This package insert follows the Pharmaceuticals, Medical devices and Other Therapeutic Products Act of Japan.

In Vitro Diagnostics
Certification No. 224ADAMX00107000

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This package insert must be read carefully prior to use.

Arbekacin assay kit
(Classification No.: 42929000)

Nanopia TDM Arbekacin

General Precautions

1. This product is for in vitro diagnostic use, and must not be used for any other purposes.
2. Clinicians should make a comprehensive clinical decision based on assay results in conjunction with clinical symptoms and other examination results.
3. Please read carefully the "PRECAUTIONS" section, particularly under "Effects on Laboratory Tests" of the package insert of each drug, for information on the influence to the assay result that medications administered to the patient have. Please also read carefully the "2) Cross-reactivity," under "2. Interfering Substances," in the "Procedural Precautions" section, as well as "2. Precautions for Assessment" in the "Assessment of Assay Results" section, of this package insert.
4. This product should be used only as directed in this package insert. Reliability of results cannot be guaranteed if there are any deviations from the instructions in this package insert.
5. If the reagent accidentally comes in contact with eyes and/or mouth, rinse immediately with ample water as first aid, and consult the doctor if required.
6. Carefully read the operating instructions for each type of automated analyzers prior to using this product. Parameters for each type of analyzers are available, and can be requested from SEKISUI MEDICAL CO., LTD. if required.
7. Perform a quality control test prior to assay to ensure accuracy.
8. ABK Antibody Solution 1 contains human-derived components that have been confirmed to be negative for HBs antigens, HIV antibodies, and HCV antibodies. However, handle this reagent with great care in the same manner as the samples, because it is potentially infectious.

Description (Kit Components)

Component: Ingredients
ABK Antibody Solution 1: Anti-arbekacin mouse monoclonal antibody
ABK Latex Reagent 2: Arbekacin-coated latex

Intended Use

Measurement of arbekacin in serum or plasma

Arbekacin is an aminoglycoside antimicrobial agent. It is resistant to various aminoglycoside-inactivating enzymes and exhibits strong antimicrobial activity against staphylococci, including methicillin-resistant Staphylococcus aureus (MRSA), as well as against Pseudomonas aeruginosa. Because of its strong antimicrobial activity against staphylococci, arbekacin is expected to be useful for MRSA infection.
Clinically significant adverse reactions to arbekacin include shock, convulsions, eighth cranial nerve disorders, and acute renal failure. To avoid these adverse reactions, monitoring the blood concentration of arbekacin after administration is recommended.[1)] Monitoring is also important to promote the appropriate use of antimicrobial agents based on PK/PD[2)].

Assay Principle

1. Assay Principle

When a certain amount of anti-arbekacin antibody is added and reacted with a sample, consumption of the antibody depends on its content in the sample. When arbekacin-coated latex is added, residual anti-arbekacin antibody reacts with the latex and forms aggregates.
Since the extent of aggregation depends on the arbekacin concentration in the sample, the arbekacin concentration can be determined by measuring aggregation as the absorbance.

Sample (arbekacin) + Anti-arbekacin antibody
⟶ Antigen-antibody reaction

Unreacted anti-arbekacin antibody + arbekacin-coated latex
⟶ Aggregation by antigen-antibody reaction

2. Features

1) Because an anti-arbekacin monoclonal antibody is used, this product shows excellent sensitivity and accuracy.
2) Liquid reagents, ready-to-use.
3) It can be measured using the automated analyzers commonly used.

Procedural Precautions **

1. Properties of Samples and Sampling Methods

1) Samples
Serum and plasma (EDTA plasma) may be used.
2) Storage of samples
(1) After separation of serum (plasma), samples may be stored for up to 7 days in a refrigerator. If samples cannot be measured within 7 days of serum (plasma) separation, store them at −30°C or lower and measure them within 14 days. Stored samples should be brought to room temperature (15–30°C) before use.
(2) Arbekacin may undergo degradation if there is a high concentration of a β-lactam antibiotic in the sample. Perform assay immediately after collection of blood or store the sample frozen.[3)]
(3) Samples may be frozen and thawed up to twice.

3) Caution must be exercised, because a separating agent, etc. in the blood collection tube may affect assay values.[4)]
4) Sampling should be performed after removing insoluble matter from the sample. Very cloudy specimens should be centrifuged before assay.

2. Interfering substances

1) Assay results are not affected by unconjugated bilirubin (up to 19.4 mg/dL), conjugated bilirubin (up to 20.3 mg/dL), hemoglobin (up to 491 mg/dL), formazin turbidity (up to 1410 FTU), or rheumatoid factors (up to 500 IU/mL).
2) Cross-reactivity
The following table summarizes the cross-reactivity between arbekacin and other drugs.

Substance	Concentration tested (μg/mL)	Cross-reactivity (%)
Amikacin	15	> 70
Gentamicin	11	ND
Kanamycin A	61	1
Kanamycin B	61	ND
Neomycin	60	ND
Netilmicin	20	–3
Sisomicin	60	–1
Streptomycin	150	ND
Teicoplanin	150	0
Tobramycin	25	2
Vancomycin	100	0
Isepamicin	330	0

ND: Not Detectable

3. Others

1) Always use Arbekacin Calibrator for Nanopia for calibration.
2) Precautions for assay range
If the arbekacin concentration in the sample exceeds the measurement range, dilute the sample with arbekacin-free serum, and perform re-measurement.

Dosage/Administration (Assay Procedure) *

1. Preparation of reagents

Reagent (1): ABK Antibody Solution 1 is ready to use.
Reagent (2): ABK Latex Reagent 2 is ready to use.
Before using this product, gently invert the ABK Latex Reagent 2 bottle to mix it thoroughly, and check that there are no bubbles.

2. Assay Procedure

This product is compatible with various types of automated analyzer. An example of the assay procedure is indicated below.

Sample 3.0 μL + Reagent (1) 105 μL → 37°C Approx. 5 min → Reagent (2) 120 μL → 37°C Approx. 1 min → Measurement (Absorbance I※) → 37°C Approx. 4 min → Measurement (Absorbance II※) → Calculation of concentration

※Absorbance I and II: Absorbance at 700 nm
Calibration material: Arbekacin Calibrator for Nanopia (Manufacture's assigned value)

Assessment of Assay Results *

1. Reference standard range

It has been reported that the maximum blood concentration of arbekacin is related to its efficacy and the recommended therapeutic range is 15–20 μg/mL, but there is no clear evidence for the upper limit.[3] It has also been reported that the risk of adverse reactions increases with an increase in the frequency of abnormally high maximum and minimum blood concentrations, and that the trough value should be < 1–2 μg/mL from the standpoint of protecting renal function.[3] Since the therapeutic concentrations and toxic concentrations may overlap, interpretation of assay results should also be based on the patient's clinical findings and other examination results. It is recommended that the blood concentration of arbekacin should be measured in a sufficient number of samples for statistical analysis and that its therapeutic range should be determined by each medical institution.

2. Precautions for Assessment

1) There may be reactions or interfering reactions with non-target substances. If assay results appear to be unreliable, repeat the measurement (if necessary, after dilution) or try another analytical methods.
2) This product shows cross-reactivity with amikacin. Accurate assay values cannot be obtained with samples from patients receiving amikacin.

Performance

1. Sensitivity

1) Absorbance of standard solution (0.0 μg/mL) is 3200 (Abs. × 10000).
2) The ratio between the absorbance with the standard solution (0.0 μg/mL) and that with another standard solution (2.0 μg/mL) is 55–85%.

2. Accuracy: 80–120 % of the expected assay value

3. Within-run Reproducibility:

Coefficient of variation ≤ 10 %
(Test methods used for 1.–3. are in-house methods.)

4. Measurement Range[5)]: (On Hitachi 7170 automated analyzer)

Minimum detection sensitivity was 0.6μg/mL.
Upper measurement limit is 30.0μg/mL.

5. Correlation[5)]

Serum N=70 r=0.997 y=0.98x–0.25
Control method: Approved in vitro diagnostic (fluorescence polarization immuno assay)

6. Standard Material

Arbekacin (in-house standard material)

Precautions for Use or Handling

1. Precautions for Handling (to Ensure Safety)

1) All samples used in the test should be handled as a material possibly infected with HIV, HBV, HCV, or other viruses. To prevent infection, use disposable gloves and avoid mouth pipetting

during the test.
2) Sodium azide is added as an antiseptic agent in this product. Therefore, if the reagent comes in accidentally contact with eyes, mouth or skin, rinse immediately with ample water as first aid, and consult the doctor if required.

2. Precautions for use

1) This product should be stored as directed, without freezing. Freezing can deteriorate the reagents, which can produce inaccurate results. Therefore, avoid using the reagents which have been previously frozen.
2) Do not use expired reagents. Use of such reagents cannot guarantee the reliability of measurement values.
3) Do not replenish the reagents.
4) After completion of measurement, this product should be tightly stoppered and stored in a refrigerator.
5) Do not mix materials from different kit lot numbers.
6) Do not perform the assay under direct sunlight

3. Precautions for Disposal

1) Before disposal, used samples and their containers must be immersed in sodium hypochlorite solution at a concentration of greater than 0.1% for longer than 1 hour or autoclaved at 121ºC for 20 minutes.
2) To prevent infections from spilled samples or solutions containing samples, wipe the spilled area thoroughly with disinfectants such as sodium hypochlorite solution at a concentration of greater than 0.1%.
3) The reagents and treated samples should be discarded as medical waste or industrial waste according to the waste disposal regulations.
4) The reagents should be disposed of in accordance with the Water Pollution Control act or related regulations.
5) Sodium azide has been added as an antiseptic agent in this product. It can react with lead or copper pipes to produce the highly explosive metal azide. Therefore, the reagent should be flushed with large amounts of water during disposal.

4. Other precautions

Do not use the containers for other purposes.

Storage and Shelf Life *

1. Storage temperature: 2–8°C
2. Shelf life: 1 year from the date of manufacture (The expiration date is printed on the outer package.)

Packaging

Name		Package
Nanopia TDM Arbekacin	ABK Antibody Solution 1	1 × 11 mL
	ABK Latex Reagent 2	1 × 12.5 mL

References *

1) Package insert of Habekacin Injection 25mg, 75mg, 100mg, and 200mg. Japanese.
2) Kizu J. et al.: Jpn J Chemother, 58(4), 2010. Japanese.
3) Japanese Society of Chemotherapy, Japanese Society of Therapeutic Drug Monitoring: A revised edition of guidelines for therapeutic drug monitoring of antimicrobials, 2016. Japanese.
4) Dasgupta A., Dean R., et al. : Am J Clin Pathol. 101(4).1994.
5) SEKISUI MEDICAL CO., LTD. In house data. Japanese.

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