OTHER REQUIREMENTS:
- Water Determination
- Particulate Matter
- pH
- Sterility Tests
- Bacterial Endotoxins Test

CONSTITUTED SOLUTION:
Water adjusted with 1 N sodium hydroxide to a pH of 8.1±0.1.

SPECIFIC 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: 90.0%±115.0% of the labeled amount of C_{18}H_{17}N_{6}O_{6}s, calculated on the anhydrous and sodium carbonate-free basis.
- Performance Tests
- 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 Water (40:40:40:880)"
- System suitability solution: 1 mg/mL of USP Cefpiramide RS in 0.01 N sodium hydroxide. Heat this solution at 95°C 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 x 15- to 30-cm; 5- to 10-μm packing L7,15 (933)
- 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.

Cefpiramide

C_{25}H_{24}N_{8}O_{7}S_{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)acetamido)-2-(o-hydroxyphenyl)acetamido)-3-[(1-methyl-1H-tetrazol-5-yl)thio]methyl]-8-oxo-[6R,7β,7β(R)]-; (68,7R)-7-(R,2-(4-Hydroxy-6-methylnicotinamido)-2-(o-hydroxyphenyl)acetamido)-3-[(1-methyl-1H-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_{18}H_{17}N_{6}O_{6}s, 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

Official from August 1, 2012
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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 7.0 ± 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:
  \[ \text{Result} = \left( \frac{r_U}{r_S} \right) \times \left( \frac{M_2}{M_1} \right) \times \left( \frac{C_U}{C_S} \right) \times F \times 100 \]
  \[ r_U = \text{peak response of 5-mercapto-1-methyltetrazole from the Sample solution} \]
  \[ r_S = \text{peak response of 5-mercapto-1-methyltetrazole from the Standard solution} \]
  \[ M_1 = \text{molecular weight of 5-mercapto-1-methyltetrazole, 115.14} \]
  \[ M_2 = \text{molecular weight of sodium 5-mercapto-1-methyltetrazole, 138.13} \]
  \[ C_S = \text{concentration of USP Cefpiramide RS in the Standard solution (mg/mL)} \]
  \[ C_U = \text{concentration of Cefpiramide in the Sample solution (mg/mL)} \]
  \[ F = \text{conversion factor, 0.001 mg/µg} \]
  Calculate the percentage of each other impurity in the portion of Cefpiramide taken:
  \[ \text{Result} = \left( \frac{r_U}{r_S} \right) \times \left( \frac{C_U}{C_S} \right) \times P \times 100 \]
  \[ r_U = \text{peak response of each other impurity from the Sample solution} \]
  \[ r_S = \text{peak response of each other impurity from the Standard solution} \]
  \[ P = \text{potency of cefpiramide in USP Cefpiramide RS (µg/mg)} \]
  \[ \text{Acceptance criteria: See Table 1.} \]

SPECIFIC TESTS
- OPTICAL ROTATION, Specific Rotation (7815)
  Sample solution: 10 mg/mL, in dimethylformamide
  Acceptance criteria: \(-100^\circ\) to \(-112^\circ\)
- CRYSTALITY (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, 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.
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$_{8}$O$_{7}$S$_{2}$).

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) (USP)
  System suitability solution: 1 mg/mL of USP Cefpiramide RS in 0.01 N sodium hydroxide. Heat this solution at 95°C 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 (USP)
    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
    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$_{8}$O$_{7}$S$_{2}$) withdrawn from the container, or in the portion of constituted solution taken:

\[ \text{Result} = \left( \frac{r_u}{r_s} \right) \times \left( \frac{C_l}{C_u} \right) \times 100 \]

- $r_u$ = peak response of the Sample solution
- $r_s$ = peak response of the Standard solution
- $C_l$ = 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$_{3}$N$_{3}$O$_{2}$S 381.4
4-[5-(4-Methylphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl]benzenesulfonylamide;
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$_{3}$N$_{3}$O$_{2}$S, 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