Hetero Drugs Limited (Unit-I)

Sy.No.s. 213, 214 & 255, Bonthapally Village, Gummadidala Mandal, Sangareddy District, Telangana state, INDIA.
Phone : + 091-8458-275314/ 275777,Fax:+91-8458-275271

HETERO DRUGS LIMITED QUALITY ASSURANCE RELEASED

CERTIFICATE OF ANALYSIS

Product	: Nebivolol Hydrochloride	Reference STP No.	: NB-011-04, NB-005-03
Batch No	: NB17100215	Reference	: In-House
Date of Manufacture	: October - 2017	Batch Quantity	: 26.41 Kg
Analytical Report No.	: NB0241/17	Date of Analysis	: 27/10/2017
		Retest Date	: September - 2022
		Status	: Initial certification

S.No.	Test	Specifications	Results	Reference
1	Description	A white to off white crystalline powder	A white crystalline powder	Visual inspection
2	Solubility	Sparingly soluble in dimethylformamide, slightly soluble in Methanol, Very slightly soluble in water and practically insoluble in 0.1M HCl.	Complies	Visual inspection
3	Identification by a) IR	The infra red absorption spectrum of the finely ground sample in KCl dispersion compressed into a disc should exhibits maxima only at the same wave numbers as that of asimilar preparation of Nebivolol Hydrochloride Working Standard.	Matches with the standard spectrum	Ph.Eur.<2.2.24>
	b) HPLC	The retention time of the principal peak obtained in Assay preparation-1 should matches with that of the standard preparation.	Matches with the standard	In-House
	c) Chlorides test	Should meet the requirement for chloride.	Complies	Ph.Eur.<2.3.1>
	d)XRD	The diffractogram of the test sample should match with that of Nebivolol HCl working standard.	Matches with the standard diffractogram	Ph.Eur.<2.9.33>
4	Melting Range	Should be between 225.0°C and 235.0°C	225.6°C to 226.8°C	Ph.Eur.<2.2.14>
5	Chloride content (on dried basis)	Should be between 7.8 % w/w and 8.5 % w/w	8.0 % w/w	In-House
6	Loss on drying	Not more than 1.0 % w/w	0.20 % w/w	Ph.Eur.<2.2.32>
7	Palladium content	Not be more than 5 ppm	Less than 1 ppm (QL=0.2 ppm)	In-House
8	Sulfated ash	Not more than 0.1 % w/w	0.06 % w/w	Ph.Eur.<2.4.14>
9	Heavy Metals	Not more than 0.002 % w/w	Less than 0.002 % w/w	Ph.Eur.<2.4.8> Method-C
10	Chromatographic purity byHPLC	[2S*[1R*, 5R* (S*)]]-α,α' – [iminobis(methylene)bis[6-fluoro-3,4-dihydro-2H-1-benzopyran-2-methanol] Related compound-A : Not more than 0.15 %	0.02% (QL=0.004%)	In-House
		Related compound-A + Related compound -B (from chiral purity by HPLC) : Not more than 0.15 %	0.02%	
		Maximum single unknown impurity : Not more than 0.10 %	0.03%	
		Total impurities : Not more than 0.50 %	0.04%	
11	Chiral purity by HPLC	[2S*[1R*, 5S* (S*)]]-α,α' – [iminobis(methylene)bis [6-fluoro-3,4-dihydro-2H-1-benzopyran-2-methanol] Related compound-B : : Not more than 0.15 %	Below QL (QL=0.02%)	In-House
		Nebivolol D-Isomer : Should be between 48.5 to 51.5 %	49.6%	
		Nebivolol L-Isomer : Should be between 48.5 to 51.5 %	50.4%	

Compiled by : Date : 27/10/2017

Checked by : Date : 27/10/17

Authorised signatory : Date : 27/10/17

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S.No.	Test	Specifications	Results	Reference
12	Residual solvents by GC* (Method-I)	Methanol : Not more than 1500 ppm	79 ppm (QL=7ppm)	In-House
		Ethanol : Not more than 1000 ppm	Below QL (QL=13ppm)	
		Di-isopropyl ether : Not more than 50 ppm	Below QL (QL=8ppm)	
		Ethyl acetate : Not more than 1000 ppm	Below QL (QL=23ppm)	
		Toluene : Not more than 400 ppm	Below QL (QL=15ppm)	
	Residual solvents by GC* (Method-II)	Acetic acid : Not more than 5000 ppm	Below QL (QL=200ppm)	
13	Assay by HPLC (on dried basis)	Should be between 98.5 % w/w and 101.5 % w/w	100.5 % w/w	In-House
14	Monomethyl amine content by IC	Should not be more than 100 ppm	35 ppm	In-House
15	FOB & B-spot content by HPLC	(±)-[1S*(S*)]-6-Fluoro-3,4dihydro-2-oxiranyl-2H-1-Benzopyran (FOB): Should be not more than 37 ppm	Below QL (QL=12ppm)	In-House
		(±)-[1S*(R*)]-6-Fluoro-3,4dihydro-2-oxiranyl-2H-1-Benzopyran (B-spot): Should be not more than 37 ppm	Below QL (QL=12ppm)	
16	Particle size analysis	d(0.90) should be less than 25µm	11 µm	In-House

* No potential for the class-1 solvents as specified by ICH to be present in Nebivolol hydrochloride, as they are not used in the manufacturing process. The material if tested for these solvents, will comply with the established standards.

The product **conforms** to the above Specifications.

Compiled by : Date : 27/10/2017

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Authorised signatory : Date : 27/10/17