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Ampicillin and Sulbactam for Injection

» Ampicillin and Sulbactam for Injection is a sterile, dry mixture of Ampicillin Sodium and Sulbactam Sodium. It contains the equivalent of not less than 90.0 percent and not more than 115.0 percent of the labeled amounts of ampicillin ($C_{16}H_{19}N_3O_4S$) and sulbactam ($C_8H_{11}NO_5S$), the labeled amounts representing proportions of ampicillin to sulbactam of 2:1. It contains not less than 563 µg of ampicillin and 280 µg of sulbactam per mg, calculated on the anhydrous basis.

Packaging and storage—Preserve as described in *Packaging and Storage Requirements ⟨659⟩, Injection Packaging, Packaging for constitution*.

USP Reference standards ⟨11⟩—

USP Ampicillin RS
USP Sulbactam RS

Constituted solution—At the time of use, it meets the requirements for *Injections and Implanted Drug Products ⟨1⟩, Specific Tests, Completeness and clarity of solutions.*

Identification—The retention times of the major peaks in the chromatogram of the *Assay preparation* correspond to those in the chromatogram of the *Standard preparation*, as obtained in the *Assay*.

Bacterial Endotoxins Test ⟨85⟩ —It contains not more than 0.17 USP Endotoxin Unit in a portion equivalent to 1 mg of a mixture of ampicillin and sulbactam (0.67 and 0.33 mg, respectively).

Sterility Tests ⟨71⟩ —It meets the requirements when tested as directed for *Membrane Filtration* under *Test for Sterility of the Product to be Examined.*

pH ⟨791⟩: between 8.0 and 10.0, in a solution containing 10 mg of ampicillin and 5 mg of sulbactam per mL.

Water Determination, *Method I* ⟨921⟩: not more than 2.0%.

Particulate Matter in Injections ⟨788⟩: meets the requirements for small-volume injections.

Other requirements—It meets the requirements for *Uniformity of Dosage Units ⟨905⟩* and for *Labeling ⟨7⟩, Labels and Labeling for Injectable Products*.

Assay—

0.005 M Tetrabutylammonium hydroxide—Dilute 6.6 mL of a 40% solution of tetrabutylammonium hydroxide with water to obtain 1800 mL of solution. Adjust with 1 M phosphoric acid to a pH of 5.0 ± 0.1, dilute with water to 2000 mL, and mix.

Mobile phase—Prepare a filtered and degassed mixture of *0.005 M Tetrabutylammonium hydroxide* and acetonitrile (1650:350). Make adjustments if necessary (see *System Suitability* under *Chromatography ⟨621⟩*).

Standard preparation—Quantitatively dissolve accurately weighed quantities of USP Ampicillin RS and USP Sulbactam RS in *Mobile phase* to obtain a solution having known concentrations of about 0.6 mg of ampicillin per mL and 0.3 mg of sulbactam per mL. [Note—Inject this solution promptly.]

Resolution solution—Prepare a solution of USP Sulbactam RS in 0.01 N sodium hydroxide containing 0.3 mg per mL, and allow to stand for 30 minutes. Adjust with phosphoric acid to a pH of 5.0 ± 0.1. Transfer 5 mL of the solution to a 25-mL volumetric flask, add 4.25 mL of acetonitrile, dilute with *0.005 M Tetrabutylammonium hydroxide* to volume, and mix. Transfer 1 mL of this solution to a second 25-mL volumetric flask, add 15 mg of USP Ampicillin RS, dilute with *Mobile phase* to volume, and mix. [Note—Inject this solution promptly.]

Assay preparation 1—Mix the contents of a container of Ampicillin and Sulbactam for Injection. Quantitatively dissolve an accurately weighed portion of the powder in *Mobile phase* to obtain a solution having a concentration of about 1 mg of the powder per mL. [Note—Inject this solution promptly.]

Assay preparation 2 (where it is represented as being in a single-dose container)— Constitute a container of Ampicillin and Sulbactam for Injection with a volume of water, accurately measured, corresponding to the volume of solvent specified in the labeling. Withdraw the total withdrawable contents from the container, using a suitable hypodermic needle and syringe, and dilute quantitatively, and stepwise if necessary, with *Mobile phase* to obtain a solution containing about 0.6 mg of ampicillin per mL and 0.3 mg of sulbactam per mL. [Note—Inject this solution promptly.]

Assay preparation 3 (where the label states the quantities of ampicillin and sulbactam in a given volume of constituted solution)— Constitute a container of Ampicillin and Sulbactam for Injection with a volume of water, accurately measured, corresponding to the volume of solvent specified in the labeling. Dilute an accurately measured volume of the constituted solution quantitatively, and stepwise if necessary, with *Mobile phase* to obtain a solution containing about 0.6 mg of ampicillin per mL and 0.3 mg of sulbactam per mL. [Note—Inject this solution promptly.]

Chromatographic system (see *Chromatography ⟨621⟩*)—The liquid chromatograph is equipped with a 230-nm detector and a 4-mm × 30-cm column containing packing L1. The flow rate is about 2 mL per minute. Chromatograph the *Resolution solution*, and record the responses as directed for *Procedure:* the relative retention times are about 0.7 for ampicillin and 1.0 for sulbactam alkaline degradation product; and the

resolution, *R*, between ampicillin and sulbactam alkaline degradation product is not less than 4.0. Chromatograph the *Standard preparation*, and record the responses as directed for *Procedure:* the relative retention times are about 0.35 for ampicillin and 1.0 for sulbactam; the column efficiency determined from the sulbactam peak is not less than 3500 theoretical plates; the tailing factor is not more than 1.5; and the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 10 µL) of the *Standard preparation* and the appropriate *Assay preparation* into the chromatograph, record the chromatograms, and measure the areas for the major peaks. Calculate the quantities, in µg, of ampicillin ($C_{16}H_{19}N_3O_4S$) and of sulbactam ($C_8H_{11}NO_5S$) in the portion of Ampicillin and Sulbactam for Injection taken by the same formula:

$$(C_S P/C_U)(r_U/r_S)$$

in which C_S is the concentration, in mg per mL, of the appropriate USP Reference Standard in the *Standard preparation; P* is the assigned content, in µg per mg, of the appropriate USP Reference Standard; C_U is the concentration, in mg per mL, of Ampicillin and Sulbactam for Injection in *Assay preparation 1*, based on the weight, in mg, of powder removed from the container and the extent of dilution; and r_U and r_S are the peak areas for the appropriate analyte obtained from *Assay preparation 1* and the *Standard preparation*, respectively. Calculate the quantities of ampicillin ($C_{16}H_{19}N_3O_4S$) and of sulbactam ($C_8H_{11}NO_5S$) withdrawn from the container, or in the volume of constituted solution taken by the same formula:

$$(L/D)(C_S P)(r_U/r_S)$$

in which *L* is the labeled quantity, in mg, of ampicillin or sulbactam, as appropriate, in the container or in the volume of constituted solution taken; *D* is the concentration, in mg per mL, of ampicillin or sulbactam in *Assay preparation 2* or *Assay preparation 3*, on the basis of the labeled quantity, in mg, of ampicillin or sulbactam, as appropriate, in the container and the extent of dilution; r_U and r_S are the peak areas for the appropriate analyte obtained from *Assay preparation 2* or *Assay preparation 3* and the *Standard preparation*, respectively; and the other terms are as defined above.

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

Topic/Question	Contact	Expert Committee
AMPICILLIN AND SULBACTAM FOR INJECTION	Documentary Standards Support	SM12020 Small Molecules 1
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM12020 Small Molecules 1

Chromatographic Database Information: Chromatographic Database

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