Certificate of Analysis

Product Name	Caspofungin Acetate		
Batch No.	6882307022	**Manufacturing Date**	2023.07.15
Batch Size	1507.62g	**Test Date**	2023.07.18
Quantity	200.0g	**Release Date**	2023.08.07
Standard	In-house specification	**Retest Date**	2025.07.14
Storage Condition	Preserve in tight, light resistant containers. Store at -70°C ± 5°C		

Test Items	**Acceptance Criteria**	**Test Results**
Description	White to off-white powder.	Conforms
Solubility	Freely soluble in 0.1 mol/L hydrochloric acid, water, DMF and DMSO, soluble in ethanol or methanol.	Conforms
Specific rotation	Between -103° and -108°, calculated on the anhydrous, solvent-free basis.	-104.9°
Identification	1. The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the test for *Assay*.	Conforms
	2. The IR absorption spectrum of the preparation of the test specimen exhibits maxima only at the same wavelengths as that of a similar preparation of the reference standard.	Conforms
pH	5.0 to 7.0	6.0
Water	6.0% to 10.0%	7.9%
Clarity and color of solution	The solution is clear and any opalescence produced is not more pronounced than that of reference suspension I; any color produced is not more intense than that of reference solution Y_7.	Conforms
Residue on ignition	Not more than 0.1%.	0.02%
Acetate	Between 9.0% and 11.0%, calculated on the anhydrous, solvent-free basis.	9.9%
Ethylenediamine	Not more than 285 ppm.	62ppm
Related compound A	Not more than 0.5%.	<0.05%(0.01%)
Residual solvents	Tetrahydrofuran: Not more than 720 ppm	<20ppm(Non-detected)
	Ethyl acetate: Not more than 5000 ppm	<30ppm(11ppm)
	Acetonitrile: Not more than 410 ppm	<90ppm(Non-detected)
	Dichloromethane: Not more than 600 ppm	<130ppm(Non-detected)
	Methanol: Not more than 3000 ppm	<80ppm (30ppm)
	Ethanol: Not more than 5000 ppm	304ppm
	1-Propanol: Not more than 5000 ppm	<160ppm(Non-detected)
Microbial limit	Total aerobic microbial count: Not more than 100 cfu/g	<1cfu/g
	Total yeasts and molds count: Not more than 10 cfu/g	<1cfu/g
	Escherichia coli: Not detected per g.	Non-detected

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Test Items	**Acceptance Criteria**	**Test Results**
Related compounds	Related compound B (RRT = 0.75): Not more than 0.10%	<0.05% (Non-detected)
	Related compound C: Not more than 1.0%	0.10%
	Related compound D (RRT = 1.37): Not more than 0.15%	<0.05% (Non-detected)
	Related compound E (RRT = 1.80): Not more than 0.5%	0.13%
	Related compound F (RRT = 2.19): Not more than 0.2%	0.08%
	Related compound G (RRT = 2.22): Not more than 0.15%	<0.05% (0.04%)
	PB_0: Not more than 0.10%	<0.05% (Non-detected)
	Intermediate **II**: Not more than 0.10%	<0.05% (0.01%)
	Intermediate **III**: Not more than 0.10%	<0.05% (Non-detected)
	Individual unspecified impurity: Not more than 0.10%	<0.05% (0.02%,RRT=2.07)
	Total impurities: Not more than 2.0% (Disregard any unspecified impurity peaks less than 0.05%)	0.30%
Bacterial endotoxins	Less than 0.5 EU/mg.	＜0.5 EU/mg
Assay	Contains 96.5% to 101.5% of $C_{52}H_{88}N_{10}O_{15}\cdot 2C_2H_4O_2$, calculated on the anhydrous, solvent-free basis.	99.5%

Conclusion: The test results indicate that the product complies with the acceptance criteria.

Note: Risk assessment for elemental impurities on Caspofungin Acetate had been done according to ICH Q3D and USP <232>. All known and potential sources of elemental impurities that may carry over into Caspofungin Acetate drug substance have been evaluated in three production batches of final drug substance. The results of the evaluation show that their levels are consistently less than control threshold (30% of the concentration limit calculated using Option 2a in ICH Q3D), hence no additional control on potential elemental impurities is required.

Related compound A:
1-[(4*R*,5*S*)-5-[(2-aminoethyl)amino]-N2-[(10*R*,12*S*)-10,12-dimethyl-1-oxotetradecyl]-4-hydroxy-L-ornithine]-5-[(3R)-3-hydroxy-L-ornithine]-Pneumocandin C_0

Related compound C:
1-[(4*R*,5*S*)-5-[(2-aminoethyl)amino]-N2-[(10R,12S)-10,12-dimethyl-1-oxotetradecyl]-4-hydroxy-L-ornithine]-2-L-serine-5-[(3R)-3-hydroxy-L-ornithine]-Pneumocandin B_0 bi-acetate

PB_0:
(4*R*,5*R*)-N2-[(10*R*,12*S*)-10,12-dimethyl-1-oxotetradecyl]-4,5-dihydroxy-L-ornithyl-L-threonyl-(4R)-4-hydroxy-L-prolyl-(4*S*)-4-hydroxy-4-(4-hydroxyphenyl)-L-threonyl -(3*R*)-3-hydroxy-L-glutamoyl-3-hydroxy-(3*S*)- L-proline -(6->1)-lactam

Intermediate II: 5-[(3R)-3-hydroxy-L-ornithine]-Pneumocandin B_0

Intermediate III: 1-[(4*R*,5*R*)-N2-[(10*R*,12*S*)-10,12-dimethyl-1-oxotetradecyl]-4-hydroxy-5-[(2-(2-ethylhexyloxy)-2-oxoethyl)thio]-L-ornithine]-5-[(3*R*)-3-hydroxy-L-ornithine]-Pneumocandin B_0 acetate

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