

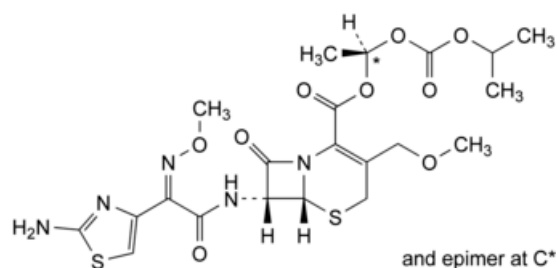


Edition: BP 2025 (Ph. Eur. 11.6 update)

Cefpodoxime Proxetil

[General Notices](#)

(Ph. Eur. monograph 2341)



$C_{21}H_{27}N_5O_9S_2$ 557.6 87239-81-4

Action and use

Cephalosporin antibacterial.

Ph Eur

DEFINITION

(1*RS*)-1-[[[(1-Methylethoxy)carbonyl]oxy]ethyl (6*R*,7*R*)-7-[[[(2*Z*)-2-(2-aminothiazol-4-yl)-2-(methoxyimino)acetyl]amino]-3-(methoxymethyl)-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate.

Semi-synthetic product derived from a fermentation product.

Content

94.0 per cent to 102.0 per cent (anhydrous substance).

CHARACTERS

Appearance

White or pale yellow or light brown, amorphous powder.

Solubility

Very slightly soluble or practically insoluble in water, very soluble in acetonitrile and in methanol, freely soluble in anhydrous ethanol.

IDENTIFICATION

Infrared absorption spectrophotometry (2.2.24).

Comparison [cefpodoxime proxetil CRS](#).

TESTS

Diastereoisomer ratio

Liquid chromatography (2.2.29) as described under Assay. Use the normalisation procedure.

Limit Test solution:

- the ratio of the area of the peak due to cefpodoxime proxetil diastereoisomer II to the sum of the areas of the peaks due to cefpodoxime proxetil diastereoisomers I and II is between 0.5 and 0.6.

Related substances

Liquid chromatography (2.2.29). Prepare the solutions immediately before use or store them at 2-8 °C.

Solvent mixture [glacial acetic acid R](#), [acetonitrile R](#), [water R](#) (2:99:99 V/V/V).

Test solution Dissolve 50 mg of the substance to be examined in the solvent mixture and dilute to 50.0 mL with the solvent mixture.

Reference solution (a) Dilute 1.0 mL of the test solution to 100.0 mL with the solvent mixture.

Reference solution (b) Dissolve 5 mg of [cefpodoxime proxetil for peak identification CRS](#) (containing impurities B, C and D) in 5.0 mL of the solvent mixture.

Reference solution (c) Dissolve 5 mg of [cefpodoxime proxetil for impurity H identification CRS](#) in 5.0 mL of the solvent mixture.

Column:

- size: $l = 0.15\text{ m}$, $\varnothing = 4.6\text{ mm}$;
- stationary phase: [end-capped octadecylsilyl silica gel for chromatography R](#) (5 μm);
- temperature: maintain at a constant temperature of 20 °C.

Mobile phase:

- mobile phase A: [anhydrous formic acid R](#), [methanol R](#), [water R](#) (1:400:600 V/V/V);
- mobile phase B: [anhydrous formic acid R](#), [water R](#), [methanol R](#) (1:50:950 V/V/V);

Time (min)	Mobile phase A (per cent V/V)	Mobile phase B (per cent V/V)
0 - 65	95	5
65 - 145	95 → 15	5 → 85
145 - 155	15	85

Flow rate 0.6 mL/min.

Detection Spectrophotometer at 254 nm.

Injection 20 μL .

Identification of impurities Use the chromatogram supplied with [cefpodoxime proxetil for peak identification CRS](#) and the chromatogram obtained with reference solution (b) to identify the peaks due to impurities B, C and D; use the

chromatogram supplied with [cefpodoxime proxetil for impurity H identification CRS](#) and the chromatogram obtained with reference solution (c) to identify the peaks due to impurity H.

Relative retention With reference to cefpodoxime proxetil diastereoisomer II (retention time = about 58 min): diastereoisomer I of impurity B = about 0.68; diastereoisomer I of cefpodoxime proxetil = about 0.74; impurity C = about 0.82; diastereoisomer II of impurity B = about 0.85; impurity D (2 peaks) = about 0.88 and 1.13; peaks due to diastereoisomers of impurity H: between about 1.9 and 2.3.

System suitability:

- the chromatogram obtained with reference solution (b) is similar to the chromatogram supplied with [cefpodoxime proxetil for peak identification CRS](#);
- **resolution**: minimum 6.0 between the peaks due to cefpodoxime proxetil diastereoisomers I and II in the chromatogram obtained with reference solution (a);
- **peak-to-valley ratio**: minimum 1.1, where H_p = height above the baseline of the peak due to diastereoisomer II of impurity B and H_v = height above the baseline of the lowest point of the curve separating this peak from the peak due to impurity C in the chromatogram obtained with reference solution (b).

Limits:

- **impurity C**: not more than twice the sum of the areas of the 2 principal peaks in the chromatogram obtained with reference solution (a) (2.0 per cent);
- **impurity D (sum of the 2 diastereoisomers)**: not more than the sum of the areas of the 2 principal peaks in the chromatogram obtained with reference solution (a) (1.0 per cent);
- **impurity H (sum of the diastereoisomers)**: not more than the sum of the areas of the 2 principal peaks in the chromatogram obtained with reference solution (a) (1.0 per cent);
- **impurity B (sum of the 2 diastereoisomers)**: not more than 0.5 times the sum of the areas of the 2 principal peaks in the chromatogram obtained with reference solution (a) (0.5 per cent);
- **any other impurity**: for each impurity, not more than 0.2 times the sum of the areas of the 2 principal peaks in the chromatogram obtained with reference solution (a) (0.2 per cent);
- **total**: not more than 4 times the sum of the areas of the 2 principal peaks in the chromatogram obtained with reference solution (a) (4.0 per cent);
- **disregard limit**: 0.05 times the sum of the areas of the 2 principal peaks in the chromatogram obtained with reference solution (a) (0.05 per cent).

Water (2.5.12)

Maximum 2.5 per cent, determined on 0.500 g.

ASSAY

Liquid chromatography ([2.2.29](#)).

Solution A 20 mg/L solution of [anhydrous citric acid R](#) in [acetonitrile R](#).

Test solution Dissolve 30.0 mg of the substance to be examined in solution A and dilute to 50.0 mL with solution A.

Reference solution Dissolve 30.0 mg of [cefpodoxime proxetil CRS](#) in solution A and dilute to 50.0 mL with solution A.

Column:

- **size**: $l = 0.15$ m, $\varnothing = 4.6$ mm;
- **stationary phase**: [end-capped octadecylsilyl silica gel for chromatography R](#) (5 μ m);
- **temperature**: 40 °C.

Mobile phase [methanol R](#), [water R](#) (9:11 V/V).

Flow rate 0.8 mL/min.

Detection Spectrophotometer at 240 nm.

Injection 10 µL.

Run time 1.2 times the retention time of cefpodoxime proxetil diastereoisomer II.

Retention time Cefpodoxime proxetil diastereoisomer II = about 30 min.

System suitability Reference solution:

— [resolution](#): minimum 4.0 between the peaks due to cefpodoxime proxetil diastereoisomers I and II.

Calculate the percentage content of $C_{21}H_{27}N_5O_9S_2$ from the sum of the areas of the 2 peaks due to the diastereoisomers and using the declared content of [cefpodoxime proxetil CRS](#).

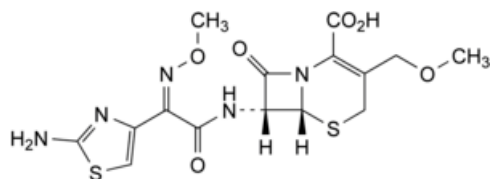
STORAGE

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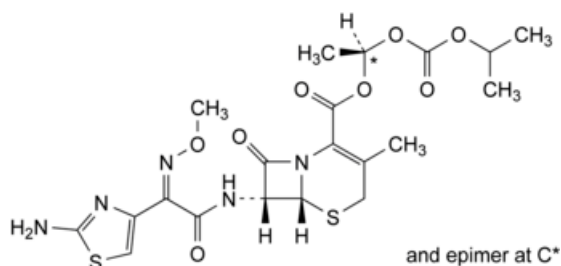
IMPURITIES

Specified impurities B, C, D, H.

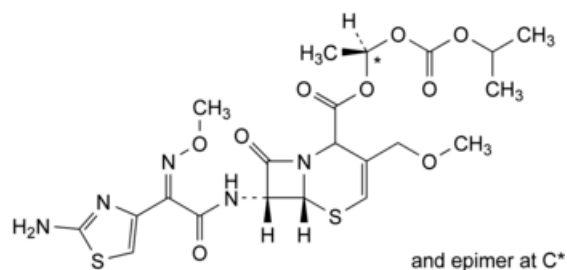
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph [Substances for pharmaceutical use \(2034\)](#). It is therefore not necessary to identify these impurities for demonstration of compliance. See also [5.10. Control of impurities in substances for pharmaceutical use](#)) A, E, F, G.



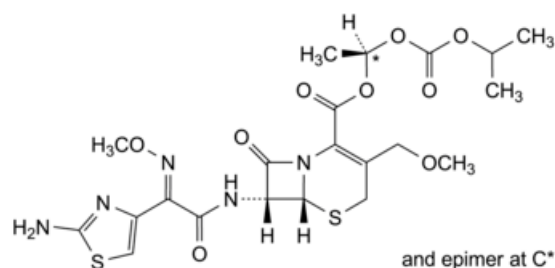
A. (6R,7R)-7-[[[(2Z)-2-(2-aminothiazol-4-yl)-2-(methoxyimino)acetyl]amino]-3-(methoxymethyl)-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid (cefpodoxime),



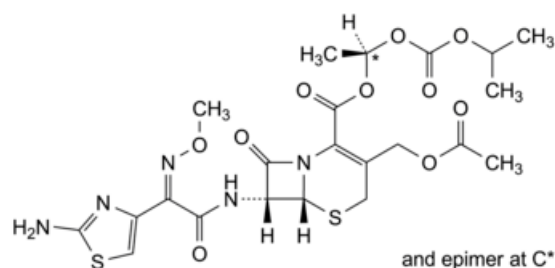
B. (1RS)-1-[[[(1-methylethoxy)carbonyloxy]ethyl (6R,7R)-7-[[[(2Z)-2-(2-aminothiazol-4-yl)-2-(methoxyimino)acetyl]amino]-3-methyl-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate (ADCA-analogue of cefpodoxime proxetil),



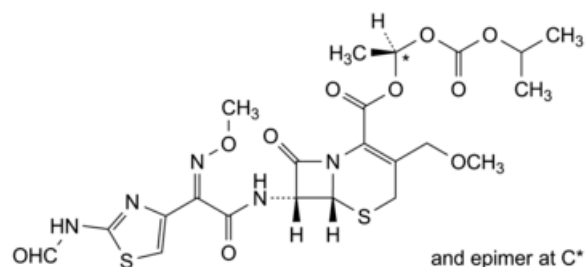
C. (1*RS*)-1-[[[(1-methylethoxy)carbonyl]oxy]ethyl (6*R*,7*R*)-7-[[[(2*Z*)-2-(2-aminothiazol-4-yl)-2-(methoxyimino)acetyl]amino]-3-(methoxymethyl)-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-3-ene-2-carboxylate (delta-2-cefpodoxime proxetil),



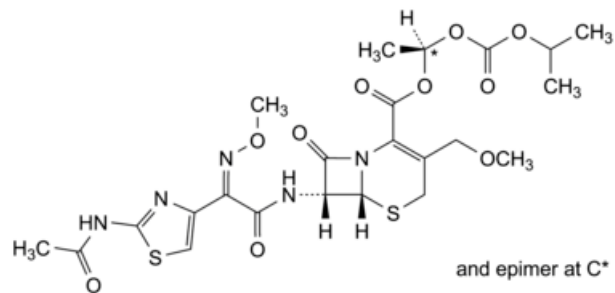
D. (1*RS*)-1-[[[(1-methylethoxy)carbonyl]oxy]ethyl (6*R*,7*R*)-7-[[[(2*E*)-2-(2-aminothiazol-4-yl)-2-(methoxyimino)acetyl]amino]-3-(methoxymethyl)-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate (anti-cefpodoxime proxetil),



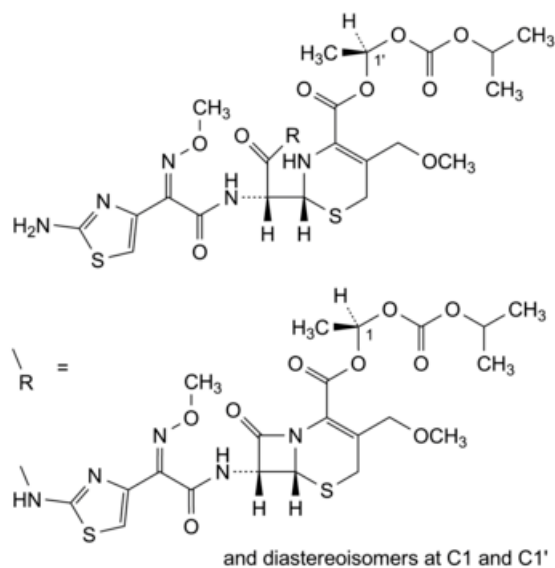
E. (1*RS*)-1-[[[(1-methylethoxy)carbonyl]oxy]ethyl (6*R*,7*R*)-3-(acetoxymethyl)-7-[[[(2*Z*)-2-(2-aminothiazol-4-yl)-2-(methoxyimino)acetyl]amino]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate (ACA-analogue of cefpodoxime proxetil),



F. (1*RS*)-1-[[[(1-methylethoxy)carbonyl]oxy]ethyl (6*R*,7*R*)-7-[[[(2*Z*)-2-[(2-formylamino)thiazol-4-yl)-2-(methoxyimino)acetyl]amino]-3-(methoxymethyl)-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate (*N*-formyl cefpodoxime proxetil),



G. (1*RS*)-1-[[[(1-methylethoxy)carbonyl]oxy]ethyl (6*R*,7*R*)-7-[[[(2*Z*)-[2-(2-acetylthiazol-4-yl)]-2-(methoxyimino)acetyl]amino]-3-(methoxymethyl)-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate (*N*-acetyl-cefpodoxime proxetil),



H. mixture of the diastereoisomers of 1-[[[(1-methylethoxy)carbonyl]oxy]ethyl (6*R*,7*R*)-7-[[[(2*Z*)-2-[2-[[[(2*R*)-2-[[[(2*Z*)-2-(2-aminothiazol-4-yl)]-2-(methoxyimino)acetyl]amino]-2-[[[(2*R*)-5-(methoxymethyl)-4-[[1-[[[(1-methylethoxy)carbonyl]oxy]ethoxy]carbonyl]-3,6-dihydro-2*H*-1,3-thiazin-2-yl]acetyl]amino]thiazol-4-yl]-2-(methoxyimino)acetyl]amino]-3-(methoxymethyl)-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylate (cefpodoxime proxetil dimer).

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