Vancomycin II

Customer Service
United States: 1-877-4ABBOTT
International: Call your Abbott Representative

This package insert must be read carefully prior to product use. Package insert instructions must be followed accordingly. Reliability of assay results cannot be guaranteed if there are any deviations from the instructions in this package insert.

Key to symbols used

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Read Highlighted Changes
Revised November, 2005
INTENDED USE
The AxSYM Vancomycin II assay is a reagent system for the quantitative measurement of vancomycin, an antibiotic drug, in serum or plasma. The measurements obtained are used in the diagnosis and treatment of vancomycin overdose and in monitoring levels of vancomycin to ensure appropriate therapy.

SUMMARY AND EXPLANATION OF TEST
The AxSYM Vancomycin II assay utilizes Fluorescence Polarization Immunoassay (FPIA) technology. The AxSYM Vancomycin II Reagents and sample are pipetted in the following sequence:

**SAMPLING CENTER**
- Sample and all AxSYM Vancomycin II Reagents required for one test are pipetted into a sampling probe into various positions of a Reaction Vessel (RV).
- Sample and Solution 4 (Line Diluent) are transferred into one well of the RV.
- The prediluent solution and Solution 4 (Line Diluent) are transferred to the cuvette of the RV.
- The RV is immediately transferred into the Processing Center. Further pipetting is done in the Processing Center with the processing probe.

**PROCESSING CENTER**
- An aliquot of the predilution mixture and Solution 4 (Line Diluent) are transferred to the cuvette of the RV.
- A second aliquot of the predilution mixture is transferred to the cuvette along with the Vancomycin II Antibody and the Vancomycin II Fluorescein Tracer.
- Vancomycin from the sample and the Vancomycin II Fluorescein Tracer compete for binding sites on the antibody molecule.
- The intensity of polarized fluorescent light is measured by the FPIA optical assembly.

For further information, refer to the AxSYM System Operations Manual, Section 3.

**REAGENTS**

**REAGENT PACK, 100 TESTS**
- AxSYM Vancomycin II Reagent Pack (5B75-20): 5B75-20 includes these items for the AxSYM Vancomycin II Assay:
  - 1 Bottle (15.0 mL) < 0.01% Vancomycin II Fluorescein Tracer in buffer
  - 1 Bottle (8.6 mL) Pretreatment Solution. Surfactant in TRIS buffer.
  - 1 Bottle (15.1 mL) < 0.01% Vancomycin II Fluorescein Tracer in buffer containing surfactant and stabilizers.
  - 3 Bottles (8 mL each) of AxSYM Vancomycin II Controls contain accurately measured amounts of vancomycin prepared in buffered dextrose and stabilizers.

**CALIBRATORS**
AxSYM Vancomycin II Standard Calibrators (5B75-01)
- 6 Bottles (6 mL A, 4 mL each B-F) of AxSYM Vancomycin II Standard Calibrators. Standard Calibrator A is buffered dextrose and stabilizers. Standard Calibrators B-F contain accurately measured amounts of vancomycin prepared in buffered dextrose and stabilizers to yield the following concentrations:

<table>
<thead>
<tr>
<th>Concentration</th>
<th>Bottle</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>µg/mL &amp; mg/L</td>
<td>µmol/L</td>
<td>µg/mL &amp; mg/L</td>
</tr>
<tr>
<td>CONTROL A</td>
<td>7.00</td>
<td>4.83</td>
</tr>
<tr>
<td>CONTROL B</td>
<td>35.00</td>
<td>24.15</td>
</tr>
<tr>
<td>CONTROL C</td>
<td>75.00</td>
<td>51.75</td>
</tr>
</tbody>
</table>

**EXPLANATION OF TEST**
- Vancomycin is a glycopeptide antibiotic which is bactericidal against many gram-positive and some gram-negative cocci. It is useful in therapy of severe staphylococcal (including methicillin-resistant staphylococci) infections in patients who cannot receive or who have failed to respond to the penicillins and cephalosporins. Vancomycin HCl has been used successfully alone in the treatment of staphylococcal (including methicillin-resistant staphylococci) endocarditis. Because of its ototoxicity, vancomycin should be used with care in patients with renal insufficiency. Concurrent and sequential use of other neurotoxic and/or nephrotoxic antimicrobial agents (e.g. amikacin, ciprofloxacin, tobramycin) requires careful monitoring of vancomycin.

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**WARRANTS AND PRECAUTIONS**
- In Vitro Diagnostic Use.

**SAFETY PRECAUTIONS**
- **CAUTION:** This product requires the handling of human specimens. It is recommended that all human sourced materials are considered potentially infectious and be handled in accordance with the OSHA Standard on Bloodborne Pathogens. Safety Level II or other appropriate biosafety practices should be used for materials that contain or are suspected of containing infectious agents.
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- The AxSYM Probe Cleaning Solution (2% Tetraethylammoniumhydroxide (TEAH)).
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**PROBE CLEANING SOLUTION**
- 2 Bottles (240 mL each) AxSYM Probe Cleaning Solution containing 2% Tetraethylammoniumhydroxide (TEAH).
- Solution 4 (Line Diluent) (8A46)

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**REAGENT PACK, 100 TESTS**
- AxSYM Vancomycin II Reagent Pack (5B75-20)
- AxSYM Vancomycin II Calibration Standard (5B75-01)
- AxSYM Vancomycin II Control (5B75-10)
- AxSYM Vancomycin II Cleaning Solution (2% TEAH).

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**REAGENT PACK, 100 TESTS**
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- AxSYM Vancomycin II Calibration Standard (5B75-01)
- AxSYM Vancomycin II Control (5B75-10)
- AxSYM Vancomycin II Cleaning Solution (2% TEAH).
For product not classified as dangerous per European Directive 1999/45/EC as amended - Safety data sheet available for professional user on request.

HANDLING PRECAUTIONS

• Do not use into beyond the expiration date or a maximum of 112 cumulative hours on-board the AxSYM System.
• Do not mix reagents from different Reagent packs.
• AxSYM Vancomycin II Reagents are susceptible to bubbles/foaming and require inspection and removal of bubbles before loading. If bubbles are present, refer to the AxSYM System Operations Manual, Section 2, for instructions on removing bubbles from Reagent packs.

For a more detailed discussion of the safety and handling precautions during system operation, including disposal of sodium azide containing solutions.

STORAGE INSTRUCTIONS

The AxSYM Vancomycin II Reagent Pack must be stored at 2-8°C. The AxSYM Vancomycin II Reagent Pack may be used immediately after removal from the refrigerator. Do not freeze the AxSYM Vancomycin II Reagent Pack. Calibrators and controls should be returned to 2-8°C storage immediately after use.

The AxSYM Vancomycin II Reagent Pack may be on-board the AxSYM System for a maximum of 112 cumulative hours; for example, 14 eight hour shifts. Refer to the AxSYM System Operations Manual, Sections 2, 5 and Appendices, for further information on tracking on-board time.

Reagents are stable until the expiration date when stored and handled as directed.

INSTRUMENT PROCEDURE

Assay File Installation

The AxSYM Vancomycin II Assay File must be installed on the AxSYM System from one of the following software disks, prior to performing the Vancomycin II assay:

• 2C44-01, or higher (112 hours on-board Stability)
• 3G35-01, or higher (112 hours on-board Stability)

Reagent Freezing is not required. For proper installation procedures.

AxSYM Vancomycin II Assay Parameters

The default values for the assay parameters used for the AxSYM Vancomycin II assay are listed below. Assay parameters that can be edited contain a (>) symbol. These parameters can be displayed and edited according to the procedure in the AxSYM System Operations Manual, Section 2, in order to obtain values for the parameters with (>). Review the specific Assay Parameter screen. Press PRINT to print the assay parameters.

<table>
<thead>
<tr>
<th>Assay Parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Long Assay Name (English): Vancomycin_II</td>
</tr>
<tr>
<td>6 Abbrev Assay Name (English): Vanc_II</td>
</tr>
<tr>
<td>11 Assay Number: 668</td>
</tr>
<tr>
<td>12 Assay Version: *</td>
</tr>
<tr>
<td>13 Calibration Version: *</td>
</tr>
<tr>
<td>14 Assay File Revision: *</td>
</tr>
<tr>
<td>15 Assay Enabled = ON</td>
</tr>
<tr>
<td>17 Assay Type: PPVA</td>
</tr>
<tr>
<td>18 Standard Cal Reps = 2</td>
</tr>
<tr>
<td>21 Cal A Concentration: 0.00</td>
</tr>
<tr>
<td>22 Cal B Concentration: 5.00</td>
</tr>
<tr>
<td>23 Cal C Concentration: 10.00</td>
</tr>
<tr>
<td>24 Cal D Concentration: 25.00</td>
</tr>
<tr>
<td>25 Cal E Concentration: 50.00</td>
</tr>
<tr>
<td>26 Cal F Concentration: 100.00</td>
</tr>
<tr>
<td>43 Default Dilution Protocol = UNDILUTED</td>
</tr>
<tr>
<td>44 Default Calibration Method = Standard Calibration</td>
</tr>
<tr>
<td>65 Selected Result Concentration Units &gt; µg/mL</td>
</tr>
<tr>
<td>66 Selected Result Decimal Places &gt; 2</td>
</tr>
<tr>
<td>67 Blank Image background intensity: *</td>
</tr>
<tr>
<td>68 Min Trace-Min net intensity: *</td>
</tr>
<tr>
<td>71 Low Limit-Normal/Therapeutic Range lower limit &gt; 0.00</td>
</tr>
<tr>
<td>74 Hi Limit-Normal/Therapeutic Range upper limit &gt; 0.00</td>
</tr>
<tr>
<td>75 Low Extreme Value &gt; 3.00</td>
</tr>
<tr>
<td>76 High Extreme Value &gt; 100.00</td>
</tr>
<tr>
<td>91 Low Range Undiluted: *</td>
</tr>
<tr>
<td>92 High Range Undiluted: *</td>
</tr>
<tr>
<td>96 Low Range Dil1: *</td>
</tr>
<tr>
<td>97 High Range Dil1: *</td>
</tr>
<tr>
<td>101 Low Range Dil2: *</td>
</tr>
<tr>
<td>102 High Range Dil2: *</td>
</tr>
</tbody>
</table>

NOTES:

1. Parameter 45. Selected result concentration unit can be edited to the alternate results units µmol/L or mg/L.
2. Values associated with the low and high extreme flags, Assay Parameters 475 and 476 are assay specific and should not be edited.

SAMPLE COLLECTION AND PREPARATION FOR ANALYSIS

• Serum or plasma (collected in sodium heparin, citrate, EDTA, or oxalate collection tubes) may be used in the AxSYM Vancomycin II assay.
• The AxSYM System does not provide the capability of verifying sample type. It is the responsibility of the operator to verify the correct sample type(s) is(are) used in the Vancomycin II assay.
• Ensure that complete clot formation has taken place prior to centrifugation. Some samples, especially those from patients receiving anticoagulant or thrombolytic therapy, may exhibit increased clotting time. If the sample is centrifuged before a complete clot forms, the presence of fibrin may cause erroneous results.
• Specimens containing particulate matter or red blood cells may give inconsistent results and should be centrifuged before testing (recommended 8,000-10,000 RCF* x 10 minutes).
• Samples may be stored for up to 24 hours at 2-8°C prior to being tested. If testing will be delayed more than 24 hours, the serum or plasma should be separated from the clot or red blood cells and stored frozen at -10°C or colder for up to 168 hours.
• To minimize the effects of evaporation, all samples (patients, controls and calibrators) should be tested within 3 hours of being placed on-board the AxSYM System. Refer to the AxSYM System Operations Manual, Section 5, for a detailed discussion of on-board sample storage constraints.
• Inspect all samples for bubbles. Remove bubbles prior to analysis.
• When shipped, samples must be packaged and labeled in compliance with applicable federal and international regulations covering the transport of clinical samples and etiologic agents.

REFERENCE CITRIFUGAL FORCE

SAMPLE VOLUME

The sample volume required to perform a single undiluted vancomycin test on the AxSYM System varies depending on the type of sample container used. For sample cups, a ROUTINE test requires 150 µL and a STAT test requires 94 µL. For every additional vancomycin test performed (ROUTINE or STAT) from the same sample container, an additional 44 µL of sample is required.

The sample cup minimum volumes for both ROUTINE and STAT tests (undiluted or diluted) are calculated by the AxSYM System. They are displayed on the Order screen at the time the test(s) is(are) ordered. When using Host Order Query, the Order screen Information and Orderlist Report are not available. Refer to the AxSYM System Operations Manual, Section 5, for a detailed discussion of on-board sample storage constraints.

The AxSYM Probe Cleaning Solution and Solution 4 (Line Diluent) must be stored at 15-30°C.
To obtain the recommended volume requirements for AxSYM Vancomycin II Calibrators and Controls, hold the bottles vertically and dispense 4 drops of each calibrator or control into each respective sample cup. 

AxSYM Vancomycin II PROCEDURE

Materials Provided

- SB75-01 AxSYM Vancomycin II Standard Calibrators
- SB75-10 AxSYM Vancomycin II Controls
- 8A46 Calibration Reagents
- 8A45-05 SOLVENT CLEANING SOLUTION
- 8A76-01 SAMPLE CUPS
- Pipette and pipette tips (optional) to deliver the volumes specified on the Order screen.

CAUTION:

- For optimal performance it is important to follow the routine maintenance procedures defined in the AxSYM System Operations Manual, Section 1. If your laboratory requires more frequent maintenance, follow those procedures.

- Assay Procedure

Sections 5 and 6 of the AxSYM System Operations Manual can be easily removed for use at the instrument. They contain detailed steps for performing assay calibration and sample testing procedures. Prior to ordering tests, confirm that the System inventory of Reaction Vessels (RVs), bulk solutions and waste levels are acceptable.

The operator may obtain an Orderlist Report by pressing PRINT. The printout contains sample placement information and minimum STAT sample cup volume requirements for all tests ordered. When using Host Order Query the Orderlist Report is not available. Refer to the AxSYM System Operations Manual, Section 5: Ordering Patient Samples, for a description of the Host Order Query option.

CAUTION: When operating the AxSYM System, always observe the following:

- The system status must be WARMING, READY, READY or STOPPED before adding or removing sample segments, reagent packs or Reaction Vessels (RVs).
- When only performing FPNA assays, the instrument homest all motors and may display “Error Code 508 Matrix cell not detected, rap door, processing center”. Select OK to proceed with testing the FPNA assay.
- Do not open the interior waste door or the AxSYM Processing Center cover while any test is in process. If opened, all processing will stop.
- Tests in progress will be terminated and must be repeated.
- When testing is completed, it is recommended that samples and the AxSYM Vancomycin II Reagent Pack are removed from the Sampling Center to maximize the on-board reagent pack use. Store Reagent Packs at 2-8°C.

QUALITY CONTROL PROCEDURES

CALIBRATION

The AxSYM Vancomycin II assay must be calibrated using a Standard Calibration (6-point) procedure.

Standard Calibration

To perform a Standard Calibration, test the AxSYM Vancomycin II Standard Calibrators A, B, C, D, E, and F in duplicate. A single sample of all levels of vancomycin controls must be tested as a means of evaluating the assay calibration.

Once the AxSYM Vancomycin II calibration is accepted and stored, all subsequent samples may be tested without further calibration unless:

- A reagent pack with a new lot number is used.
- Control values are out of their specified range.
- Refer to the AxSYM System Operations Manual, Section 1, for:
  - Setting up an assay calibration.
  - When recalibration may be necessary.

Calibration Verification

The AxSYM System verifies that the results of an assay calibration meet the specifications assigned to selected validity parameters. An error message will appear when the calibration fails to meet a specification. Refer to the AxSYM System Operations Manual, Section 10, for an explanation of the corrective actions for the error code. Refer to the AxSYM System Operations Manual Appendices, for an explanation of the calibration validity parameters that may be used by the AxSYM System.
according to the following equation:

\[ \text{Volume of Sample} = \frac{\text{Concentration} \times \text{Manual Dilution Factor}}{\text{Final Sample Concentration}} \]

**EXPECTED VALUES**

Strong correlations have been shown between serum levels of vancomycin and both therapeutic effect and toxicity in specific patient types. Peak serum levels of vancomycin in the range of 20 to 40 µg/mL, and trough blood levels of 3.0-10.0 µg/mL, are suggested for optimal therapeutic effectiveness. In the presence of impaired renal function, unnecessarily high blood levels of vancomycin (approximately 90 µg/mL) may damage the eighth cranial nerve and cause deafness.6,7

**SPECIFIC PERFORMANCE CHARACTERISTICS**

**PRECISION**

Precision was determined as described in National Committee for Clinical Laboratory Standards (NCCLS) protocol EP5-T210 (including an additional estimate of between day precision) using assay controls with 7.0, 35.0, and 75.0 µg/mL, of vancomycin added. Results from these studies typically yielded CV’s of less than 7%. The following are representative results from pooled data from one reagent lot tested across four instruments for a total of twelve precision studies.

**SPECIFICITY**

Cross-reactivity was tested for compounds whose chemical structure or concurrent usage could cause potential interference with the AxSYM Vancomycin II assay.

Cross-reactivity testing has demonstrated that vancomycin crystalline degradation product 1 (CDP-1) at concentrations of 10, 20 and 50 µg/mL, cross-reacts less than the sensitivity of the assay in the absence of vancomycin. When CDP-1 is tested in the presence of vancomycin, at the same indicated concentrations (10-50 µg/mL), the change in vancomycin measured is less than the assay sensitivity. CDP-1 may accumulate in patients with impaired renal function.1,12

The following compounds were tested in the absence of vancomycin up to 500 µg/mL, after adding a known quantity of each to human serum. Methotrexate was tested up to 227 µg/mL. Each compound yielded results less than the sensitivity of the assay (2.00 µg/mL).

**INTERFERENCE**

The compounds listed below, added to human serum, resulted in less than 10% error in detecting added drug when assayed with the AxSYM Vancomycin II assay.
ACCURACY BY CORRELATION

The Abbott AxSYM Vancomycin II assay was compared to commercially available Fluorescence Polarization Immunoassays and to an HPLC method standardized with the United States Pharmacopoeia (USP) standard. The results of the specimen testing are shown in the following table.

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Number of Observations</th>
<th>Intercept</th>
<th>Slope</th>
<th>Correlation Coefficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abbott AxSYM Vancomycin II vs. Abbott AxSYM Vancomycin*</td>
<td>217</td>
<td>-1.08</td>
<td>1.03</td>
<td>0.99</td>
</tr>
<tr>
<td>Abbott TDx®/TDxFLx® Vancomycin**</td>
<td>209</td>
<td>-0.09</td>
<td>1.01</td>
<td>0.98</td>
</tr>
<tr>
<td>HPLC***</td>
<td>202</td>
<td>2.17</td>
<td>0.97</td>
<td>0.98</td>
</tr>
</tbody>
</table>

* Sample Range (AxSYM Vancomycin II): 2.04 to 90.65 µg/mL, includes 44 spiked samples ranging from 41.03 to 90.65 µg/mL.
** Sample Range (AxSYM Vancomycin II): 2.04 to 90.65 µg/mL, includes 43 spiked samples ranging from 41.03 to 90.65 µg/mL.
*** Sample Range (AxSYM Vancomycin II): 2.04 to 90.65 µg/mL, includes 42 spiked samples ranging from 41.12 to 90.65 µg/mL.

BIBLIOGRAPHY

7. Arnhitt JP. Laboratory monitoring of antimicrobial therapy. American Association for Clinical Chemistry Therapeutic Drug Monitoring Continuing Education and Quality Control Program 1981; April: 141.

Related Reading


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