MEDICAL COVERAGE POLICY	
SERVICE:	**Nogapendekin alfa inbakicept (Anktiva®)**
Policy Number:	**314**
Effective Date:	**1/1/2025**
Last Review:	**10/14/2024**
Next Review:	**10/14/2025**

Important note: *Unless otherwise indicated, medical policies will apply to all lines of business. Medical necessity as defined by this policy does not ensure the benefit is covered. This medical policy does not replace existing federal or state rules and regulations for the applicable service or supply. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan documents. See the member plan specific benefit plan document for a complete description of plan benefits, exclusions, limitations, and conditions of coverage. In the event of a discrepancy, the plan document always supersedes the information in this policy.*

SERVICE: Nogapendekin alfa inbakicept (Anktiva®)

PRIOR AUTHORIZATION: Required

POLICY: Please review the plan's EOC (Evidence of Coverage) or Summary Plan Description (SPD) for details.

For Medicare plans, please refer to appropriate Medicare NCD (National Coverage Determination) or LCD (Local Coverage Determination). Medicare NCD or LCD specific InterQual criteria may be used when available. If there are no applicable NCD or LCD criteria, use the criteria set forth below.

For Medicaid plans, please confirm coverage as outlined in the Texas Medicaid Provider Procedures Manual | TMHP (TMPPM). Texas Mandate HB154 is applicable for Medicaid plans.

Baylor Scott & White Health Plan (BSWHP) may consider nogapendekin alfa inbakicept (Anktiva®) medically necessary for the treatment of members with non-muscle invasive bladder cancer (NMIBC) when ALL of the following criteria are met:

1. Member is 18 years of age or older; **AND**
2. Documentation of BCG unresponsive non-muscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS) with all of the following:
    a. High-grade; **AND**
    b. Urothelial (transitional cell) histology
        i. Mixed histology tumors with predominant transitional cell histology is supported

    AND
    c. BCG unresponsive defined by one of the following:
        i. Persistent or recurrent CIS within 12 months of receiving at least 5 of 6 doses of an initial BCG induction PLUS at least 2 doses as part of maintenance treatment or a second induction; **OR**
        ii. Recurrent high-grade Ta/T1 disease within 6 months of receiving at least 5 of 6 doses of an initial BCG induction PLUS at least 2 doses as part of maintenance treatment or a second induction; **OR**
        iii. T1 high-grade disease at the first evaluation following 5 of 6 doses of BCG as an initial induction course

AND

3. Medication is prescribed by a physician who specializes in oncology or urology; **AND**

4. Medication will be prescribed in combination with BCG; **AND**
5. Member meets one of the following:
    a. Documented trial and failure, intolerance, or contraindication to pembrolizumab (Keytruda) AND nadofaragene firdenovec-vncg (Adstiladrin); **OR**
    b. Member is established on nogapendekin; **OR**
    c. Texas Mandate HB1584, Texas Insurance Code (TIC) sec. 1369.213, or TIC sec. 1369.0546 are applicable

Approval duration is the shortest of clinically appropriate indication, 6 months, or requested duration.

BACKGROUND:

Bladder cancer is the sixth most common type of cancer in the U.S. The American Cancer Society (ACS) estimates that 83,730 new cases of bladder cancer will be diagnosed in the U.S. in 2021, and that 17,200 people will die of the disease. Bladder cancer incidence increases with age; the average age at diagnosis is 73 years. The disease is approximately 3 times more common in men than in women. According to the National Cancer Institute (NCI), an estimated 723,745 people were living with bladder cancer in the U.S. in 2018.

Urothelial carcinoma, also known as transitional cell carcinoma, accounts for 90% of bladder cancers diagnosed in the U.S. (ACS, 2019a). Approximatively 75% of patients with urothelial carcinoma have non-muscle invasive bladder cancer (NMIBC), also known as "superficial" bladder cancer.

The primary treatment for NMIBC is TURBT. Patients who underwent TURBT during diagnostic work-up typically undergo a second, more extensive TURBT after diagnosis is confirmed. Adjuvant intravesical therapy with bacillus Calmette-Guérin (BCG) is strongly recommended for patients with newly diagnosed high-risk NMIBC; these patients have a 60% to 70% chance of cancer recurrence and a 10% to 45% chance of progression to muscle-invasive or metastatic bladder cancer within 5 years. Although intravesical BCG in addition to repeat TURBT is an effective primary treatment for NMIBC, 30% to 50% of patients have disease unresponsive to BCG, increasing their risk for cancer progression and mortality. The U.S. Food and Drug Administration (FDA) defines BCG-unresponsive NMIBC as being at least 1 of the following (FDA, 2018):

- Persistent or recurrent CIS alone or with recurrent Ta/T1 (noninvasive papillary disease/tumor invades the subepithelial connective tissue) disease within 12 months of completion of adequate BCG therapy
- Recurrent high-grade Ta/T1 disease within 6 months of completion of adequate BCG therapy
- T1 high-grade disease at the first evaluation following an induction BCG course

The standard of care for patients with high-risk BCG-unresponsive NMIBC is radical cystectomy, which is potentially curative. However, radical cystectomy is associated with substantial morbidity and decreased quality of life; many patients are either unfit or unwilling to undergo the surgery. The FDA has approved intravenously-administered pembrolizumab (Keytruda®) and nadofaragene firadenovec-vncg (Adstiladrin®) for high-risk BCG-unresponsive NMIBC in patients with CIS with or without

papillary tumors.

The U.S. Food and Drug Administration (FDA) approved ImmunityBio's nogapendekin alfa inbakicept-pmln (Anktiva®) plus Bacillus Calmette-Guérin (BCG) on April 22, 2024, for the treatment of patients with BCG-unresponsive non-muscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS), with or without papillary tumors. It is a first-in-class interleukin (IL)-15 receptor agonist and administered intravesically. Efficacy of Anktiva was evaluated in the Phase 2/3 QUILT-3.032 trial (NCT03022825), a single-arm, multicenter study of 77adults with BCG-unresponsive, high-risk NMIBC with CIS with or without Ta/T1 papillary disease following transurethral resection.

The complete response (CR) rate was 62%, with 95% confidence interval (CI) 51% - 73%. The duration of response (DOR), as of the November 2023 cut-off, was more than 47 months and ongoing. The final median DOR has yet to be determined. The prolonged DOR beyond 24 months with Anktiva/BCG exceeds the benchmark for the magnitude of meaningful clinical results suggested by a panel of experts from the International Bladder Cancer Group (IBCG). In total, 58% of patients with a CR had a DOR ≥12 months and 40% had a DOR ≥24 months. Adverse events were consistent with those reported with BCG alone.

Texas Mandate HB1584 and Texas Insurance Code (TIC) sec, 1369.213 state step therapy will not be required for a non-preferred drug when use is

1) consistent with best practices for the treatment of stage-four advanced, metastatic cancer or an associated condition;
2) supported by peer-reviewed, evidence-based literature; AND
3) approved by the United States Food and Drug Administration

TIC sec. 1369.0546 states step therapy will not be required for a non-preferred drug when use is contraindicated or expected to be ineffective or cause harm based on submitted clinical documentation and/or medical literature.

CODES:

Important note: *Due to the wide range of applicable diagnosis codes and potential changes to codes, an inclusive list may not be presented, but the following codes may apply. Inclusion of a code in this section does not guarantee that it will be reimbursed, and patient must meet the criteria set forth in the policy language.*

CPT Codes:	
HCPCS Codes:	C9169 - Injection, nogapendekin alfa inbakicept-pmln, for intravesical use, 1 microgram J9999 – not otherwise classified, antineoplastic drugs
ICD10 codes:	
ICD10 Not covered:	

POLICY HISTORY:

Status	Date	Action
New	10/14/2024	New policy

REFERENCES:

The following scientific references were utilized in the formulation of this medical policy. BSWHP will continue to review clinical evidence related to this policy and make modifications based upon the evolution of the published clinical evidence. Should additional scientific studies become available, and they are not included in the list, please forward the reference(s) to BSWHP so the information can be reviewed by the Medical Coverage Policy Committee (MCPC) and the Quality Improvement Committee (QIC) to determine if a modification of the policy is in order.

1. Adstiladrin [package insert]. Ferring Pharmaceuticals. Kastrup, Denmark. Available at: https://ferringusa.com/wp-content/uploads/sites/12/2024/05/ADSTILADRIN-USPI-CLEAN-5.2024.pdf
2. Adstiladrin. NCCN Drugs & Biologics Compendium. Available at: https://www.nccn.org/professionals/drug_compendium/content/
3. Anktiva [package insert]. ImmunityBio, Inc. Culver City, CA. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/761336s000lbl.pdf
4. Anktiva. NCCN Drugs & Biologics Compendium. Available at: https://www.nccn.org/professionals/drug_compendium/content/
5. “Bladder Cancer.” Cancers, 1999, https://medlineplus.gov/bladdercancer.html.
6. “Cancer of the Urinary Bladder - Cancer Stat Facts.” SEER, https://seer.cancer.gov/statfacts/html/urinb.html. Accessed 16 Aug. 2024.
7. Chamie K, Change SS, Kramolowsky E, Et al. IL-15 superagonist NAI in BCG-unresponsive non-muscle-invasive bladder cancer. NEJM Evid 2023; 2:EVIDoa2200167. Available at: https://evidence.nejm.org/doi/full/10.1056/EVIDoa2200167
8. Chang, Sam S et al. “Diagnosis and Treatment of Non-Muscle Invasive Bladder Cancer: AUA/SUO Guideline.” The Journal of urology vol. 196,4 (2016): 1021-9. doi:10.1016/j.juro.2016.06.049
9. Chehroudi, Ali Cyrus, and Peter C Black. “Emerging intravesical therapies for the management of bacillus Calmette-Guérin (BCG)-unresponsive non-muscle-invasive bladder cancer: Charting a path forward.” Canadian Urological Association journal = Journal de l'Association des urologues du Canada vol. 14,6 (2020): 204-213. doi:10.5489/cuaj.6101
10. “Key Statistics for Bladder Cancer.” Cancer.org, https://www.cancer.org/cancer/types/bladder-cancer/about/key-statistics.html. Accessed 16 Aug. 2024.
11. Keytruda [package insert]. Merck & Co, Inc. Whitehouse Station, NJ. Available at: https://www.merck.com/product/usa/pi_circulars/k/keytruda/keytruda_pi.pdf
12. Keytruda. NCCN Drugs & Biologics Compendium. Available at: https://www.nccn.org/professionals/drug_compendium/content/
13. Matulewicz, Richard S, and Gary D Steinberg. “Non-muscle-invasive Bladder Cancer: Overview and Contemporary Treatment Landscape of Neoadjuvant Chemoablative Therapies.” Reviews in urology vol. 22,2 (2020): 43-51.
14. Packiam, Vignesh T et al. “Non-muscle-invasive bladder cancer: Intravesical treatments beyond Bacille Calmette-Guérin.” Cancer vol. 123,3 (2017): 390-400. doi:10.1002/cncr.30392
15. Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). National

Comprehensive Cancer Network, Inc. 2024. All rights reserved. Accessed June 27, 2024. To view the most recent and complete version of the guideline, go online to NCCN.org.

16. "What Is Bladder Cancer?" Cancer.org, https://www.cancer.org/cancer/types/bladder-cancer/about/what-is-bladder-cancer.html. Accessed 16 Aug. 2024.

***Note**:*
Health Maintenance Organization (HMO) products are offered through Scott and White Health Plan dba Baylor Scott & White Health Plan, and Scott & White Care Plans dba Baylor Scott & White Care Plan. Insured PPO and EPO products are offered through Baylor Scott & White Insurance Company. Scott and White Health Plan dba Baylor Scott & White Health Plan serves as a third-party administrator for self-funded employer-sponsored plans. Baylor Scott & White Care Plan and Baylor Scott & White Insurance Company are wholly owned subsidiaries of Scott and White Health Plan. These companies are referred to collectively in this document as Baylor Scott & White Health Plan.

RightCare STAR Medicaid is offered through Scott and White Health Plan in the Central Texas Medicaid Rural Service Area (MRSA); FirstCare STAR is offered through SHA LLC dba FirstCare Health Plans (FirstCare) in the Lubbock and West MRSAs; and FirstCare CHIP is offered through FirstCare in the Lubbock Service Area.