TEVA CZECH INDUSTRIES S.R.O., Ostravska 29/305, 747 70 OPAVA-KOMAROV, CZECH REPUBLIC

PRODUCT SPECIFICATIONS AND CERTIFICATE OF ANALYSIS

Product Name: CYCLOSPORINE
Control No.: 74151000218
Order No.: JU80019802
Client Packing Order: 4500013301
Customer Name: TEVA CZECH INDUSTRIES S.R.O.
Quantity: 134.200 KG
Quality Market: EUR
Manufacturing Site: Opava. Czech Republic
Original Analysis Date: July 2018
Manufacturing Date: July 2018
Re Test date: July 2023
Packaging and storage: Preserve in tight, light-resistant containers at a temperature up to 25 °C.

TESTS AND METHODS	SPECIFICATIONS	RESULTS*
	SV-741410-01, rev.1 TESTS	
Description *Visual*	White or almost white powder.	Complies
Identity (IR) *EP 2.2.24*	IR spectrum of the tested substance exhibits maxima at the same wavelengths as the spectrum of the reference standard obtained under the same conditions.	Complies
Identity (HPLC) *EP, AM-QC-LC002*	The retention time of the principle peak in chromatogram of tested sample corresponds to the retention time of the peak in chromatogram of the reference standard	Complies
Assay (HPLC) *EP, AM-QC-LC002*	98.5 to 101.5 % calculated on dried substance	100.8%

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TESTS AND METHODS	SPECIFICATIONS	RESULTS*
	SV-741410-01, rev.1 TESTS	
Related substances *EP, AM-QC-LC002*		
[Abu]5cyclosporine	NMT 0.30 %	Less than 0.02%
Cyclosporine U	NMT 0.40 %	0.08%
Cyclosporine H	NMT 0.30 %	Less than 0.02%
Dihydrocyclosporine A + cyclosporine V	NMT 0.60 %	0.31%
Cyclosporine D	NMT 0.20 %	0.05%
Isocyclosporine A	NMT 0.50 %	0.13%
Any unspecified impurities	NMT 0.10 %	0.07%
Total impurities	NMT 1.20 %	0.71%
Appearance of solution *EP (2.2.1)* clarity	Clear	Complies
Appearance of solution *EP (2.2.2) Method II* colour	NMT Y5, BY5 or R7	Complies
Specific optical rotation *EP, (2.2.7)*	-193 to -185 ° calculated on dried substance	-189°
Loss on drying *EP, (2.2.32)*	NMT 2.0 %	0.5%

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TESTS AND METHODS	SPECIFICATIONS	RESULTS*
SV-741410-01, rev.1 TESTS		
Residual solvents *EP (5.4), AM-QC-GC001*		
Acetone	NMT 2000 ppm	13ppm
Toluene	NMT 100 ppm	Less than 5ppm
Hexanes	NMT 100 ppm	Less than 1ppm
Ethyl acetate	NMT 100 ppm	Less than 10ppm
Factors TESTS		
Assay (PhEur) as is	no limit	99.5%
Assay (USP) as is	no limit	99.5%
CS12, rev.0 TESTS		
Particle size *AM-QC-OT001*		
50 %	NMT 12 um	3um
90 %	NMT 25 um	6um
IH-01 TESTS		
Heavy metals *EP (2.4.8), method C*	NMT 20 ppm	Less than 20ppm

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TESTS AND METHODS	SPECIFICATIONS	RESULTS*
	IH-01 TESTS	
Residual solvents *EP (5.4), AM-QC-GC001* methanol	NMT 100 ppm	Less than 15ppm

Remarks:
1. Conforms to the requirements of the SV-741410-01, rev.1 and Factors and CS12, rev.0 and IH-01 Specifications.
2. Conforms to the current EP monograph.
3. The following residual solvents Class 1, as defined in the ICH Q3C, benzene, carbon tetrachloride, 1,2-Dichloroethane, 1,1-Dichloroethene and 1,1,1- Trichloroethane are not present in the Active Pharmaceutical ingredient.
4. The product meets the requirements for residual solvents USP <467>, EP 5.4 and ICH guide Q3C.
5. The product has been produced and controlled in compliance with GMP rules and valid documentation. Tested parameters comply with the approved specification.
6. We declare that the batch was produced according to the currently valid R1-CEP 2002-152-Rev 04.

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Released by Quality Control Manager:	Signature**: PP\ Martina Stonova 27 July 2018 10:46:09
Bohumir Biba	Print Date: 27 July 2018
	QA Approval: Marek Dominik

(*) Upon completion of the 'Results' column this document becomes a certificate of analysis **End of C.O.A.**

(**) This document was signed electronically and this is the manifestation of the electronic signature.