Reconstitution Stability Report of

Ceftriaxone Sodium for Injection 1.0g

Purpose: the insert of Ceftriaxone Sodium for Injection specifies that the time period of ceftriaxone sodium for injection remaining stable after being dissolved in solution should be stated. The study is carried out to confirm the stability of ceftriaxone sodium for injection 1g after being dissolved in the diluents described in the insert (0.9% Sodium Chloride Injection; 1% Lidocaine HCL Injection; 0.45% Sodium Chloride + 2.5% Dextrose Injection; 5% Dextrose Injection; 10% Dextrose Injection; Dextran 40 Dextrose Injection; Hydroxyethyl Starch 200/0.5 Injection; Sterile Water for Injection).

Method: Determine the test of description, pH, particulate matter, sterility, bacterial endotoxins and assay of Ceftriaxone Sodium for injection 1g in different time period after reconstitution. Apparatus and method refer to USP34.

1. Reagents:

Ceftriaxone Sodium for injection 1g, 0.9% Sodium Chloride Injection; 1% Lidocaine HCL Injection; 0.45% Sodium Chloride + 2.5% Dextrose Injection; 5% Dextrose Injection; 10% Dextrose Injection; Dextran 40 Dextrose Injection; Hydroxyethyl Starch 200/0.5 Injection; Sterile water for injection.

2. Procedure:

Intravenous Administration

1） Take 12 vials of ceftriaxone sodium for injection 1g samples, divide the samples into 2 groups, 6 vials each group, dissolve the samples completely in 10ml of sterile water for injection respectively (approximately equivalent to a concentration of 100mg/ml). Place 6 vials at 30±2°C and determine the description, pH, particulate matter, sterility, bacterial endotoxins and assay at 0h, 6h and 12h respectively. Place the 6 vials of another group at 2-8°C and determine description, pH, particulate matter, sterility, bacterial endotoxins and assay at 0h,

12h and 24h.

2） Take 84 vials of ceftriaxone sodium for injection 1g samples, divide the samples into 2 groups, 42 vials each group, dissolve the samples completely in 40 ml of diluent solutions (Table 1) (equivalent to a concentration of 25mg/ml). After reconstitution, place 42 vials from one group at 30±2°C and determine description, pH, particulate matter, sterility, bacterial endotoxins and assay at 0h, 6h and 12h respectively. Place 42 vials of the other group at 2-8°C and determine description, pH, particulate matter, sterility, bacterial endotoxins and assay at 0h, 12h and 24h.

Table 1 Reconstitution solutions

1	0.9% Sodium Chloride Injection
2	0.45% Sodium Chloride + 2.5% Dextrose Injection
3	5% Dextrose Injection
4	10% Detrose Injection
5	Dextran 40 Dextrose Injection
6	Hydroxyethyl Starch 200/0.5 Injection
7	Sterile Water for Injection

Intramuscular Administration:

Take 12 vials of ceftriaxone sodium for injection 1g samples, dissolve completely in 3.5ml of 1% Lidocaine HCL injection, after reconstitution, place 6 vials at 30±2°C and determine the description, pH, particulate matter, sterility, bacterial endotoxins and assay at 0h, 6h and 12h respectively. Place the 6 vials of another group at 2-8°C and determine description, pH, particulate matter, sterility, bacterial endotoxins and assay at 0h, 12h and 24h.

3. Test results

- Test results of description (see Tab. 2)
- Test results of pH (see Tab. 3)

- Test results of particulate matter (see Tab. 4)
- Test results of sterility (see Tab. 5)
- Test results of bacterial endotoxins (see Tab. 6)
- Test results of assay (see Tab. 7)

4. Results analysis

According to the insert of Ceftriaxone Sodium for Injection 1g, we have carried out the stability study concerning 8 reconstitution solutions, 3 concentrations, 2 storage conditions and 6 determination items, analyze as follows with the test results:

1） In the test results under description test, no change of description in all of the compatible solutions, the test results are stable both at 2-8°C and at 30±2°C, however conform with the quality specification.

2） In the test results under pH test, little change of pH in all of the compatible solutions, the test results at 2-8°C are more stable than those at 30±2°C, however conform with the quality specification.

3） In the test results under the test of particulate matter, little change of particulate matter in all of the compatible solutions, the test results at 2-8°C are more stable than those at 30±2°C, however conform with the quality specification.

4） In the test results under sterility test, no change of sterility in all of the compatible solutions, the test results are stable both at 2-8°C and at 30±2°C, however conform with the quality specification.

5） In the test results under the test of bacterial endotoxins, little change of bacterial endotoxins in all of the compatible solutions, the test results at 2-8°C are more stable than those at 30±2°C, however conform with the quality specification.

6） In the test results under Assay test, the relative assay determined value decreases gradually with the increasing storage time, the test results at 2-8°C are more stable than those at 30±2°C, however conform with the quality specification.

5. Conclusion

The results show: After being reconstituted in the above solutions, Ceftriaxone Sodium for Injection (Batch No.: XD5110801, strength: 1.0g) produced by NCPC Hebei Huamin Pharmaceutical Co., Ltd remains stable for the time period specified in insert: remain stable at 30±2°C for 12h, remains stable at 2-8°C for 24h. Therefore, the datas of Reconstitution Stability study of Ceftriaxone Sodium for Injection verify the product complies with the related regulations in insert, and can meet the safety requirement of clinical administration.

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Tab. 2 Description data summary of ceftriaxone sodium for injection (USP)

Time (h) / Items		30±2°C			2-8°C		
		Acceptable criteria: light pale yellow solution					
		0	6	12	0	12	24
IV 100mg/ml	Sterile water for injection	light pale yellow solution	light pale yellow solution	light pale yellow solution	light pale yellow solution	light pale yellow solution	light pale yellow solution
IV 25mg/ml	0.9% Sodium Chloride Injection	light pale yellow solution	light pale yellow solution	light pale yellow solution	light pale yellow solution	light pale yellow solution	light pale yellow solution
	0.45% Sodium Chloride + 2.5% Dextrose Injection	light pale yellow solution	light pale yellow solution	light pale yellow solution	light pale yellow solution	light pale yellow solution	light pale yellow solution
	5% Dextrose Injection	light pale yellow solution	light pale yellow solution	light pale yellow solution	light pale yellow solution	light pale yellow solution	light pale yellow solution
	10% Dextrose Injection	light pale yellow solution	light pale yellow solution	light pale yellow solution	light pale yellow solution	light pale yellow solution	light pale yellow solution
	Dextran 40 Dextrose Injection	light pale yellow solution	light pale yellow solution	light pale yellow solution	light pale yellow solution	light pale yellow solution	light pale yellow solution
	Hydroxyethyl Starch 200/0.5 Injection	light pale yellow solution	light pale yellow solution	light pale yellow solution	light pale yellow solution	light pale yellow solution	light pale yellow solution
	Sterile water for injection	light pale yellow solution	light pale yellow solution	light pale yellow solution	light pale yellow solution	light pale yellow solution	light pale yellow solution
IM 1g/3.5ml	1% Lidocaine HCL Injection	light pale yellow solution	light pale yellow solution	light pale yellow solution	light pale yellow solution	light pale yellow solution	light pale yellow solution

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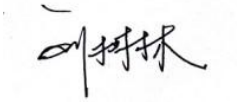

Tab. 3 pH data summary of ceftriaxone sodium for injection (USP)

Time (h) / Items		30±2°C			2-8°C		
		Acceptable criteria: 6.0 to 8.0					
		0	6	12	0	12	24
IV 100mg/ml	Sterile water for injection	6.9	6.9	6.8	6.8	6.8	6.8
IV 25mg/ml	0.9% Sodium Chloride Injection	6.8	6.8	6.9	6.7	6.7	6.8
	0.45% Sodium Chloride + 2.5% Dextrose Injection	6.7	6.8	6.8	6.8	6.8	6.7
	5% Dextrose Injection	6.8	6.8	6.7	6.7	6.7	6.7
	10% Dextrose Injection	6.7	6.8	6.7	6.8	6.9	6.9
	Dextran 40 Dextrose Injection	6.8	6.8	6.9	6.9	6.9	6.8
	Hydroxyethyl Starch 200/0.5 Injection	6.9	6.9	7.0	6.8	6.8	6.9
	Sterile water for injection	6.9	6.8	6.9	6.9	6.9	6.8
IM 1g/3.5ml	1% Lidocaine HCL Injection	6.9	6.9	6.8	6.7	6.7	6.8

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Tab. 4 Particulate matter data summary of ceftriaxone sodium for injection (USP)

Items \ Time (h)			30±2°C			2-8°C		
			Acceptable criteria: ≥ 10 μm: NMT 6000 per container ≥ 25 μm: NMT 600 per container					
			0	6	12	0	12	24
IV 100mg/ml	Sterile water for injection	≥ 10 μm	110	132	146	101	130	171
		≥ 25 μm	54	69	88	52	78	95
IV 25mg/ml	0.9% Sodium Chloride Injection	≥ 10 μm	106	120	132	102	121	150
		≥ 25 μm	48	60	78	44	72	93
	0.45% Sodium Chloride + 2.5% Dextrose Injection	≥ 10 μm	100	113	125	115	143	175
		≥ 25 μm	46	65	77	43	67	84
	5% Dextrose Injection	≥ 10 μm	104	121	144	105	130	153
		≥ 25 μm	38	47	68	37	67	85
	10% Dextrose Injection	≥ 10 μm	112	129	143	111	129	160
		≥ 25 μm	67	87	55	53	77	90
	Dextran 40 Dextrose Injection	≥ 10 μm	114	132	156	102	130	151
		≥ 25 μm	51	69	87	53	78	95
	Hydroxyethyl Starch 200/0.5 Injection	≥ 10 μm	101	119	142	103	131	160
		≥ 25 μm	42	67	89	44	72	93
	Sterile water for injection	≥ 10 μm	121	143	165	113	133	165
		≥ 25 μm	41	52	75	48	59	74
IM 1g/3.5ml	1% Lidocaine HCL Injection	≥ 10 μm	101	132	146	101	118	143
		≥ 25 μm	22	45	63	54	77	89

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Tab. 5 Sterility data summary of ceftriaxone sodium for injection (USP)

Items \ Time (h)		30±2°C			2-8°C		
		Acceptable criteria: sterile solution					
		0	6	12	0	12	24
IV 100mg/ml	Sterile water for injection	sterile solution	sterile solution	sterile solution	sterile solution	sterile solution	sterile solution
IV 25mg/ml	0.9% Sodium Chloride Injection	sterile solution	sterile solution	sterile solution	sterile solution	sterile solution	sterile solution
	0.45% Sodium Chloride + 2.5% Dextrose Injection	sterile solution	sterile solution	sterile solution	sterile solution	sterile solution	sterile solution
	5% Dextrose Injection	sterile solution	sterile solution	sterile solution	sterile solution	sterile solution	sterile solution
	10% Dextrose Injection	sterile solution	sterile solution	sterile solution	sterile solution	sterile solution	sterile solution
	Dextran 40 Dextrose Injection	sterile solution	sterile solution	sterile solution	sterile solution	sterile solution	sterile solution
	Hydroxyethyl Starch 200/0.5 Injection	sterile solution	sterile solution	sterile solution	sterile solution	sterile solution	sterile solution
	Sterile water for injection	sterile solution	sterile solution	sterile solution	sterile solution	sterile solution	sterile solution
IM 1g/3.5ml	1% Lidocaine HCL Injection	sterile solution	sterile solution	sterile solution	sterile solution	sterile solution	sterile solution

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Tab. 6 Bacterial endotoxins data summary of ceftriaxone sodium for injection (USP)

Items \ Time (h)		30±2°C			2-8°C		
		Acceptable criteria: ≤ 0.20 EU/mg					
		0	6	12	0	12	24
IV 100mg/ml	Sterile water for injection	< 0.20EU/mg	< 0.20EU/mg	< 0.20EU/mg	< 0.20EU/mg	< 0.20EU/mg	< 0.20EU/mg
IV 25mg/ml	0.9% Sodium Chloride Injection	< 0.20EU/mg	< 0.20EU/mg	< 0.20EU/mg	< 0.20EU/mg	< 0.20EU/mg	< 0.20EU/mg
	0.45% Sodium Chloride + 2.5% Dextrose Injection	< 0.20EU/mg	< 0.20EU/mg	< 0.20EU/mg	< 0.20EU/mg	< 0.20EU/mg	< 0.20EU/mg
	5% Dextrose Injection	< 0.20EU/mg	< 0.20EU/mg	< 0.20EU/mg	< 0.20EU/mg	< 0.20EU/mg	< 0.20EU/mg
	10% Dextrose Injection	< 0.20EU/mg	< 0.20EU/mg	< 0.20EU/mg	< 0.20EU/mg	< 0.20EU/mg	< 0.20EU/mg
	Dextran 40 Dextrose Injection	< 0.20EU/mg	< 0.20EU/mg	< 0.20EU/mg	< 0.20EU/mg	< 0.20EU/mg	< 0.20EU/mg
	Hydroxyethyl Starch 200/0.5 Injection	< 0.20EU/mg	< 0.20EU/mg	< 0.20EU/mg	< 0.20EU/mg	< 0.20EU/mg	< 0.20EU/mg
	Sterile water for injection	< 0.20EU/mg	< 0.20EU/mg	< 0.20EU/mg	< 0.20EU/mg	< 0.20EU/mg	< 0.20EU/mg
IM 1g/3.5ml	1% Lidocaine HCL Injection	< 0.20EU/mg	< 0.20EU/mg	< 0.20EU/mg	< 0.20EU/mg	< 0.20EU/mg	< 0.20EU/mg

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Tab. 7 Assay data summary of ceftriaxone sodium for injection (USP)

Time (h) / Items		30±2°C			2-8°C		
		Acceptable criteria: relative assay should more than 95%					
		0	6	12	0	12	24
IV 100mg/ml	Sterile water for injection	100%	98.5%	97.1%	100%	99.5%	97.3%
IV 25mg/ml	0.9% Sodium Chloride Injection	100%	97.2%	96.6%	100%	99.4%	98.5%
	0.45% Sodium Chloride + 2.5% Dextrose Injection	100%	98.3%	96.1%	100%	98.5%	97.5%
	5% Dextrose Injection	100%	97.5%	96.4%	100%	98.5%	96.4%
	10% Dextrose Injection	100%	97.7%	95.6%	100%	98.1%	96.2%
	Dextran 40 Dextrose Injection	100%	98.3%	95.8%	100%	100%	98.5%
	Hydroxyethyl Starch 200/0.5 Injection	100%	97.5%	96.4%	100%	99.1%	98.1%
	Sterile water for injection	100%	98.0%	95.1%	100%	98.7%	97.3%
IM 1g/3.5ml	1% Lidocaine HCL Injection	100%	97.6%	95.4%	100%	97.4%	96.7%

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