

Certificate of Analysis

检验报告单

检验报告编号：CP190058

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|-------------------|--|---|------------------------|---|
| Product 品名 | Heparin Calcium 肝素钙 | | Batch No. 批号 | YN010711809004 |
| Quantity 批量 | 2.720Kg | | Specification 规格 | EP9.3 |
| MFG. Date 生产日期 | Year Month Day | 2018 年 09 月 25 日 | Retest Date 复验期 | Year Month Day 2020 年 09 月 24 日 |
| Test Date 检测日期 | Year Month Day | 2018 年 10 月 08 日 | Report Date 报告日期 | Year Month Day 2019 年 03 月 19 日 |
| MFG Line 生产车间 | Line P1 P1 车间 | | Storage condition 储存条件 | Storage in airtight container below 25°C 置于密闭容器中，在 25°C 以下保存 |
| Items 项目 | Specifications 检验标准 | | | Results 检验结果 |
| Origin 来源 | The intestinal mucosa of healthy pigs suitable for human consumption. 适用于人类的健康猪肠粘膜 | | | Complies 符合规定 |
| Characters 性状 | Appearance 外观 | White or almost white powder, hygroscopic powder. 白色或类白色，吸湿性粉末 | | Complies 符合规定 |
| | Solubility 溶解性 | Freely soluble in water 易溶于水 | | Complies 符合规定 |
| Identification 鉴别 | A. It complies with the requirements described under assay. 符合“含量”分析项目下的要求 | | | Complies 符合规定 |
| | The ratio of anti-factor Xa activity to anti-factor IIa activity determined as described under Assay, ranges between 0.9-1.1 B. 抗 Xa 与抗 IIa 的比值在 0.9-1.1 之间 | | | 1.0 |
| | C. NMR | The large heparin calcium must be present: 2.05ppm, 3.29ppm(doublet), 4.37ppm, 5.35ppm and 5.43ppm, all within ± 0.03 ppm; The ¹ H-NMR spectrum obtained with the test sample and that obtained with heparin calcium for NMR identification CRS are compared qualitatively after the 2 spectra have been normalised 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 per cent compared to the height of the heparin signal at 5.42ppm are present in the ranges 0.10-2.00ppm, 2.10-3.10ppm and 5.70-8.00ppm; signals from the solvent or process-related substances may be present and have to be identified to be accepted. 肝素钙主要峰信号应为 2.05、3.29(d)、4.37、5.35 和 5.43，均可在其值的 ± 0.03 ppm 范围内；调整测试样品和肝素钙 NMR 鉴别化学参考标准品的 H-NMR 图谱强度一致后，对 2 者进行定性比较；硫酸皮肤素的甲基信号应在 2.08 ± 0.02 ppm；在 0.10~2.00、2.10~3.10、5.70~8.00 ppm 范围内不允许有峰高大于 5.43 ppm 处峰高值的 4% 的未识别峰出现；允许溶剂及相关添加物的峰出现，但这些峰必须鉴别且可接受。 | | Complies 符合规定 Contract analysis (委托检验) |
| | D: HPLC | 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). 样品溶液 (a) 和标准溶液 (c) 所获得图谱中主要峰的保留时间和峰形均相似。 | | Complies 符合规定 |
| E. Calcium 钙 | It gives the reactions of calcium 呈正反应 | | Complies 符合规定 | |
| Tests 检测 | Appearance of solution 溶液外观 | Clarity: The solution is clear 澄清度：澄清 | | Complies 符合规定 |
| | | Color: not more intensely colored than intensity 5 of the range of reference solutions of the most appropriate colour (2.2.2, Method II) 颜色：不深于 BY5 | | Complies 符合规定 |

| | | | | |
|---|--|--|------------------------|--|
| Product 品名 | Heparin Calcium 肝素钙 | | Batch No. 批号 | YN010711809004 |
| Quantity 批量 | 2.720Kg | | Specification 规格 | EP9.3 |
| MFG. Date 生产日期 | Year Month Day | 2018 年 09 月 25 日 | Retest Date 复验期 | Year Month Day 2020 年 09 月 24 日 |
| Test Date 检测日期 | Year Month Day | 2018 年 10 月 08 日 | Report Date 报告日期 | Year Month Day 2019 年 03 月 19 日 |
| MFG Line 生产车间 | Line P1 P1 车间 | | Storage condition 储存条件 | Storage in airtight container below 25°C 置于密闭容器中, 在 25°C 以下保存 |
| Items 项目 | Specifications 检验标准 | | | Results 检验结果 |
| | pH | 5.5 ~ 8.0 | | 7.0 |
| | Nucleic Impurities 核酸杂质 | ≤ 0.15(260nm) | | 0.054 |
| | Protein 蛋白 | ≤0.5%(Based on dried substance) ≤0.5% (以干品计) | | 0.04% |
| | Related Substances 相关物质 | Not more than the area of the peak due to dermatan sulfate and chondroitin sulfate in the chromatogram obtained with reference solution (e)(2.0 per cent) No peak with an area greater than 0.01 times 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 0.02 per cent) 待测溶液 (b) 中硫酸皮肤素和硫酸软骨素的峰面积不大于参考溶液 (e) 中硫酸皮肤素和硫酸软骨素的峰面积 (2.0%) ; 其他单个杂质峰面积不得大于对照溶液 (e) 中的硫酸皮肤素和硫酸软骨素的峰面积之和的 0.01 倍 (0.02%) 。 | | Complies 符合规定 |
| | Nitrogen 氮 | 1.5%~2.5%(Based on dried substance) 1.5%~2.5%(以干品计) | | 2.0% |
| | Calcium 钙 | 9.5%~11.5%(Based on dried substance) 9.5%~11.5%(以干品计) | | 11.1% |
| | Loss on drying 干燥失重 | ≤8.0% | | 5.3% |
| | Residual Solvent 残留溶剂 | ≤0.5% (ethanol) ≤0.5% (乙醇) | | 0.05% |
| | Heavy metal 重金属 | ≤ 30ppm | | Complies 符合规定 |
| | Bacterial endotoxins 细菌内毒素 | ≤0.01EU/IU | | Complies 符合规定 |
| Microbial Limits 微生物检查 | Total Plate Count : ≤ 100 CFU/g | 菌落总数 : ≤ 100 CFU/g | | <10 CFU/g |
| | Mould and Yeast : ≤ 10 CFU/g | 霉菌和酵母菌菌落 : ≤ 10 CFU/g | | <10 CFU/g |
| | Bile-tolerant : absent /g | 耐胆汁的革兰阴性菌 : 不得检出/g | | 未检出 Absent |
| | Escherichia coli : absent /g | 大肠埃希菌 : 不得检出/g | | 未检出 Absent |
| | Staphylococcus aureus : absent/g | 金黄色葡萄球菌 : 不得检出/g | | 未检出 Absent |
| | Saimonella : absent/10g | 沙门菌 : 不得检出/10g | | 未检出 Absent |
| Assay/Potency 含量/效价 | Anti-factor IIa activity based on "dried substance": NLT 180iu/mg 以干品计算, 每 1mg 的抗IIa 因子含量不得少于 180IU | | | 248 IU/mg |
| Conclusion : <u>comply</u> (comply/fail) with the specifications of EP9.3. 结论 : 结果 <u>符合</u> (符合/不符合) EP9.3 规定 | | | | |

Tabulator /Date: 陈小平
2019.03.19

QC Manager/Date: 朱斌
2019.03.19

QA Reviewed by/Date: 孙燕
2019.03.19

Certificate of Analysis

检验报告单

检验报告编号：CP190059

| | | | | |
|----------------------|--|--|---|--|
| Product 品名 | Heparin Calcium 肝素钙 | | Batch No. 批号 | YN010711809005 |
| Quantity 批量 | 3.014Kg | | Specification 规格 | EP9.3 |
| MFG. Date 生产日期 | Year Month Day 2018 年 09 月 27 日 | Retest Date 复验期 | Year Month Day 2020 年 09 月 26 日 | |
| Test Date 检测日期 | Year Month Day 2018 年 10 月 08 日 | Report Date 报告日期 | Year Month Day 2019 年 03 月 19 日 | |
| MFG Line 生产车间 | Line P1 P1 车间 | Storage condition 储存条件 | Storage in airtight container below 25°C 置于密闭容器中，在 25°C 以下保存 | |
| Items 项目 | Specifications 检验标准 | | | Results 检验结果 |
| Origin 来源 | The intestinal mucosa of healthy pigs suitable for human consumption. 适用于人类的健康猪肠粘膜 | | | Complies 符合规定 |
| Characters 性状 | Appearance 外观 | White or almost white powder, hygroscopic powder. 白色或类白色，吸湿性粉末 | | Complies 符合规定 |
| | Solubility 溶解性 | Freely soluble in water 易溶于水 | | Complies 符合规定 |
| Identification 鉴别 | A. It complies with the requirements described under assay. 符合“含量”分析项目下的要求 | | | Complies 符合规定 |
| | The ratio of anti-factor Xa activity to anti-factor IIa activity determined as described under Assay, ranges between 0.9-1.1 B. 抗 Xa 与抗 IIa 的比值在 0.9-1.1 之间 | | | 0.9 |
| | C. NMR | The large heparin calcium must be present: 2.05ppm, 3.29ppm(doublet), 4.37ppm, 5.35ppm and 5.43ppm, all within ± 0.03 ppm; The ¹ H-NMR spectrum obtained with the test sample and that obtained with heparin calcium for NMR identification CRS are compared qualitatively after the 2 spectra have been normalised 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 per cent compared to the height of the heparin signal at 5.42ppm are present in the ranges 0.10-2.00ppm, 2.10-3.10ppm and 5.70-8.00ppm; signals from the solvent or process-related substances may be present and have to be identified to be accepted. 肝素钙主要峰信号应为 2.05、3.29(d)、4.37、5.35 和 5.43，均可在其值的 ± 0.03 ppm 范围内；调整测试样品和肝素钙 NMR 鉴别化学参考标准品的 ¹ H-NMR 图谱强度一致后，对二者进行定性比较；硫酸皮肤素的甲基信号应在 2.08 ± 0.02 ppm；在 0.10~2.00、2.10~3.10、5.70~8.00 ppm 范围内不允许有峰高大于 5.43 ppm 处峰高值的 4% 的未识别峰出现；允许溶剂及相关添加物的峰出现，但这些峰必须鉴别且可接受。 | | Complies 符合规定 Contract analysis (委托检验) |
| | D: HPLC | 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). 样品溶液 (a) 和标准溶液 (c) 所获得图谱中主要峰的保留时间和峰形均相似。 | | Complies 符合规定 |
| E. Calcium E. 钙 | It gives the reactions of calcium 呈正反应 | | Complies 符合规定 | |
| Tests 检测 | Appearance of solution 溶液外观 | Clarity : The solution is clear 澄清度 : 澄清 | | Complies 符合规定 |
| | | Color: not more intensely colored than intensity 5 of the range of reference solutions of the most appropriate colour (2.2.2, Method II) 颜色 : 不深于 BY5 | | Complies 符合规定 |

| Product 品名 | Heparin Calcium 肝素钙 | | Batch No. 批号 | YN010711809005 |
|---|--|--|------------------------|--|
| Quantity 批量 | 3.014Kg | | Specification 规格 | EP9.3 |
| MFG. Date 生产日期 | Year Month Day | 2018 年 09 月 27 日 | Retest Date 复验期 | Year Month Day 2020 年 09 月 26 日 |
| Test Date 检测日期 | Year Month Day | 2018 年 10 月 08 日 | Report Date 报告日期 | Year Month Day 2019 年 03 月 19 日 |
| MFG Line 生产车间 | Line P1 P1 车间 | | Storage condition 储存条件 | Storage in airtight container below 25°C 置于密闭容器中, 在 25°C 以下保存 |
| Items 项目 | Specifications 检验标准 | | | Results 检验结果 |
| | pH | 5.5 ~ 8.0 | | 7.0 |
| | Nucleic Impurities 核酸杂质 | ≤ 0.15(260nm) | | 0.054 |
| | Protein 蛋白 | ≤0.5%(Based on dried substance) ≤0.5% (以干品计) | | 0.05% |
| | Related Substances 相关物质 | Not more than the area of the peak due to dermatan sulfate and chondroitin sulfate in the chromatogram obtained with reference solution (e)(2.0 per cent) No peak with an area greater than 0.01 times 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 0.02 per cent) 待测溶液 (b) 中硫酸皮肤素和硫酸软骨素的峰面积不大于参考溶液 (e) 中硫酸皮肤素和硫酸软骨素的峰面积 (2.0%) ; 其他单个杂质峰面积不得大于对照溶液 (e) 中的硫酸皮肤素和硫酸软骨素的峰面积之和的 0.01 倍 (0.02%) 。 | | Complies 符合规定 |
| | Nitrogen 氮 | 1.5%~2.5%(Based on dried substance) 1.5%~2.5%(以干品计) | | 2.0% |
| | Calcium 钙 | 9.5%~11.5%(Based on dried substance) 9.5%~11.5%(以干品计) | | 11.2% |
| | Loss on drying 干燥失重 | ≤8.0% | | 4.8% |
| | Residual Solvent 残留溶剂 | ≤0.5% (ethanol) ≤0.5% (乙醇) | | 0.05% |
| | Heavy metal 重金属 | ≤ 30ppm | | Complies 符合规定 |
| | Bacterial endotoxins 细菌内毒素 | ≤0.01EU/IU | | Complies 符合规定 |
| Microbial Limits 微生物检查 | Total Plate Count : ≤ 100 CFU/g | 菌落总数 : ≤ 100 CFU/g | | <10 CFU/g |
| | Mould and Yeast : ≤ 10 CFU/g | 霉菌和酵母菌菌落 : ≤ 10 CFU/g | | <10 CFU/g |
| | Bile-tolerant : absent /g | 耐胆汁的革兰阴性菌 : 不得检出/g | | 未检出 Absent |
| | Escherichia coli : absent /g | 大肠埃希菌 : 不得检出/g | | 未检出 Absent |
| | Staphylococcus aureus : absent/g | 金黄色葡萄球菌 : 不得检出/g | | 未检出 Absent |
| | Saimonella : absent/10g | 沙门菌 : 不得检出/10g | | 未检出 Absent |
| Assay/Potency 含量/效价 | Anti-factor IIa activity based on "dried substance": NLT 180iu/mg 以干品计算, 每 1mg 的抗IIa 因子含量不得少于 180IU | | | 249 IU/mg |
| Conclusion : <u>comply</u> (comply/fail) with the specifications of EP9.3. 结论 : 结果 <u>符合</u> (符合/不符合) EP9.3 规定 | | | | |

 Tabulator /Date: 陈小琴
2019.03.19

 QC Manager/Date: 朱线
2019.03.19

 QA Reviewed by/Date: 安公基
2019.03.19

Certificate of Analysis

检验报告单

检验报告编号：CP190060

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|----------------------|--|---|---|--|
| Product 品名 | Heparin Calcium 肝素钙 | | Batch No. 批号 | YN010711809006 |
| Quantity 批量 | 3.024Kg | | Specification 规格 | EP9.3 |
| MFG. Date 生产日期 | Year Month Day 2018 年 09 月 30 日 | Retest Date 复验日期 | Year Month Day 2020 年 09 月 29 日 | |
| Test Date 检测日期 | Year Month Day 2018 年 10 月 08 日 | Report Date 报告日期 | Year Month Day 2019 年 03 月 19 日 | |
| MFG Line 生产车间 | Line P1 P1 车间 | Storage condition 储存条件 | Storage in airtight container below 25°C 置于密闭容器中，在 25°C 以下保存 | |
| Items 项目 | Specifications 检验标准 | | | Results 检验结果 |
| Origin 来源 | The intestinal mucosa of healthy pigs suitable for human consumption. 适用于人类的健康猪肠粘膜 | | | Complies 符合规定 |
| Characters 性状 | Appearance 外观 | White or almost white powder, hygroscopic powder. 白色或类白色，吸湿性粉末 | | Complies 符合规定 |
| | Solubility 溶解性 | Freely soluble in water 易溶于水 | | Complies 符合规定 |
| Identification 鉴别 | A. It complies with the requirements described under assay. 符合“含量”分析项目下的要求 | | | Complies 符合规定 |
| | The ratio of anti-factor Xa activity to anti-factor IIa activity determined as described under Assay, ranges between 0.9-1.1 B. 抗 Xa 与抗 IIa 的比值在 0.9-1.1 之间 | | | 1.0 |
| | C. NMR | The large heparin calcium must be present: 2.05ppm, 3.29ppm(doublet), 4.37ppm, 5.35ppm and 5.43ppm, all within ± 0.03 ppm; The ¹ H-NMR spectrum obtained with the test sample and that obtained with heparin calcium for NMR identification CRS are compared qualitatively after the 2 spectra have been normalised 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 per cent compared to the height of the heparin signal at 5.42ppm are present in the ranges 0.10-2.00ppm, 2.10-3.10ppm and 5.70-8.00ppm; signals from the solvent or process-related substances may be present and have to be identified to be accepted. 肝素钙主要峰信号应为 2.05、3.29(d)、4.37、5.35 和 5.43，均可在其值的 ± 0.03 ppm 范围内；调整测试样品和肝素钙 NMR 鉴别化学参考标准品的 H-NMR 图谱强度一致后，对 2 者进行定性比较；硫酸皮肤素的甲基信号应在 2.08 ± 0.02 ppm；在 0.10~2.00, 2.10~3.10, 5.70~8.00 ppm 范围内不允许有峰高大于 5.43 ppm 处峰高值的 4% 的未识别峰出现；允许溶剂及相关添加物的峰出现，但这些峰必须鉴别且可接受。 | | Complies 符合规定 Contract analysis (委托检验) |
| | D: HPLC | 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). 样品溶液 (a) 和标准溶液 (c) 所获得图谱中主要峰的保留时间和峰形均相似。 | | Complies 符合规定 |
| E. Calcium E. 钙 | It gives the reactions of calcium 呈正反应 | | Complies 符合规定 | |
| Tests 检测 | Appearance of solution 溶液外观 | Clarity : The solution is clear 澄清晰度：澄清 | | Complies 符合规定 |
| | | Color: not more intensely colored than intensity 5 of the range of reference solutions of the most appropriate colour (2.2.2, Method II) 颜色：不深于 BY5 | | Complies 符合规定 |

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|---|--|--|---------------------------|--|
| Product 品名 | Heparin Calcium 肝素钙 | | Batch No. 批号 | YN010711809006 |
| Quantity 批量 | 3.024Kg | | Specification 规格 | EP9.3 |
| MFG. Date 生产日期 | Year Month Day 2018 年 09 月 30 日 | | Retest Date 复验日期 | Year Month Day 2020 年 09 月 29 日 |
| Test Date 检测日期 | Year Month Day 2018 年 10 月 08 日 | | Report Date 报告日期 | Year Month Day 2019 年 03 月 19 日 |
| MFG Line 生产车间 | Line P1 P1 车间 | | Storage condition 储存条件 | Storage in airtight container below 25°C 置于密闭容器中, 在 25°C 以下保存 |
| Items 项目 | Specifications 检验标准 | | | Results 检验结果 |
| | pH | 5.5 ~ 8.0 | | 7.0 |
| | Nucleic Impurities 核酸杂质 | ≤ 0.15(260nm) | | 0.056 |
| | Protein 蛋白 | ≤0.5%(Based on dried substance) ≤0.5% (以干品计) | | 0.05% |
| | Related Substances 相关物质 | Not more than the area of the peak due to dermatan sulfate and chondroitin sulfate in the chromatogram obtained with reference solution (e)(2.0 per cent) No peak with an area greater than 0.01 times 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 0.02 per cent) 待测溶液 (b) 中硫酸皮肤素和硫酸软骨素的峰面积不大于参考溶液 (e) 中硫酸皮肤素和硫酸软骨素的峰面积 (2.0%) ; 其他单个杂质峰面积不得大于对照溶液 (e) 中的硫酸皮肤素和硫酸软骨素的峰面积之和的 0.01 倍 (0.02%) 。 | | Complies 符合规定 |
| | Nitrogen 氮 | 1.5%~2.5%(Based on dried substance) 1.5%~2.5%(以干品计) | | 2.0% |
| | Calcium 钙 | 9.5%~11.5%(Based on dried substance) 9.5%~11.5%(以干品计) | | 11.0% |
| | Loss on drying 干燥失重 | ≤8.0% | | 4.4% |
| | Residual Solvent 残留溶剂 | ≤0.5% (ethanol) ≤0.5% (乙醇) | | 0.05% |
| | Heavy metal 重金属 | ≤ 30ppm | | Complies 符合规定 |
| | Bacterial endotoxins 细菌内毒素 | ≤0.01EU/IU | | Complies 符合规定 |
| Microbial Limits 微生物检查 | Total Plate Count : ≤ 100 CFU/g | 菌落总数 : ≤ 100 CFU/g | | <10 CFU/g |
| | Mould and Yeast : ≤ 10 CFU/g | 霉菌和酵母菌菌落 : ≤ 10 CFU/g | | <10 CFU/g |
| | Bile-tolerant : absent /g | 耐胆汁的革兰阴性菌 : 不得检出/g | | 未检出 Absent |
| | Escherichia coli : absent /g | 大肠埃希菌 : 不得检出/g | | 未检出 Absent |
| | Staphylococcus aureus : absent/g | 金黄色葡萄球菌 : 不得检出/g | | 未检出 Absent |
| | Saimonella : absent/10g | 沙门菌 : 不得检出/10g | | 未检出 Absent |
| Assay/Potency 含量/效价 | Anti-factor IIa activity based on "dried substance": NLT 180iu/mg 以干品计算, 每 1mg 的抗IIa 因子含量不得少于 180IU | | | 237 IU/mg |
| Conclusion : <u>comply</u> (comply/fail) with the specifications of EP9.3. 结论 : 结果 <u>符合</u> (符合/不符合) EP9.3 规定 | | | | |

Tabulator /Date: 陈小琴
2019.03.19

QC Manager/Date: 朱斌
2019.03.19

QA Reviewed by/Date: 张燕
2019.03.19