Adstiladrin (nadofaragene firadenovec-vncg)
PAM – 066

Iowa Medicaid Program	Prior Authorization	**Effective Date**	07/01/2023
Revision Number	2	**Last Reviewed**	01/17/2025
Reviewed By	Medicaid Medical Director	**Next Review**	01/16/2026
Approved By	Medicaid Clinical Advisory Committee	**Approved Date**	01/19/2024

Overview

Medication: [1]	nadofaragene firadenovec-vncg
Brand Name:	Adstiladrin®
Pharmacologic Category:	Antineoplastics; adeno-associated virus (AAV) vector-based gene therapy, non-replicating
FDA-Approved Indication(s):	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
How Supplied:	Provided in a carton containing 4 vials. Each vial has a nominal concentration of 3 x 10^{11} viral particles per mL (vp/mL) and contains an extractable volume of not less than 20 mL.
Dosage and Administration:	• For intravesical instillation only (not for IV use, topical use, or oral administration) • 75 mL instilled once every 3 months into the bladder via a urinary catheter at a concentration of 3 x 10^{11} viral particles per mL (vp/mL) • Continue until unacceptable toxicity or recurrent high-grade (HG) non-muscle invasive bladder cancer
Benefit Category:	Medical

Descriptive Narrative

High-risk, non-muscle invasive bladder cancer (NMIBC) is defined as the presence of high-grade Ta (confined to urothelium), any T1 (invading lamina propria), or CIS (high-grade flat lesions). Standard treatment for high-risk NMIBC includes transurethral resection of bladder tumor (TURBT), followed by immunotherapy with intravesical Bacillus Calmette-Guérin (BCG) that includes induction and maintenance therapy for up to 3 years.

BCG treatment fails in up to 50% of patients. In patients with BCG-unresponsive NMIBC, who are at high risk for progression to muscle-invasive or metastatic urothelial carcinoma, the standard of care is radical cystectomy. However, cystectomy is associated with high rates of 90-day post-operative mortality;

generally, 1 to 7 percent in younger patients who have no comorbidities seen at academic medical centers, and up to 15 percent in elderly patients in the SEER database. One intravesical therapy, valrubicin, is approved for patients who are ineligible for cystectomy, but has a low complete response rate (18 percent) and minimal use due to perceived lack of efficacy. A systemic PD-1 inhibitor, pembrolizumab, administered intravenously, was approved for this population in January 2020 based on a complete response (CR) rate of 41% and median duration of response (DoR) of 16 months.[2]

Abbreviations and Staging System for Bladder Cancer

ABBREVIATIONS	
BCG	Bacillus Calmette-Guérin
CIS	carcinoma in situ
CR	complete response
DoR	duration of response
HG	high-grade
NMIBC	non-muscle invasive bladder cancer
PD-1	programmed death protein 1
TURBT	transurethral resection of bladder tumor
SEER	Surveillance, Epidemiology, and End Results (SEER) Program

From the American Joint Committee on Cancer (AJCC) TNM Staging System for Bladder Cancer 8th ed. (2017)[3]	
T	Primary Tumor
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
Ta	Noninvasive papillary carcinoma
Tis	Urothelial carcinoma in situ: “flat tumor”
T1	Tumor invades lamina propria (subepithelial connective tissue)
T2	Tumor invades muscularis propria
pT2a	Tumor invades superficial muscularis propria (inner half)
pT2b	Tumor invades deep muscularis propria (outer half)
T3	Tumor invades perivesical tissue
pT3a	Microscopically
pT3b	Macroscopically (extravesical mass)
T4	Extravesical tumor directly invades any of the following: prostatic stroma, seminal vesicles, uterus, vagina, pelvic wall, abdominal wall
T4a	Extravesical tumor invades prostatic stroma, seminal vesicles, uterus, vagina
T4b	Extravesical tumor invades pelvic wall, abdominal wall

American Urological Association (AUA) Risk Stratification for Non-Muscle Invasive Bladder Cancer [4]

Low Risk	Intermediate Risk	High Risk

• Papillary urothelial neoplasm of low malignant potential
• Low grade urothelial carcinoma
  ○ Ta and
  ○ ≤ 3 cm and
  ○ Solitary
	• Low grade urothelial carcinoma
	  ○ T1 or
	  ○ > 3 cm or
	  ○ Multifocal or
	  ○ Recurrence within 1 year
	• High grade urothelial carcinoma
	  ○ Ta and
	  ○ ≤ 3 cam and
	  ○ Solitary
		• High grade urothelial carcinoma
		  ○ CIS or
		  ○ T1 or
		  ○ > 3 cm or
		  ○ Multifocal
		• Very high-risk features (any):
		  ○ BCG unresponsive [a]
		  ○ Variant histologies [b]
		  ○ Lymphovascular invasion
		  ○ Prostatic urethral invasion

Within each of these risk strata, a patient may have more or fewer concerning features that can influence care.		

[a] Kamat AM, et al. J Clin Oncol 2016;34:1935-1944. [b] Montironi R, et al. Int J Surg Pathol 2005;13:143-153.

Guidelines

The National Comprehensive Cancer Network (NCCN) publishes guidelines for the prevention, diagnosis, and management of malignancies across the continuum of care. The NCCN Guidelines® are a comprehensive set of guidelines detailing the sequential management decisions and interventions that currently apply to 97 percent of cancers affecting patients in the United States. The guidelines are developed and updated by 61 individual panels, comprising over 1,700 clinicians and oncology researchers from the 33 NCCN Member Institutions.

Guidelines are reviewed and updated on a continual basis to ensure that the recommendations take into account the most current evidence. To view the most recent and complete version of the guidelines, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way.[5,6]

The information referenced at the time of this policy writing/revision is from the NCCN Guidelines® for (note version number and effective date):[7]

- Bladder Cancer (v.5.2024 – October 28, 2024)

NCCN Guidelines® Recommendation(s) in Bladder Cancer
NMIBC, BCG-Unresponsive or BCG-Intolerant: Initial Management a. Nadofaragene firadenovec-vncg (select patients) i. High-risk NMIBC with CIS, with or without papillary: Category 2A ii. High-risk NMIBC with high-grade papillary Ta/T1 only tumors without CIS: Category 2B **BCG:** Bacillus Calmette-Guerin **CIS:** carcinoma in situ **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

NCCN Categories of Evidence and Consensus (all recommendations are category 2A unless otherwise indicated)	
Category 1	Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2A	Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
Category 2B	Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
Category 3	Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

NCCN Categories of Preference (all recommendations are considered appropriate)	
Preferred intervention	Interventions that are based on superior efficacy, safety, and evidence; and, when appropriate, affordability.
Other recommended intervention	Other interventions that may be somewhat less efficacious, more toxic, or based on less mature data; or significantly less affordable for similar outcomes.
Useful in certain circumstances	Other interventions that may be used for select patient populations (defined with recommendation).

Eastern Cooperative Oncology Group (ECOG) Performance Status Scale [8]

Developed by the Eastern Cooperative Oncology Group (ECOG), now part of the ECOG-ACRIN Cancer Research Group, and published in 1982, the ECOG Performance Status Scale describes a patient's level of functioning in terms of their ability to care for themselves, daily activity, and physical ability (walking, working, etc.). It is used by doctors and researchers to assess how a patient's disease is progressing, how the disease affects the daily living abilities of the patient, and to determine appropriate treatment and prognosis.

Grade	ECOG Performance Status [Synonyms: WHO/Zubrod score]
0	Fully active, able to carry on all pre-disease performance without restriction.
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework, office work.
2	Ambulatory and capable of all self-care but unable to carry out any work activities; up and about more than 50% of waking hours.
3	Capable of only limited self-care; confined to bed or chair more than 50% of waking hours.
4	Completely disabled; cannot carry on any self-care; totally confined to bed or chair.
5	Dead.

Criteria

Prior authorization is required.

Adstiladrin® is considered medically necessary when **ALL** of the following are met:

1. Diagnosis of non-muscle invasive bladder cancer (NMIBC) which is characterized as high-risk, with carcinoma in situ (CIS), and with or without papillary tumors; **AND**
2. Disease is Bacillus Calmette-Guérin (BCG)-unresponsive; **AND**
3. Member is 18 years of age or older; **AND**
4. Member has an Eastern Cooperative Oncology Group (ECOG) status of 0, 1, or 2; **AND**
5. Member is ineligible for or has elected not to undergo cystectomy; **AND**
6. Prescribed by, or in consultation with, an oncologist; **AND**
7. Request meets one of the following (a or b):
    a. Regimen prescribed does not exceed 75 mL [at a concentration of 3×10^{11} viral particles per mL (vp/mL)] as an intravesical instillation once every 3 months; or,
    b. Regimen is supported by clinical practice guidelines (i.e., must be recommended in NCCN Guidelines®). Supporting clinical documentation must be provided with any request for which regimen prescribed does not align with FDA-approved labeling.

Adstiladrin® is considered medically necessary for continuation of therapy when **ALL** of the following are met:

1. Member is currently receiving medication through the Iowa Medicaid benefit or has previously met initial approval criteria; **AND**
2. Documentation of positive clinical response to therapy, as demonstrated by freedom from high-grade disease recurrence and an acceptable toxicity profile; **AND**
3. Prescribed by, or in consultation with, an oncologist; **AND**
4. Request meets one of the following (a or b):
    a. Regimen prescribed does not exceed 75 mL [at a concentration of 3×10^{11} viral particles per mL (vp/mL)] as an intravesical instillation once every 3 months; or,
    b. Regimen is supported by clinical practice guidelines (i.e., must be recommended in NCCN Guidelines®). Supporting clinical documentation must be provided with any request for which regimen prescribed does not align with FDA-approved labeling.

Approval Duration and Quantity Limits

	Initial Authorization	Subsequent Authorization(s)
Approval Duration	6 months	12 months
Quantity Limits	4 vials every 90 days	4 vials every 90 days

Coding and Product Information

The following list(s) of codes and product information are provided for reference purposes only and may not be all inclusive. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment, nor does the exclusion of a code imply that its association to the HCPCS code is inappropriate.

HCPCS	Description
J9029	Injection, nadofaragene firadenovec-vncg, per therapeutic dose

ICD-10	Description
C67.0 – C67.9	Malignant neoplasm of bladder

NDC (Strength)	Labeler	Dosage	Pkg Size	Pkg Qty	Units /Pkg
55566-1050-00 (single vial, volume 20 mL, nominal concentration of 3×10^{11} vp/mL when thawed)	Ferring Pharmaceuticals, Inc. (55566)	per treatment dose	1	EA	1
55566-1050-01 (available only as a carton of 4 vials)					

Compliance

1. Should conflict exist between the policy and applicable statute, the applicable statute shall supersede.
2. Federal and State law, as well as contract language, including definitions and specific contract provisions or exclusions, take precedence over medical policy and must be considered first in determining eligibility for coverage.
3. Medical technology is constantly evolving, and Iowa Medicaid reserves the right to review and update medical policy on an annual or as-needed basis.

Medical necessity guidelines have been developed for determining coverage for member benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. Medical necessity guidelines are developed for selected physician-administered medications found to be safe and proven to be effective in a limited, defined population or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in the service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. Criteria are revised and updated annually, or more frequently if new evidence becomes available that suggests needed revisions.

References

[1] Adstiladrin® prescribing information (08/2024). Ferring Pharmaceuticals, Inc.: Parsippany, NJ. Available online: www.adstiladrinhcp.com. Accessed November 1, 2024.

[2] BLA 125700: Summary Basis for Regulatory Action. December 16, 2022. Available online at www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/adstiladrin. Accessed December 1, 2023.

[3] Amin MB, Edge SB, Greene F, et al., eds. AJCC Cancer Staging Manual, 8th ed. New York: Springer International Publishing; 2017.

[4] Chang SS, Boorjian SA, Chou R, et al. Diagnosis and treatment of non-muscle invasive bladder cancer: AUA/SUO guideline. J Urol 2016;196:1021-1029.

[5] National Comprehensive Cancer Network (NCCN). Guidelines Process: About Clinical Practice Guidelines. Available online at www.nccn.org. Accessed July 29, 2024.

[6] National Comprehensive Cancer Network (NCCN). Guidelines Process: Development and Update of Guidelines. Available online at www.nccn.org. Accessed July 29, 2024.

[7] NCCN Clinical Practice Guidelines in Oncology. The NCCN Guidelines® are a work in progress that may be refined as often as new significant data becomes available. To view the most recent and complete version, go online to NCCN.org. NCCN Guidelines® referenced (note version number and effective date):

- Bladder Cancer (v.5.2024 – October 28, 2024)

[8] Oken M, Creech R, Tormey D, et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. Am J Clin Oncol. 1982;5:649-655. PMID 7165009.

Development of utilization management criteria may also involve research into other state Medicaid programs, other payer policies, consultation with experts and review by the Medicaid Clinical Advisory Committee (CAC). These sources may not be referenced individually unless they are specifically published and are otherwise applicable to the criteria at issue.

Criteria Change History

Change Date	Changed By	Description of Change	Version
[mm/dd/yyyy]	CAC		
Signature			

Change Date	Changed By	Description of Change	Version
[mm/dd/yyyy]	CAC		
Signature			

Change Date	Changed By	Description of Change	Version
01/17/2025	CAC	Annual review. Added "American Urological Association (AUA) Risk Stratification for Non-Muscle Invasive Bladder Cancer" to Descriptive Narrative. Updated NCCN Guidelines®.	2
Signature William (Bill) Jagiello, DO			

Change Date	Changed By	Description of Change	Version
01/19/2024	CAC	Criteria implementation.	1
Signature William (Bill) Jagiello, DO			

CAC = Medicaid Clinical Advisory Committee