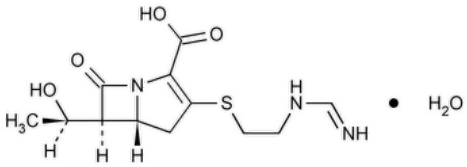
Status: Currently Official on 18-Feb-2025
Official Date: Official as of 01-May-2020
Document Type: USP Monographs
DocId: GUID-CC70FD72-CB80-4EDA-9396-4F5B9DDCA154_4_en-US
DOI: https://doi.org/10.31003/USPNF_M40020_04_01
DOI Ref: 5lt42

Imipenem



$C_{12}H_{17}N_3O_4S \cdot H_2O$ 317.36

1-Azabicyclo[3.2.0]hept-2-ene-2-carboxylic acid, 6-(1- hydroxyethyl)-3-[[2-(iminomethyl)amino]ethyl]thio]-7-oxo-, monohydrate, [5*R*-[5α,6α(*R**)]]-. (5*R*,6*S*)-3-[[2-(Formimidoylamino)ethyl]thio]-6-[(*R*)-1- hydroxyethyl]-7-oxo-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylic acid monohydrate CAS RN®: 74431-23-5; UNII: 71OTZ9ZE0A.

Anhydrous 299.35 CAS RN®: 64221-86-9; UNII: Q20IM7HE75.

» Imipenem contains the equivalent of not less than 98.0 percent and not more than 101.0 percent of imipenem monohydrate ($C_{12}H_{17}N_3O_4S \cdot H_2O$).

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

Labeling—Where it is intended for use in preparing injectable dosage forms, the label states that it is sterile.

USP Reference standards ⟨11⟩—

USP Imipenem Monohydrate RS

Change to read:

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

Specific rotation ⟨781S⟩: between +84° and +89°.

Test solution: 5 mg per mL, in a pH 7 buffer. Prepare the pH 7 buffer solution as follows. Dissolve 5 g of monobasic potassium phosphate and 11 g of dibasic potassium phosphate in 900 mL of water, adjust with phosphoric acid or 5 N sodium hydroxide to a pH of 7, dilute with water to 1000 mL, and mix.

Crystallinity ⟨695⟩: meets the requirements.

Bacterial Endotoxins Test ⟨85⟩ (where the label states that Imipenem is sterile)—It contains not more than 0.17 USP Endotoxin Unit per mg.

Sterility Tests ⟨71⟩ (where the label states that Imipenem is sterile)—It meets the requirements when tested as directed for *Membrane Filtration* under *Test for Sterility of the Product to be Examined*, 6 g of specimen dissolved in 200 mL of *Fluid A* being used.

Loss on drying (see *Thermal Analysis* ⟨891⟩)—[Note—The quantity taken for the determination may be adjusted, if necessary, for instrument sensitivity. Weight loss occurring at temperatures above about 160°, indicative of decomposition, is not to be interpreted as *Loss on drying*.] Determine the percentage of volatile substances by thermogravimetric analysis on an appropriately calibrated instrument, using 5 to 10 mg of Imipenem, accurately weighed. Heat the specimen under test at a rate of 20° per minute under vacuum. Record the thermogram to 200°, and calculate the weight loss at the plateau or inflection point at about 150°: it loses not less than 5.0% and not more than 8.0% of its weight.

Residue on ignition ⟨281⟩: not more than 0.2%.

Solvents—

Internal standard solution—Add 1 mL of *n*-propyl alcohol to 2000 mL of water, and mix.

Standard preparation—Transfer 1.0 mL of acetone and 2.0 mL of isopropyl alcohol to a 1000-mL volumetric flask, dilute with water to volume, and mix. Transfer 1.0 mL of this solution and 5.0 mL of *Internal standard solution* to a 25-mL volumetric flask, dilute with water to volume, and mix. Each mL of this *Standard preparation* contains 31.6 µg of acetone and 63.2 µg of isopropyl alcohol.

Test preparation—Transfer about 250 mg of Imipenem, accurately weighed, to a 10-mL volumetric flask, add 4.0 mL of 1 N ammonium hydroxide, and dissolve by swirling. Add 2.0 mL of *Internal standard solution*, dilute with water to volume, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The gas chromatograph is equipped with a flame-ionization detector and a 3-mm × 1.8-m column containing 10% phase G16 on support S5. The column temperature is programmed to operate at 70° for 8 minutes, then to increase at a rate of 32° per minute to 170°, and to maintain the temperature at 170° for 8 minutes. The injection port is maintained at 200°, the detector is maintained at 250°, and helium is used as the carrier gas at a flow rate of about 19 mL per minute. Chromatograph the *Standard preparation*, and record the peak responses as directed under *Procedure*: the relative retention times are about 0.3 for acetone, 0.5

for isopropyl alcohol, and 1.0 for *n*-propyl alcohol, and the relative standard deviation of each of the ratios of the response of the respective analyte peak to the response of the *n*-propyl alcohol peak for replicate injections is not more than 5%.

Procedure—[NOTE—Use peak areas where peak responses are indicated.] Separately inject equal volumes (about 2 µL) of the *Standard preparation* and the *Test preparation* into the chromatograph, using the solvent (water) flush technique, record the chromatograms, and measure the responses for the acetone, isopropyl alcohol, and *n*-propyl alcohol peaks. Calculate the percentages of acetone and isopropyl alcohol in the portion of Imipenem taken by the same formula:

$$(C/W)(R_U/R_S)$$

in which C is the concentration, in µg per mL, of the appropriate analyte in the *Standard preparation; W* is the quantity, in mg, of Imipenem taken to prepare the *Test preparation;* and R_U and R_S are the ratios of the peak response of each of the corresponding analytes to the peak responses of *n*-propyl alcohol obtained from the *Test preparation* and the *Standard preparation,* respectively. Add the percentages of acetone and isopropyl alcohol found: the total is not more than 0.25%.

Assay—

Mobile phase—Dissolve 0.54 g of monobasic potassium phosphate in 3600 mL of water, adjust with 0.5 N sodium hydroxide or 0.5 M phosphoric acid to a pH of 6.8 ± 0.1, dilute with water to make 4000 mL of solution, and mix. Filter this solution through a filter of 0.5-µm or finer porosity, and degas. Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Standard preparation—Dissolve an accurately weighed quantity of USP Imipenem Monohydrate RS in *Mobile phase* to obtain a solution having a known concentration of about 0.4 mg per mL. Store this solution in an ice bath, and discard after 8 hours.

Assay preparation—Transfer about 100 mg of Imipenem, accurately weighed, to a 250-mL volumetric flask, dissolve in and dilute with *Mobile phase* to volume, and mix. Store this solution in an ice bath, and discard the unused portion after 8 hours.

Chromatographic system (see *CHROMATOGRAPHY* ⟨621⟩)—The liquid chromatograph is equipped with a 300-nm detector and a 4.6-mm × 30-cm column that contains packing L1, and is maintained at a temperature of 30 ± 1.0°. The flow rate is about 1.5 mL per minute. Chromatograph the *Standard preparation,* and record the peak responses as directed for *Procedure:* the column efficiency determined from the analyte peak is not less than 600 theoretical plates, and the relative standard deviation for replicate injections is not more than 1.0%.

Procedure—Separately inject equal volumes (about 10 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in mg, of imipenem monohydrate ($C_{12}H_{17}N_3O_4S \cdot H_2O$) in the portion of Imipenem taken by the formula:

$$(317.36/299.35)(0.25CP)(r_U/r_S)$$

in which 317.36 and 299.35 are the molecular weights of imipenem monohydrate and anhydrous imipenem, respectively; C is the concentration, in mg per mL, of USP Imipenem Monohydrate RS in the *Standard preparation; P* is the content, in µg per mg, of anhydrous imipenem ($C_{12}H_{17}N_3O_4S$) in USP Imipenem Monohydrate RS; and r_U and r_S are the imipenem peak responses obtained from the *Assay preparation* and the *Standard preparation,* respectively.

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

Topic/Question	Contact	Expert Committee
IMIPENEM	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

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 43(3)

Current DocID: GUID-CC70FD72-CB80-4EDA-9396-4F5B9DDCA154_4_en-US
DOI: https://doi.org/10.31003/USPNF_M40020_04_01
DOI ref: 5lt42