

Utilization Management and Clinical Medical Policy

Policy Name: Nogapendekin alfa inbakicept-pmln (Anktiva®)	Policy Number: MP-RX-FP-154-24	Scope: <input checked="" type="checkbox"/> MMM MA <input checked="" type="checkbox"/> MMM MultiHealth	Origination Date: 8/7/2024	Effective Date: 5/6/2026
			Last Review Date: 5/6/2026	Frequently Revision: Annual

Service Category:

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| <input type="checkbox"/> Anesthesia | <input type="checkbox"/> Medicine Services and Procedures |
| <input type="checkbox"/> Surgery | <input type="checkbox"/> Evaluation and Management Services |
| <input type="checkbox"/> Radiology Procedures | <input type="checkbox"/> DME/Prosthetics or Supplies |
| <input type="checkbox"/> Pathology and Laboratory Procedures | <input checked="" type="checkbox"/> Other: Part B Drugs |

Service Description:

This document addresses the use of Nogapendekin alfa inbakicept-pmln (Anktiva®), an interleukin-15 (IL-15) receptor agonist approved by the Food and Drug Administration (FDA) to be used in combination with Bacillus Calmette-Guérin (BCG) for the treatment of adult patients with BCG- unresponsive nonmuscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS) with or without papillary tumors.

Background Information:

Bladder cancer affects around 390,000 people and causes 150,000 deaths annually worldwide. In developed regions like North America and Western Europe, most bladder cancers are urothelial. About 70%-80% of new urothelial bladder cancer cases are non-muscle invasive (which is found in the tissue that lines the inner surface of the bladder and hasn't spread into the bladder wall), encompassing Ta (papillary), T1 (submucosal invasive), and Tis (carcinoma in situ [CIS]), which constitute approximately 70%, 20%, and 10% of non-muscle invasive cases, respectively.

Treatment for intermediate or high-risk NMIBC usually involves transurethral resection of the bladder tumor (TURBT) followed by Bacillus Calmette-Guérin (BCG) intravesical therapy. This cancer type has the highest recurrence rate among all cancers, with the majority of patients experiencing a recurrence. Even with optimal treatment, there's a significant risk of recurrence or progression to advanced disease. Specifically, 30% to 40% of NMIBC patients will face recurrence despite adequate BCG treatment, and up to 50% of those who initially respond completely to BCG will eventually relapse. Patients unresponsive to BCG therapy have limited treatment options and require novel interventions.

Anktiva in combination with BCG was evaluated in QUILT-3.032, a single-arm, multicenter trial in adults with BCG-unresponsive, high-risk NMIBC with CIS with or without Ta/T1 papillary disease following transurethral resection. In the FDA evaluable population of 77 patients, the complete response (CR) rate was 62%. Among patients who achieved CR, 58% had a duration of response of at least 12 months and 40% had a duration of response of at least 24 months. Treatment consisted of induction followed by maintenance therapy for up to 37 months.

Delaying cystectomy in patients with BCG-unresponsive CIS may increase the risk of development of muscle-invasive or metastatic bladder cancer; if a complete response is not achieved after a second induction course of Anktiva with BCG, cystectomy should be reconsidered.

The recommended dose of nogapendekin alfa inbakicept-pmln is 400 mcg, administered intravesically with BCG once a week for 6 weeks as induction therapy. If CR is not achieved at month 3, a second induction course may be given. For maintenance after induction therapy, the dose is 400 mcg with BCG once a week for 3 weeks at months 4, 7, 10, 13, and 19 (for a total of 15 doses). For patients with an ongoing CR at month 25 or later,

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maintenance instillations with BCG can be given once a week for 3 weeks at months 25, 31, and 37 for up to 9 additional instillations. Treatment should be discontinued if disease persists after the second induction, if there is recurrence or progression of the disease, or if there is unacceptable toxicity. The maximum treatment duration is 37 months.

Definitions and Measures

- Carcinoma in situ (CIS): This refers to a flat, high-grade lesion confined to the bladder lining.
- BCG: Bacillus Calmette-Guerin
- BCG unresponsive: Defined as persistent disease following adequate BCG therapy [≥ 5 of 6 induction doses plus ≥ 2 doses of maintenance or of 2nd induction], disease recurrence after an initial tumor-free state following adequate BCG therapy, or Ta/T1 disease following a single induction course of BCG.
- ECOG or Eastern Cooperative Oncology Group Performance Status: A scale and criteria used by doctors and researchers to assess how an individual's disease is progressing, assess how the disease affects the daily living abilities of the individual, and determine appropriate treatment and prognosis. This scale may also be referred to as the WHO (World Health Organization) or Zubrod score which is based on the following scale:
 - 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, for example, light house work, 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
- Metastasis: The spread of cancer from one part of the body to another; a metastatic tumor contains cells that are like those in the original (primary) tumor and have spread.
- Non-Muscle Invasive Bladder Cancer (NMIBC) with CIS: Involves flat, high-grade lesions (CIS) that are confined to the bladder lining. CIS is always high-grade and can be present with or without concurrent Ta/T1 papillary tumors.

Approved Indications

- A. Nogapendekin alfa inbakicept-pmln (Anktiva®) is indicated by the FDA to be used with Bacillus Calmette-Guérin (BCG) for the treatment of adult patients with BCG- unresponsive nonmuscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS) with or without papillary tumors.

Other Uses

- A. None.

Utilization Management and Clinical Medical Policy

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Medical Necessity Guidelines:

When a drug is being reviewed for coverage under a member’s medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Nogapendekin alfa inbakicept-pmln (Anktiva®)

A. Criteria For Initial Approval (*Provider must submit documentation [such as office chart notes, lab results, pathology reports, imaging studies, and any other pertinent clinical information] supporting the patient’s diagnosis for the drug and confirming that the patient has met **all** approval criteria.*)

Requests for Nogapendekin alfa inbakicept-pmln (Anktiva®) may be approved if the following criteria are met:

- i. The patient is 18 years of age or older (Label, NCCN 2A); **AND**
- ii. The patient has a diagnosis of BCG-unresponsive, high-risk, non-muscle invasive bladder cancer (NMIBC) (NCCN 2A); **AND**
- iii. with carcinoma in situ (CIS), with or without papillary tumors (Label, NCCN 2A); **AND**
- iv. The patient has an Eastern Cooperative Oncology Group (ECOG) performance status of 0–2; **AND**
- v. The patient has *one* of the following:
 - A. Carcinoma in situ (CIS) with or without papillary tumors (Label, NCCN 2A); **OR**
 - B. Ta/T1 papillary tumors without CIS (NCCN 2A); **OR**
 - C. Cytology-positive, imaging- and cystoscopy-negative, bladder-positive recurrent or persistent disease (NCCN 2A); **AND**
- vi. The patient is using in combination with BCG (Label, NCCN 2A); **AND**
- vii. The patient is using as one of the following:
 - A. Initial management (NCCN 2A); **OR**
 - B. First induction cycle (Label); **OR**
 - C. Second induction cycle (Label); **AND**
 1. It has been at least 3 months since the previous induction cycle; **AND**
 2. There is evidence that complete response was not achieved at month 3 after the initial induction cycle; **OR**
 - D. Maintenance therapy at months 4, 7, 10, 13, and 19 after induction cycle(s) (Label); **OR**
 - E. Maintenance therapy at months 25, 31, and 37 after induction cycle(s) (Label); **AND**
 1. It is documented that the patient has an ongoing complete response at month 25 or later.

B. Criteria For Continuation of Therapy

- i. MMM considers continuation of Nogapendekin alfa inbakicept-pmln (Anktiva®) therapy medically necessary in members requesting reauthorization for an indication listed in Section A above (Criteria for Initial Approval) when there is no evidence of unacceptable toxicity or

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disease progression while on the current regimen. The following information should be submitted for reauthorization:

- A. A current oncology note documenting the patient’s response to treatment showing no progression of disease.
- B. Current cystoscopy findings, urine cytology results, and pathology/biopsy/TURBT findings, as appropriate, showing no disease persistence after second induction, no recurrence or progression, and no unacceptable toxicity.
- ii. Reauthorization of Nogapendekin alfa inbakicept-pmln (Anktiva®) will be considered medically necessary in the following scenarios:
 - A. Administration of a second induction cycle when there is evidence that complete response was not achieved at month 3.
 - B. Maintenance treatment at months 4, 7, 10, 13 and 19.
 - C. For patients with evidence of ongoing complete response at month 25 and later, additional maintenance instillations with BCG may be administered once a week for 3 weeks at months 25, 31, and 37.
- iii. Discontinue for disease persistence after second induction, disease recurrence or progression, unacceptable toxicity, or a maximum of 37 months.

C. Authorization Duration

- i. Initial Approval Duration: Up to 6 months
- ii. Reauthorization Approval Duration: Up to 6 months (maximum duration of therapy is 37 months)

D. Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

- i. Nogapendekin alfa inbakicept-pmln (Anktiva®) may not be approved for individuals with muscle-invasive (T2–T4), locally advanced, metastatic, or extra-vesical (i.e., urethra, ureter, or renal pelvis) urothelial carcinoma.

Utilization Management and Clinical Medical Policy

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Limits or Restrictions:

A. Therapeutic Alternatives

The list below includes preferred alternative therapies recommended in the approval criteria and may be subject to prior authorization.

- i. N/A

B. Quantity Limitations

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. The chart below includes dosing recommendations as per the FDA-approved prescribing information.

Drug	Recommended Dosing Schedule	Quantity Limitations
Nogapendekin alfa inbakicept-pmln (Anktiva®) 400 mcg/0.4 ml solution in a single-dose vial	<ul style="list-style-type: none"> • For induction: 400 mcg administered intravesically with BCG once a week for 6 weeks. A second induction course may be administered if complete response is not achieved at month 3. • For maintenance: 400 mcg administered intravesically with BCG once a week for 3 weeks at months 4, 7, 10, 13 and 19. For patients with an ongoing complete response at month 25 and later, additional maintenance instillations with BCG may be administered once a week for 3 weeks at months 25, 31, and 37. 	<ul style="list-style-type: none"> • Induction: One 400 mcg/0.4mL single dose vial per week, up to a maximum of 6 vials per induction cycle (for a maximum of two induction cycles at least three months apart) • Maintenance: One 400 mcg/0.4mL single dose vial per week, up to a maximum of 3 vials per maintenance cycle.
Exceptions		
None		

Utilization Management and Clinical Medical Policy

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Codes Information:

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

ICD-10 Diagnostic Codes:

Codes	Description
C67.0	Malignant neoplasm of trigone of bladder
C67.1	Malignant neoplasm of dome of bladder
C67.2	Malignant neoplasm of lateral wall of bladder
C67.3	Malignant neoplasm of anterior wall of bladder
C67.4	Malignant neoplasm of posterior wall of bladder
C67.5	Malignant neoplasm of bladder neck
C67.6	Malignant neoplasm of ureteric orifice
C67.7	Malignant neoplasm of urachus
C67.8	Malignant neoplasm of overlapping sites of bladder
C67.9	Malignant neoplasm of bladder, unspecified
D09.0	Carcinoma in situ of bladder
Z85.51	Personal history of malignant neoplasm of bladder.

HCPCS Codes:

Codes	Description
J9028	Injection, nogapendekin alda inbakicept-pml, for intravesical use, 1 mcg [Anktiva]

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Reference Information:

1. Anktiva [package insert]. Culver City, CA; Altor BioSciences, LLC; April 2024. Accessed March 31, 2026.
2. Black P. Treatment of recurrent or persistent non-muscle invasive urothelial carcinoma of the bladder. Topic last updated June 13, 2024. Available at: https://www.uptodate.com/contents/treatment-of-recurrent-or-persistent-non-muscle-invasive-urothelial-carcinoma-of-the-bladder?search=non-muscle%20invasive%20urothelial%20bladder%20cancer%20unresponsive%20to%20BCG&source=search_result&selectedTitle=2%7E150&usage_type=default&display_rank=2#H3121780479
3. FDA Resources for Information | Approved Drugs. FDA approves nogapendekin alfa inbakicept-pmln for BCG-unresponsive non-muscle invasive bladder cancer. April 22, 2024. Available at: <https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-nogapendekin-alfa-inbakicept-pmln-bcg-unresponsive-non-muscle-invasive-bladder-cance>
4. Karim Chamie et al. Final clinical results of pivotal trial of IL-15RαFc super-agonist N-803 with BCG in BCG-unresponsive CIS and papillary non-muscle-invasive bladder cancer (NMIBC). JCO 40, 4508-4508(2022). DOI:10.1200/JCO.2022.40.16_suppl.4508. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/38320011>
5. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). Bladder Cancer. Version 1.2026 — March 16, 2026. Available at: https://www.nccn.org/professionals/physician_gls/pdf/bladder.pdf.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.

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Policy History:

Type of Review	Summary of Changes	P&T Approval Date	UM/CMPC Approval Date
Annual Review	Updated Background Information to align with the current FDA Prescribing Information and NCCN recommendations by revising the service description for consistency with labeled use; updating the background section with current, label-aligned clinical trial and safety language; clarifying the FDA-approved indication and treatment sequencing; revising the Criteria for Initial Approval to reflect use in adult patients with BCG-unresponsive, high-risk non-muscle invasive bladder cancer (NMIBC) treated in combination with BCG, including carcinoma in situ (CIS) with or without papillary tumors, Ta/T1 papillary tumors without CIS, and cytology-positive, imaging- and cystoscopy-negative, bladder-positive recurrent or persistent disease, and incorporating the applicable evidence levels (Label, NCCN 2A); updating continuation language to reflect disease-appropriate surveillance and discontinuation criteria; adding the exclusion for muscle-invasive, locally advanced, metastatic, or extravesical urothelial carcinoma; correcting coding and nomenclature, including the J9028 descriptor and ICD-10 history code; correcting the vial concentration in quantity limitations; and updating the reference section to the current prescribing information and NCCN bladder cancer guideline. Administrative update to incorporate new policy template.	5/1/2026	5/6/2026
Annual Review	Minimal changes; word formatting. Coding changes: J9999 removed, J9028 added Injection, nogapendekin alfa inbakicept-pml, for intravesical use, 1 mcg [Anktiva].	7/17/2025	8/8/2025
Policy Inception	New Medical Policy creation	7/29/2024	8/7/2024