Estudio de estabilidad del reconstituido y diluido.

IN-USE STABILITY STUDIES

BLEOMYCIN SULFATE for Injection 15 units

KOREA UNITED PHARM. INC.

1. PROTOCOL

1.1. Product Name : BLEOMYCIN SULFATE for Injection 15 units

1.2. Active Ingredient : Bleomycin Sulfate

1.3. Analysis Date : June 04, 2018 ~ June 07, 2018

1.4. Conc. of Reconstitution : 3 units/mL, 1.2 units/mL

1.5. Method of Reconstitution : The BLEOMYCIN SULFATE 15 units vial should be reconstituted with 5 mL of sterile water for injection and sterile bacteriostatic water for injection. 60 units of BLEOMYCIN SULFATE are dissolved in 50 mL of sodium chloride for injection 0.9%.

1.6. Storage Condition : The reconstituted solution is stored at room temperature (30°C) for up to 24 hours.

1.7. Test Products

Batch No.	Mfg. Date	Exp. Date	Batch Size
1174604	June 19, 2016	June 18, 2018	5,000 Vials
1174801	February 14, 2018	February 13, 2020	5,000 Vials
1174802	February 18, 2018	February 17, 2020	5,000 Vials

1.8. Test Parameters

Test	Requirements
Description	Visual Inspection
pH	Between 4.5 and 6.0
Assay	Between 90.0% and 120.0%
Content of Bleomycins	A_2 : Between 55% and 70%
	B_2 : Between 25% and 32%
	B_4 : Not more than 1%
	A_2 & B_2 : Not less than 90%

1.9. Test Conditions

Diluents	Conditions	Concentration
Sterile water for injection	For 24 hours at room temperature (30°C)	3 units/mL
Sterile bacteriostatic water for injection	For 24 hours at room temperature (30°C)	3 units/mL
Sodium chloride for injection 0.9%	For 24 hours at room temperature (30°C)	1.2 units/mL

1.10. Test Plans

Conditions	Sampling Intervals (hours)
Sterile water for injection for 24 hours at room temperature (30°C)	Initial, 12, 24
Sterile bacteriostatic water for injection for 24 hours at room temperature (30°C)	Initial, 12, 24
Sodium chloride for injection 0.9% for 24 hours at room temperature (30°C)	Initial, 12, 24

2. RESULT

2.1. Sterile water for injection for 24 hours at room temperature (30°C)

1) Batch No. 1174604

Test	Specification	Initial	12 hours	24 hours
Description	Clear, colorless solution	Conforms	Conforms	Conforms
pH	Between 4.5 and 6.0	5.2	5.2	5.3
Assay	Between 90.0% and 120.0%	102.5	100.9	98.5
Content of Bleomycins	A_2 : Between 55% and 70%	67.5	67.8	67.5
	B_2 : Between 25% and 32%	31.5	31.2	30.8
	B_4 : Not more than 1%	0.2	0.4	0.5
	A_2 & B_2 : Not less than 90%	98.1	97.5	97.3

2) Batch No. 1174801

Test	Specification	Initial	12 hours	24 hours
Description	Clear, colorless solution	Conforms	Conforms	Conforms
pH	Between 4.5 and 6.0	5.1	5.2	5.2
Assay	Between 90.0% and 120.0%	104.8	102.4	98.1
Content of Bleomycins	A_2 : Between 55% and 70%	68.7	68.0	67.5
	B_2 : Between 25% and 32%	30.5	30.3	29.8
	B_4 : Not more than 1%	0.2	0.4	0.5
	A_2 & B_2 : Not less than 90%	98.5	98.0	97.5

3) Batch No. 1174802

Test	Specification	Initial	12 hours	24 hours
Description	Clear, colorless solution	Conforms	Conforms	Conforms
pH	Between 4.5 and 6.0	5.1	5.2	5.3
Assay	Between 90.0% and 120.0%	103.5	100.4	98.1
Content of Bleomycins	A_2 : Between 55% and 70%	68.8	68.3	68.5
	B_2 : Between 25% and 32%	30.2	29.7	29.9
	B_4 : Not more than 1%	0.2	0.5	0.5
	A_2 & B_2 : Not less than 90%	98.7	98.1	97.9

2.2. Sterile bacteriostatic water for injection for 24 hours at room temperature (30°C)

1) Batch No. 1174604

Test	Specification	Initial	12 hours	24 hours
Description	Clear, colorless solution	Conforms	Conforms	Conforms
pH	Between 4.5 and 6.0	5.1	5.2	5.3
Assay	Between 90.0% and 120.0%	100.5	100.9	97.9
Content of Bleomycins	A_2 : Between 55% and 70%	66.9	67.8	67.0
	B_2 : Between 25% and 32%	30.5	31.2	31.0
	B_4 : Not more than 1%	0.3	0.4	0.5
	A_2 & B_2 : Not less than 90%	97.4	97.5	96.3

2) Batch No. 1174801

Test	Specification	Initial	12 hours	24 hours
Description	Clear, colorless solution	Conforms	Conforms	Conforms
pH	Between 4.5 and 6.0	5.2	5.2	5.2
Assay	Between 90.0% and 120.0%	103.5	101.0	98.5
Content of Bleomycins	A_2 : Between 55% and 70%	69.2	68.7	67.9
	B_2 : Between 25% and 32%	30.1	29.9	29.1
	B_4 : Not more than 1%	0.2	0.2	0.4
	A_2 & B_2 : Not less than 90%	98.7	98.3	97.8

3) Batch No. 1174802

Test	Specification	Initial	12 hours	24 hours
Description	Clear, colorless solution	Conforms	Conforms	Conforms
pH	Between 4.5 and 6.0	5.1	5.2	5.2
Assay	Between 90.0% and 120.0%	104.2	102.5	100.8
Content of Bleomycins	A_2 : Between 55% and 70%	68.4	68.3	68.1
	B_2 : Between 25% and 32%	29.9	29.5	29.7
	B_4 : Not more than 1%	0.2	0.3	0.3
	A_2 & B_2 : Not less than 90%	98.3	97.8	97.5

2.3. Sodium chloride for injection 0.9% for 24 hours at room temperature (30°C)

1) Batch No. 1174604

Test	Specification	Initial	12 hours	24 hours
Description	Clear, colorless solution	Conforms	Conforms	Conforms
pH	Between 4.5 and 6.0	5.2	5.3	5.3
Assay	Between 90.0% and 120.0%	99.8	98.1	95.9
Content of Bleomycins	A_2 : Between 55% and 70%	67.3	67.0	66.7
	B_2 : Between 25% and 32%	30.2	29.5	29.3
	B_4 : Not more than 1%	0.4	0.6	0.7
	A_2 & B_2 : Not less than 90%	97.1	95.9	94.2

2) Batch No. 1174801

Test	Specification	Initial	12 hours	24 hours
Description	Clear, colorless solution	Conforms	Conforms	Conforms
pH	Between 4.5 and 6.0	5.3	5.3	5.3
Assay	Between 90.0% and 120.0%	101.8	99.9	98.3
Content of Bleomycins	A_2 : Between 55% and 70%	69.0	68.4	68.1
	B_2 : Between 25% and 32%	30.0	29.3	29.5
	B_4 : Not more than 1%	0.3	0.4	0.5
	A_2 & B_2 : Not less than 90%	98.1	97.6	97.1

3) Batch No. 1174802

Test	Specification	Initial	12 hours	24 hours
Description	Clear, colorless solution	Conforms	Conforms	Conforms
pH	Between 4.5 and 6.0	5.2	5.2	5.3
Assay	Between 90.0% and 120.0%	103.4	100.3	98.9
Content of Bleomycins	A_2 : Between 55% and 70%	68.5	68.1	68.0
	B_2 : Between 25% and 32%	29.7	29.5	29.3
	B_4 : Not more than 1%	0.2	0.2	0.3
	A_2 & B_2 : Not less than 90%	98.7	98.0	97.8

3. CONCLUSION

The stability test of the reconstituted solution performed for 24 hours at room temperature (30°C). The satisfactory result was found in the stability test, conforming to the required specifications. Therefore, the stability test of this product is guaranteed for a period of 24 hours at room temperature (30°C).

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Mr. Ki-Young Do
QC/QA Director

KOREA UNITED PHARM. INC.