nadofaragene firadenovec-vncg (Adstiladrin®)

Policy # 00860
Original Effective Date: 01/08/2024
Current Effective Date: 01/08/2024

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider nadofaragene firadenovec-vncg (Adstiladrin®)‡ for the treatment of high-risk Bacillus Calmette-Guérin (BCG)-unresponsive non-Muscle Invasive Bladder Cancer (NMIBC) to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility for the use of nadofaragene firadenovec-vncg (Adstiladrin) will be considered when all of the following criteria are met:

- Initial
  - Patient has a diagnosis of non-muscle invasive bladder cancer (NMIBC); AND
  - Patient has high-risk Bacillus Calmette-Guérin (BCG)-unresponsive disease (i.e., persistent or recurrent disease unresponsive to ≥2 courses of BCG in the last 12 months); AND
  - ONE of the following:
    - Patient has carcinoma in situ (CIS) with or without high-grade papillary Ta/T1 tumors; OR
    - Patient has high-grade papillary Ta/T1 tumors without CIS; AND
  - Dose will not exceed 75 mL every three months.
- Continuation
  - Patient has received an initial authorization; AND
  - There is no evidence of muscle-invasive (muscularis propria) or metastatic disease; AND

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- According to treating provider, tumor continues to respond to therapy (e.g., absence of high-risk recurrence or progression); AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Dose will not exceed 75 mL every three months.

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the continued use of nadofaragene firadenovec-vncg (Adstiladrin) when the cancer is no longer responding to the therapy to be **not medically necessary.****

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of nadofaragene firadenovec-vncg (Adstiladrin) when patient selection criteria are not met (except those denoted above as **not medically necessary****) to be **investigational.***

Background/Overview

Adstiladrin is a gene therapy indicated for the treatment of adult patients with high-risk Bacillus Calmette-Guérin (BCG)-unresponsive non-Muscle Invasive Bladder Cancer (NMIBC). It is comprised of a non-replicating adenovirus vector that delivers a copy of the interferon-alfa 2b gene to the bladder urothelium, leading to transient local expression of IFNα2b, which is thought to have anti-tumor effects. It is indicated to be administered via intravesical instillation every 3 months until disease progression or unacceptable toxicity. Patients who are immunocompromised or immunodeficient should avoid Adstiladrin exposure since they may be at risk for disseminated infection due to low levels of replication-competent adenovirus. Since this therapy may be used as an alternative to cystectomy, the package insert warns that delaying cystectomy could lead to the development of metastatic bladder cancer, which can be lethal.

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Bladder cancer is a malignancy in which abnormal tissue develops in the lining of the bladder. The most common kind of bladder cancer is known as urothelial bladder cancer or transitional cell carcinoma and accounts for 90% of all bladder cancers. About 75% of these urothelial bladder cancers are classified as non-muscle invasive. Non-muscle invasive bladder cancer (NMIBC) includes Ta tumors, T1 tumors, and Tis (carcinoma in situ [CIS]). Treatment of bladder cancer depends on a variety of factors, but can include cytotoxic chemotherapy, radiation, surgery, or immunotherapy. A 6-week intravesical administration of BCG, a live attenuated form of *Mycobacterium bovis*, is the standard-of-care (SOC) induction therapy for patients with intermediate or high-risk disease. Patients with high-risk disease may also go on to receive maintenance treatment; however, more than half of patients who receive initial treatment with BCG will experience disease recurrence and progression within 1 year. Radical cystectomy (removal of the bladder) is considered the standard of care for any patient with BCG-unresponsive high-grade NMIBC, but it carries a high morbidity rate and risk of mortality. The National Comprehensive Cancer Network (NCCN) guidelines for bladder cancer recommend Adstiladrin for patients with BCG-unresponsive, high risk, NMIBC with CIS (with or without papillary) and state that it may also be considered for patients with BCG-unresponsive, high-risk, NMIBC with high-grade papillary Ta/T1 only tumors without CIS.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Adstiladrin was approved in December 2022 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.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

The efficacy of Adstiladrin was evaluated in an open-label, multicenter, single-arm trial in 103 adults with BCG-unresponsive, high-risk, non-muscle invasive bladder cancer with carcinoma in situ (CIS)

with or without papillary tumors following transurethral resection, of whom 98 were considered evaluable for response. BCG-unresponsive high-risk NMIBC was defined as persistent disease following adequate BCG therapy, disease recurrence after an initial tumor-free state following adequate BCG therapy, or T1 disease following a single induction course of BCG. Adequate BCG was defined as the administration of at least five of six doses of an initial induction course plus either of: at least two of three doses of maintenance therapy or at least two of six doses of a second induction course. Prior to treatment, all patients had undergone transurethral resection of bladder tumor (TURBT) to remove all resectable disease. Residual CIS not amenable to complete resection was allowed. The trial excluded patients with extra-vesical (i.e., urethra, ureter, or renal pelvis), muscle invasive (T2-T4), or metastatic urothelial carcinoma.

Patients received Adstiladrin 75 mL intravesical instillation (3×10^{11} vp) once every three months for up to 12 months (four doses) or until unacceptable toxicity or recurrent high-grade NMIBC. Patients without evidence of high grade recurrence were allowed to continue Adstiladrin treatment every three months.

The major efficacy outcome measures were complete response (CR) at any time (as defined by negative results for cystoscopy and urine cytology) and duration of response. Low-grade (Ta) papillary disease was not considered a recurrence for the purposes of evaluating CR. CR was assessed at 3, 6, 9, and 12 months by cystoscopy and cytology. Random bladder biopsy of five sites was conducted in patients remaining in CR at Month 12. In the 98 evaluable patients, the complete response rate was found to be 51% (95% CI 41%, 61%) with a median duration of response of 9.7 months (range: 3, 52+). Forty-six percent of patients who responded had a duration of response of greater than or equal to 12 months.

References

1. Adstiladrin [package insert]. Ferring Pharmaceuticals. Kastrup, Denmark. Updated September 2023.
2. Adstiladrin New Drug Review. IPD Analytics. Updated January 2023.
3. National Comprehensive Cancer Network (NCCN). Clinical practice guidelines in oncology Bladder Cancer. Version 3.2023. Updated May 2023.

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Policy History

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12/07/2023 Medical Policy Committee review
12/13/2023 Medical Policy Implementation Committee approval. New policy.
Next Scheduled Review Date: 12/2024

Coding

The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2022 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

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Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	No code
HCPCS	J9029
ICD-10 Diagnosis	All related Diagnoses

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and

C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.