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CERTIFICATE OF ANALYSIS No. JP 19105/UP2

Name of Product: **Digoxin Micronized**

Batch No: **051019/M**

Release date: 06.11.2019

Manufacturing date: 10/2019

Retest date: 08/2022

No.	Analysis	Specification limits	Test results
1.	Characterization	white or almost white powder or colorless crystals	conforms
2.	Identification		conforms
2.1	IR spectrum (EP)	IR spectrum complying with that of the reference standard	conforms
2.3	Retention time (EP, USP)	conforms standard	conforms
3.	Appearance of 0.5% solution: in methanol: methylene chloride 1:1 (v/v), clarity	clear and colorless	conforms
4.	Solubility		conforms
4.1.	in water	practically insoluble	conforms
4.2.	in a mixture methylene chloride – methanol 1:1 (v/v)	soluble	conforms
4.3.	in alcohol	slightly soluble	conforms
5.	Specific optical rotation calcd. on dry substance $[\alpha]_D^{20}$; (2% solution in a mixture of methylene chloride and methanol (1:1)), [°]	+13.9 ÷ +15.9	+ 15.4
6.	Chromatographic purity		conforms
6.1	Chromatographic purity – by HPLC (EP)		conforms
6.1.1	digitoxin (A), not more than, [%]	0.5	0.20
6.1.2.	gitoxin (B), not more than, [%]	0.5	0.11
6.1.3.	digoxigenin (C), not more than, [%]	1.0	0.03
6.1.4.	diginatin (E), not more than, [%]	1.0	0.42
6.1.5.	digoxigenin bisdigitoxoside (F), not more than, [%]	2.5	0.68
6.1.6.	neodigoxin (G), not more than, [%]	0.8	0.07
6.1.7.	lanatoside C (H), not more than, [%]	0.2	n.d.
6.1.8.	digoxigenin tetrakisdigitoxoside (K), not more than, [%]	1.0	0.41
6.1.9.	impurity of unknown structure (L), not more than, [%]	0.3	0.03
6.1.10.	any other impurity, not more than, [%]	0.2	conforms (max. 0.16)
6.1.11.	sum of impurities other than, A, B, C, E, F, G, K, L, not more than, [%]	0.7	0.27

Approved
06.11.2019

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6.1.12.	total sum of impurities, not more than, [%]	3.5	2.22
6.2.	Chromatographic purity – by HPLC (USP)		conforms
6.2.1.	gitoxin (B), not more than [%]	0.5	0.10
6.2.2.	digitoxin (A), not more than [%]	0.5	0.20
6.2.3.	total impurities, not more than [%]	3.5	2.30
7.	Loss on drying		conforms
7.1	Loss on drying (0.5g sample over P_2O_5 at room temperature under vacuum), not more than, [%] (EP)	1.0	0.3
7.2	Loss on drying, (vacuum at 105° for 1h), not more than, [%] (USP)	1.0	0.4
8.	Sulphated ash (1g sample), not more than, [%]	0.1	0.06
9.	Residue on ignition, not more than, [%]	0.5	0.3
10.	Residual organic solvents		conforms
10.1.	methanol, not more than, [ppm]	3 000	80
10.2.	methylene chloride, not more than, [ppm]	600	110
10.3.	acetone, not more than, [ppm]	5 000	10
10.4.	DMSO, not more than, [ppm]	5 000	800
11.	Assay of Digoxin		conforms
11.1.	Assay of Digoxin, calcd. on dry substance, [%] (EP)	96.0 – 102.0	101.9
11.2.	Assay of Digoxin, [%] (USP)	95.0 – 101.0	100.0
12.	Particle size distribution, not less than [µm]	50 % below 12 µm	8
		90 % below 24 µm	18
		99 % below 48 µm	33

This batch has been manufactured, tested, packaged and released in accordance with the ICH Q7 / EU GMP Guide Part II.
The Product corresponds with the requirements of current Ph. Eur. and USP.
The Digoxin Micronized batch 051019/M complies as per the above registered specification.

Signature: [illegible] (Head of Quality / Qualified Person) Date: 06.11.2019