HEALTHCARE PROFESSIONAL GUIDE

▼ANKTIVA® (nogapendekin alfa inbakicept)

2 mg/ mL

Subcutaneous Injection

Healthcare Professional Guide for healthcare providers to ensure safe use of ANKTIVA in combination with immune checkpoint inhibitors for the treatment of adult patients with metastatic non-small cell lung cancer (NSCLC) with disease progression on or after standard of care (immune checkpoint inhibitors alone or in combination with chemotherapy). Patients with actionable genomic alteration should have disease progression on approved therapy for these alterations, before using ANKTIVA in combination with immune checkpoint inhibitors.

- 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 subcutaneous ANKTIVA in the treatment of patients with metastatic non-small cell lung cancer with disease progression on or after standard of care (immune checkpoint inhibitors alone or in combination with chemotherapy) in order to further minimise important selected risks.

Please read this information carefully before prescribing the product.

SELECT IMPORTANT SAFETY INFORMATION

- **<u>Very common side effects (may affect more than 1 in 10 people)</u>**
  - Injection site reactions (redness, pain, itching, swelling),
  - Chills,
  - Fatigue,
  - Pyrexia,
  - Nausea,
  - Flu-like illness,
  - Loss of appetite

- **<u>Common side effects (may affect up to 1 in 10 people)</u>**
  - Vomiting,
  - Diarrhea,
  - Dizziness,
  - Headache,
  - Rash or skin redness,
  - Myalgia and arthralgia,
  - Increased ALT and AST,
  - Anemia,
  - Hypotension

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 is indicated in combination with immune checkpoint inhibitors for the treatment of adult patients with metastatic NSCLC with disease progression on or after standard of care (immune checkpoint inhibitors alone or in combination with chemotherapy). Patients with actionable genomic

alteration should have disease progression on approved therapy for these alterations, before using ANKTIVA in combination with immune checkpoint inhibitors.

This indication is approved under accelerated approval based on the increase of ALC associated with overall survival in single arm study. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory clinical trials.

Limitation of Evidence of Benefit:

- Insufficient evidence of benefit for the use of ANKTIVA in combination with immune checkpoint inhibitors in NSCLC with baseline ALC < $1.0 \times 10^3/\mu L$.
- Experience is limited to patients with a baseline absolute lymphocyte counts (ALC) ≥ $1.0 \times 10^3/\mu L$ who are maintained above this level after treatments.

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 metastatic NSCLC, subcutaneous use only. ANKTIVA should NOT be administered by intravesical, intravenous, or intramuscular use.
- Do not shake.
- ANKTIVA is recommended at a fixed dose of 1 mg, administered subcutaneously, using standard technique.
- Please refer to section 4.2 of the SPC for additional information and comprehensive instructions.
    - For instructions on subcutaneous administration, see section 6.6 of the SPC.

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

Injection Site Reactions (Including Cellulitis):

- Risk factors/clinical context: Subcutaneous administration is associated with local injection site reactions (e.g., erythema, pain, pruritus, swelling). Risk may be increased by improper injection technique, repeated injection at the same site, or pre-existing dermatologic conditions.
- Risk mitigation in clinical development: Monitoring of local tolerability; symptomatic management; and assessment of clinically significant local reactions (e.g., cellulitis) including treatment interruption/discontinuation as clinically indicated.

Flu-Like Symptoms:

- Risk factors/clinical context: Transient chills, pyrexia and influenza-like symptoms are consistent with immune activation and were commonly observed with NAI +CPI. Risk may be higher early in treatment or in patients with comorbidities (e.g., frailty, cardiopulmonary disease).
- Risk mitigation in clinical development: Vital sign monitoring and supportive care (e.g., antipyretics) as needed, clinical evaluation to rule out infection, dose delay/withholding per protocol for clinically significant events.

Gastrointestinal Adverse Events (Nausea, Diarrhoea; Colitis):

- Risk factors/clinical context: Nausea, diarrhoea, vomiting and abdominal pain may occur with NAI + CPI. Given concomitant CPI use, immune-mediated colitis remains an important differential diagnosis for persistent or severe diarrhoea.
- Routine risk minimisation (Saudi SPC/label): Gastrointestinal adverse reactions (e.g., nausea, diarrhoea, vomiting, abdominal pain; colitis) are described for systemic administration. Clinicians should manage suspected immune-mediated GI toxicity per established CPI guidance when appropriate.

Hepatic Enzyme Elevation:

- Risk factors/clinical context: Transaminase and other hepatic laboratory elevations were reported with NAI + CPI. Patients with hepatic metastases, pre-existing liver disease, viral hepatitis or concomitant hepatotoxic medications may be at increased risk.
- Risk mitigation in clinical development: Periodic laboratory monitoring (including liver function tests) and management of clinically significant abnormalities, including treatment interruption and appropriate diagnostic work-up.

Respiratory Failure (including fatal cases; Treatment Related):

- Risk factors/clinical context: Pneumonitis and respiratory failure have been reported with NAI + CPI. Underlying lung disease, prior thoracic radiotherapy, pulmonary infection, and prior CPI-related pneumonitis may increase risk.
- Risk mitigation in clinical development: Monitoring for respiratory symptoms; prompt evaluation(including imaging and infection work-up) for suspected pneumonitis; treatment interruption and management per standard CPI immune-related pneumonitis guidance (including corticosteroids) as clinically indicated.

Hypovolemic Shock (Rare, Treatment Related):

- Risk factors/clinical context: Hypotension and rare serious events (including hypovolaemic shock) have been reported. Contributing factors may include dehydration, infection, concurrent medications, or acute systemic inflammatory responses.

Risk mitigation in clinical development: Vital sign monitoring; assessment and correction of volume status; evaluation for infection; and treatment interruption/discontinuation for clinically significant hypotension or shock per protocol and standard of care.

Pericardial Effusion / Valvular Dysfunction (Rare; Treatment Related):

- Pericardial effusion and tricuspid valve incompetence were each reported as NAI-related serious TEAEs (1% each) and as grade ≥3 NAI-related events (1% each) in the NSCLC safety population.
- Risk factors/clinical context: Cardiac events including pericardial effusion were reported rarely with NAI + CPI. Underlying cardiac disease, malignancy-related effusions, and immune-mediated pericarditis/pericardial effusion in the context of CPI therapy are potential contributing factors.

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:

There are no data on the presence of ANKTIVA in either animal or human milk or its effects on the breastfed child or on milk production. Because of the potential for serious adverse reactions in breastfed children, women are advised not to breastfeed during treatment with ANKTIVA and for 2 weeks after the final dose.

Fertility:

There are no clinical data on the effects of treatment on fertility.

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