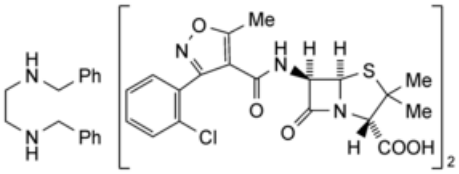
Edition: BP 2025 (Ph. Eur. 11.6 update)

Cloxacillin Benzathine

General Notices



$C_{16}H_{20}N_2,(C_{19}H_{18}ClN_3O_5S)_2$ 1112.1 *32222-55-2*

Action and use

Penicillin antibacterial.

Preparations

Cloxacillin Benzathine Intramammary Infusion (Dry Cow)

Ampicillin Trihydrate and Cloxacillin Benzathine Intramammary Infusion (Dry Cow)

DEFINITION

Cloxacillin Benzathine is *N,N'*-dibenzylethylenediammonium bis[(6*R*)-6-(3-*o*-chlorophenyl-5-methylisoxazole-4-carboxamido)penicillanate]. It contains not less than 92.0% of $C_{16}H_{20}N_2,(C_{19}H_{18}ClN_3O_5S)_2$ and not less than 20.0% and not more than 22.0% of benzathine, $C_{16}H_{20}N_2$, each calculated with reference to the anhydrous substance.

CHARACTERISTICS

A white or almost white powder.

Slightly soluble in *water*; freely soluble in *methanol*; slightly soluble in *ethanol (96%)* and in *propan-2-ol*.

IDENTIFICATION

A. The *infrared absorption spectrum*, Appendix II A, is concordant with the *reference spectrum* of cloxacillin benzathine *(RSV 12)*.
B. Shake 0.1 g with 1 mL of 1M *sodium hydroxide* for 2 minutes, add 2 mL of *ether*, shake for 1 minute and allow to separate. Evaporate 1 mL of the ether layer to dryness, dissolve the residue in 2 mL of *glacial acetic acid* and add 1 mL of *dilute potassium dichromate solution*. A golden yellow precipitate is produced.
C. Shake 50 mg with 10 mL of *water* and filter. To 5 mL of the filtrate add a few drops of *silver nitrate solution*. No precipitate is produced. Heat 50 mg with 2 mL of *alcoholic potassium hydroxide solution* on a water bath for 15 minutes, add 15 mg of *activated charcoal*, shake and filter. Acidify the filtrate with 2M *nitric acid*. The solution yields reaction A characteristic of *chlorides*, Appendix VI.

TESTS

Water

Not more than 5.0% w/w, Appendix IX C. Use 0.5 g.

ASSAY

For cloxacillin benzathine

To 60 mg add 40 mL of *methanol*, shake to dissolve, add 25 mL of 1M *sodium hydroxide* and allow to stand for 30 minutes. Add 27.5 mL of 1M *hydrochloric acid* and sufficient *water* to produce 100 mL, mix, transfer 20 mL of the solution to a stoppered flask, add 30 mL of *0.01M iodine VS*, close the flask with a wet stopper and allow to stand for 15 minutes protected from light. Titrate the excess of iodine with 0.02M *sodium thiosulfate VS*, using *starch mucilage*, added towards the end of the titration, as indicator. Add a further 12 mg of the substance being examined to 10 mL of *water*, swirl to disperse, add 30 mL of *0.01M iodine VS* and titrate immediately with 0.02M *sodium thiosulfate VS*, using *starch mucilage*, added towards the end of the titration, as indicator. The difference between the titrations represents the volume of *0.01M iodine VS* equivalent to the total penicillins present. Calculate the content of $C_{16}H_{20}N_2$,$(C_{19}H_{18}ClN_3O_5S)_2$ from the difference obtained by carrying out the assay simultaneously using *cloxacillin benzathine BPCRS* and from the declared content of $C_{16}H_{20}N_2$,$(C_{19}H_{18}ClN_3O_5S)_2$ in *cloxacillin benzathine BPCRS*.

For benzathine

To 1 g add 30 mL of a saturated solution of *sodium chloride* and 10 mL of 5M *sodium hydroxide*, shake well, and extract with four 50 mL quantities of *ether*. Wash the combined extracts with three 10 mL quantities of *water*, extract the combined washings with 25 mL of *ether* and add the extract to the main ether solution. Evaporate the ether solution to low bulk, add 2 mL of *absolute ethanol* and evaporate to dryness. To the residue add 50 mL of *anhydrous acetic acid* and titrate with *0.1M perchloric acid VS*, using 0.1 mL of *1-naphtholbenzein solution* as indicator. Repeat the operation without the substance being examined. The difference between the titrations represents the amount of perchloric acid required to neutralise the liberated base. Each mL of *0.1M perchloric acid VS* is equivalent to 12.02 mg of $C_{16}H_{20}N_2$.

STORAGE

Cloxacillin Benzathine should be kept in an airtight container. If the material is sterile, the container should be sterile, tamper-evident and sealed so as to exclude micro-organisms.

LABELLING

The label states, where applicable, that the material is sterile.

Cloxacillin Benzathine intended for use in the manufacturer of either a parenteral dosage form or an intramammary infusion without a further appropriate sterilisation procedure complies with the following additional requirement.

Sterility

Complies with the *test for sterility*, Appendix XVI A.