510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K230827

B Applicant

Hardy Diagnostics

C Proprietary and Established Names

HardyDisk AST Rezafungin 5µg (RZF5)

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
JTN	Class II	21 CFR 866.1620 - Antimicrobial Susceptibility Test Disc	MI - Microbiology

II Submission/Device Overview:

A Purpose for Submission:

To obtain a substantial equivalence determination for Rezafungin Antimicrobial Susceptibility Test Disk

B Measurand:

Rezafungin 5µg

C Type of Test:

Antimicrobial Susceptibility Test Disks

III Intended Use/Indications for Use:

A Intended Use(s):

HardyDisk AST Disks are used for semi-quantitative *in vitro* susceptibility testing by the agar diffusion test procedure (Kirby- Bauer). Standardized methods for agar diffusion testing have been described for Enterobacterales, *Staphylococcus* spp., *Pseudomonas* spp., *Acinetobacter* spp., *Listeria monocytogenes*, *Enterococcus* spp., and by modified procedures, *Candida* spp., *Haemophilus* spp., *Neisseria gonorrhoeae*, *Neisseria meningitidis* and *Streptococcus* spp., including *Streptococcus pneumoniae*.

B Indication(s) for Use:

HardyDisk AST Disks are used for semi-quantitative *in vitro* susceptibility testing by the agar diffusion test procedure (Kirby- Bauer). Standardized methods for agar diffusion testing have been described for Enterobacterales, *Staphylococcus* spp., *Pseudomonas* spp., *Acinetobacter* spp., *Listeria monocytogenes*, *Enterococcus* spp., and by modified procedures, *Candida* spp., *Haemophilus* spp., *Neisseria gonorrhoeae*, *Neisseria meningitidis* and *Streptococcus* spp., including *Streptococcus pneumoniae*.

Use of HardyDisk AST Rezafungin 5µg (RZF5) for *in vitro* agar diffusion susceptibility testing is indicated when there is the need to determine the susceptibility of microorganisms to Rezafungin.

HardyDisk AST Rezafungin at concentration 5µg can be used to determine the zone diameter (mm) of Rezafungin against the following microorganisms for which Rezafungin has been shown to be active both clinically and *in vitro*: *Candida albicans*, *Candida glabrata*, *Candida parapsilosis*, and *Candida tropicalis*.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

D Special Instrument Requirements:

Not applicable.

IV Device/System Characteristics:

A Device Description:

HardyDisk AST Rezafungin 5µg (RZF5) is a high quality 6mm diameter white filter paper disk that is impregnated with 5µg Rezafungin. The disks are clearly marked on both sides with RZF5, designating the agent and the drug content. The disks are supplied in plastic cartridges containing 50 disks each. HardyDisk AST Rezafungin 5µg (RZF5) is intended to be used for *in vitro* agar diffusion susceptibility testing.

B Principle of Operation:

The HardyDisk AST Disk is based on the agar diffusion (Kirby-Bauer) methodology. It utilizes dried filter paper disks impregnated with a known concentration of an antimicrobial agent that

are placed onto the test medium surface. Mueller Hinton (MH) agar supplemented with 2% glucose and 0.5 µg/mL methylene blue dye is recommended for agar diffusion testing of yeasts. Five distinct colonies (approximately 1 mm in diameter) are transferred to 5 mL of a diluent such as sterile saline (0.85%). The final inoculum density should be equivalent to a 0.5 McFarland turbidity standard. Alternatively, the inoculum can be standardized photometrically to facilitate adjustment of rapidly growing microorganisms.

Within 15 minutes of inoculum preparation, the MH agar plate supplemented with 2% glucose and 0.5 µg/mL methylene blue dye is streaked with an inoculated swab to obtain an even inoculation of organism. Disks are aseptically placed onto the agar surface with a disk dispenser and the disks are pressed down with a sterile needle or forceps to make contact with the agar surface. Agar plates are incubated in an ambient air incubator at 35±2°C for 24 hours.

After incubation, the agar medium is examined for a zone of inhibition around the disks. The zones of inhibition are measured to the nearest millimeter and compared to recognized zone size ranges for the antimicrobial agent being tested.

V Substantial Equivalence Information:

A Predicate Device Name(s):

Hardy Disk Ast Tigecycline 15µg

B Predicate 510(k) Number(s):

K062245

C Comparison with Predicate(s):

Device & Predicate Device(s):	Device: K230827	Predicate: K062245
Device Trade Name	HardyDisk AST Rezafungin 5µg (RZF5)	Hardy Disk Ast Tigecycline 15µg
General Device Characteristic Similarities		
Intended Use/Indications For Use	Antimicrobial Susceptibility Test Disks are used for *in vitro* susceptibility testing by standardized agar diffusion test procedures.	Same
Test Method	Antimicrobial Susceptibility testing using paper disks impregnated with an antimicrobial agent	Same
Methodology	Kirby-Bauer Disk Diffusion	Same

	Susceptibility Test Protocol require the user to determine categorical interpretations (S/I/R) using the measured zone diameters.	
Inoculum	Prepared from pure isolated colonies to match the turbidity equivalent of a 0.5 McFarland.	Same
Inoculum Method	Dip a sterile swab into the prepared inoculums, and streak an appropriate agar plate's surface three times. Add the disks impregnated with the antimicrobial agent to the surface of the plate. The temperature, atmospheric conditions and duration of incubation are dependent on the organism tested.	Same
Reading Method	The user will interpret the zone diameters according to established interpretive criteria for the drug.	Same
General Device Characteristic Differences		
Product Name	HardyDisk AST Rezafungin 5µg (RZF5)	Hardy Disk Ast Tigecycline 15µg
Antibiotic	Rezafungin	Tigecycline
Concentration	5µg	15µg

VI Standards/Guidance Documents Referenced:

- CLSI M27M44S 3rd ed. *Performance Standards for Antifungal Susceptibility Testing of Yeasts* (August 2022).
- CLSI M44-S3 *Zone Diameter Interpretive Standards, Corresponding Minimal Inhibitory Concentration (MIC) Interpretive Breakpoints, and Quality Control Limits for Antifungal Disk Diffusion Susceptibility Testing of Yeasts* (2018).

VII Performance Characteristics (if/when applicable):

The premarket submission for HardyDisk Rezafungin included a letter dated February 02, 2023 indicating the right of reference to NDA 217417. Descriptive characteristics were sufficient for

the HardyDisk Rezafungin 5µg (RZF5) disk based on data from microbiology disk studies evaluated by CDER which were used to generate the breakpoints identified by FDA on the susceptibility test interpretive criteria webpage. In addition, CDER concurred with the disk QC ranges that were established by CLSI. The disk data used to support this submission included data from testing organisms shown to be active *in vitro* and in clinical infections within the spectrum of activity of Rezafungin and as noted in the device's intended use.

Data obtained from stability, quality control, disk to MIC correlation, reproducibility (from disk content optimization) studies were generated in accordance with the CDER Clinical/Antimicrobial guidance, *Microbiology Data for Systemic Antibacterial Drugs-Development, Analysis, and Presentation* to ensure precise, accurate, and reproducible results.

For this review, the interpretive criteria are applied to *Candida albicans, Candida glabrata, Candida parapsilosis,* and *Candida tropicalis* according to the FDA STIC website. As required under 511A(2)(2)(B) of the Federal Food, Drug and Cosmetic Act, the following statement is included in the Precautions section of the HardyDisk AST Rezafungin 5µg package insert:

> *Per the FDA-Recognized Susceptibility Test Interpretive Criteria website, the safety and efficacy of antimicrobial drugs, for which antimicrobial susceptibility is tested by this AST device, may or may not have been established in adequate and well-controlled clinical trials for treating clinical infections due to microorganisms outside of those found in the indications and usage in the drug label. The clinical significance of susceptibility information in those instances is unknown. The approved labeling for specific antimicrobial drugs provides the uses for which the antimicrobial drug is approved.*

A Analytical Performance:

1. Precision/Reproducibility:

   N/A

2. Linearity:

   N/A

3. Analytical Specificity/Interference:

   N/A

4. Assay Reportable Range:

   N/A

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

   N/A

6. Detection Limit:

N/A

7. Assay Cut-Off:

N/A

B Comparison Studies:

1. Method Comparison with Predicate Device:

N/A

2. Matrix Comparison:

N/A

C Clinical Studies:

1. Clinical Sensitivity:

N/A

2. Clinical Specificity:

N/A

3. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):

N/A

D Clinical Cut-Off:

N/A

E Expected Values/Reference Range:

The FDA-identified susceptibility interpretive criteria for Rezafungin are listed below.

FDA-Identified Disk Diffusion Interpretive Criteria (zone diameter in mm) for Rezafungin

Organisms	Susceptible	Intermediate	Resistant
Candida abicans	≥13	-	-
Candida glabrata	≥15	-	-
Candida parapsilosis	≥9	-	-
Candida tropicalis	≥14	-	-

Exception to the recognized standard of CLSI M27M44S as noted on the FDA STIC website
For the species listed below, susceptibility test interpretive criteria are not recognized at this time:
Candida auris
Candida dubliniensis
Candida krusei

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.