

**System suitability—**

System performance: Dissolve 0.2 g of Cefcapene Pivoxil Hydrochloride in 10 mL of methanol, and warm in a water bath at 60°C for 20 minutes. After cooling, pipet 1 mL of this solution, and add exactly 10 mL of the internal standard solution and a mixture of water and methanol (1:1) to make 50 mL. When the procedure is run with 10  $\mu$ L of this solution under the above operating conditions, cefcapene pivoxil, *trans*-cefcapene pivoxil and the internal standard are eluted in this order, the ratios of the retention time of *trans*-cefcapene pivoxil and the internal standard to that of cefcapene pivoxil are about 1.8 and 2.0, respectively, and the resolution between the peaks of *trans*-cefcapene pivoxil and the internal standard is not less than 1.5.

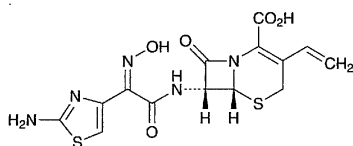
System repeatability: When the test is repeated 5 times with 10  $\mu$ L of the standard solution under the above operating conditions, the relative standard deviation of the ratios of peak area of cefcapene pivoxil to that of the internal standard is not more than 1.0%.

**Containers and storage** Containers—Tight containers.

Storage—Light-resistant, at a temperature not exceeding 5°C.

**Cefdinir**

セフジニル



$C_{14}H_{13}N_5O_5S_2$ : 395.41  
(6*R*,7*R*)-7-[(*Z*)-2-(2-Aminothiazol-4-yl)-2-hydroxyiminoacetylamino]-8-oxo-3-vinyl-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid  
[91832-40-5]

Cefdinir contains not less than 900  $\mu$ g (potency) per mg. The potency of Cefdinir is expressed as mass (potency) of cefdinir ( $C_{14}H_{13}N_5O_5S_2$ ).

**Description** Cefdinir occurs as a white to light yellow crystalline powder.

It is practically insoluble in water, in ethanol (95) and in diethyl ether.

It dissolves in 0.1 mol/L phosphate buffer solution, pH 7.0.

**Identification (1)** Determine the absorption spectra of solutions of Cefdinir and Cefdinir Reference Standard in 0.1 mol/L phosphate buffer solution, pH 7.0 (1 in 100,000) as directed under the Ultraviolet-visible Spectrophotometry, and compare these spectra: both spectra exhibit similar intensities of absorption at the same wavelengths.

(2) Determine the infrared absorption spectra of Cefdinir and Cefdinir Reference Standard as directed in the paste method under the Infrared Spectrophotometry, and compare these spectra: both spectra exhibit similar intensities of absorption at the same wave numbers.

(3) Determine the spectrum of a solution of Cefdinir in a mixture of deuterated dimethyl sulfoxide and heavy water for nuclear magnetic resonance spectroscopy (4:1) (1 in 10), using tetramethylsilane for nuclear magnetic resonance spectroscopy as an internal reference compound, as directed under the Nuclear Magnetic Resonance Spectroscopy (<sup>1</sup>H): it exhibits multiple signals, A and B, at around  $\delta$  5.0–6.1 ppm and B at around  $\delta$  6.4–7.5 ppm. The ratio of integrated intensity of each signal, A:B is about 2:1.

**Absorbance**  $E_{1\text{ cm}}^{1\%}$  (287 nm): 570–610 (0.05 g, 0.1 mol/L phosphate buffer solution, pH 7.0, 5000 mL).

**Optical rotation**  $[\alpha]_D^{20}$ : –58 – –66° (0.25 g, 0.1 mol/L phosphate buffer solution, pH 7.0, 25 mL, 100 mm).

**Purity (1)** Heavy metals—Proceed with 2.0 g of Cefdinir according to Method 2, and perform the test. Prepare the control solution with 2.0 mL of Standard Lead Solution (not more than 10 ppm).

(2) Related substances—Dissolve about 0.1 g of Cefdinir in 10 mL of 0.1 mol/L phosphate buffer solution, pH 7.0. Pipet 3 mL of this solution, add tetramethylammonium hydroxide TS, pH 5.5 to make exactly 20 mL, and use this solution as the sample solution. Perform the test with 10  $\mu$ L of the sample solution as directed under the Liquid Chromatography according to the following conditions, determine the areas of each peak by the automatic integration method, and calculate the amounts of their peaks by the area percentage method: the amount of E-isomer having the relative retention time 1.5 to cefdinir is not more than 0.8%, and the amount of total peak areas other than cefdinir is not more than 3.0%.

**Operating conditions—**

**Detector:** An ultraviolet absorption photometer (wavelength: 254 nm).

**Column:** A stainless steel column 4.6 mm in inside diameter and 15 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (5  $\mu$ m in particle diameter).

**Column temperature:** A constant temperature of about 40°C.

**Mobile phase A:** To 1000 mL of tetramethylammonium hydroxide TS, pH 5.5, add 0.4 mL of 0.1 mol/L disodium dihydrogen ethylenediamine tetraacetate TS.

**Mobile phase B:** To 500 mL of tetramethylammonium hydroxide TS, pH 5.5 add 300 mL of acetonitrile for liquid chromatography and 200 mL of methanol, and add 0.4 mL of 0.1 mol/L disodium dihydrogen ethylenediamine tetraacetate TS.

**Flowing of the mobile phase:** Control the gradient by mixing the mobile A and B as directed in the following table.

Time after injection of the sample (min)	Mobile phase A (%)	Mobile phase B (%)
0–2	95	5
2–22	95→75	5→25
22–32	75→50	25→50
32–37	50	50
37–38	50→95	50→5
38–58	95	5

Flow rate: 1.0 mL per minute. The retention time of cefdinir is about 22 minutes under this condition.

Time span of measurement: About 40 minutes after injection of the sample solution.

*System suitability—*

Test for required detection: Pipet 1 mL of the sample solution, add tetramethylammonium hydroxide TS, pH 5.5 to make exactly 100 mL, and use this solution as the test solution for system suitability. Pipet 1 mL of the test solution for system suitability, add tetramethylammonium hydroxide TS, pH 5.5 to make exactly 10 mL. Confirm that the peak area of cefdinir obtained from 10  $\mu$ L of this solution is equivalent to 7 to 13% of that obtained from 10  $\mu$ L of the test solution for system suitability.

System performance: Dissolve 0.03 g of Cefdinir Reference Standard and 2 mg of cefdinir lactam ring-cleavage lactones in 3 mL of 0.1 mol/L phosphate buffer solution, pH 7.0, add tetramethylammonium hydroxide TS, pH 5.5, to make 20 mL. When the procedure is run with 10  $\mu$ L of this solution under the above operating conditions, peak 1 and peak 2 of cefdinir lactam ring-cleavage lactones separated into 4 peaks, cefdinir, peak 3 and peak 4 of remaining cefdinir lactam ring-cleavage lactones are eluted in this order. Relative retention time of peak 3 of cefdinir lactam ring-cleavage lactone to the retention time of cefdinir is not less than 1.09. The number of theoretical steps and the symmetry coefficient of the peak of cefdinir are not less than 7000 steps and not more than 3.0, respectively.

System repeatability: When the test is repeated 3 times with 10  $\mu$ L of the test solution for system suitability under the above operating conditions, the relative standard deviation of the peak areas of cefdinir is not more than 2.0%.

**Water** Not more than 2.0% (1 g, volumetric titration, direct titration. Use a mixture of formamide for water determination and methanol for water determination (2:1) instead of methanol for water determination).

**Assay** Weigh accurately an amount of Cefdinir and Cefdinir Reference Standard equivalent to about 0.02 g (potency), dissolve each in 0.1 mol/L phosphate buffer solution, pH 7.0 to make exactly 100 mL, and use these solutions as the sample solution and the standard solution. Perform the test with 5  $\mu$ L of the sample solution and the standard solution as directed under the Liquid Chromatography according to the following conditions, and calculate the peak areas,  $A_T$  and  $A_S$ , of cefdinir of the solutions.

$$\begin{aligned} & \text{Amount } [\mu\text{g (potency)}] \text{ of cefdinir } (\text{C}_{14}\text{H}_{13}\text{N}_5\text{O}_5\text{S}_2) \\ &= \text{amount } [\text{mg (potency)}] \text{ of Cefdinir Reference} \\ & \text{Standard} \times \frac{A_T}{A_S} \times 1000 \end{aligned}$$

*Operating conditions—*

**Detector:** An ultraviolet absorption photometer (wavelength: 254 nm).

**Column:** A stainless steel column 4.6 mm in inside diameter and 15 cm in length, packed with octadecylsilanized silica gel for liquid chromatography (5  $\mu$ m in particle diameter).

**Column temperature:** A constant temperature of about 40°C.

**Mobile phase:** To 1000 mL of tetramethylammonium hydroxide TS, pH 5.5, add 0.4 mL of 0.1 mol/L disodium dihydrogen ethylenediamine tetraacetate TS. To 900 mL of

this solution add 60 mL of acetonitrile for liquid chromatography and 40 mL of methanol.

Flow rate: Adjust the flow rate so that the retention time of cefdinir is about 8 minutes.

*System suitability—*

System performance: Dissolve 2 mg of Cefdinir Reference Standard and 5 mg of cefdinir lactam ring-cleavage lactones in 10 mL of 0.1 mol/L phosphate buffer solution, pH 7.0. When the procedure is run with 5  $\mu$ L of this solution under the above operating conditions, peak 1 and peak 2 of cefdinir lactam ring-cleavage lactones separated into 4 peaks, cefdinir, peak 3 and peak 4 of remaining cefdinir lactam ring-cleavage lactones are eluted in this order. The resolution between the peak 2 of cefdinir lactam ring-cleavage lactone and that of cefdinir is not less than 1.2. The number of theoretical steps and the symmetry coefficient of the peak of cefdinir are not less than 2000 steps and not more than 1.5, respectively.

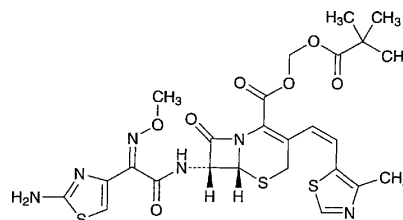
System repeatability: When the test is repeated 6 times with 5  $\mu$ L of the standard solution under the above operating conditions, the relative standard deviation of the peak areas of cefdinir is not more than 1.0%.

**Containers and storage** Containers—Tight containers.

Storage—Light-resistant.

## Cefditoren Pivoxil

セフジトレン ピボキシル



$\text{C}_{25}\text{H}_{28}\text{N}_6\text{O}_7\text{S}_3$ : 620.72

2,2-Dimethylpropanoyloxymethyl (6R,7R)-7-[(Z)-2-(2-aminothiazol-4-yl)-2-methoxyiminoacetyl-amino]-3-[(Z)-2-(4-methylthiazol-5-yl)ethenyl]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate [117467-28-4]

Cefditoren Pivoxil contains not less than 780  $\mu$ g (potency) per mg, calculated on the anhydrous basis. The potency of Cefditoren Pivoxil is expressed as mass (potency) of cefditoren ( $\text{C}_{19}\text{H}_{18}\text{N}_6\text{O}_5\text{S}_3$ : 506.59).

**Description** Cefditoren Pivoxil occurs as a light yellowish white to light yellow crystalline powder.

It is sparingly soluble in methanol, slightly soluble in acetonitrile and in ethanol (95), and practically insoluble in water.

It dissolves in dilute hydrochloric acid.

**Identification (1)** Dissolve 5 mg of Cefditoren Pivoxil in 3 mL of hydroxylammonium chloride-ethanol TS, allow to stand for 5 minutes, add 1 mL of acidic ammonium iron (III) sulfate TS and shake: a red-brown color develops.

(2) Dissolve 1 mg of Cefditoren Pivoxil in 1 mL of di-