



STUDIES FOR THE CONSTITUTED SOLUTION OF BENZATHINE BENZYL PENICILLIN 1.2MEGA POWDER FOR INJECTION

ABSTRACT For the stability study of the reconstituted solution of benzylpenicillin base 1.2mega (as benzathine benzylpenicillin) powder for injection in sterile water for injection. Each vial was dissolved in 3ml of the solvent, at low temperature (LT, 2-8°C) and room temperature (20-30°C). Content, pH and visual appearance of the admixture were inspected. Benzylpenicillin concentrations were determined by HPLC method followed by the registered test method.

Key Words **Benzylpenicillin** **Stability** **HPLC**

1 PREPARE

1.1 APPARATUS AND REAGENTS

HPLC: chromatogram system:

Apparatus no. : LC-20At SPD-20A

Column : Hanbang C18 NO.09021106

Wavelength : 220-nm detector and a 4.0-mm × 25-cm column packed with end-capped octadecylsilyl silica gel for chromatography R (5 μm)

Method : external standard method

Flow rate : 1.000ml/min pressure : 10.5MPa

Sensitivity : 1.0000Aufs Tem. : 22°C,

Inject amount : 20μl

PHS-3TC precision acidity meter;

benzathine benzylpenicillin CRS ;

Benzylpenicillin base 1.2mega (as benzathine benzylpenicillin) powder for injection, made by Reyoung pharma, LOT 131011, LOT 131012 and LOT 131013.

1.2 TEST STOCK SOLUTIONS

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Dissolve one vial with LOT 131011 in 3.ml of the solvent (Sterile water for injection), remarked as stock solution 01; and repeat the same procedure with LOT131012 and LOT131013, and remarked as stock solution02 and stock solution03; stored under low temperature(LT, 2-8℃).

Repeat the procedure to prepare stock solution 04, stock solution 05 and stock solution 06, stored under room temperature (20-30℃).

2. INSPECTION OF APPEARANCE OF TEST STOCK SOLUTION

Follow the registered test methods, and inspect the appearance of the test stock solutions.

3. ASSAY CONTENT OF BENZYL PENICILLIN

HPLC method was used to determine the content of benzylpenicillin in solutions prepared by the requirements indicated under the assay of the registered method from test stock solution.

4. TEST RESULTS

Low temperature: The appearance, pH and the content of the prepared solutions also comply with the prescribed specification at the 3 day, and the content of benzylpenicillin descends to a low value at the 4 day.

Room temperature: From the table, we could see at the first 24h, the appearance, pH and the content could comply with the specification in the solvent.but they failed pass the acceptable value at the 32h.



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TABLE pH, APPEARANCE and CONTENT (stored under low temperature, 2-8°C)

LOT 131011

	0 day	1day	2 day	3 day	4 day
Appearance White suspension	White suspension	White suspension	White suspension	White suspension	White suspension
pH Not more than 0.2 ml of 0.02 M sodium hydroxide is required to change the color of the indicator to blue.	Complies	Complies	Complies	Complies	Complies
Content 95%-105%	101.5	99.22	98.89	95.02	93.77

LOT 131012

	0 day	1day	2 day	3 day	4 day
Appearance White suspension	White suspension	White suspension	White suspension	White suspension	White suspension
pH Not more than 0.2 ml of 0.02 M sodium hydroxide is required to change the color of the indicator to blue.	Complies	Complies	Complies	Complies	Complies
Content 95%-105%	101.3	99.94	98.80	95.07	93.51

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LOT 131013

	0 day	1 day	2 day	3 day	4 day
Appearance White suspension	White suspension	White suspension	White suspension	White suspension	White suspension
pH Not more than 0.2 ml of 0.02 M sodium hydroxide is required to change the color of the indicator to blue.	Complies	Complies	Complies	Complies	Complies
Content 95%-105%	101.4	99.74	98.58	95.07	93.51

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**TABLE pH , APPEARANCE and CONTENT (stored under room temperature,
20-30℃)**

LOT 131011

	0h	8h	16h	24h	32h
Appearance White suspension	White suspension	White suspension	White suspension	White suspension	White suspension
pH Not more than 0.2 ml of 0.02 M sodium hydroxide is required to change the color of the indicator to blue.	Complies	Complies	Complies	Complies	Complies
Content 95%-105%	101.5	99.94	98.87	95.69	94.65

LOT 131012

	0h	8h	16h	24h	32h
Appearance White suspension	White suspension	White suspension	White suspension	White suspension	White suspension
pH Not more than 0.2 ml of 0.02 M sodium hydroxide is required to change the color of the indicator to blue.	Complies	Complies	Complies	Complies	Complies
Content 95%-105%	101.3	99.98	98.80	95.61	94.64

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LOT 131013

	0h	8h	16h	24h	32h
Appearance White suspension	White suspension	White suspension	White suspension	White suspension	White suspension
pH Not more than 0.2 ml of 0.02 M sodium hydroxide is required to change the color of the indicator to blue.	Complies	Complies	Complies	Complies	Complies
Content 95%-105%	101.4	99.98	98.44	95.28	94.66

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5. CONCLUSION

Product	Batch No.	Preparation	Storage	Shelf Life
Benzathine benzylpenicillin 1.2mega powder for injection	131011	See the details under 1.2	Low temperature(2-8℃)	3 days
			Room temperature (20-30℃)	24 hour
Benzathine benzylpenicillin 1.2mega powder for injection	131012	See the details under 1.2	Low temperature(2-8℃)	3 days
			Room temperature (20-30℃)	24 hour
Benzathine benzylpenicillin 1.2mega powder for injection	131013	See the details under 1.2	Low temperature(2-8℃)	3 days
			Room temperature (20-30℃)	24 hour

STORAGE CONDITIONS:

The constituted solution of benzathine benzylpenicillin 1.2mega powder for injection should be stored under a low temperature (2-8℃) for not more than 3days, and room temperature (20-30℃) for not more than 24 hour. From a microbiological point of view, once opened, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user.

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