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Cloxacillin Benzathine Intramammary Infusion

DEFINITION

Cloxacillin Benzathine Intramammary Infusion is a suspension of Cloxacillin Benzathine in a suitable oil vehicle. It has a potency equivalent to NLT 90.0% and NMT 120.0% of the labeled amount of cloxacillin ($C_{19}H_{18}ClN_3O_5S$).

IDENTIFICATION

Change to read:

• **A.** ▲**Spectroscopic Identification Tests ⟨197⟩, *Infrared Spectroscopy*: 197K**▲ (CN 1-May-2020)

Sample: Transfer a quantity of Intramammary Infusion, equivalent to 500 mg of cloxacillin, to a 50-mL centrifuge tube. Add 25 mL of toluene, mix, and centrifuge. Decant and discard the toluene. Wash the residue with four 25-mL portions of toluene, sonicating for 30 s after each addition of toluene. Dry the residue under vacuum over silica gel.

Acceptance criteria: Meets the requirements

ASSAY

• **Procedure**

Buffer: 0.1 M monobasic sodium phosphate in water prepared by dissolving 55.2 g of monobasic sodium phosphate in water, and diluting with water to 4 L

Mobile phase: Acetonitrile and *Buffer* (1:3). Adjust with phosphoric acid or 1 N sodium hydroxide to a pH of 4.6 ± 0.2. Pass through a 0.45-µm nylon filter, and degas. [Note—The retention time of cloxacillin is very sensitive to the acetonitrile content of the *Mobile phase*.]

Diluent: 0.05 M monobasic sodium phosphate in water. Mix acetonitrile and the resulting solution (2:3). Adjust with phosphoric acid or 1 N sodium hydroxide to a pH of 6.4.

Standard solutions: In duplicate, 112 µg/mL of USP Cloxacillin Sodium RS in *Diluent*

Sample solutions: Nominally 100 µg/mL of cloxacillin prepared as follows. In duplicate, quantitatively express the entire contents of a syringe of Intramammary Infusion into a 500-mL volumetric flask. Add 300 mL of methanol, and stir for 45 ± 1 min. Dilute with methanol to volume, and stir for an additional 10 ± 1 min. Immediately transfer 45 mL of the resulting solution to a 50-mL polypropylene centrifuge tube, and centrifuge for 10 min. From the supernatant remove an aliquot, and dilute with a sufficient volume of *Diluent* to prepare a solution containing nominally 100 µg/mL of cloxacillin.

Chromatographic system

(See *Chromatography ⟨621⟩, System Suitability*.)

Mode: LC

Detector: UV 220 nm

Column: 4.6-mm × 25-cm; 10-µm packing L1

Column temperature: 40°

Flow rate: 1.5 mL/min

Injection volume: 10 µL

System suitability

Samples: *Standard solutions*

Suitability requirements: Peak areas of the two *Standard solutions* agree within 98%–102%.

Tailing factor: NMT 2.0

Relative standard deviation: NMT 2%

Analysis

Samples: *Standard solutions* and *Sample solutions*

Calculate the percentage of the labeled amount of cloxacillin ($C_{19}H_{18}ClN_3O_5S$) in each syringe of Intramammary Infusion taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

r_U = average peak areas of cloxacillin from the *Sample solutions*

r_S = average peak areas of cloxacillin from the *Standard solutions*

C_S = concentration of cloxacillin in the *Standard solutions* (µg/mL)

C_U = nominal concentration of cloxacillin in the *Sample solutions* (µg/mL)

Acceptance criteria: 90.0%–120.0%

SPECIFIC TESTS

• **Sterility Tests ⟨71⟩:** Where the label states that it is sterile, it meets the requirements when tested as directed in *Test for Sterility of the Product to Be Examined, Direct Inoculation of the Culture Medium*, except use Fluid Thioglycollate Medium containing polysorbate 80 solution (1 in 200) and an amount of sterile penicillinase sufficient to inactivate the cloxacillin in each tube, use Soybean–Casein Digest Medium containing polysorbate 80 solution (1 in 200) and an amount of sterile penicillinase sufficient to inactivate the cloxacillin in each tube, and shake the tubes once daily.

• **Water Determination,** *Method I* ⟨921⟩

Analysis: Use 20 mL of a mixture of toluene and methanol (7:3) in place of methanol in the titration vessel.

Acceptance criteria: NMT 1.0%

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** Preserve in disposable syringes that are well-closed containers, except that where the Intramammary Infusion is labeled as sterile, the individual syringes or cartons are sealed and tamper-proof so that sterility is assured at time of use.

• **Labeling:** Label it to indicate that it is for veterinary use only. Intramammary Infusion that is sterile may be so labeled.

• **USP Reference Standards** ⟨11⟩

USP Cloxacillin Benzathine RS

USP Cloxacillin Sodium RS

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
CLOXACILLIN BENZATHINE INTRAMAMMARY INFUSION	Documentary Standards Support	SM32020 Small Molecules 3

Chromatographic Database Information: Chromatographic Database

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