Blue Cross Blue Shield Blue Care Network of Michigan

Nonprofit corporations and independent licensees of the Blue Cross and Blue Shield Association

Medical benefit drug policies are a source for BCBSM and BCN medical policy information only. These documents are not to be used to determine benefits or reimbursement. Please reference the appropriate certificate or contract for benefit information. This policy may be updated and therefore subject to change.

Effective Date: 10/12/2023

Adstiladrin® (nadofaragene firadenovec-vncg)

HCPCS: J9029

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

A. Coverage of the requested drug is provided when all the following are met:
   a. FDA approved indication
   b. FDA approved age
   c. Prescribed by or in consultation with an oncologist or urologist
   d. Must be Bacillus Calmette-Guérin (BCG) unresponsive defined as:
      i. Having received at least 2 previous courses of BCG within a 12-month period defined as
         a) At least 5 of 6 induction BCG instillations and at least 2 out of 3 instillations of maintenance BCG
            OR
         b) At least two of six instillations of a second induction course where maintenance BCG is not given
      ii. Recurrence of high-grade Ta or T1 non-muscle-invasive bladder cancer within 6 months of disease-free state after BCG therapy
      iii. Recurrence of carcinoma in situ (CIS) within 12 months of disease-free state after BCG therapy
      iv. Persistent high-grade Ta or CIS or progression to T1 disease after BCG therapy
   e. All visible papillary tumors must be resected and those with persistent T1 disease on transurethral resection of bladder tumor (TURBT) should undergo an additional re-TURBT within 14 to 60 days prior to beginning Adstiladrin
   f. ECOG performance score less than or equal to 2
   g. Must not have concomitant upper tract urothelial carcinoma or urothelial carcinoma within the prostatic urethra
   h. Trial and failure, contraindication, OR intolerance to the preferred drugs as listed in BCBSM/BCN's utilization management medical drug list

B. Quantity Limitations, Authorization Period and Renewal Criteria
   a. Quantity Limits: Align with FDA recommended dosing
   b. Authorization Period: Aligns with FDA recommended or guideline supported treatment duration and provided for at least 60 days and up to 6 months at a time

c. Renewal Criteria: Continue until unacceptable toxicity or recurrent high-grade (HG) non-muscle invasive bladder cancer (NMIBC)

***Note: Coverage and approval duration may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at http://www.cms.hhs.gov/. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Background Information:

- Bladder cancer is one of the more common forms of cancer. Approximately 75% - 80% of newly diagnosed bladder cancers are classified as NMIBC – a type of cancer that has grown through the lining of the bladder but hasn't yet invaded the muscle layer. This type of cancer is associated with high rates of recurrence (between 30 to 80%) and the risk of progression to invasive and metastatic disease.

- Treatment and care of patients with high-risk NMIBC, including those with CIS, often involves removing the tumor followed by BCG bladder instillation therapy to reduce the risk of recurrence. Few effective treatment options exist for patients who develop BCG-unresponsive disease. The failure to achieve a complete response, or the disappearance of all signs of cancer as seen on cystoscopy, biopsied tissue, and urine, is associated with an increased risk of death or a disease-worsening event.

- Adstiladrin is a non-replicating adenoviral vector-based gene therapy indicated for the treatment of adult patients with high-risk BCG-unresponsive NMIBC with CIS with or without papillary tumors. It offers an additional treatment option in a historically limited space.

- The 2023 National Comprehensive Cancer Network Bladder Cancer Treatment Guidelines recommend TURBT for staging followed by a single dose of intravesicular mitomycin or gemcitabine as the first step in treatment. Following the tumor evaluation, if the tumor is considered high-grade, BCG is the preferred adjuvant therapy and intravesicular mitomycin or gemcitabine provide additional options to those who aren't candidates for BCG therapy. BCG is typically given weekly for 6 weeks at induction followed by maintenance of 3 weekly instillations at month 3, 6, 12, 18, 24, 30, and 36. Two 6-week BCG induction courses should be completed before the patient is considered non-responsive to the therapy. If patients have had recurrence or are considered non-responsive to BCG therapy, cystectomy, Keytruda®, or Adstiladrin are currently recommended as second-line therapies.

- Safety and efficacy were evaluated in CS-003, an open-label, multicenter, single-arm trial in 157 adults with BCG-unresponsive, high-risk, NMIBC with 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 at least two of three doses of maintenance therapy or at least two of six doses of a second induction course. Patients were excluded from the trial if they had an ECOG score greater than 2 or had concomitant upper tract urothelial carcinoma or urothelial carcinoma within the prostatic urethra. All visible papillary tumors were resected and those with persistent T1 disease on TURBT should undergo an additional re-TURBT within 14 to 60 days prior to beginning therapy. Patients received Adstiladrin once every three months for up to 12 months, until unacceptable toxicity, or recurrent high-grade NMIBC. Overall, 51% of enrolled patients using Adstiladrin therapy achieved a complete response and median duration of response was 9.7 months. Forty-six percent of responding patients remained in complete response for at least one year.

References:

1. Adstiladrin [prescribing information]. Kastrup, Denmark: Ferring Pharmaceuticals; December 2022.
2. Boorjian SA, Alemozaffar M, Konet 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 Jan; 22 (1): 107 - 17.
3. National Comprehensive Cancer Network. Baldder cancer (Version 3.2023). 2023 May 25. Available at: https://www.nccn.org/professionals/physician_gls/pdf/bladder.pdf. Accessed on August 23, 2023.

<table>
<tr><th colspan="3">Policy History</th></tr>
<tr><th>#</th><th>Date</th><th>Change Description</th></tr>
<tr><td>1.2</td><td>Effective Date: 10/12/2023</td><td>Updated to include a urologist as part of the prescriber requirements</td></tr>
<tr><td>1.1</td><td>Effective Date: 05/01/2023</td><td>UM medical management system update for MAPPO and BCNA
<table>
<tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr>
<tr><td>BCBS</td><td>Yes</td></tr>
<tr><td>BCN</td><td>Yes</td></tr>
<tr><td>MAPPO</td><td>Yes</td></tr>
<tr><td>BCNA</td><td>Yes</td></tr>
</table></td></tr>
<tr><td>1.0</td><td>Effective Date: 02/02/2023</td><td>New policy - replaces previously approved preliminary criteria
UM medical management system update for BCBSM and BCN
<table>
<tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr>
<tr><td>BCBS</td><td>Yes</td></tr>
<tr><td>BCN</td><td>Yes</td></tr>
<tr><td>MAPPO</td><td>No</td></tr>
<tr><td>BCNA</td><td>No</td></tr>
</table></td></tr>
</table>

** The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or http://dailymed.nlm.nih.gov/dailymed/index.cfm.*

Blue Cross Blue Shield/Blue Care Network of Michigan
Medication Authorization Request Form

Blue Cross Blue Shield Blue Care Network of Michigan

Nonprofit corporations and independent licensees of the Blue Cross and Blue Shield Association

This form is to be used by participating physicians to obtain coverage for **drugs covered under the medical benefit**. For commercial members only, please complete this form and submit via fax to 1-877-325-5979. If you have any questions regarding this process, please contact BCBSM Provider Relations and Servicing or the Medical Drug Helpdesk at 1-800-437-3803 for assistance.

PATIENT INFORMATION	PHYSICIAN INFORMATION
Name	**Name**
ID Number	**Specialty**
D.O.B. ☐Male ☐Female	**Address**
Diagnosis	**City /State/Zip**
Drug Name	**Phone/Fax: P**: ( ) - **F**: ( ) -
Dose and Quantity	**NPI**
Directions	**Contact Person**
Date of Service(s)	**Contact Person Phone / Ext.**

STEP 1: DISEASE STATE INFORMATION

1. Is this request for: ☐ Initiation ☐ Continuation *Date patient started therapy:* _____
2. Administered by patient or a medical professional? ☐ patient (self) ☐ health care professional (physician, nurse, etc.)
3. Site of administration? ☐ Provider office/Home infusion ☐ Other: _____
   ☐ Hospital outpatient facility (go to #4) *Reason for Hospital Outpatient administration:* _____
   ☐ Hospital inpatient facility for Car-T therapy only (for example: Kymriah, Yescarta, or Tecartus) (go to #5)
4. Please specify location of administration if hospital outpatient infusion: _____
5. Please specify location of administration if hospital inpatient infusion: _____
6. Please provide the NPI number for the place of administration: _____
7. **Initiation AND Continuation of therapy:**
   a. What is the patient's diagnosis? _____
   b. What other medication has the patient received for their condition? Please list_____
      i. Please describe the response to previous therapies:
      _____
   c. Will the patient be receiving any other treatment for the listed condition while on this medication? Please list:
      _____
   d. Please list any labs values important for diagnosing or monitoring this patient's condition:
      _____
8. **Continuation of therapy:**
   a. Has the patient progressed while on this medication? ☐ yes ☐ no
   b. How has the patient's condition changed while on this medication?
      ☐ Improved: Please describe: _____
      ☐ Stable: please describe: _____
      ☐ Worsened; Please describe: _____
      ☐ Other; Please describe: _____

Chart notes are required for the processing of all requests. Please add any other supporting medical information necessary for our review **(required)**

Coverage will not be provided if the prescribing physician's signature and date are not reflected on this document.

☐ Request for expedited review: I certify that applying the standard review time frame may seriously jeopardize the life or health of the member or the member's ability to regain maximum function

Physician's Name **Physician Signature** **Date**

Step 2: Checklist	☐ Form Completely Filled Out ☐ Provide chart notes	☐ Attach test results
Step 3: Submit	**By Fax: BCBSM Specialty Pharmacy Mailbox 1-877-325-5979**	**By Mail: BCBSM Specialty Pharmacy Program P.O. Box 312320, Detroit, MI 48231-2320**

7/26/2018, 9/18/2018; 1/31/2020; 3/17/2020; 8/9/2021