# HEALTHCARE PROFESSIONAL GUIDE

ANKTIVA® (nogapendekin alfa inbakicept)

1 mg/ mL

**Intravesical Instillation**

Healthcare Professional Guide for healthcare providers to ensure safe use of ANKTIVA in combination with Bacillus Calmette-Guérin (BCG) is indicated for the treatment of adult patients with high-risk BCG-unresponsive non-muscle invasive bladder cancer (NMIBC) of carcinoma in situ (CIS) with or without papillary disease.

- This document is approved by The Executive Directorate of Pharmacovigilance, at SFDA.
- These materials describe recommendations to minimize or prevent important risks of the drug.
- See the ANKTIVA SPC for more information on possible side effects of ANKTIVA.

*This educational material is mandatory as a condition of the marketing authorisation of intravesical ANKTIVA in the treatment of adult patients with high-risk BCG-unresponsive non-muscle invasive bladder cancer (NMIBC) of carcinoma in situ (CIS) with or without papillary disease in order to further minimise important selected risks.*

*Please read this information carefully before prescribing the product.*

**SELECT IMPORTANT SAFETY INFORMATION**

**Very Common side effects (may affect more than 1 in 10 people)**

- Dysuria,
- Pollakiuria,
- Haematuria,
- Micturition urgency,
- Fatigue

**Common side effects (may affect up to 1 in 10 people)**

- Bladder spasm, urinary retention, urinary hesitation, nocturia), lower urinary tract discomfort, urinary incontinence, cystitis noninfective, urinary tract pain, bladder pain, bladder irritation, and urge incontinence,
- Chills,
- Night sweats,
- Nausea,
- Diarrhoea,
- Decreased appetite,
- Pruritus,
- Rash,
- Muscular weakness,
- Penile pain, penile burning sensation, prostatitis, benign prostatic hyperplasia, and vulvovaginal burning sensation,
- Dehydration,
- Vomiting,
- Influenza like illness,
- Asymptomatic bacteriuria, and bacteriuria,
- Anaemia, macrocytic anaemia, blood creatinine increased, leukocytosis, and bacteraemia,
- Dizziness,
- Constipation,
- Myalgia, abdominal pain, lower abdominal pain, and suprapubic pain,
- Arthalgia,
- Sepsis

**PATIENT ALERT CARD**

All patients receiving treatment with ANKTIVA should be given a Patient Alert Card by their healthcare professional. This Patient Alert Card is to be carried by the patient at all times. These materials are to educate patients and their caregivers on the important risks, how to mitigate them, and the need to report any signs or symptoms of these potential adverse events to their treating doctor immediately.

Treating doctors should advise their patients to keep the Patient Alert Card with them at all times and show it to any healthcare professional who may treat them.

This includes any doctor, pharmacist, nurse or dentist they see - not just the specialist who prescribes their ANKTIVA.

To obtain copies of the Patient Alert Card, please contact ImmunityBio Medical Information department at Company contact point below.

**WHAT IS ANKTIVA?**

Nogapendekin alfa inbakicept is a complex consisting of two nogapendekin alfa bound to inbakicept, produced by recombinant DNA technology.

ANKTIVA in combination with Bacillus Calmette-Guérin (BCG) is indicated for the treatment of adult patients with high-risk BCG-unresponsive non-muscle invasive bladder cancer (NMIBC) of carcinoma in situ (CIS) with or without papillary disease.

Method of Administration

- To enhance the traceability of biological medicinal products, the name and batch number of the administered product should be clearly documented.
- For BCG-unresponsive NMIBC, intravesical use only. ANKTIVA should NOT be administered by subcutaneous or intravenous or intramuscular use.
- Do not shake.
- ANKTIVA is recommended at a dose of 400 micrograms. It is administered intravesically as a mixture with BCG (recommended at a dose of 50 mL). The mixture is instilled into the bladder through the urinary catheter.
- After instillation is completed, the catheter is removed. The ANKTIVA and BCG admixture is retained in the bladder for up to 2 hours and then voided.
- Please refer to section 4.2 of the SPC for additional information and comprehensive instructions.
    - For instructions on dilution of the medicinal product before intravesical administration, see section 6.6 of the SPC.

**IMPORTANT RISKS ASSOCIATED WITH ANKTIVA PLUS BCG USE AND HOW TO MITIGATE THEM:**

- **Severe systemic BCG-infections/reactions:**
    - Fever above 39°C that does not resolve within 12 hours despite antipyretic therapy must be considered as systemic BCG infection. Other systemic BCG infection symptoms may include malaise and/or influenza-like symptoms (fever, rigors, malaise, myalgia, and chills) and may accompany the localized, irritative bladder symptoms. Systemic BCG infections may also be manifested by pneumonitis, hepatitis, cytopenia, vasculitis, infective aneurysm, or sepsis after a period of fever and malaise during which symptoms progressively increase. Such presentations require immediate clinical confirmatory diagnosis to assess for systemic BCG infection. See Summary of Product Characteristics for the specific BCG being used.
    - Careful clinical monitoring of all patients after each intravesical BCG instillation is required to detect early signs of systemic BCG infection.
    - Patients with symptoms of therapy-induced systemic BCG infection should be adequately treated with anti-tuberculosis drugs according to treatment regimens used for tuberculosis infections. In all cases of systemic BCG infections, further treatment with ANKTIVA plus BCG must be discontinued.
- **Risk of muscle invasive and metastatic bladder cancer with delayed cystectomy:**
    - If patients with NMIBC CIS with or without papillary are medically eligible for cystectomy and do not have a complete response (absence of disease or low-grade Ta) to treatment after an induction course of ANKTIVA with BCG at the 12 weeks assessment, re-induction is indicated or reconsider cystectomy. The risk of developing muscle invasive or metastatic bladder cancer, increases the longer cystectomy is delayed in the presence of persisting CIS with or without papillary NMIBC.
    - Of the 100 evaluable patients with BCG-unresponsive CIS treated with ANKTIVA with BCG in QUILT-3.032, 10% (n = 10), (0.049, 0.176), progressed to muscle invasive (T2 or greater) bladder cancer, including 2 during the treatment period.
- **Use in pregnancy:** There were no reported pregnancies while on treatment with ANKTIVA. Women of childbearing potential have to use effective contraception during treatment and for 1 week after the last dose. Treatment is not recommended during pregnancy and in women of childbearing potential not using effective contraception.
- **Breast-feeding:** No effects on the breastfed newborn/infant are anticipated since the systemic exposure of the breast-feeding woman to nogapendekin alfa inbakicept (ANKTIVA) following intravesical administration is negligible (below the limit of quantitation). There are no data on the presence of nogapendekin alfa inbakicept (ANKTIVA) in human milk, or the effects on the breastfed child, or on milk production. Treatment can be used during breast-feeding.
- **Fertility:** There are no clinical data on the effects of treatment on fertility. No effects on fertility are expected since systemic exposure to nogapendekin alfa inbakicept following intravesical administration is below the limit of quantitation.

**CALL FOR REPORTING**

- Consult the SPC before prescribing, preparing or administering ANKTIVA.
- For full information on all possible adverse events please see the SPC.
- Adverse reactions should also be reported to ImmunityBio Medical Information via the Company contact point that is provided below.
- In case of any adverse events – including any possible side effects not listed in the leaflet – or product complaints associated with the use of ANKTIVA, please talk to the HCP or report the details in accordance with the national requirements via the national spontaneous reporting systems to:

***Local Agent Contact:***
Contact ImmunityBio at our agent (Cigalah Healthcare Company)
**Address:** Othman bin Affan Street, Mammoun Building
Ground Floor, Pharmacovigilance Department.
**Postal Address:** P O Box 19435 Jeddah 21435 Saudi Arabia.
**Hot line:** +966-539455825
**Office Tel:** +966-12-6148000

To report Adverse Events/Product Complaint or any Medical Information Inquiries,
Please contact us at **Email**: Drug-Safety@Cigalah.com.sa

The National Pharmacovigilance Centre at Saudi Food and Drug Authority (SFDA):
Land Line: 19999
**Email:** npc.drug@sfda.gov.sa
**Website:** https://ade.sfda.gov.sa