CONCORD BIOTECH LIMITED

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CERTIFICATE OF ANALYSIS

Product	TACROLIMUS USP	A. R. No.	CBL-03518255
Batch No.	03518255	Mfg. Date	Dec 2018
Batch size	1772 g	Retest Date	Nov 2021

S.N.	Tests	Specifications	Observations
1	Description	White crystals or white crystalline powder	White crystalline powder
2	Solubility	Very soluble in methanol ,freely soluble in N,N dimethyl formamide and inethanol (95%) and practically insoluble in water.	Very soluble in methanol ,freely soluble in N,N dimethyl formamide and inethanol (95%) and practically insoluble in water.
3	Identification (a) By IR (b) By HPLC	The Infrared absorption spectrum of the preparation of the sample exhibits maxima only at the same wavelengths as that of a similar preparation of the corresponding reference standard/ working standard. The retention time of the major peak of the sample solution corresponds to that the standard solution as obtained in the assay test.	The Infrared absorption spectrum of the preparation of the sample exhibits maxima only at the same wavelengths as that of a similar preparation of the corresponding working standard. Standard RT : 25.1 minutes Sample RT : 25.4 minutes Complies
4	Water (by KF)	Not more than 4.0 %	2.1%
5	Optical rotation on an " as is" basis 10mg/ml in N,Ndimethylformamide	Between -110° and -115°	-113°
6	Residue on ignition	NMT 0.1 %	0.03%
7	Organic impurities (By HPLC) (Procedure 2)		
	Ascomycin Desmethyl tacrolimus Tacrolimus 8-epimer Tacrolimus 8-propyl analog Any individual unspecified impurity Total impurities (Exoluding Tacrolimus open ring and Tacrolimus 19-epimer)	NMT 0.50 % NMT 0.1 % NMT 0.15 % NMT 0.15 % NMT 0.10 % NMT 1.0 %	<0.05 % <0.05 % Not detected Not detected 0.05% 0.05%
8	Content of Tautomers (By HPLC)		
	Tacrolimus open ring (Tautomer I) Tacrolimus 19-epimer (Tautomer II) Sum of Tacrolimus open ring and Tacrolimus 19-epimer	NMT 0.5 % NMT 1.0 % NMT 1.0 %	<0.05 % 0.30% 0.30 %
9	Assay (By HPLC)	98.0 % to 102.0 % $C_{44}H_{69}NO_{12}$, calculated on the anhydrous and solvent- free basis	100.3 %
Additional Tests			
10	Residual solvents (By GC Headspace)		
	Acetone Di isopropyl ether Ethyl acetate Acetonitrile Toluene Hexane	NMT 1000 ppm NMT 100 ppm NMT 2000 ppm NMT 400 ppm NMT 250 ppm NMT 250 ppm	Below detection limit Below detection limit Below detection limit Below detection limit Below detection limit Below detection limit
11	Particle size distribution (By Malvern)	d(0.1): NMT 20 µm d(0.5): NMT 50 µm d(0.9): NMT 100 µm	4 µm 16 µm 62 µm
12	Microbial tests:		
	Total viable aerobic count Total mold and yeast count Test for specified microorganisms E. coli S. aureus Pseudomonas aeruginosa Salmonella spp.	NMT 1000 cfu / g NMT 100 cfu / g Should be Absent / g Should be Absent / g Should be Absent / g Should be Absent /10 g	Less than 10 cfu/g Less than 10 cfu/g Absent/g Absent/g Absent/g Absent/10g
13	Bacterial endotoxins	NMT 25 EU/mg	Less than 25 EU/mg

Storage: Store in airtight container up to 25°C.
Remarks: The material complies as per USP and in-house specification no SPC/QC/FP/031-08.
Date of Report: Dec 25, 2018

Compiled By (QC)
(B.N.Panchal-Sr.AM)
Date: 25/12/18

Checked By (QC)
(N.S.Jagad-DGM)
Date: 25/12/2018

Approved By (QA)
(T.K.Saha-DGM)
Date: 26/12/2018

Fecha Entrada: 29-01-2019

7084

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TACROLIMUS GRANEL

8 432780 070843

Lote: 0082364

QC-00204826

109581-93-3

804,02

C44H69NO12xH2O

•PELIGRO H301 Tóxico en caso de ingestión.P264 Lavarse concienzudamente tras la manipulación.P270 No comer, beber ni fumar durante su utilización.P301+P310 EN CASO DE INGESTIÓN: Llamar inmediatamente a un CENTRO DE INFORMACIÓN TOXICOLÓGICA o a un médico.P321 Se necesita un tratamiento específico (ver ... en este etiqueta).P330 Enjuagarse la boca.P405 Guardar bajo llave.P501 Eliminar el contenido/el recipiente en conformidad con la normativa local, regional, nacional o internacional.

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GUINAMA
ABSOLUTA CALIDAD

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CERTIFICATE OF ANALYSIS

Product	TACROLIMUS MONOHYDRATE Ph.Eur.	A. R. No.	CBL-03518255A
Batch No.	03518255	Mfg. Date	Dec 2018
Batch size	1772 g	Retest Date	Nov 2021

S.N.	Tests	Specifications	Observations
1	Appearance	White or almost white crystalline powder	White crystalline powder
2	Solubility	Practically insoluble in water, soluble in ethanol (96%) and practically insoluble in heptane	Practically insoluble in water, soluble in ethanol (96%) and practically insoluble in heptane
3	Identification by IR	The Infrared absorption spectrum of the preparation of the sample exhibits maxima only at the same wavelengths as that of a similar preparation of the corresponding EP reference standard/ working standard.	The Infrared absorption spectrum of the preparation of the sample exhibits maxima only at the same wavelengths as that of a similar preparation of the corresponding working standard.
4	Appearance of solution	The solution is clear and not more intensely coloured than reference solution GY_7.	The solution is clear and not more intensely coloured than reference solution GY_7.
5	Related substance (by HPLC)		
	Ascomycin (Impurity A) Tacrolimus 8-epimer (Impurity D) Tacrolimus 8-propyl analog (Impurity E) Any individual unspecified impurity Total impurities (exoluding Tacrolimus compound I and Tacrolimus compound II)	Maximum 0.5 % Maximum 0.15 % Maximum 0.15 % Maximum 0.10 % Maximum 1.0 %	Below disregard limit Not detected Not detected Below disregard limit Nil
6	Water (by KF)	1.5 % to 4.0%	2.1%
7	Sulphated Ash	Maximum 0.1 %	0.03%
8	Assay (By HPLC)	97.0 % to 102.0 % for the sum of Tacrolimus, Tacrolimus compound I and Tacrolimus compound II on the anhydrous substance basis	99.5%
Additional Tests			
9	Residual solvents (By GC Headspace)		
	Acetone Di isopropyl ether Ethyl acetate Acetonitrile Toluene Hexane	NMT 1000 ppm NMT 600 ppm NMT 2000 ppm NMT 400 ppm NMT 250 ppm NMT 250 ppm	Below detection limit Below detection limit Below detection limit Below detection limit Below detection limit Below detection limit
10	Partiole size distribution	For information	d(0.1): 4 µm d(0.5): 16 µm d(0.9): 62 µm
11	Microbial tests:		
	Total viable aerobic count Total mold and yeast count Test for specified microorganism E.coli S.aureus Pseudomonas aeruginosa Candida albicans Clostridium sporogenes Bile tolerant gram - negative bacteria Salmonella spp	NMT 1000 cfu/g NMT 100 cfu/g Should be absent/g Should be absent/g Should be absent/g Should be absent/g Should be absent/g Should be absent/g Should be absent/10g	Less than 10 cfu/g Less than 10 cfu/g Absent/g Absent/g Absent/g Absent/g Absent/g Absent/g Absent/10g

Storage: Store in airtight container up to 25°C.
Remarks: The material compiles as per Ph.Eur and in-house specification no STP/QC/FP/120-00.
Date of Report: Jan 05,2019

Compiled By (QC)
(D.N.Panchal-Sr.AM)
Date: 05/01/19

Checked By (QC)
(S.K.Jha-GM)
Date: 05/01/2019

Approved By (QA)
(T.K.Saha-DGM)
Date: 07/01/2019

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