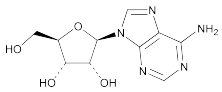
ADDITIONAL REQUIREMENTS
- **PACKAGING AND STORAGE:** Preserve in well-closed containers.
- **USP REFERENCE STANDARDS** ⟨**11**⟩
  USP Adenine RS

Adenosine



$C_{10}H_{13}N_5O_4$ 267.25
6-Amino-9-β-D-ribofuranosyl-9*H*-purine;
9-β-D-Ribofuranosyladenine [58-61-7].

DEFINITION
Adenosine contains NLT 99.0% and NMT 101.0% of $C_{10}H_{13}N_5O_4$, calculated on the dried basis.

IDENTIFICATION
- **INFRARED ABSORPTION** ⟨**197M**⟩**:** NMT 0.1%

ASSAY
- **ADENOSINE**
  Sample: 200 mg of Adenosine previously dried at 105 ° for 2 h
  Titrimetric system
  (See *Titrimetry* ⟨541⟩.)
  Mode: Direct titration
  Titrant: 0.1 N perchloric acid VS
  Endpoint detection: Potentiometric
  Blank: 50 mL of glacial acetic acid
  Analysis: Dissolve in 50 mL of glacial acetic acid and titrate with 0.1 N perchloric acid VS. Calculate the percentage of Adenosine ($C_{10}H_{13}N_5O_4$) in the portion taken:

$$\text{Result} = [(V - B) \times N \times F \times 100]/W$$

V = *Sample* titrant volume (mL)
B = *Blank* titrant volume (mL)
N = titrant normality (mEq/mL)
F = equivalency factor: 267.25 mg/mEq
W = weight of the *Sample* (mg)

  Acceptance criteria: 99.0%–101.0% on the dried basis

IMPURITIES
- **RESIDUE ON IGNITION** ⟨**281**⟩**:** NMT 0.1%
- **HEAVY METALS,** *Method II* ⟨**231**⟩**:** NMT 10 ppm
- **LIMIT OF AMMONIA**
  Sample solution: Suspend 0.5 g in 10 mL of water. Stir for 30 s, and pass through a coarse filter. Dilute the filtrate with water to 15 mL, and use the filtrate.
  Standard solution: 0.4 µg/mL of ammonium chloride in water
  Analysis: To the *Sample solution* and the *Standard solution* add 0.3 mL of alkaline mercuric–potassium iodide TS, cap the test tubes, and allow to stand for 5 min.
  Acceptance criteria: The *Sample solution* does not exhibit a more intense yellow color than that of the *Standard solution* (NMT 4 ppm of ammonia).
- **LIMIT OF CHLORIDE**
  Sample solution: Suspend 0.2 g in 10 mL of water. Stir for 30 s, pass through a coarse filter, and use the filtrate.
  Standard solution: 2.3 µg/mL of sodium chloride in water
  Analysis: To the *Sample solution* and 10 mL of the *Standard solution* add 1 mL of nitric acid and 1 mL of silver nitrate TS, and dilute each solution with water to 40 mL. Allow the solutions to stand for 5 min, protected from light.
  Acceptance criteria: When viewed against a dark background, the *Sample solution* is not more turbid than the *Standard solution* (NMT 0.007% chloride).
- **LIMIT OF SULFATE**
  Sample solution: Suspend 0.75 g in 15 mL of water. Stir for 30 s, pass through a coarse filter, and use the filtrate.
  Standard solution: Add 0.15 mL of 0.020 N sulfuric acid to 15 mL of water.
  Analysis: To the *Sample solution* and the *Standard solution* add 2 mL of barium chloride TS and 1 mL of 3 N hydrochloric acid, dilute each solution with water to 30 mL, and mix. Allow the solutions to stand for 5 min.
  Acceptance criteria: The *Sample solution* is not more turbid than the *Standard solution* (NMT 0.02% sulfate).
- **ORGANIC IMPURITIES**
  Solution A: 6.8 g/L of potassium hydrogen sulfate and 3.4 g/L of tetrabutylammonium hydrogen sulfate in water. Adjust with 2 N potassium hydroxide to a pH of 6.5.
  Solution B: 0.1 g/L of sodium azide solution
  Mobile phase: *Solution A* and *Solution B* (60:40)
  System suitability solution: 0.2 mg/mL each of Adenosine and inosine in *Mobile phase*
  Sample solution: 1.0 mg/mL of Adenosine in *Mobile phase*
  Chromatographic system
  (See *Chromatography* ⟨621⟩, *System Suitability*.)
  Mode: LC
  Detector: UV 254 nm
  Column: 4.6-mm × 25-cm; 5-µm packing L1
  Flow rate: 1.5 mL/min
  Injection size: 20 µL
  System suitability
  Sample: *System suitability solution*
  Suitability requirements
  Resolution: NLT 9.0 between adenosine and inosine
  Tailing factor: NMT 2.5
  Relative standard deviation: NMT 2.0%
  [NOTE—Chromatograph the *Sample solution*, and adjust the run time to at least twice the retention time of the major peak.]
  Analysis
  Sample: *Sample solution*
  Calculate the percentage of each impurity in the portion of Adenosine taken:

$$\text{Result} = (r_U/r_T) \times 100$$

r_U = peak response of each impurity from the *Sample solution*
r_T = sum of all the responses for all peaks from the *Sample solution*

  Acceptance criteria
  Individual impurities: NMT 0.1% each of guanosine, inosine, and uridine, and NMT 0.2% of adenine
  Total impurities: NMT 0.5%

SPECIFIC TESTS
- **MELTING RANGE OR TEMPERATURE** ⟨**741**⟩**:** 233°–238°
- **OPTICAL ROTATION,** *Specific Rotation* ⟨**781S**⟩**:** −68° to −72°
  Test solution: 20 mg/mL in sodium hydroxide solution (1 in 20), determined on a sample previously dried at 105 ° for 2 h
- **ACIDITY OR ALKALINITY:** Suspend 1 g in 20 mL of carbon dioxide-free water. Stir for 30 s, and pass through a coarse filter. To each of two 10-mL portions of the filtrate add 0.1 mL of bromocresol purple TS.
  Acceptance criteria: NMT 0.3 mL of 0.01 N sodium hydroxide is required to produce a blue-violet color in one portion. NMT 0.1 mL of 0.01 N hydrochloric acid is required to produce a yellow color in the other portion.
- **LOSS ON DRYING** ⟨**731**⟩**:** Dry a sample at 105 ° for 2 h: it loses NMT 0.5% of its weight.

ADDITIONAL REQUIREMENTS
- **PACKAGING AND STORAGE:** Preserve in tight, light-resistant containers, and store at controlled room temperature.

• **USP REFERENCE STANDARDS** ⟨11⟩
USP Adenosine RS

Adenosine Injection

» Adenosine Injection is a sterile solution of Adenosine in Water for Injection. It may contain Sodium Chloride. It contains not less than 90.0 percent and not more than 110.0 per cent of the labeled amount of adenosine ($C_{10}H_{13}N_5O_4$).

Packaging and storage—Preserve in tight, single-dose containers, preferably of Type I glass, and store at controlled room temperature.

USP Reference standards ⟨11⟩**—**
USP Adenosine RS
USP Endotoxin RS

Identification—The retention time of the adenosine peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation,* as obtained in the *Assay*.

Bacterial endotoxins ⟨85⟩**—**When the product is used for rapid intravenous injection, it contains not more than 11.62 USP Endotoxin Units per mg of adenosine. When the product is used for continuous peripheral intravenous infusion, it contains not more than 5.95 USP Endotoxin Units per mg of adenosine.

pH ⟨791⟩**:** between 4.5 and 7.5.

Particulate matter ⟨788⟩**:** meets the requirements for small-volume injections.

Chromatographic purity—

Mobile phase, *System suitability solution*, *Standard preparation*, *System sensitivity solution*, and *Chromatographic system*—Proceed as directed in the *Assay*.

Test solution—Use the stock solution reserved from the *Assay preparation*.

Procedure—Inject a volume (about 10 µL) of the *Test solution* into the chromatograph, record the chromatogram, and measure the peak responses. Calculate the percentage of each impurity in the volume of Injection taken by the formula:

$$100(r_i / r_s)$$

in which r_i is the peak response for each impurity, and r_s is the sum of the responses of all of the peaks: not more than 1.0% of any individual impurity is found, and not more than 1.5% of total impurities is found.

Other requirements—It meets the requirements under *Injections* ⟨1⟩.

Assay—

Mobile phase—Dissolve 2.0 g of monobasic potassium phosphate in 800 mL of water. Add 5 mL of 1.0 *M* tetrabutylammonium dihydrogen phosphate solution, dilute with water to 980 mL, and mix. Add 20 mL of acetonitrile, mix, filter, and degas. Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

System suitability solution—Dissolve accurately weighed quantities of USP Adenosine RS and inosine in warm water (50° to 55°), and dilute quantitatively, and stepwise if necessary, with water to obtain a solution having known concentrations of about 0.03 mg each of adenosine and inosine per mL.

Standard preparation—Dissolve an accurately weighed quantity of USP Adenosine RS in warm water (50° to 55°), and dilute quantitatively, and stepwise if necessary, with water to obtain a solution having a known concentration of about 0.03 mg per mL. If sodium chloride is present in the Injection, add 0.01 mL of sodium chloride solution (0.9 in 100) per mL of the anticipated final volume of the *Standard preparation* before the addition of the warm water.

System sensitivity solution—Pipet 3.0 mL of the *Standard preparation* into a 200-mL volumetric flask, dilute with water to volume, and mix.

Assay preparation—Transfer an accurately measured volume of Injection, equivalent to about 30 mg of adenosine, to a 100-mL volumetric flask, dilute with water to volume, and mix. Reserve a portion of this stock solution for use in the test for *Chromatographic purity*. Pipet 5.0 mL of the stock solution into a 50-mL volumetric flask, dilute with water to volume, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 254-nm detector and a 3.9-mm × 30-cm column that contains packing L1. The flow rate is about 2.5 mL per minute. Chromatograph the *System suitability solution*, and record the peak responses as directed for *Procedure:* the tailing factor for the adenosine peak is not more than 2.0; and the resolution, *R,* between adenosine and inosine is not less than 6.0. Similarly chromatograph the *Standard preparation:* the relative standard deviation for replicate injections is not more than 1.5%. Chromatograph the *System sensitivity solution*, and adjust the run time to 2 1/2 times the retention time of adenosine.

Procedure—Separately inject equal volumes (about 10 µL) of the *Assay preparation* and the *Standard preparation* into the chromatograph, record the chromatograms, and measure the areas of the adenosine peak responses. Calculate the quantity, in mg, of adenosine ($C_{10}H_{13}N_5O_4$) in each mL of the Injection taken by the formula:

$$CD(r_U / r_S)$$

in which *C* is the concentration, in mg per mL, of USP Adenosine RS in the *Standard preparation; D* is the concentration, in mg per mL, of adenosine in the *Assay preparation*, based on the labeled quantity per mL and the extent of dilution; and r_U and r_S are the peak responses for adenosine obtained from the *Assay preparation* and the *Standard preparation,* respectively.

Medical Air

» Medical Air is a natural or synthetic mixture of gases consisting largely of nitrogen and oxygen. It contains not less than 19.5 per cent and not more than 23.5 per cent, by volume, of O_2.

Packaging and storage—Preserve in cylinders or in a low pressure collecting tank. Containers used for Medical Air are not to be treated with any toxic, sleep-inducing, or narcosis-producing compounds, and are not to be treated with any compound that would be irritating to the respiratory tract when the Medical Air is used.

NOTE—Reduce the container pressure by means of a regulator. Measure the gases with a gas volume meter downstream from the detector tube in order to minimize contamination or change of the specimens.
The various detector tubes called for in the respective tests are listed under *Reagent Specifications* in the section *Reagents, Indicators, and Solutions*.

Labeling—Where it is piped directly from the collecting tank to the point of use, label each outlet "Medical Air."

Water and oil—Support 1 container in an inverted position (with the valve at the bottom) for 5 minutes. Cautiously open the valve slightly, maintaining the container in an inverted position. Vent the gas with a barely audible flow against a stainless steel mirror for a few seconds: no liquid is discernible on the mirror.

Odor—Carefully open the container valve to produce a moderate flow of gas. Do not direct the gas stream toward the face,