Hangzhou Huarong Pharm Co.,Limited

No. 5 Yongfuqiao Road, Gongshu District, Hangzhou, Zhejiang Province, China.
TEL: 0086-571-86758373 FAX: 0086-571-81131109

Certificate of Analysis

品名：肝素钠 批号：KH3-2305027 批数量：87.992Kg
Commodity: Heparin sodium Batch number: KH3-2305027 Quantity of Lot: 87.992Kg

生产日期：2023.05.17 报告日期：2023.06.06 有效期至：2026.04
Date of manufacture:May 17,2023 Date of report:June 06,2023 Expiry Date:Apr,2026

检验依据 Acceptance Criteria		EP11.0	
检验项目 Items tests		标准规定 Specifications	检验结果 Test results
*性状 *Appearance		白色或类白色粉末，具有引湿性，易溶于水。 White or almost white, hygroscopic powder, freely soluble in water.	白色粉末 White powder
鉴别 Identification	A.	符合活性检验的描述。 It complies with the requirements described under Assay.	符合活性检验的描述。 It complies with the requirements described under Assay.
	B.Anti-FXa/ Anti-FIIa	0.9~1.1	1.0
	C.氢谱检测 Nuclear magnetic resonance spectrometry	必须在2.04ppm、3.27ppm (成对)、4.34 ppm、5.22ppm和5.42ppm处存在肝素钠的主峰，误差在± 0.03ppm内；利用测试样品和肝素钠核磁鉴别标准品获得^{1}H-NMR谱，两种氢谱在进行归一化后定量比较以获得相似强度。在2.08±0.02 ppm处可能存在硫酸皮肤素峰；在0.10~2.00ppm、2.10~3.10ppm和 5.70 ~8.00ppm区域不得存在超过5.42ppm峰高4%的信号；溶剂或工艺相关物质如存在必须确定；在3.35ppm~4.55ppm区域某些肝素信号峰强度可能不同。 The large heparin sodium signals must be present: 2.04ppm, 3.27ppm (doublet), 4.34ppm, 5.22ppm and 5.42 ppm, all within ± 0.03ppm. The H-NMR spectrum obtained with the test sample and that obtained with heparin sodium for NMR identification CRS are compared qualitatively after the 2 spectra have been normalized so as to have a similar intensity; Dermatan sulfate with a methyl signal at 2.08±0.02 ppm may be observed; no unidentified signals larger than 4 percent compared to the height of the heparin signal at 5.42 ppm are present in the ranges 0.10-2.00 ppm, 2.10-3.10 ppm and 5.70-8.00ppm ;signals from the solvent or process related substances may be present and have to be identified to be accepted; variation in the intensity of some signal regions of the spectrum of heparin may occur; the intensity -variable regions are between 3.35 ppm and 4.55 ppm, where the signal pattern is approximately kept but intensity varies.	在 2.04ppm、3.27ppm (成对)、4.34 ppm、5.22ppm 和 5.42ppm 处存在肝素钠的主峰，误差在± 0.03ppm 内；样品溶液谱图与对照品谱图相似，并且峰的信号强度相似。在 2.08±0.02 ppm 处存在硫酸皮肤素峰；在 0.10~2.00ppm 、2.10~3.10ppm 和 5.70 ~8.00ppm 区域不存在超过 5.42ppm 峰高 4%的信号；残留溶剂峰的信号出现在 1.18ppm 附近。 The large heparin sodium signals is present: 2.04ppm, 3.27ppm(doublet), 4.34ppm, 5.22ppm and 5.42 ppm, all with in ± 0.03 ppm. The spectrum of sample solution is similar to that of Heparin sodium RS and the signal of the peak is similar. Dermatan sulfate signal exists at 2.08±0.02 ppm; no unidentified signals larger than 4 percent compared to the height of the heparin signal at 5.42 ppm are present in the ranges 0.10-2.00 ppm, 2.10-3.10 ppm and 5.70-8.00ppm ; The signals of residue solvent is present near 1.18ppm.

HUARONG PHARMACEUTICAL 杭州华鎔医药有限公司 HANGZHOU CO.,LTD. QC

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检验依据 Acceptance Criteria		EP11.0	
检验项目 Items tests		标准规定 Specifications	检验结果 Test results
鉴别 Identification	D.液相鉴别 Liquid chromatography	供试品溶液(a)主峰的保留时间和峰形应与对照溶液(c)主峰的保留时间一致 The principal peak in the chromatogram obtained with test solution (a) is similar in retention time and shape to the principal peak in the chromatogram obtained with reference solution (c).	供试品溶液(a)主峰的保留时间和峰形应与对照溶液(c)主峰的保留时间一致 The principal peak in the chromatogram obtained with test solution (a) is similar in retention time and shape to the principal peak in the chromatogram obtained with reference solution (c).
	E. 钠 Sodium	见“检查”中钠含量项 It complies with the test for sodium (see Tests)	符合规定 Complies
检查 Test	水溶液外观 Appearance of solution	澄清无色；如显色，不得超过对照溶液 5。 The solution is clear and not more intensely coloured than intensity 5 of the range of reference solutions of the most appropriate colour.	澄清；颜色浅于对照溶液 5。 The solution is clear and not more intensely coloured than intensity 5 of the range of reference solutions of the most appropriate colour.
	pH	5.5~8.0	6.6
	核酸 Nucleotidic impurities	260nm≤0.15	0.055
	蛋白质（干品） Protein(dried substance)	≤0.5%	0.05%
	有关物质 Related substances	—硫酸皮肤素和硫酸软骨素和：其峰面积不得超过对照溶液(e)中对应峰面积（2.0%）； —其他杂质：忽略出现在初始等度洗脱步骤的峰，谱图中不得有超过对照溶液(e)中硫酸皮肤素和硫酸软骨素峰面积的 0.01 倍(0.02%)的峰。 —Sum of dermatan sulfate and chondroitin sulfate: not more than the area of the corresponding peak in the chromatogram obtained with reference solution (e) (2.0 percent) —Any other impurity: No peak with an area greater than 0.01times the area of the peak due to dermatan sulfate and chondroitin sulfate in the chromatogram obtained with reference solution (e) is detected (corresponding to a disregard limit of 0.02percent). Disregard any peaks that appear during the initial isocratic step.	—硫酸皮肤素和硫酸软骨素峰面积和少于对照溶液(e)中对应峰面积（2.0%）； —忽略出现在初始等度洗脱步骤的峰，谱图中无超过对照溶液(e)中硫酸皮肤素和硫酸软骨素峰面积的 0.01 倍(0.02%)的峰。 Sum of dermatan sulfate and chondroitin sulfate not more than the area of the corresponding peak in the chromatogram obtained with reference solution (e) (2.0 percent). Any other impurity: No peak with an area greater than 0.01times the area of the peak due to dermatan sulfate and chondroitin sulfate in the chromatogram obtained with reference solution (e) is detected (corresponding to a disregard limit of 0.02percent). Disregard any peaks that appear during the initial isocratic step.

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检验项目 Items tests		标准规定 Specifications						检验结果 Test results
检查 Test	氮含量（干品） Nitrogen (dried substance)	1.5%~2.5%						2.0%
	钠含量（干品） Sodium (dried substance)	10.5%~13.5%						12.4%
	元素杂质 Elemental Impurities	元素 Element	Li	V	Co	Ni	Cu	As: 0.001 Cd: 0 Hg: 0 Pb: 0.01
		限度 Limit(μg/g)	25	1	0.5	2	30	
		元素 Element	As	Cd	Sb	Hg	Pb	
		限度 Limit(μg/g)	1.5	0.2	9	0.3	0.5	
	干燥失重 Loss on drying	≤8.0%						3.6%
	细菌内毒素 Bacterial endotoxins	<0.01 IU/抗 IIa 因子活性 <0.01 IU/ Anti-factor IIa U activity						<0.01 IU/ Anti-factor IIa U activity
	残留溶剂 Residue solvent	≤5000ppm						402pm
微生物项目 Micro organisms	总需氧菌 TAMC	≤100CFU/g						<10 CFU/g
	霉菌及酵母菌 TYMC	≤10CFU/g						<10 CFU/g
	大肠埃希菌 Escherichia coli	不得检出 Negative						未检出 Negative
	沙门菌 Salmonella	不得检出 Negative						未检出 Negative
活性 activity	抗 IIa 因子活性 Anti-factor IIa activity	≥180 IU/mg						262 IU/mg
	抗 Xa 因子活性 Anti-factor Xa activity	/						253 IU/mg
结论 Conclusion	肝素钠的质量符合 EP11.0 的要求。 The analytical results of the substance show that heparin sodium complies with the requirements of EP 11.0 standards.							

备注：引湿性和溶解性只检测工艺验证批次。
Note: Hygroscopicity and solubility only be detected in process validation batches.

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