1,2,3-Propanetricarboxylic acid, 2-hydroxy-, gallium-^{67}*Ga* (1:1) salt.
Gallium-^{67}*Ga* citrate (1:1) [41183-64-6; 52260-70-5].

» Gallium Citrate Ga 67 Injection is a sterile aqueous solution of radioactive, essentially carrier-free gallium citrate Ga 67 suitable for intravenous administration. It contains not less than 90.0 percent and not more than 110.0 per cent of the labeled amount of ^{67}Ga as citrate expressed in megabecquerels (microcuries or millicuries) per mL at the time indicated in the labeling. Other chemical forms of radioactivity do not exceed 3.0 per cent of the total radioactivity. It may contain a preser vative or stabilizer.

Packaging and storage—Preserve in single-dose or multiple-dose containers.

Labeling—Label it to include the following, in addition to the information specified for *Labeling* under *Injections* ⟨1⟩: the time and date of calibration; the amount of ^{67}Ga as labeled gallium citrate expressed as total megabecquerels (MBq) (microcuries [μCi] or millicuries [mCi]) and concentration as megabecquerels (μCi or mCi) per mL at the time of calibration; the expiration date and time; and the statement "Caution—Radioactive Material." The labeling indicates that in making dosage calibrations, correction is to be made for radioactive decay, and also indicates that the radioactive half-life of ^{67}Ga is 78.26 hours.

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

Bacterial endotoxins ⟨85⟩**—**It meets the requirements of the *Bacterial Endotoxins Test*, the limit of endotoxin content being not more than 175/ *V* USP Endotoxin Unit per mL of the Injection, when compared with the USP Endotoxin RS , in which *V* is the maximum recommended total dose, in mL, at the expiration date or time.

pH ⟨791⟩: between 4.5 and 8.0.

Radiochemical purity—Place 10 to 20 μL of Injection about 3 cm from one end of a 3- × 55-cm strip of chromatographic paper (see *Chromatography* ⟨621⟩). While spots are wet, immediately develop the chromatogram at room temperature to the 14-cm mark by ascending chromatography, using a solvent system consisting of a mixture of 1.36 g of sodium acetate and 0.58 mL of glacial acetic acid in each 100 mL of water. Allow the strip to partially dr y, cover with clear tape, and determine the radioactivity distribution by scanning the chromatogram with a suitable collimated radiation detector: not less than 97.0% of the total radioactivity is found as gallium citrate when measured at the solvent front (R_F value equal to or greater than 0.9).

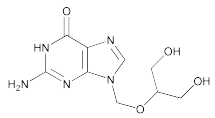
Radionuclide identification (see *Radioactivity* ⟨821⟩**)—**Its gamma-ray spectrum is identical to that of a specimen of ^{67}Ga of known purity that exhibits major photopeaks having energies of 93.3, 184.6, and 300.2 KeV.

Radionuclidic purity—Using a suitable counting assembly (see *Selection of a Counting Assembly* under *Radioactivity* ⟨821⟩), determine the radionuclidic purity of the Injection: not less than 99% of the total radioactivity is present as ^{67}Ga at the time of calibration.

Other requirements—It meets the requirements under *Injections* ⟨1⟩, except that the Injection may be distributed or dispensed prior to the completion of the test for *Sterility*, the latter test being started on the day of manufacture, and except that it is not subject to the recommendation on *Volume in Container.*

Assay for radioactivity—Using a suitable counting assembly (see *Selection of a Counting Assembly* under *Radioactivity* ⟨821⟩), determine the radioactivity in MBq (μCi or mCi) per mL of Gallium Ga 67 Injection by use of a calibrated system as directed under *Radioactivity* ⟨821⟩.

Ganciclovir



$C_9H_{13}N_5O_4$ 255.23
6*H*-Purin-6-one, 2-amino-1,9-dihydro-9-[[2-hydroxy-1-(hydroxymethyl)ethoxy]methyl]-;
9-[[2-Hydroxy-1-(hydroxymethyl)ethoxy]methyl]guanine [82410-32-0].

DEFINITION
Ganciclovir contains NLT 98.0% and NMT 102.0% of $C_9H_{13}N_5O_4$, calculated on the anhydrous basis.

IDENTIFICATION
- **A. Infrared Absorption** ⟨197K⟩
- **B. Ultraviolet Absorption** ⟨197U⟩
  Sample solution: 10 μg/mL in methanol

ASSAY
- **Procedure**
  Solution A: Trifluoroacetic acid and water (0.5 in 1000)
  Mobile phase: Acetonitrile and *Solution A* (1:1)
  System suitability solution: 0.1 mg/mL each of USP Ganciclovir RS and USP Ganciclovir Related Compound A RS in *Mobile phase*. [Note—Sonicate the solution if necessar y.]
  Standard solution: 0.22 mg/mL of USP Ganciclovir RS in *Mobile phase*
  Sample solution: 0.22 mg/mL of Ganciclovir in *Mobile phase*
  Chromatographic system
  (See *Chromatography* ⟨621⟩, *System Suitability*.)
  Mode: LC
  Detector: UV 254 nm
  Column: 4.6-mm × 25-cm; packing L9
  Column temperature: 40°
  Flow rate: 1.5 mL/min
  Injection size: 20 μL
  System suitability
  Sample: *System suitability solution*
  [Note—The relative retention times for ganciclovir related compound A and ganciclovir are 0.9 and 1.0, respectively.]
  Suitability requirements
  Resolution: NLT 1.4 between ganciclovir and ganciclovir related compound A
  Column efficiency: NLT 5000 theoretical plates
  Tailing factor: NMT 1.4
  Relative standard deviation: NMT 1.0%
  Analysis
  Samples: *Standard solution* and *Sample solution*
  Calculate the per centage of $C_9H_{13}N_5O_4$ in the portion of Ganciclovir taken:

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

r_U = peak response from the *Sample solution*
r_S = peak response from the *Standard solution*
C_S = concentration of USP Ganciclovir RS in the *Standard solution* (mg/mL)
C_U = concentration of Ganciclovir in the *Sample solution* (mg/mL)

Acceptance criteria: 98.0%–102.0% on the anhydrous basis

IMPURITIES

Inorganic Impurities

- **HEAVY METALS,** *Method II* ⟨**231**⟩**:** NMT 20 ppm
- **RESIDUE ON IGNITION** ⟨**281**⟩**:** NMT 0.1%

Organic Impurities

- **PROCEDURE**

Solution A, Mobile phase, System suitability solution, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay.*

Sample solution: 0.22 mg/mL of Ganciclovir in *Mobile phase*

Analysis

Sample: *Sample solution*

Calculate the percentage of each impurity in the portion of Ganciclovir taken:

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

r_U = peak response for each impurity in the *Sample solution*

r_T = sum of the responses of all the peaks

Acceptance criteria

Ganciclovir related compound A: NMT 0.5%

Total impurities: NMT 1.5%

SPECIFIC TESTS

- **WATER DETERMINATION,** *Method I* ⟨**921**⟩**:** NMT 6.0%

[NOTE—Ganciclovir is extremely hygroscopic.]

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in well-closed containers. Store at 25°, excursions permitted between 15 ° and 30°.
- **USP REFERENCE STANDARDS** ⟨**11**⟩

USP Ganciclovir RS

USP Ganciclovir Related Compound A RS

Ganciclovir for Injection

» Ganciclovir for Injection is a freeze-dried powder prepared by the neutralization of Ganciclovir with the aid of Sodium Hydroxide. It contains not less than 90.0 per cent and not more than 110.0 percent of the labeled amount of ganciclovir ($C_9H_{13}N_5O_4$), calculated on the anhydrous basis.

Caution—Handle Ganciclovir for Injection with great care, as it is a potent cytotoxic agent and suspected carcinogen.

Packaging and storage—Preserve in *Containers for Sterile Solids,* as described under *Injections* ⟨1⟩. Store between 15 ° and 30°, unless otherwise specified by the manufacturer. Protect from moisture.

Labeling—Label it to state that it is to be handled with great care because it is a potent cytotoxic agent and suspected carcinogen.

USP Reference standards ⟨11⟩**—**

USP Endotoxin RS

USP Ganciclovir RS

Constituted solution—At the time of use, it meets the requirements for *Constituted Solutions* under *Injections* ⟨1⟩.

Identification—The retention time of the major 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⟩**—**It contains not more than 0.84 Endotoxin Unit per mg of Ganciclovir for Injection.

Sterility ⟨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 10.8 and 11.4, in the solution constituted as directed in the labeling.

Water, *Method I* ⟨921⟩**—**Proceed as directed in the chapter, except to use the following modifications. Use a mixture of anhydrous formamide and methanol (1:1) in place of methanol as the titration vessel solvent. The *Reagent* volume required in order to condition the titration vessel solvent is not greater than 10% of the initial volume of solvent. The concentration of Ganciclovir for Injection in the titration vessel is not greater than 7 mg per mL. Not more than 3.0% is found.

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

Assay—

Mobile phase—Dissolve 1.4 g of monobasic ammonium phosphate and 2.0 g of phosphoric acid in 500 mL of water in a 1000-mL volumetric flask. Dilute with water to volume, mix, filter, and degas. Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Internal standard solution—Transfer about 75 mg of hypoxanthine to a 500-mL volumetric flask, dissolve in and dilute with water to volume, and mix.

Standard stock preparation—Dissolve an accurately weighed amount of USP Ganciclovir RS in water to obtain a solution having a known concentration of about 250 µg per mL.

Standard preparation—Transfer 20.0 mL of the *Standard stock preparation* and 10.0 mL of the *Internal standard solution* to a 100-mL volumetric flask. Dilute with *Mobile phase* to volume, and mix.

Assay stock preparation—Constitute Ganciclovir for Injection in a portion of water, quantitatively transfer with water to a suitable volumetric flask, and dilute with water to volume to obtain a solution having a concentration of about 1 mg per mL.

Assay preparation—Transfer 5.0 mL of the *Assay stock preparation* and 10.0 mL of the *Internal standard solution* to a 100-mL volumetric flask, dilute with *Mobile phase* to volume, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 254-nm detector and a 4.6-mm × 10-cm column that contains packing L1. The flow rate is about 1.2 mL per minute. Chromatograph the *Standard preparation,* and record the peak responses as directed for *Procedure:* the relative retention times are about 0.7 for hypoxanthine and 1.0 for ganciclovir; the resolution, *R,* between hypoxanthine and ganciclovir is not less than 3.0; the column efficiency is not less than 1000 theoretical plates; the tailing factor is not more than 2.0; 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 *Assay preparation* into the chromatograph, record the chromatograms, and measure the peak response ratios for the major peaks. Calculate the quantity, in mg, of ganciclovir ($C_9H_{13}N_5O_4$) in the container of Ganciclovir for Injection taken by the formula:

$$CD(R_U / R_S)$$

in which C is the concentration, in mg per mL, of USP Ganciclovir RS in the *Standard preparation; D* is the dilution factor, in mL, used to prepare the *Assay preparation;* and R_U and R_S are the peak response ratios of ganciclovir to the internal standard obtained from the *Assay preparation* and the *Standard preparation,* respectively.