In Vitro Diagnostics
Marketing Notification No. 13A2X00197223001
**Revised: January, 2017 (3rd edition)
*Revised: April,2014(2nd edition)

This package insert must be read carefully prior to use.

Vancomycin assay kit
(Classification No.: 30414000)

Nanopia TDM Vancomycin

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. The influence of medications administered to the patient on assay results is described in the "PRECAUTIONS" section, particularly under "Effects on Laboratory Tests," of the package insert of each drug. Please also read "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. VCM Antibody Solution 1 contains materials of human origin that have been shown to be negative for HBs antigen, HIV (AIDS viruses) antibodies, and HCV antibodies. However, this reagent (as well as the specimens) should be considered potentially infectious and handled with great care.

Description (Kit Components)

Component: Ingredients
VCM Antibody Solution 1: Mouse anti-vancomycin monoclonal antibody
VCM Latex Reagent 2: Vancomycin-coated latex

Intended Use

Measurement of the vancomycin in serum or plasma

Vancomycin is a glycopeptide antibiotic isolated from the species *Amycolatopsis orientalis*. It shows potent antimicrobial activity against Gram-positive bacteria and is also effective against methicillin-resistant *Staphylococcus aureus* (MRSA), which is a multidrug-resistant organism. Therefore, it is currently used as the first-line drug for the treatment of MRSA around the world.
The most important adverse reactions to vancomycin include renal dysfunction and hearing impairment. Since these reactions are associated with the blood concentration of the drug, they can generally be avoided by monitoring blood levels.[1)] Monitoring the blood concentration of vancomycin is also important for implementing proper use of this antimicrobial agent based on PK/PD.[2)]

Assay Principle

1. Assay Principle

When a certain amount of anti-vancomycin antibody is added to a specimen the anti-vancomycin antibody binds to vancomycin until it has reacted with all of the available vancomycin in the specimen. Then vancomycin-coated latex is added, which react with the residual anti-vancomycin antibody, leading to agglutination. Since the extent of agglutination depends on the concentration of vancomycin in the specimen, the vancomycin concentration can be determined by measuring the absorbance as an indicator of agglutination.

Specimen (vancomycin) + Anti-vancomycin antibody ⟶ Antigen-antibody reaction

Residual anti-vancomycin antibody + Vancomycin-coated latex ⟶ Agglutination via an antigen-antibody reaction

2. Features

1) A highly specific monoclonal antibody enables highly sensitive and precise measurement.
2) Liquid reagents, ready-to-use.
3) Applicable to various automated analyzers.

Procedural Precautions **

1. Properties of Samples and Sampling Methods

1) Samples
Serum and plasma (heparin plasma and EDTA plasma) may be used.
2) Storage of samples[1)]
(1) After separation of serum or plasma, specimens may be stored for up to 7 days in a refrigerator. If secimens cannot be measured within 7 days of separation, store at -20°C and measure within 28 days.
Bring samples to room temperature (15–30 °C) before use.
(2) Specimens may be frozen and thawed up to twice.
3) The separating agent or other substances in a blood collection tube may influence the assay results. Attention should be paid to this risk.[3)]
4) Remove insoluble matter from specimens before performing the sampling procedure. Centrifuge heavily turbid specimens before measurement.

2. Interfering substances

1) Assay results are not affected by free bilirubin

(up to 18.7 mg/dL), conjugated bilirubin (up to 19.7 mg/dL), hemoglobin (up to 498 mg/dL), formazin turbidity (up to 1440 FTU), and rheumatoid factor (up to 450 IU/mL).

2) Cross-reactivity

Cross-reactivity with vancomycin analogs and various other agents is detailed in the tables below.

(1) Vancomycin analogs

Substance	Concentration tested (μg/mL)	Cross-reactivity (%)
Crystalline Degradation Product-I (CDP-I)	100	3.69
Teicoplanin	100	1.2

(2) Drugs commonly prescribed with vancomycin

Substance	Concentration tested (μg/mL)	Cross-reactivity (%)
Acetaminophen	500	0.05
Amikacin	500	-0.02
Amphotericin B	500	-0.07
Ampicillin	500	0.08
Bendroflumethiazide	500	0.05
Caffeine	500	0.04
Carbenicillin	500	0.06
Cefamandole nafate	500	-0.17
Cefazolin	500	-0.04
Cefalexin	500	-0.11
Cephalosporin	500	-0.05
Cephalothin	500	-0.14
Chloramphenicol	500	0.03
Chlorothiazide	500	0.16
Clindamycin	500	0.09
Erythromycin	500	-0.11
Etacrynic acid	500	-0.01
Ethambutol	500	0.06
5-Fluorocytosine	500	-0.14
Furosemide	500	0.05
Fusidic acid	500	0.05
Gentamicin	500	0.01
Hydrochlorothiazide	500	0.06
Ibuprofen	500	-0.07
Isoniazid	500	-0.05
Kanamycin A	500	0.05
Kanamycin B	500	0.07
Lincomycin	500	0.01
Methotrexate	500	-0.11
Methylprednisolone	500	-0.04
Nalidixic acid	500	-0.17
Naproxen	500	-0.03
Neomycin sulfate	500	0.12
Niacin	500	0.03
Nitrofurantoin	500	0.03
Oxytetracycline	500	-0.07
Penicillin G	500	-0.01
Penicillin V	500	0.01
Phenacetin	500	-0.04
Prednisolone	500	0.02
Prednisone	500	0.03
Rifampicin	500	0.07
Salicylic acid	500	0.10
Sisomicin	500	0.07
Spectinomycin	500	-0.05
Sulfadiazine	500	-0.03
Sulfamethoxazole	500	0.00
Sulfisoxazole	500	-0.02
fuTetracycline	500	0.04
Tobramycin	500	-0.16
Trimethoprim	500	-0.04

3. Others

1) Always use Vancomycin Calibrator for Nanopia for calibration.
2) Precautions for assay range
   If the concentration of sample exceeds assay range, dilute the sample with saline and repeat the measurement.

Dosage/Administration (Assay Procedure) **

1. Preparation of reagents

Reagent (1): VCM Antibody Solution 1 is ready to use.
Reagent (2): VCM Latex Reagent 2 is ready to use.
Before using this product, gently invert the VCM 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 μL + Reagent (1) 125 μL → 37°C Approx. 5 min → Reagent (2) 125 μL → 37°C Approx. 1 min → Measurement (Absorbance I※)

→ 37°C Approx. 2 min → Measurement (Absorbance II※)

→ Calculation of concentration

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

Assessment of Assay Results **

1. Reference standard range

According to guidelines, vancomycin should be administered at doses that obtain trough levels of 10 to 15 μg/mL in order to achieve a therapeutic concentration, while trough levels of 15 to 20 μg/mL are recommended to obtain a good clinical response in patients with bacteremia, endocarditis,

osteomyelitis, meningitis, pneumonia (nosocomial pneumonia and nursing and healthcare-associated pneumonia), or severe skin or soft tissue infections.[4] However, therapeutic and toxic concentrations of this agent may overlap. Therefore, interpretation of assay results should also be based on the patient's clinical findings and other examination results.

It is recommended that the therapeutic concentration range of vancomycin be determined at each institution by measuring the blood concentration in a statistically adequate number of specimens.

2. 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.

Performance

1. Sensitivity

1) Absorbance of standard solution (0.0 μg/mL) is ≥ 1900 (Abs. × 10000)
2) The difference of absorbance between standard solution (0.0 μg/mL) and another standard solution (5.0 μg/mL) is ≥ 600 (Abs. × 10000)

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

3. Within-run Reproducibility:

Coefficient of variation ≤ 15 %

(Test methods used for 1.–3. are in-house methods.)

4. Measurement Range[5]: (On Hitachi 7180 automated analyzer)

2.5–100 μg/mL

5. Correlation[5]

Serum N=51 r=0.985 y=0.95x+1.8

Control method: Approved in vitro diagnostic (enzyme immunoassay)

6. Standard Material

Vancomycin (United States Pharmacopeia)

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 puroduct. 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 Vancomycin	VCM Antibody Solution 1	1 × 15 mL
	VCM Latex Reagent 2	1 × 15 mL

Constituent reagents are available in other configurations. For further details please contact SEKISUI MEDICAL CO., LTD.

References ***

1) Iga T., Inui K., eds.-auths.: Practical Manual of TDM for Pharmacists and Pharmacy Students. Tokyo, Japan: Jiho, Inc.;172(2004)
2) Sohara Y. et al: Mebio 28(7), 47(2011)
3) Dasgupta A., Dean R., et al.:Am J Clin Pathol.101(4) 456-461(1994)
4) Japanese Society of Chemotherapy and Japanese Society of Therapeutic Drug Monitoring: Practice Guidelines for Therapeutic drug monitoring of Antibiotics, p35-58 (2016)
5) In house data, SEKISUI MEDICAL CO., LTD.

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