r_S = sum of the peak responses of cefamandole and cefamandole nafate from the *Standard solution*
C_S = concentration of USP Cefamandole Nafate RS in the *Standard solution* (mg/mL)
C_U = nominal concentration of cefamandole in *Sample solution 1* or in *Sample solution 2* (mg/mL)
M_{r1} = molecular weight of cefamandole, 462.50
M_{r2} = molecular weight of cefamandole nafate, 512.49
P = potency of USP Cefamandole Nafate RS (mg/mg)

Calculate the potency, in µg/mg, of cefamandole ($C_{18}H_{18}N_6O_5S_2$) in the portion of Cefamandole Nafate for Injection taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times (M_{r1}/M_{r2}) \times P \times F$$

r_U = sum of the peak responses of cefamandole and cefamandole nafate from *Sample solution 1* or *Sample solution 2*
r_S = sum of the peak responses of cefamandole and cefamandole nafate from the *Standard solution*
C_S = concentration of USP Cefamandole Nafate RS in the *Standard solution* (mg/mL)
C_U = nominal concentration of cefamandole in *Sample solution 1* or *Sample solution 2* (mg/mL)
M_{r1} = molecular weight of cefamandole, 462.50
M_{r2} = molecular weight of cefamandole nafate, 512.49
P = potency of USP Cefamandole Nafate RS (mg/mg)
F = conversion factor, 1000 µg/mg

Acceptance criteria: 810–1000 µg/mg of $C_{18}H_{18}N_6O_5S_2$, calculated on the anhydrous and sodium carbonate-free basis; 90.0%–115.0% of the labeled amount of $C_{18}H_{18}N_6O_5S_2$ ■1S *(USP35)*

PERFORMANCE TESTS

- **UNIFORMITY OF DOSAGE UNITS** ⟨**905**⟩
  Procedure for content uniformity: Perform the *Assay* on individual containers using *Sample solution 1* or *Sample solution 2*, or both, as appropriate.
  Acceptance criteria: Meets the requirements

SPECIFIC TESTS

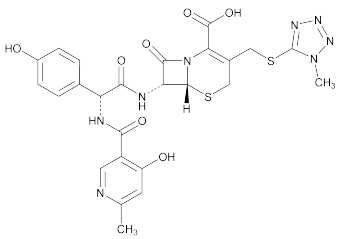
- **CONSTITUTED SOLUTION:** At the time of use, it meets the requirements for *Injections* ⟨1⟩, *Constituted Solutions*.
- **BACTERIAL ENDOTOXINS TEST** ⟨**85**⟩**:** NMT 0.15 USP Endotoxin Unit/mg of cefamandole
- **STERILITY TESTS** ⟨**71**⟩**:** It meets the requirements for *Test for Sterility of the Product to Be Examined, Membrane Filtration*.
- **pH** ⟨**791**⟩
  Sample solution: 100 mg/mL
  Acceptance criteria: 6.0–8.0, determined after 30 min
- **PARTICULATE MATTER** ⟨**788**⟩**:** Meets the requirements for small-volume injections
- **WATER DETERMINATION,** *Method I* ⟨**921**⟩**:** NMT 3.0%
- **OTHER REQUIREMENTS:** It meets the requirements under *Injections* ⟨1⟩.

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in *Containers for Sterile Solids* as described under *Injections* ⟨1⟩.

- **USP REFERENCE STANDARDS** ⟨**11**⟩
  USP Cefamandole Nafate RS
  USP Endotoxin RS

Cefpiramide



$C_{25}H_{24}N_8O_7S_2$ 612.64

5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[[[(4-hydroxy-6-methyl-3-pyridinyl)carbonyl]amino](4-hydroxyphenyl)acetyl]amino]-3-[[(1-methyl-1*H*-tetrazol-5-yl)thio]methyl]-8-oxo, [6*R*-[6α,7β (*R**)]]-; (6*R*,7*R*)-7-[(*R*)-2-(4-Hydroxy-6-methylnicotinamido)-2-(*p*-hydroxyphenyl)acetamido]-3-[[(1-methyl-1*H*-tetrazol-5-yl)thio]methyl]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid [70797-11-4].

DEFINITION

Cefpiramide contains NLT 974 µg/mg and NMT 1026 µg/mg of $C_{25}H_{24}N_8O_7S_2$, calculated on the anhydrous basis.

IDENTIFICATION

- **A. INFRARED ABSORPTION** ⟨**197K**⟩
- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

Change to read:

- **PROCEDURE**
  Buffer: 1.36 g/L of monobasic potassium phosphate in water adjusted with 1 N sodium hydroxide to a pH of 6.8 ± 0.1 prior to final dilution
  Mobile phase: Tetrahydrofuran, acetonitrile, methanol, and *Buffer* ■(40:40:40:880)■1S *(USP35)*
  System suitability solution: 1 mg/mL of USP Cefpiramide RS in 0.01 N sodium hydroxide. Heat this solution at 95° for 10 min. Mix 1 mL of this solution with 19 mL of *Mobile phase*. This solution contains a mixture of cefpiramide and cefpiramide lactone.
  Standard solution: 0.25 mg/mL of USP Cefpiramide RS in *Mobile phase*
  Sample solution: 0.25 mg/mL of Cefpiramide in *Mobile phase*
  Chromatographic system
  (See *Chromatography* ⟨621⟩, *System Suitability*.)
  Mode: LC
  Detector: UV 254 nm
  Column: ■4.0-mm × 15- to 30-cm; 5- to 10-µm packing L7■1S *(USP35)*
  Flow rate: 1.5 mL/min
  Injection size: 20 µL
  System suitability
  Samples: *System suitability solution* and *Standard solution*
  [NOTE—The relative retention times for cefpiramide and cefpiramide lactone are about 0.7 and 1.0, respectively.]

Suitability requirements
Resolution: NLT 5 between cefpiramide lactone and cefpiramide, *System suitability solution*
■1S *(USP35)*
Tailing factor: 0.95–1.4, *Standard solution*
Relative standard deviation: NMT 2.0%, *Standard solution*
Analysis
Samples: *Standard solution* and *Sample solution*
Calculate the quantity, in µg, of cefpiramide ($C_{25}H_{24}N_8O_7S_2$) in each mg of the portion of Cefpiramide taken:

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

r_U = peak response from the *Sample solution*
r_S = peak response from the *Standard solution*
C_S = concentration of USP Cefpiramide RS in the *Standard solution* (mg/mL)
C_U = concentration of Cefpiramide taken to prepare the *Sample solution* (mg/mL)
P = potency of cefpiramide in USP Cefpiramide RS (mg/mg)
F = conversion factor, 1000 µg/mg
Acceptance criteria: 974–1026 µg/mg on the anhydrous basis

IMPURITIES

Change to read:

- **ORGANIC IMPURITIES**
System suitability solution, Chromatographic system, and **System suitability:** Proceed as directed in the *Assay*.
Buffer: 4.08 g/L of monobasic potassium phosphate in water, adjusted with 1 N sodium hydroxide to a pH of 7.5 ± 0.1 prior to final dilution
Mobile phase: Methanol and *Buffer* (250:750)
Standard stock solution: 0.15 mg/mL of sodium 5-mercapto-1-methyltetrazole and 0.25 mg/mL of USP Cefpiramide RS in *Buffer*
Standard solution: 3 µg/mL of sodium 5-mercapto-1-methyltetrazole and 5 µg/mL of USP Cefpiramide RS from the *Standard stock solution* in *Mobile phase*
Sample solution: 0.5 mg/mL of Cefpiramide in *Mobile phase*
***N*-Ethylmaleimide solution:** 40 mg/mL of *N*-ethylmaleimide in methanol
Test preparation: 10 mg/mL of sodium 5-mercapto-1-methyltetrazole in *N-Ethylmaleimide solution* in a stoppered centrifuge tube. Sonicate for 15 min.
Analysis
Samples: *Standard solution* and *Sample solution*
Determine the water content of sodium 5-mercapto-1-methyltetrazole by the titrimetric method (see *Water Determination* ⟨921⟩), using 5.0 mL of the *Test preparation*.
Calculate the percentage of 5-mercapto-1-methyltetrazole in the portion of Cefpiramide taken:

$$\text{Result} = (r_U/r_S) \times (M_{r1}/M_{r2}) \times (C_S/C_U) \times F \times 100$$

r_U = peak response of 5-mercapto-1-methyltetrazole from the *Sample solution*
r_S = peak response of 5-mercapto-1-methyltetrazole from the *Standard solution*
M_{r1} = molecular weight of 5-mercapto-1-methyltetrazole, 115.14
M_{r2} = molecular weight of anhydrous sodium 5-mercapto-1-methyltetrazole, 138.13
C_S = concentration of sodium 5-mercapto-1-methyltetrazole, corrected for water, in the *Standard solution* (µg/mL)
C_U = concentration of Cefpiramide in the *Sample solution* (mg/mL)
F = conversion factor, 0.001 mg/µg
Calculate the percentage of each other impurity in the portion of Cefpiramide taken:

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

r_U = peak response of each other impurity from the *Sample solution*
r_S = peak response of cefpiramide from the *Standard solution*
C_S = concentration of USP Cefpiramide RS in the *Standard solution* (µg/mL)
C_U = concentration of Cefpiramide in the *Sample solution* (µg/mL)
P = potency of cefpiramide in USP Cefpiramide RS (µg/mg)
Acceptance criteria: See *Table 1*.

Table 1

Name	Relative Retention Time	Acceptance Criteria, NMT (%)
5-Mercapto-1-methyltetrazole	■0.20■1S *(USP35)*	0.7
Cefpiramide	1.0	—
Any other individual impurity	—	0.7
Total impurities	—	2.0

SPECIFIC TESTS

- **OPTICAL ROTATION,** *Specific Rotation* ⟨**781S**⟩
Sample solution: 10 mg/mL, in dimethylformamide
Acceptance criteria: –100° to –112°
- **CRYSTALLINITY** ⟨**695**⟩**:** Meets the requirements
- **pH** ⟨**791**⟩
Sample solution: 5-mg/mL suspension in water
Acceptance criteria: 3.0–5.0
- **WATER DETERMINATION,** *Method I* ⟨**921**⟩**:** NMT 9.0%
- **PYROGEN TEST** ⟨**151**⟩
Sample solution: 50 mg/mL of cefpiramide in Sterile Water for Injection
Test dose: 1.0 mL/kg of the *Sample solution*
Acceptance criteria: Where the label states that Cefpiramide is sterile, or it must be subjected to further processing during the preparation of injectable dosage forms, it meets the requirements.
- **STERILITY TESTS** ⟨**71**⟩**:** Where the label states that Cefpiramide is sterile, it meets the requirements when tested as directed for *Test for Sterility of the Product to Be Examined, Membrane Filtration*.

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight containers.
- **LABELING:** Where it is intended for use in preparing injectable dosage forms, the label states that it is sterile or must be subjected to further processing during the preparation of injectable dosage forms.

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

Cefpiramide for Injection

DEFINITION
Cefpiramide for Injection contains NLT 90.0% and NMT 120.0% of the labeled amount of cefpiramide ($C_{25}H_{24}N_8O_7S_2$).

IDENTIFICATION
• **A.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY

Change to read:

• **PROCEDURE**
Buffer: 1.36 g/L of monobasic potassium phosphate in water adjusted with 1 N sodium hydroxide to a pH of 6.8 ± 0.1 before final dilution
Mobile phase: Tetrahydrofuran, acetonitrile, methanol, and *Buffer* ■(40:40:40:880)■1S *(USP35)*
System suitability solution: 1 mg/mL of USP Cefpiramide RS in 0.01 N sodium hydroxide. Heat this solution at 95° for 10 min. Dilute 1 mL of this solution with *Mobile phase* to 20 mL. This solution contains a mixture of cefpiramide and cefpiramide lactone.
Standard solution: 0.25 mg/mL of USP Cefpiramide RS in *Mobile phase*
Sample solution 1 (where it is represented as being in a single-dose container): Constitute a container of Cefpiramide for Injection in a volume of water corresponding to the volume of diluent specified in the labeling. Withdraw all of the withdrawable contents, using a suitable hypodermic needle and syringe, and dilute with *Mobile phase* to obtain a solution containing the nominal equivalent of 0.25 mg/mL of cefpiramide.
Sample solution 2 (where the label states the quantity of cefpiramide in a given volume of constituted solution): Constitute a container of Cefpiramide for Injection in a volume of water equivalent to the volume of diluent specified in the labeling. Dilute the constituted solution with water to obtain a solution nominally containing 0.25 mg/mL of cefpiramide.
Chromatographic system
(See *Chromatography* ⟨621⟩*, System Suitability*.)
Mode: LC
Detector: UV 254 nm
Column: ■4.0-mm × 15- to 30-cm; 5- to 10-µm packing L7■1S *(USP35)*
Flow rate: 1.5 mL/min
Injection size: 20 µL
System suitability
Samples: *System suitability solution* and *Standard solution*
[NOTE—The relative retention times for cefpiramide and cefpiramide lactone are 0.7 and 1.0, respectively.]
Suitability requirements
Resolution: NLT 5 between cefpiramide lactone and cefpiramide, *System suitability solution* ■■1S *(USP35)*
Tailing factor: 0.95–1.4, *Standard solution*
Relative standard deviation: NMT 2.0%, *Standard solution*
Analysis
Samples: *Standard solution* and *Sample solution 1* or *Sample solution 2*

Calculate the percentage of cefpiramide ($C_{25}H_{24}N_8O_7S_2$) withdrawn from the container, or in the portion of constituted solution taken:

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

r_U = peak response of the *Sample solution*
r_S = peak response of the *Standard solution*
C_S = concentration of USP Cefpiramide RS in the *Standard solution* (mg/mL)
C_U = nominal concentration of cefpiramide in *Sample solution 1* or *Sample solution 2* (mg/mL)
Acceptance criteria: 90.0%–120.0%

SPECIFIC TESTS
• **PYROGEN TEST** ⟨**151**⟩
Sample solution: 50 mg/mL of cefpiramide from Cefpiramide for Injection in Sterile Water for Injection
Test dose: 1.0 mL/kg of the *Sample solution*
Acceptance criteria: Meets the requirements
• **STERILITY TESTS** ⟨**71**⟩**:** It meets the requirements when tested as directed for *Test for Sterility of the Product to Be Examined, Membrane Filtration*.
• **pH** ⟨**791**⟩
Sample solution: Equivalent to 100 mg/mL of cefpiramide from Cefpiramide for Injection
Acceptance criteria: 6.0–8.0 in water
• **WATER DETERMINATION,** *Method I* ⟨**921**⟩**:** NMT 3.0%
• **PARTICULATE MATTER IN INJECTIONS** ⟨**788**⟩**:** It meets the requirements for small-volume injections.

ADDITIONAL REQUIREMENTS
• **PACKAGING AND STORAGE:** Preserve as described in *Injections* ⟨1⟩*, Containers for Sterile Solids*.
• **USP REFERENCE STANDARDS** ⟨**11**⟩
USP Cefpiramide RS

Add the following:

■Celecoxib

$C_{17}H_{14}F_3N_3O_2S$ 381.4
4-[5-(4-Methylphenyl)-3-(trifluoromethyl)-1*H*-pyrazol-1-yl] benzenesulfonamide;
p-[5-*p*-Tolyl-3-(trifluoromethyl)pyrazol-1-yl] benzenesulfonamide [169590-42-5].

DEFINITION
Celecoxib contains NLT 98.0% and NMT 102.0% of $C_{17}H_{14}F_3N_3O_2S$, calculated on the anhydrous basis.

IDENTIFICATION
• **A. INFRARED ABSORPTION** ⟨**197**⟩**:** [NOTE—Methods ⟨197A⟩, ⟨197K⟩, or ⟨197M⟩ under *Infrared Absorption* may be used.]
[NOTE—If the spectra obtained show differences, dissolve the substance to be examined and the Reference Standard separately in isopropyl alcohol, evaporate to dryness, and record the new spectra.]
• **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the *Assay*.

ASSAY
• **PROCEDURE**
Buffer: 2.7 g/L of monobasic potassium phosphate adjusted with phosphoric acid to a pH of 3.0 ± 0.2