (IFNα2b). Adstiladrin® is designed to deliver a

copy of a gene encoding a human interferon- alfa 2b (IFNα2b) to the bladder urothelium. Intravesical instillation of Adstiladrin® results in cell transduction and transient local expression of the IFNα2b protein that is anticipated to have anti- tumor effects.

After treatment with a single intravesical 75 mL dose of Adstiladrin® (3 × 1011 viral particles per mL), 53·4% (n=151) of patients with carcinoma in situ (with or without a high-grade Ta or T1 tumor) had a complete response within 3 months of the first dose and this response was maintained in 45·5% of patients at 12 months.

Adstiladrin® is approved for the treatment of adult patients with high-risk Bacillus Calmette-Guérin (BCG)-unresponsive non-muscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS) with or without papillary tumors. Animal reproductive and developmental toxicities studies have not been conducted.

CLINICAL EVIDENCE

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice. The efficacy of Adstiladrin® was evaluated in a phase 3, multicenter, open-label, repeat-dose study done in 33 centers (hospitals and clinics) in the USA in patients aged 18 years or older, with BCG-unresponsive non-muscle-invasive bladder cancer and an Eastern Cooperative Oncology Group status of 2 or less. Patients received a single intravesical 75 mL dose of Adstiladrin® (3×10^{11} viral particles per mL). Repeat dosing at months 3, 6, and 9 was done in the absence of high-grade recurrence. The study is ongoing with a 4-year treatment and monitoring phase. The primary endpoint was the proportion of patients with a complete response in the carcinoma in situ cohort at any time within 12 months after the first dose of Adstiladrin®. 55 (53·4%) of 103 patients (95% CI 43·3 to 63·3) in the carcinoma in situ cohort had a complete response, with all complete responses noted at month 3.

CODING

Note*:* The Current Procedural Terminology (CPT®), Healthcare Common Procedure Coding System (HCPCS), and the 10th revision of the International Statistical Classification of Diseases and Related Health Problems (ICD-10) codes that *may* be listed in this policy are for reference purposes only. Listing of a code in this policy does not imply that the service is covered and is not a guarantee

of payment. Other policies and coverage guidelines may apply. When reporting services, providers/facilities should code to the highest level of specificity using the code that was in effect on the date the service was rendered. This list may not be all inclusive.

CPT® is a registered trademark of the American Medical Association.

HCPCS Code	Description
J9029	Intravesical instillation, nadofaragene firadenovec-vncg, per therapeutic dose Nadofaragene firadenovec-vncg (Adstiladrin®).

ICD-10 Codes	Description
N/A	N/A

DISCLAIMER

Approval or denial of payment does not constitute medical advice and is neither intended to guide nor influence medical decision making. Policy Bulletins are developed by us to assist in administering plan benefits and constitute neither offers of coverage nor medical advice. This Policy Bulletin may be updated and therefore is subject to change. For Health Choices (Medicaid) and Children's Health Insurance Program (CHIP) products: Any requests for services that do not meet criteria set in PARP will be evaluated on a case-by-case basis.

POLICY HISTORY

This section provides a high-level summary of changes to the policy since the previous version.

Summary	Version	Version Date
New policy.	A	7/1/2024

REFERENCES

1. Boorjian SA, Alemozaffar M, 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.* Lancet Oncol. 2021;22(1):107-117. doi:10.1016/S1470-2045(20)30540-4.

2. *Package Insert - ADSTILADRIN*. U.S. Food and Drug Administration: 2022. Available at https://www.fda.gov/media/164029/download

3. Stewart J. *Adstiladrin*. Drugs.com: 2022. Available at: https://www.drugs.com/adstiladrin.html#warnings