Nogapendekin alfa inbakicept (ANKTIVA)
National Drug Monograph
June 2025
VA Pharmacy Benefits Management Services and National Formulary Committee

The purpose of VA National Formulary Committee drug monographs is to provide a focused drug review for making formulary decisions. The Product Information or other resources should be consulted for detailed and most current drug information.

FDA APPROVAL INFORMATION	**Description / MOA**	Nogapendekin alfa, bound to an IgG1 Fc fusion protein inbakicept (NAI) (N-803), is an interleukin-15 (IL-15) receptor agonist that binds to IL-15 receptors on T cells and NK cells, resulting in proliferation and activation of NK, CD8+, and memory T cells without proliferation of Treg cells, showing antitumor activity with and without BCG.
	Indication Under Review	Use with BCG for BCG-unresponsive nonmuscle invasive bladder cancer (NMIBC) with carcinoma in situ (CIS) with or without papillary tumors.
	Dosage Regimen	Induction: 400mcg intravesically with BCG weekly for 6 weeks (may require 2nd induction). Maintenance: 400mcg intravescially with BCG once a week for 3 weeks at months 4, 7, 10, 13, and 19. If complete response at week 25 or later, may continue maintenance with BCG weekly for 3 weeks months 25, 31, and 37.
	Dosage Forms Under Review	Solution for intravesical use.

EFFICACY CONSIDERATIONS	**Trial**	Quilt-3.032 trial[1]
	Design	P2, SA, MC, BCG-unresponsive,
	Population	3 cohorts: A=CIS ± Ta/T1 B=Ta/T1 with complete resection C= CIS ± Ta/T1 (monotherapy-discontinued)
	Demographics	mAge:71; Male:74-87%; mPrior BCG doses: 12
	Intervention	NAI 400 mcg BCG intravesically weekly x6 =induction; if residual CIS or high-grade Ta may be repeated x1 Month 6: cystoscopy: lack of disease or low-grade Ta- Maintenance if not disease/low-grade Ta: NAI 400 mcg + BCG weekly x 3; repeat at months 3,6; 9; 12; 18; if continued lack of disease/low-grade Ta then NAI + BCG weekly x3 at months 21, 24, 30, and 36
	Comparator	None
	Results	**Cohort A- Complete Response (CR) and Duration of Response (DoR)** **CR 71% ; 13/82 received reinduction; mDoR (CR): 26.6 months** **3, 6, and 12 months CR rates: 55%, 56%, 45%** 24 months PFS: 85.7% 24 months OS: 94.3% Cystectomy rate: Responders 9% (5/58) All 16% (13/82) **Cohort B-Disease-Free Survival (DFS) at 12 months** **mDFS at 12 months: 19.3 months** DFS at 12, 18, 24 months: 55.4%, 51.1%, 48.3% 24 month DFS: 88.8% 24 months OS: 91.7% Cystectomy rate: 7%
	Notes	**NCCN BCG-Unresponsive** Cystectomy-preferred **Other recommended regimens (cat 2A):** Intravescial chemotherapy Pembrolizumab Nadofaragene firadenovec Nogapendekin alpha inbakicept + BCG **VA Oncology Clinical Pathway: BCG Unresponsive** **Alternative options:** After Shared Decision Making: Cystectomy Intravesical chemotherapy Pembrolizumab Nadofaragene firadenovec

P2=phase 2; SA=single arm; MC=multi-center; CIS=carcinoma in situ; Ta=noninvasive papillary disease; T1=tumor invades subepithelial connective tissue; BCG=Bacillus Calmette-Guerin; PFS=progression-free survival; OS=overall survival

SAFETY CONSIDERATI		
	Boxed Warnings	None
	Contraindications	None
	Other Warnings	• Risk of lethal metastatic disease by delaying cystectomy
	Top 5 AEs	Dysuria, hematuria, urinary frequency, urination urgency, urinary track infection
	Drug Interactions	None

VHA PLACE IN THERAPY		
	Potential Use in VHA	• The current gold standard for treatment of non-muscle invasive bladder cancer (NMIBC) is radical cystectomy. The gold standard for non-surgical treatment of NMIBC for patients who are not candidates for cystectomy or who desire to preserve their bladder is BCG. BCG triggers a variety of localized immune responses. • However, there are large unresponsive/recurrence rates after BCG treatment. Also, the BCG shortage continues, with only 1 manufacturer in the United States. • None of the optional non-surgical treatments for BCG unresponsive NMIBC have been compared to each other; the optimal treatment for BCG unresponsive disease has not been established. • Intravesical treatment with either nadofaragene firadenovec or nogapendekin alfa inbakicept plus BCG have demonstrated clinical responses, have less toxicity than systemic treatments, and can be given in the outpatient setting. Alternatively, intravesical treatment with sequential gemcitabine and docetaxel is an alternative but outcomes have only been reported in a retrospective series of patients. • The ongoing BCG shortage may interfere with nogapendekin alfa inbakicept as a therapeutic choice. • For systemic therapy, pembrolizumab offers some durable responses, but has more toxicities.

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References

[1] Chamie K, et al. IL-15 superagonist NAI in BCG-unresponsive non-muscle -invasive bladder cancer. NEJM Evid 2022; 2: DOI: 10.1056/EVIDoa2200167