Anktiva®

(nogapendekin alfa inbakicept-pmln)

400 mcg/0.4 mL, solution for intravesical instillation

Summary of Product Characteristics

Date of Preparation: August 2026. UK-Onc-Ankt-01414.

▼ **This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.**

1. NAME OF THE MEDICINAL PRODUCT

ANKTIVA 400 microgram concentrate for intravesical suspension

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each single-dose vial contains 400 micrograms nogapendekin alfa inbakicept in 0.4 mL solution (1 mg/mL).

Nogapendekin alfa inbakicept is an interleukin-15 (IL-15) receptor superagonist. It is a soluble complex consisting of two nogapendekin alfa units (a human IL-15N72D variant) bound to a single inbakicept unit [a dimeric human IL-15Rα sushi domain/ human IgG1 Fc fusion protein].

Nogapendekin alfa inbakicept is produced in Chinese hamster ovary (CHO) cells by recombinant DNA technology.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Concentrate for intravesical suspension.

Clear to slightly opalescent, colourless to slightly yellow solution, pH 7.4.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

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

4.2 Posology and method of administration

For preparation of the BCG ANKTIVA admixture see section 6.6.

Posology

Induction therapy

ANKTIVA is recommended at a dose of 400 micrograms; 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.

Maintenance therapy

After BCG and ANKTIVA induction therapy, ANKTIVA is recommended at a dose of 400 micrograms administered intravesically 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 complete response at month 25 and later, maintenance instillations with BCG may be administered once a week for 3 weeks at months 25, 31, and 37 for a maximum of 9 additional instillations.

The recommended duration of treatment is until disease persistence after second induction, disease recurrence or progression, unacceptable toxicity, or a maximum of 37 months.

Special populations

Elderly

No dose adjustments are necessary in the elderly population.

Of the total number of patients in clinical studies of ANKTIVA for BCG unresponsive NMIBC, 84% were 65 years of age or older and 40% were 75 years or older. Clinical studies of ANKTIVA did not include sufficient numbers of younger adult patients to determine if patients 65 years of age and older respond differently than younger adult patients.

Paediatric population

The safety and efficacy of ANKTIVA in children have not been established.

Method of administration

For instructions on dilution of the medicinal product before administration, see section 6.6.

Administering the medicinal product

The admixture of ANKTIVA in combination with BCG is instilled into the bladder via a catheter. After instillation is complete, the catheter is removed.

The ANKTIVA in combination with BCG admixture is retained in the bladder for 2 hours and then voided. Patients unable to retain the suspension for 2 hours should be allowed to void sooner, if necessary. Do not repeat the dose if the patient voids before 2 hours.

See BCG Summary of Product Characteristics for information on retention in the bladder and patient positioning during bladder instillation.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

For Intravesical Use Only. Do NOT administer ANKTIVA by subcutaneous or intravenous or intramuscular routes.

Risk of metastatic bladder cancer with delayed cystectomy

Delaying cystectomy in patients with BCG-unresponsive CIS could lead to development of muscle invasive or metastatic bladder cancer, which can be lethal. The risk of developing muscle invasive or metastatic bladder cancer increases the longer cystectomy is delayed in the presence of persisting CIS.

Of the 77 evaluable patients with BCG-unresponsive CIS treated with ANKTIVA with BCG in QUILT-3.032, 10% (n = 8) progressed to muscle invasive (T2 or greater) bladder cancer, including 7 during the treatment period. Three patients had progression determined at the time of cystectomy. The median time between determination of persistent or recurrent CIS and progression to muscle-invasive disease was 107 days (range: 0 – 210).

If patients with CIS do not have a complete response to treatment after a second induction course of ANKTIVA with BCG, reconsider cystectomy.

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Excipients

This medicinal product contains less than 1 mmol potassium (39 mg) per dose, i.e. essentially “potassium-free”.

This medicinal product contains less than 1 mmol sodium (23 mg) per dose, i.e. essentially “sodium-free”.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.

4.6 Fertility, pregnancy, and lactation

Women of childbearing potential/contraception

The pregnancy status in women of childbearing potential has to be verified prior to initiating treatment with ANKTIVA. Advise females of reproductive potential to use effective contraception during treatment with ANKTIVA and for 1 week after the last dose.

Pregnancy

No effects during pregnancy are anticipated, since systemic exposure to nogapendekin alfa inbakicept following intravesical administration is below the limit of quantitation.

Systemic exposure of nogapendekin alfa inbakicept (ANKTIVA) following intravesical administration of the approved dosage of ANKTIVA was below the limit of quantitation (see section 5.2). Based on its mechanism of action, ANKTIVA may cause fetal harm when administered to a pregnant woman if systemic exposure occurs (see section 5.1). There are no available data on ANKTIVA use in pregnant women to inform a drug-associated risk. Animal reproductive and developmental toxicity studies have not been conducted with nogapendekin alfa inbakicept.

Breast-feeding

No effects on the breastfed newborn/infant are anticipated since the systemic exposure (see section 5.2) 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. ANKTIVA can be used during breast-feeding.

Fertility

Systemic exposure of nogapendekin alfa inbakicept (ANKTIVA) following intravesical administration of the approved dosage of ANKTIVA was below the limit of quantitation (see section 5.2). No clinical data are available on the possible effects of ANKTIVA on fertility. There were no notable effects in the male and female reproductive organs in rats and monkeys administered ANKTIVA subcutaneously and intravenously based on the 13-week and the 1-month repeat-dose toxicity studies, respectively (see section 5.3).

4.7 Effects on ability to drive and use machines

ANKTIVA has no or negligible influence on the ability to drive and use machines since systemic absorbption is below the limit of quantification.

4.8 Undesirable effects

Summary of the safety profile

The most common adverse reactions were those related to bladder instillation: dysuria, haematuria, pollakiuria, and micturition urgency. Also common was fatigue.

The safety profile presented below is based on data obtained from clinical trial QUILT-3.032 where ANKTIVA in combination with BCG was administered to subjects (aged 50 to 91 years) (Table 1).

The safety profile of ANKTIVA plus BCG was comparable to that of BCG monotherapy.

Tabulated list of adverse reactions

Adverse reactions reported are listed according to the following frequency: very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1 000 to < 1/100); rare (≥ 1/10 000 to < 1/1 000); very rare (< 1/10 000) and not known (cannot be estimated from the available data). Adverse drug reactions (ADRs) are organised by MedDRA System Organ Class (SOC). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

Table 1 summarises the incidence of treatment related adverse events, from trial QUILT-3.032, which represents the total subjects treated with ANKTIVA and BCG.

Table 1: Adverse reactions reported in clinical trials with ANKTIVA in combination with BCG

Infections and infestations	
Common	Urinary tract infection, Cystitis
Metabolism and nutrition disorders	
Common	Decreased appetite, Dehydration
Nervous system disorders	
Common	Headache
Respiratory, thoracic and mediastinal disorders	
Common	Dyspnoea
Gastrointestinal disorders	
Common	Diarrhoea, Nausea, Abdominal pain lower, Vomiting
Skin and subcutaneous tissue disorders	
Common	Night sweats, Pruritus, Rash
Musculoskeletal and connective tissue disorders	
Common	Arthralgia, Muscular weakness, Myalgia, Arthritis, Flank pain, Pain in extremity
Renal and urinary disorders	
Very Common	Dysuria, Pollakiuria, Haematuria, Micturition urgency
Common	Bladder spasm, Cystitis noninfective, Nocturia, Urinary tract pain, Incontinence, Urinary incontinence, Urinary retention, Urinary tract discomfort, Bladder irritation, Lower urinary tract symptoms, Polyuria, Urge incontinence, Urinary hesitation, Urine abnormality
Reproductive system and breast disorders	
Common	Prostatitis, Benign prostatic hyperplasia, Penile discharge, Penile pain, Vulvovaginal burning sensation
General disorders and administration site conditions	
Very common	Fatigue
Common	Chills, Pyrexia, Influenza like illness, Pain, Suprapubic pain
Investigations	
Common	Bacterial test positive, Blood urine present, Blood creatinine increased, Cells in urine, Blood urea increased, Glomerular filtration rate decreased

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via:

Yellow Card Scheme
Website: http://www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

There are no data indicating that an overdose may lead to any other symptoms than the described undesirable effects.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Interleukins, ATC code: L03AC03

Mechanism of action

Nogapendekin alfa inbakicept is an IL-15 receptor superagonist. IL-15 signals through a heterotrimeric receptor that is composed of the common gamma chain (γc) subunit, the beta chain (βc) subunit, and the IL-15-specific alpha subunit, IL-15 receptor α. IL-15 is trans-presented by the IL-15 receptor α to the shared IL-2/IL-15 receptor (βc and γc) on the surface of CD4+ and CD8+ T cells and NK cells.

Binding of nogapendekin alfa inbakicept to its receptor, as a lymphocyte stimulating agent, results in proliferation and activation of NK, CD8+, and memory T cells without proliferation of immuno-suppressive Treg cells. In vivo, intravesicular nogapendekin alfa inbakicept alone or in combination with BCG showed anti-tumour activity when compared to BCG alone, in a carcinogen-induced model of bladder cancer in immunocompetent rats.

Pharmacodynamic effects

The exposure-response relationship and time course of pharmacodynamic response for the safety and effectiveness of nogapendekin alfa inbakicept have not been fully characterised.

Immunogenicity

There is insufficient information to characterize the anti-drug antibody response to ANKTIVA and the effects of anti-drug antibodies on pharmacokinetics, pharmacodynamics, safety, or effectiveness of nogapendekin alfa inbakicept (ANKTIVA) products.

Clinical efficacy and safety

The efficacy of ANKTIVA was evaluated in QUILT-3.032 (NCT03022825), a single-arm, multicentre trial in 77 adults with BCG-unresponsive, high-risk, NMIBC with CIS with or without Ta/T1 papillary disease following transurethral resection.

BCG unresponsive high-risk NMIBC CIS was defined as persistent or recurrent CIS alone or with Ta/T1 disease within 12 months of completion of adequate BCG therapy. Adequate BCG therapy was defined as administration of at least 5 of 6 doses of an initial induction course plus either of at least 2 of 3 doses of maintenance therapy or at least 2 of 6 doses of a second induction course. Prior to treatment, all patients with Ta or T1 disease had undergone transurethral resection of bladder tumour (TURBT) to remove all resectable disease. Residual CIS not amenable to complete resection, fulguration, or cauterization was permitted. The trial excluded patients with history of or evidence of muscle invasive (i.e., T2, T3, T4), locally advanced, metastatic, and/or extra-vesical (i.e., urethra, ureter, or renal pelvis) bladder cancer.

Patients received 400 micrograms ANKTIVA with BCG weekly for 6 consecutive weeks during the induction treatment period and then once a week every 3 weeks at 4, 7, 10, 13, and 19 months for patients with no or low-grade disease. Patients with persistent CIS or high-grade Ta disease at 3 months were eligible to receive a second induction course. Patients with ongoing CR at 25 months were eligible to receive additional instillations once a week every 3 weeks at months 25, 31, and 37. Assessment of tumour status was performed every 3 months for up to two years. Assessment for ongoing response beyond month 24 was per local community standards. Random or cystoscopy directed biopsies were required within the first 6 months after treatment initiation. The major efficacy outcome measures were complete response (CR) at any time (as defined by negative results for cystoscopy [with TURBT/biopsies as applicable] and urine cytology) and duration of response.

The median age of patients was 73 years (range, 50 – 91 years); 86% were male; race was White (90%), Black (6%), Asian (1%), American Indian or Alaska Native (1%), or Unknown (1%); and patients had baseline ECOG performance status of 0 (83%) or 1 (17%).

Tumour characteristics at study entry were CIS without Ta/T1 papillary disease (69%), CIS with Ta papillary disease (21%) or CIS with T1 +/- Ta papillary disease (10%). Baseline high-risk NMIBC disease status was 43% refractory and 57% relapsed. The median number of prior BCG doses received was 12 doses (range: 8 – 45 doses); 13% received partial-dose prior BCG. Baseline cystoscopy imaging modality was white light (57%), blue light or narrow band imaging (40%), and unknown (3%).

Efficacy results are summarised in Table 2. Thirty-one percent (n = 24) of patients received a second induction course.

Table 2: Efficacy results in QUILT-3.032

	ANKTIVA with BCG (n=77)
Complete response rate (95% CI)	**62% (51, 73)**
Duration of response[a]	
Range in months	**0.0, 47.0+ months**
% (n) with duration ≥ 12 months	**58% (28)**
% (n) with duration ≥ 24 months	**40% (19)**

+Denotes ongoing response
[a] Based on 48 patients that achieved a complete response at any time; reflects period from the time complete response was achieved.

Paediatric population

The licensing authority has waived the obligation to submit the results of studies with nogapendekin alfa inbakicept in all subsets of the paediatric population in the treatment of malignant bladder neoplasms (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

Systemic exposure of nogapendekin alfa inbakicept (ANKTIVA) was less than 100 pg/mL following the approved recommended dosage in all patients. This was below the lower limit of quantitation in all patients.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of toxicity since the systemic exposure to nogapendekin alfa inbakicept (ANKTIVA) following intravesical administration is negligible.

The safety of nogapendekin alfa inbakicept (ANKTIVA) was evaluated by systemic routes of exposure in 1-month repeat-dose toxicity studies in four mouse and one monkey studies and in a 13-week repeat-dose toxicity study in rats. Mice were administered four intravenous or subcutaneous doses of ANKTIVA at dose levels ranging from 0.1 to 4.0 mg/kg. The lowest no observed effect dose level was 0.1 mg/kg. Rats were administered subcutaneous doses (0.1, 0.3, 1.0 mg/kg/day) once every other week for 13 weeks. The no-observed-adverse-effect (NOAEL) level was 1.0 mg/kg. Monkeys were administered intravenous doses of 0.03 and 0.1 mg/kg once a week in the 1-month study, followed by a 2-week treatment-free period. No findings of toxicological significance were observed and the NOAEL was 0.03 mg/kg in monkeys.

Animal fertility studies have not been conducted with nogapendekin alfa inbakicept (ANKTIVA). In pivotal 13-week and 1-month repeat-dose toxicology studies in rats and monkeys, respectively, there were no notable effects in the male and female reproductive organs. However, the monkeys were not sexually mature.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Disodium phosphate
Potassium dihydrogen phosphate
Sodium chloride
Water for injections
Hydrochloric acid (for pH adjustment)
Sodium hydroxide (for pH adjustment)

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.

6.3 Shelf life

36 months.

If the admixture of ANKTIVA in combination with BCG is not used immediately, store refrigerated at 2°C to 8°C and use within 2 hours.

6.4 Special precautions for storage

Store in a refrigerator (2 °C-8 °C).
Do not freeze.
Store in the original package in order to protect from light.

6.5 Nature and contents of container

0.4 mL solution in a clear type I glass vial with a chlorobutyl elastomer stopper and an aluminium alloy seal containing a yellow plastic polypropylene flip-off cap.

Pack size: 1 single-dose vial.

6.6 Special precautions for disposal

For single use only.

Do not shake.

Before administration, visually inspect the solution for particulate matter and discolouration prior to administration. Discard the vial if visible particles or discolouration are observed.

Draw 0.4 mL of ANKTIVA into a small syringe and using aseptic technique add to the saline containing the BCG suspension that has been prepared following the instructions provided in the Summary of Product Characteristics for BCG. Mix the suspension gently. Using a 60-mL syringe connected to an appropriate size needle, withdraw the ANKTIVA BCG mixture to a final volume of 50 mL.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

ImmunityBio Ireland Limited
6th Floor, 2 Grand Canal Square
Dublin 2, D02 A342
Ireland

8. MARKETING AUTHORISATION NUMBER(S)

PL 59840/0001

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

04/07/2025

10. DATE OF REVISION OF THE TEXT

06/02/2026

Notes

Notes

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard or search MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to Accord-UK LTD on 01271 385257 or email accord.pv@tepsivo.com

Anktiva®

(nogapendekin alfa inbakicept-pmln)

400 mcg/0.4 mL, solution for intravesical instillation

Date of Preparation: August 2026. UK-Onc-Ankt-01414.