

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

206473Orig1s000

MICROBIOLOGY / VIROLOGY REVIEW(S)

Division of Anti-Infective Products Clinical Microbiology Review

NDA: 206473 Linezolid in 0.9% Sodium Chloride

Date Company Submitted: 26 November 2013
Date received by CDER: 26 November 2013
Date Completed: 24 July 2014
Reviewer: Kerry Snow

NAME AND ADDRESS OF APPLICANT:

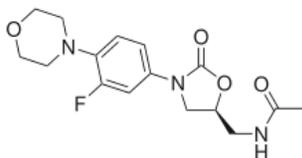
Hospira
275 North Field Drive
Department 389, Bldg H2-2
Lake Forest, IL 60064

CONTACT PERSON:

Neda Yaleh
Manager, Global Regulatory Affairs
224-212-6163

DRUG PRODUCT NAMES:

Established Name: Linezolid
Molecular Mass: 337.346 g/mol
Chemical formula: C₁₆H₂₀FN₃O₄
Chemical Name: (S)-N-[(3-[3-fluoro-4-(4-morpholinyl)phenyl]-2-oxo-5-oxalidiny]methyl)-acetamide
Chemical structure:



DOSAGE FORM AND STRENGTH:

Injection: 600 mg

Infection	Dosage, Route, and Frequency of Administration		Duration (days)
	Pediatric Patients	Adults and Adolescents	
Nosocomial pneumonia (1.1) Community-acquired pneumonia, including concurrent bacteremia (1.1) Complicated skin and skin structure infections (1.2)	10 mg/kg intravenous every 8 hours	600 mg intravenous every 12 hours	10 to 14
Vancomycin-resistant <i>Enterococcus faecium</i> infections, including concurrent bacteremia (1.3)	10 mg/kg intravenous every 8 hours	600 mg intravenous every 12 hours	14 to 28

ROUTE OF ADMINISTRATION:

IV

DISPENSED:

Rx

INDICATION:

Linezolid is an oxazolidinone-class antibacterial indicated in adults and children for the treatment of the following infections caused by susceptible Gram-positive bacteria: Nosocomial pneumonia, Community-acquired pneumonia, Complicated skin and skin structure infections, including diabetic foot infections, without concomitant osteomyelitis, (b) (4) and Vancomycin-resistant *Enterococcus faecium* infections.

RELATED DOCUMENTS:

NDA 021131

TYPE OF SUBMISSION:

New Drug Application

PURPOSE OF SUBMISSION:

The Applicant has proposed Linezolid in a 0.9% Sodium Chloride vehicle (b) (4). The Applicant also proposes to remove sodium citrate (b) (4) a higher concentration of citric acid (b) (4). The Application has been submitted in accordance with Section 505(b)(2) regulations, with NDA 021131 at its basis.

SUMMARY AND RECOMMENDATIONS:

No new information has been submitted in the Application that is pertinent for clinical microbiology review. Changes to the Microbiology section (Section 12.4) of the product labeling are proposed. Deletions to the existing labeling are indicated with strikethrough font, and additions are indicated with red font. The rationale for certain changes includes:

1. Table 12 has been modified to include resistant breakpoints for both MIC and Disk Diffusion testing of *Staphylococcus* species. This change is supported by recent literature (surveillance data and clinical studies) suggesting that isolates with MIC values at or above 8 mcg/mL (or at or below 20 mm, when tested by disk diffusion) are appropriately considered resistant to Linezolid^{1,2,3}.

References:

1. Ikeda-Dantsuji Y, Hanaki H, et al. Emergence of Linezolid-Resistant Mutants in a Susceptible-Cell Population of Methicillin-Resistant *Staphylococcus aureus*. *Antimicrob Agents Chemother*. May 2011; 55(5): 2466-2468.
2. Mendes R, Flamm R, et al. Summary of Linezolid Activity and Resistance Mechanisms Detected during the 2012 Surveillance Program for the United States (LEADER). *Antimicrob Agents Chemother*. 2014; 58(2): 1243-7.
3. Summary Minutes of the June 2009 Meeting of the Antimicrobial Susceptibility Testing Subcommittee of the Clinical and Laboratory Standards Institute (CLSI). 2009; June Meeting: page 31.

Staphylococcus aureus (including methicillin-resistant isolates)
Streptococcus agalactiae
Streptococcus pneumoniae
Streptococcus pyogenes

The following *in vitro* data are available, but their clinical significance is unknown. At least 90% of the following (b) (4) exhibit an *in vitro* minimum inhibitory concentration (MIC) less than or equal to the susceptible breakpoint for (b) (4) the safety and effectiveness of linezolid in treating clinical infections due to these (b) (4) have not been established in adequate and well-controlled clinical trials.

Gram-positive bacteria

Enterococcus faecalis (including vancomycin-resistant isolates)
Enterococcus faecium (vancomycin-susceptible isolates)
Staphylococcus epidermidis (including methicillin-resistant isolates)
Staphylococcus haemolyticus
Viridans group streptococci

Gram-negative bacteria

Pasteurella multocida

Susceptibility Test Methods

When available, the clinical microbiology laboratory should provide the results of *in vitro* susceptibility test results for antimicrobial drug products used in (b) (4) hospitals to the physician as periodic reports that describe the susceptibility profile of nosocomial and community-acquired pathogens. These reports should aid the physician in selecting an antibacterial drug product for treatment.

Dilution techniques

Quantitative methods are used to determine antimicrobial minimum inhibitory concentrations (MICs). These MICs provide estimates of the susceptibility of bacteria to antimicrobial compounds. The MICs should be determined using a standardized method^{1,2} (broth and/or agar). The MIC values should be interpreted according to criteria provided in Table 12.

Diffusion techniques

Quantitative methods that require measurement of zone diameters can also provide reproducible estimates of the susceptibility of bacteria to antimicrobial compounds. The zone size provides an estimate of the susceptibility of bacteria to antimicrobial compounds. The zone size should be determined using a standardized test method^{2,3}. This procedure uses paper disks impregnated with 30 mcg linezolid to test the susceptibility of bacteria to linezolid. The disk diffusion interpretive criteria are provided in Table 12.

Table 12. Susceptibility Test Interpretive Criteria for Linezolid

Pathogen	Susceptibility Interpretive Criteria					
	Minimal Inhibitory Concentrations (MIC in mcg/mL)			Disk Diffusion (Zone Diameters in mm)		
	S	I	R	S	I	R
<i>Enterococcus</i> spp	≤2	4	≥8	≥23	21-22	≤20
<i>Staphylococcus</i> spp ^a	≤4	---	≥8	≥21	---	≤20
<i>Streptococcus pneumoniae</i> ^a	≤2	---	---	≥21	---	---
<i>Streptococcus</i> spp other than <i>S pneumoniae</i> ^a	≤2	---	---	≥21	---	---

^a The current absence of data on resistant isolates precludes defining any categories other than “Susceptible.” Isolates yielding test results suggestive of a “nonsusceptible” category should be retested, and if the result is confirmed, the isolate should be submitted to a reference laboratory for further testing.

A report of *Susceptible* ^{(b) (4)} indicates that the antimicrobial is likely to inhibit growth of the pathogen if the antimicrobial ^{(b) (4)} drug reaches the concentration ^{(b) (4)} usually achievable at the site of infection. A report of *Intermediate* ^{(b) (4)} indicates that the result should be considered equivocal, and, if the bacteria is not fully susceptible to alternative, clinically feasible drugs, the test should be repeated. This category implies possible clinical applicability in body sites where the drug product is physiologically concentrated or in situations where a high dosage of the drug product can be used. This category also provides a buffer zone that prevents small uncontrolled technical factors from causing major discrepancies in interpretation. A report of *Resistant* ^{(b) (4)} indicates that the antimicrobial drug is not likely to inhibit growth of the pathogen if the antimicrobial ^{(b) (4)} reaches the concentration ^{(b) (4)} usually achievable at the ^{(b) (4)} site of infection; other therapy should be selected.

Quality Control

Standardized susceptibility test procedures require the use of laboratory controls to monitor and ensure the accuracy and precision of supplies and reagents used in the assay, and the techniques of the individuals performing the test^{1,2,3}. Standard linezolid powder should provide the following range of MIC values noted in Table 13. For the diffusion technique using the 30 mcg linezolid disk, the criteria in Table 13 should be achieved.

Table 13. Acceptable Quality Control Ranges for Linezolid

	Minimum Inhibitory Ranges (MIC in mcg/mL)	Disk Diffusion Ranges Zone Diameters (mm)
<i>Enterococcus faecalis</i> ATCC 29212	1-4	Not applicable
<i>Staphylococcus aureus</i> ATCC 29213	1-4	Not applicable
<i>Staphylococcus aureus</i> ATCC 25923	Not applicable	25-32
<i>Streptococcus pneumoniae</i>	0.25-2	25-34

ATCC 49619^a

^a This organism may be used for validation of susceptibility test results when testing *Streptococcus* spp. other than *S. pneumoniae*.

15 REFERENCES

1.  (b) (4)
Clinical and Laboratory Standards Institute (CLSI). Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically; Approved Standard - (b) (4) Edition. CLSI document M07-A (b) (4) Clinical and Laboratory Standards Institute, 950 West Valley Road, Suite 2500, Wayne, Pennsylvania 19087, USA, 201 (b) (4)
2.  (b) (4)
Clinical and Laboratory Standards Institute (CLSI). Performance Standards for Antimicrobial Susceptibility Testing; Twenty- (b) (4) Informational Supplement, CLSI document M100-S2 (b) (4) Clinical and Laboratory Standards Institute, 950 West Valley Road, Suite 2500, Wayne, Pennsylvania 19087, USA, 201 (b) (4)
3.  (b) (4)
Clinical and Laboratory Standards Institute (CLSI). Performance Standards for Antimicrobial Disk Diffusion Susceptibility Tests; Approved Standard – (b) (4) Edition. CLSI document M02-A1 (b) (4) Clinical and Laboratory Standards Institute, 950 West Valley Road, Suite 2500, Wayne, Pennsylvania 19087, USA, 201 (b) (4)
4.  (b) (4)

LABEL PROPOSED BY THE AGENCY

12.4 Microbiology

Mechanism of Action

Linezolid is a synthetic antibacterial agent of the oxazolidinone class, which has clinical utility in the treatment of infections caused by aerobic Gram-positive bacteria. The *in vitro* spectrum of activity of linezolid also includes certain Gram-negative bacteria and anaerobic bacteria. Linezolid binds to a site on the bacterial 23S ribosomal RNA of the 50S subunit and prevents the formation of a functional 70S initiation complex, which is essential for bacterial reproduction. The results of time-kill studies have shown linezolid to be bacteriostatic against enterococci and staphylococci. For streptococci, linezolid was found to be bactericidal for the majority of isolates.

Mechanisms of Resistance

In vitro studies have shown that point mutations in the 23S rRNA are associated with linezolid resistance. Reports of vancomycin-resistant *E. faecium* becoming resistant to linezolid during its clinical use have been published. There are reports of *Staphylococcus aureus* (methicillin-resistant) developing resistance to linezolid during clinical use. The linezolid resistance in these organisms is associated with a point mutation in the 23S rRNA (substitution of thymine for guanine at position 2576) of the organism. Also, linezolid resistance in staphylococci mediated by the enzyme methyltransferase has been reported. This resistance is mediated by the *cfr* (chloramphenicol-florfenicol) gene located on a plasmid which is transferable between staphylococci.

Interaction with Other Antimicrobials

In vitro studies have demonstrated additivity or indifference between linezolid and vancomycin, gentamicin, rifampin, imipenem-cilastatin, aztreonam, ampicillin, or streptomycin.

Linezolid has been shown to be active against most isolates of the following microorganisms, both *in vitro* and in clinical infections (b) (4) INDICATIONS AND USAGE (b) (4) (1).

Gram-positive bacteria

Enterococcus faecium (vancomycin-resistant isolates only)
Staphylococcus aureus (including methicillin-resistant isolates)
Streptococcus agalactiae
Streptococcus pneumoniae
Streptococcus pyogenes

The following *in vitro* data are available, but their clinical significance is unknown. At least 90% of the following (b) (4) exhibit an *in vitro* minimum inhibitory concentration (MIC) less than or equal to the susceptible breakpoint for (b) (4) the safety and effectiveness of linezolid in treating clinical infections due to these (b) (4) have not been established in adequate and well-controlled clinical trials.

Gram-positive bacteria

Enterococcus faecalis (including vancomycin-resistant isolates)
Enterococcus faecium (vancomycin-susceptible isolates)
Staphylococcus epidermidis (including methicillin-resistant isolates)
Staphylococcus haemolyticus
Viridans group streptococci

Gram-negative bacteria

Pasteurella multocida

Susceptibility Test Methods

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acquired pathogens. These reports should aid the physician in selecting an antibacterial drug product for treatment.

Dilution techniques

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<i>Streptococcus</i> spp other than <i>S pneumoniae</i> ^a	≤2	---	---	≥21	---	---

^a The current absence of data on resistant isolates precludes defining any categories other than "Susceptible." Isolates yielding test results suggestive of a "nonsusceptible" category should be retested, and if the result is confirmed, the isolate should be submitted to a reference laboratory for further testing.

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Quality Control

Standardized susceptibility test procedures require the use of laboratory controls to monitor and ensure the accuracy and precision of supplies and reagents used in the assay, and the techniques of the individuals performing the test^{1,2,3}. Standard linezolid powder should provide the following range of MIC values noted in Table 13. For the diffusion technique using the 30 mcg linezolid disk, the criteria in Table 13 should be achieved.

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<i>Streptococcus pneumoniae</i> ATCC 49619 ^a	0.25-2	25-34

^a This organism may be used for validation of susceptibility test results when testing *Streptococcus* spp. other than *S. pneumoniae*.

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2. Clinical and Laboratory Standards Institute (CLSI). Performance Standards for Antimicrobial Susceptibility Testing; Twenty- (b) (4) Informational Supplement, CLSI document M100-S2^{(b) (4)} Clinical and Laboratory Standards Institute, 950 West Valley Road, Suite 2500, Wayne, Pennsylvania 19087, USA, 201^{(b) (4)}
3. Clinical and Laboratory Standards Institute (CLSI). Performance Standards for Antimicrobial Disk Diffusion Susceptibility Tests; Approved Standard - (b) (4) Edition. CLSI document M02-A1^{(b) (4)} Clinical and Laboratory Standards Institute, 950 West Valley Road, Suite 2500, Wayne, Pennsylvania 19087, USA, 201^{(b) (4)}

(b) (4)

Kerry Snow, MS MT(ASCP)
Clinical Microbiology Team Leader
22 September 2014

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/s/

KERRY SNOW
09/22/2014

Product Quality Microbiology Review

11 JUL 2013

NDA: 206-473

Drug Product Name

Non-proprietary: Linezolid in 0.9% sodium chloride

Review Number: 1

Dates of Submission(s) Covered by this Review

Submit	Received	Review Request	Assigned to Reviewer
26 NOV 2013	26 NOV 2013	10 DEC 2013	16 DEC 2013
18 APR 2014	18 APR 2014	N/A	N/A
27 JUN 2014	27 JUN 2014	N/A	N/A

Applicant/Sponsor

Name: Hospira, Inc.

Address: 275 N. Field Drive
H2-2N/0392
Lake Forest, IL 60045

Representative: Neda Yaleh

Telephone: 224-212-6163

Name of Reviewer: Jessica G. Cole, PhD

Conclusion: Recommended for Approval

Product Quality Microbiology Data Sheet

- A.
1. **TYPE OF SUBMISSION:** 505(b)(2) NDA
 2. **SUBMISSION PROVIDES FOR:** New sterile drug product
 3. **MANUFACTURING SITE:**
Hospira, Inc.
Highway 301 North
Rocky Mount, NC 27801
 4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:**
 - 2 mg/mL linezolid
 - Single use intravenous injection
 - 300 mL fill in a (b) (4) mL flexible bag with a foil laminate overwrap
 5. **METHOD(S) OF STERILIZATION:** (b) (4)
(b) (4)
 6. **PHARMACOLOGICAL CATEGORY:** Antibiotic
- B. **SUPPORTING/RELATED DOCUMENTS:** None
- C. **REMARKS:** This submission is in the eCTD format. The following information request was sent to the OND project manager on 22 April 2014 and a response was received on 27 June 2014.

Microbiology Comment:

Please provide the following information or a reference to its location in the subject submission.

1. We note the inclusion of a container-closure integrity test conducted on a (b) (4) mL VisIV bag (b) (4). However, the submitted study was conducted using (b) (4). Submit container closure integrity study results that support the proposed commercial system.
2. We refer to your description of the methods and controls to monitor production cycles. Please describe how the sterilization (b) (4) are monitored in (b) (4).
3. Provide a description of the (b) (4) used during sterilization validation studies.
4. Module 3.2.P.3.5 Microbial Challenge Studies describes the preparation of (b) (4). However, the results presented in Table 11 only include (b) (4). Please explain this discrepancy.
5. Describe how the D₍₄₎^(b) for (b) (4) in 0.9% sodium chloride is determined. Indicate how often the D₍₄₎^(b) is reassessed to support the stability of the biological indicator.
6. Justify the use of a biological indicator ((b) (4) in drug product) with a D₍₄₎^(b) of (b) (4) minutes in context with the routine bioburden isolates recovered at the facility.
7. If available, more information is desired on the routine bioburden to be expected in (b) (4) product. Provide a summary of bioburden results from bulk and filled units for other (b) (4) sterilized products manufactured in (b) (4). This should include, but not be limited to, information on how many alert and action levels were exceeded and a discussion of any organisms

-
- that survived the [REDACTED] (b) (4).
8. We refer to your product and stability specification, which refer to an in-house endotoxin method in addition to the USP<85> Gel Clot method. The specification refers to the Validation of Analytical Procedures Section for more information but no information was found on the in-house method, only the USP<85> method. Please provide a description of the test method and the validation studies to support the in-house endotoxin method.
 9. We refer to the proposed sterility test and the submitted verification studies. For drug products that contain >100 mL, USP<71> requires testing of 10% of the contents, but not less than 20 mL from each unit. Your proposed test method utilizes a (b) (4) mL sample and is unacceptable. Please revise your sterility test method to be consistent with USP<71> or provide a scientific justification for the deviation. The test should be repeated on manufactured batches using the appropriate test volumes.
 10. Provide a copy or a summary of the contents of document 90.M-03060.
 11. Provide a copy or summary of Report RM BQ 11.122.
 12. Provide a comparison of [REDACTED] (b) (4) used during [REDACTED] (b) (4) sterilization validation studies.

filename: N206473R1.doc

Executive Summary**I. Recommendations**

- A. Recommendation on Approvability** - Recommended for Approval.
- B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable** – Not applicable.

II. Summary of Microbiology Assessments

- A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology** – This is a (b) (4) sterilized drug product that uses a (b) (4)
- B. Brief Description of Microbiology Deficiencies** – Not applicable.
- C. Assessment of Risk Due to Microbiology Deficiencies** – Not applicable.
- D. Contains Potential Precedent Decision(s)**- Yes No

III. Administrative

- A. Reviewer's Signature** _____
Jessica G. Cole, PhD
- B. Endorsement Block** _____
Bryan Riley, PhD
Microbiology Team Leader
- C. CC Block**
In DARRTS

11 Page(s) have been Withheld in Full as b4 (CCI/TS) immediately following this page

P.8 Stability**P.8.1 Stability Summary and Conclusion****MAINTENANCE OF MICROBIOLOGICAL CONTROL AND QUALITY: STABILITY CONSIDERATIONS**

Three (b) (4) L batches (lots 12-094-SB, 12-095-SB, and 12-096-SB) of drug product were manufactured in September 2012 and placed under long term (25°C/40% RH, 30°C/35% RH, 30°C/75% RH) and accelerated (40°C/<25% RH and 40°C/75% RH) stability conditions. The sterility and endotoxin stability specification and test methods are the same as those proposed for release. Sterility testing will occur at release, 12, 24, and 36 months while endotoxins testing will occur at release, 24, and 36 months. Under accelerated conditions endotoxin and sterility testing will occur at release, 3, and 6 months.

P.8.2 Post-Approval Stability Protocol and Stability Commitment

The first three commercial lots and one lot annually will be placed on stability and sterility and endotoxins will be tested for according to the schedule described above.

P.8.3 Stability Data

The study results were acceptable through completion of the accelerated studies and through 12 months for the long term studies. All time points were sterile with < (b) (4) EU/mL.

ADEQUATE

REVIEWER COMMENT – The stability plan and results to date are acceptable.

A APPENDICES Not applicable.

R REGIONAL INFORMATION

- R.1 Executed Batch Record** Executed batch records were provided in Module 3.2.R.
- 2. REVIEW OF COMMON TECHNICAL DOCUMENT-QUALITY (CTD-Q) MODULE 1**
- A. PACKAGE INSERT** The single use drug product is supplied ready to use and there are no quality microbiology concerns with the label.
- 3. LIST OF MICROBIOLOGY DEFICIENCIES AND COMMENTS:**
None.

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/s/

JESSICA COLE
07/11/2014

BRYAN S RILEY
07/11/2014
I concur.

PRODUCT QUALITY MICROBIOLOGY FILING CHECKLIST

NDA Number: 206-473

Applicant: Hospira

Letter Date: 26 November 2013

Drug Name: Linezolid in 0.9% Sodium Chloride

NDA Type: 505(b)(2)

Stamp Date: 26 November 2013

The following are necessary to initiate a review of the NDA application:

	Content Parameter	Yes	No	Comments
1	Is the product quality microbiology information described in the NDA and organized in a manner to allow substantive review to begin? Is it legible, indexed, and/or paginated adequately?	X		
2	Has the applicant submitted an overall description of the manufacturing processes and microbiological controls used in the manufacture of the drug product?	X		(b) (4) sterilization with (b) (4) at Rocky Mount, NC
3	Has the applicant submitted protocols and results of validation studies concerning microbiological control processes used in the manufacture of the drug product?	X		
4	Are any study reports or published articles in a foreign language? If yes, has the translated version been included in the submission for review?		X	
5	Has the applicant submitted preservative effectiveness studies (if applicable) and container-closure integrity studies?	X		(b) (4) mL flex bag
6	Has the applicant submitted microbiological specifications for the drug product and a description of the test methods?	X		
7	Has the applicant submitted the results of analytical method verification studies?	X		
8	Has the applicant submitted all special/critical studies/data requested during pre-submission meetings and/or discussions?			Not applicable
9	If sterile, are extended post-constitution and/or post-dilution hold times in the draft labeling supported by microbiological data?			Not applicable
10	Is this NDA fileable? If not, then describe why.	X		

Additional Comments: None.

Jessica G. Cole, PhD

06 January 2013

Reviewing Microbiologist

Date

Bryan Riley, PhD

Microbiology Secondary Reviewer/Team Leader

Date

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

JESSICA COLE
01/14/2014

BRYAN S RILEY
01/14/2014
I concur.

Clinical Microbiology: 45-Day Meeting Checklist NDA - Fileability
NDA 206473 Linzolid in 0.9% Sodium Chloride
Reviewer: Kerry Snow Date Review completed: 4 January 2014

On **initial** overview of the NDA application for RTF:

No.	Item	Yes	No	Comments
1	Is the clinical microbiology information (preclinical/nonclinical and clinical) described in different sections of the NDA organized in a manner to allow substantive review to begin?			N/A; no clinical microbiology information has been submitted
2	Is the clinical microbiology information (preclinical/nonclinical and clinical) described in different sections of the NDA indexed, paginated, and/or linked in a manner to allow substantive review to begin?			N/A; no clinical microbiology information has been submitted
3	Is the clinical microbiology information (preclinical/nonclinical and clinical) in different sections of the NDA legible so that substantive review can begin?			N/A; no clinical microbiology information has been submitted
4	On its face, has the applicant <u>submitted</u> <i>in vitro</i> data in necessary quantity, using necessary clinical and non-clinical strains/ isolates, and using necessary numbers of approved current divisional standard of approvability of the submitted draft labeling?			N/A; no clinical microbiology information has been submitted
5	Has the applicant <u>submitted</u> draft provisional breakpoint and interpretive criteria, along with quality control (QC) parameters, if applicable, in a manner consistent with contemporary standards, which attempt to correlate criteria with clinical results of NDA studies, and in a manner to allow substantive review to begin?			N/A; no clinical microbiology information has been submitted
6	Has the applicant <u>submitted</u> any required animal model studies necessary for approvability of the product based on the submitted draft labeling?			N/A
7	Has the applicant <u>submitted</u> all special/critical studies/data requested by the Division during pre-submission discussions?			N/A

Clinical Microbiology: 45-Day Meeting Checklist NDA - Fileability
NDA 206473 Linezolid in 0.9% Sodium Chloride
Reviewer: Kerry Snow Date Review completed: 4 January 2014

8	Has the applicant <u>submitted</u> the clinical microbiology datasets in a format which intends to correlate baseline pathogen with clinical and microbiologic outcomes exhibited by relevant pathogens isolated from test of cure or end of treatment?			N/A; no clinical microbiology information has been submitted
9	Has the applicant <u>submitted</u> a clinical microbiology dataset in a format which intends to determine resistance development by correlating changes in the phenotype (such as <i>in vitro</i> susceptibility) and/or genotype (such as mutations) of the baseline relevant pathogen with clinical and microbiologic outcome as exhibited by relevant pathogens isolated from test of cure or end of treatment?			N/A; no clinical microbiology information has been submitted
10	Has the applicant used standardized methods or if non-standardized methods were used has the applicant included full details of the method, the name of the laboratory where actual testing was done and performance characteristics of the assay in the laboratory where the actual testing was done?			N/A
11	Is the clinical microbiology draft labeling consistent with 21 CFR Parts 201, 314, 601 and current Divisional policy.	✓		
12	FROM A CLINICAL MICROBIOLOGY PERSPECTIVE, IS THIS NDA FILEABLE? IF NO, GIVE REASONS BELOW.	✓		

Any Additional Clinical Microbiology Comments:

The Application is for Linezolid in 0.9% Sodium Chloride Injection in accordance with 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, based on NDA 021131 for Zyvox, approved on 18 April 2000, the Reference Listed Drug. The Applicant states that “the composition of Hospira, Inc.’s Linezolid in 0.9% Sodium Chloride Injection ^(b)₍₄₎ Zyvox ^(b)₍₄₎ the drug product vehicle and ^(b)₍₄₎.”

No clinical microbiology information has been submitted in this Application. The Draft Labeling, included in the submission, will be reviewed by the assigned clinical microbiologist.

Reviewing Clinical Microbiologist: Kerry Snow

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/s/

KERRY SNOW
01/04/2014