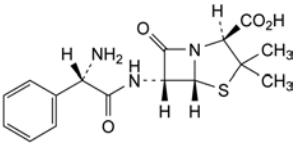
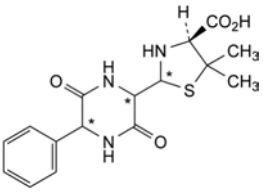
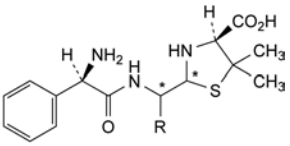


B. (2*S*,5*R*,6*R*)-6-[[(2*S*)-2-amino-2-phenylacetyl]amino]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid (L-ampicillin),

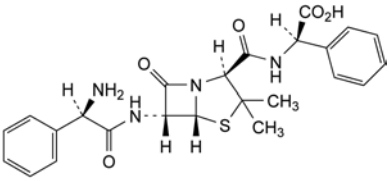


C. (4*S*)-2-(3,6-dioxo-5-phenylpiperazin-2-yl)-5,5-dimethylthiazolidine-4-carboxylic acid (diketopiperazines of ampicillin),

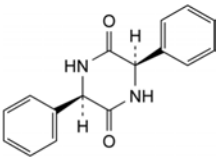


D. R = CO_2H: (4*S*)-2-[[[(2*R*)-2-amino-2-phenylacetyl]amino]-carboxymethyl]-5,5-dimethylthiazolidine-4-carboxylic acid (penicilloic acids of ampicillin),

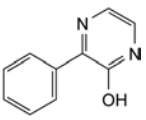
F. R = H: (2*RS*,4*S*)-2-[[[(2*R*)-2-amino-2-phenylacetyl]amino]-methyl]-5,5-dimethylthiazolidine-4-carboxylic acid (penilloic acids of ampicillin),



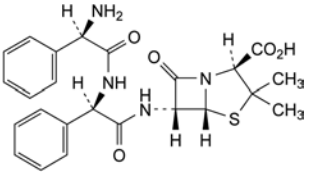
E. (2*R*)-2-[[[(2*S*,5*R*,6*R*)-6-[[(2*R*)-2-amino-2-phenylacetyl]-amino]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo-[3.2.0]hept-2-yl]carbonyl]amino]-2-phenylacetic acid (ampicillinyl-D-phenylglycine),



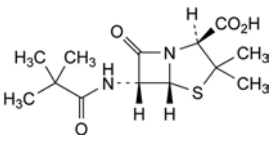
G. (3*R*,6*R*)-3,6-diphenylpiperazine-2,5-dione,



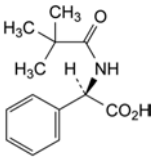
H. 3-phenylpyrazin-2-ol,



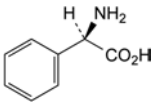
I. (2*S*,5*R*,6*R*)-6-[[(2*R*)-2-[[(2*R*)-2-amino-2-phenylacetyl]-amino]-2-phenylacetyl]amino]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid (D-phenylglycylampicillin),



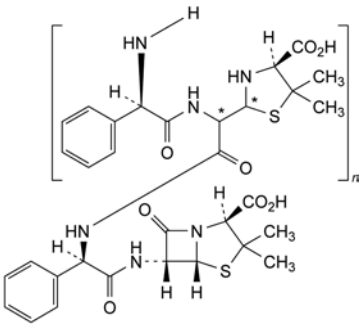
J. (2*S*,5*R*,6*R*)-6-[(2,2-dimethylpropanoyl)amino]-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid,



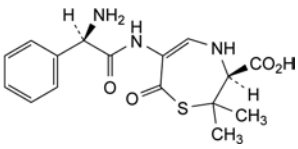
K. (2*R*)-2-[(2,2-dimethylpropanoyl)amino]-2-phenylacetic acid,



L. (2*R*)-2-amino-2-phenylacetic acid (D-phenylglycine),



M. co-oligomers of ampicillin and of penicilloic acids of ampicillin,

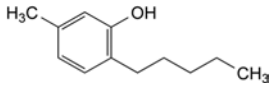


N. (3*S*)-6-[[(2*R*)-2-amino-2-phenylacetyl]amino]-2,2-dimethyl-7-oxo-2,3,4,7-tetrahydro-1,4-thiazepine-3-carboxylic acid.

01/2011:2405

AMYLMETACRESOL

Amylmetacresolum



$C_{12}H_{18}O$ M_r 178.3
[1300-94-3]

DEFINITION

5-Methyl-2-pentylphenol.

Content: 98.0 per cent to 102.0 per cent.

CHARACTERS

Appearance: clear or almost clear liquid, or solid crystalline mass, colourless or slightly yellow when freshly prepared. The substance changes colour during storage by darkening and/or discolouration to dark yellow, brownish-yellow or pink.

Solubility: practically insoluble in water, very soluble in acetone and in ethanol (96 per cent).

It solidifies at about 22 °C.

IDENTIFICATION

Infrared absorption spectrophotometry (*2.2.24*).

Preparation: film between 2 plates of *potassium bromide R*.

Comparison: *amylmetacresol CRS*.

TESTS

Related substances. Gas chromatography (*2.2.28*): use the normalisation procedure.

Internal standard solution. Dissolve 0.100 g of *butylhydroxytoluene R* in *2-propanol R* and dilute to 10.0 mL with the same solvent.

Test solution (a). Dissolve 0.1000 g of the substance to be examined in *2-propanol R* and dilute to 10.0 mL with the same solvent.

Test solution (b). To 2.0 mL of test solution (a) add 2.0 mL of the internal standard solution and dilute to 10.0 mL with *2-propanol R*.

Reference solution (a). Dissolve 10 mg of *m-cresol R* (impurity B) and 10 mg of *p-cresol R* (impurity D) in *2-propanol R* and dilute to 100.0 mL with the same solvent.

Reference solution (b). Dissolve the contents of a vial of *amylmetacresol for peak identification CRS* (containing impurities A, G and K) in 1.0 ml of *2-propanol R*.

Reference solution (c). Dissolve 0.1000 g of *amylmetacresol CRS* in *2-propanol R* and dilute to 10.0 mL with the same solvent. To 2.0 mL of this solution add 2.0 mL of the internal standard solution and dilute to 10.0 mL with *2-propanol R*.

Reference solution (d). Dilute 1.0 mL of test solution (a) to 100.0 mL with *2-propanol R*. Dilute 1.0 mL of this solution to 20.0 mL with *2-propanol R*.

Column:

- *material*: fused silica;
- *size*: *l* = 30 m, Ø = 0.25 mm;
- *stationary phase*: *macrogol 20 000 R* (film thickness 0.5 µm).

Carrier gas: *helium for chromatography R*.

Linear velocity: 33 cm/s.

Split ratio: 1:30.

Temperature:

	Time (min)	Temperature (°C)
Column	0 - 17.5	100 → 240
	17.5 - 32.5	240
Injection port		250
Detector		250

Detection: flame ionisation.

Injection: 1.0 µL of test solution (a) and reference solutions (a), (b) and (d).

Identification of impurities: use the chromatogram supplied with *amylmetacresol for peak identification CRS* and the chromatogram obtained with reference solution (b) to identify the peaks due to impurities A, G and K.

Relative retention with reference to amylmetacresol (retention time = about 16 min): impurity G (diastereoisomer 1) = about 0.51; impurity G (diastereoisomer 2) = about 0.53; impurity D = about 0.77; impurity B = about 0.78; impurity K = about 0.95; impurity A = about 0.99.

System suitability: reference solution (a):

- *resolution*: minimum 1.5 between the peaks due to impurities D and B.

Limits:

- *impurity A*: maximum 0.6 per cent;
- *impurities G* (sum of the 2 diastereoisomers), *K*: for each impurity, maximum 0.15 per cent;
- *unspecified impurities*: for each impurity, maximum 0.10 per cent;
- *total*: maximum 1.0 per cent;
- *disregard limit*: the area of the peak due to amylmetacresol in the chromatogram obtained with reference solution (d) (0.05 per cent).

Sulfated ash (*2.4.14*): maximum 0.1 per cent, determined on 1.0 g.

ASSAY

Gas chromatography (*2.2.28*) as described in the test for related substances with the following modification.

Injection: 1.0 µL of test solution (b) and reference solution (c).

Calculate the percentage content of $C_{12}H_{18}O$ from the declared content of *amylmetacresol CRS*.

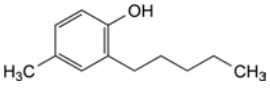
STORAGE

In an airtight, non-metallic container, protected from light.

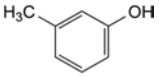
IMPURITIES

Specified impurities: A, G, K.

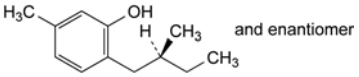
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph *Substances for pharmaceutical 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*): *B, C, D, E, F, H, I, J.*



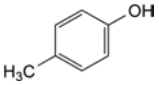
A. 4-methyl-2-pentylphenol,



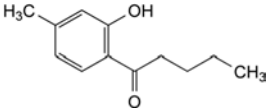
B. 3-methylphenol (*m*-cresol),



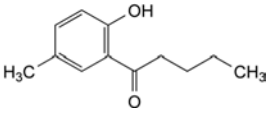
C. 5-methyl-2-[(2*RS*)-2-methylbutyl]phenol,



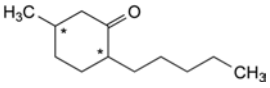
D. 4-methylphenol (*p*-cresol),



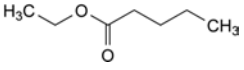
E. 1-(2-hydroxy-4-methylphenyl)pentan-1-one,



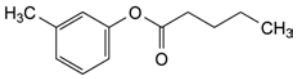
F. 1-(2-hydroxy-5-methylphenyl)pentan-1-one,



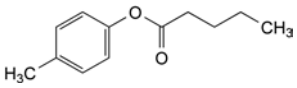
G. 5-methyl-2-pentylcyclohexanone,



H. ethyl pentanoate,



I. 3-methylphenyl pentanoate,



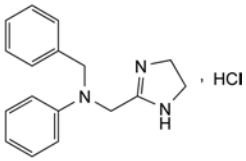
J. 4-methylphenyl pentanoate,

K. unknown structure.

01/2008:0972
corrected 6.0

ANTAZOLINE HYDROCHLORIDE

Antazolini hydrochloridum



$C_{17}H_{20}ClN_3$ M_r 301.8
[2508-72-7]

DEFINITION

Antazoline hydrochloride contains not less than 99.0 per cent and not more than the equivalent of 101.0 per cent of *N*-benzyl-*N*-[(4,5-dihydro-1*H*-imidazol-2-yl)methyl]aniline hydrochloride, calculated with reference to the dried substance.

CHARACTERS

A white or almost white, crystalline powder, sparingly soluble in water, soluble in alcohol, slightly soluble in methylene chloride.

It melts at about 240 °C, with decomposition.

IDENTIFICATION

First identification: A, D.

Second identification: B, C, D.

A. Examine by infrared absorption spectrophotometry (*2.2.24*), comparing with the spectrum obtained with *antazoline hydrochloride CRS*. Examine the substances as discs prepared using *potassium chloride R*.

B. Examine the chromatograms obtained in the test for related substances in daylight after spraying. The principal spot in the chromatogram obtained with test solution (b) is similar in position, colour and size to the principal spot in the chromatogram obtained with reference solution (b).

C. To 5 mL of solution S (see Tests) add, drop by drop, *dilute sodium hydroxide solution R* until an alkaline reaction is produced. Filter. The precipitate, washed with two quantities, each of 10 mL, of *water R* and dried in a desiccator under reduced pressure, melts (*2.2.14*) at 119 °C to 123 °C.

D. It gives reaction (a) of chlorides (*2.3.1*).

TESTS

Solution S. Dissolve 2.0 g in *carbon dioxide-free water R* prepared from *distilled water R*, heating at 60 °C if necessary. Allow to cool and dilute to 100 mL with the same solvent.

Appearance of solution. Solution S is clear (*2.2.1*) and not more intensely coloured than reference solution Y_7 (*2.2.2, Method II*).

Acidity or alkalinity. To 10 mL of solution S add 0.2 mL of *methyl red solution R*. Not more than 0.1 mL of *0.01 M hydrochloric acid* or *0.01 M sodium hydroxide* is required to change the colour of the indicator.

Related substances. Examine by thin-layer chromatography (*2.2.27*), using *silica gel* GF_{254} *R* as the coating substance. Heat the plate at 110 °C for 15 min before using.

Test solution (a). Dissolve 0.10 g of the substance to be examined in *methanol R* and dilute to 5 mL with the same solvent.

Test solution (b). Dilute 1 mL of test solution (a) to 5 mL with *methanol R*.

Reference solution (a). Dilute 0.5 mL of test solution (a) to 100 mL with *methanol R*.

Reference solution (b). Dissolve 20 mg of *antazoline hydrochloride CRS* in *methanol R* and dilute to 5 mL with the same solvent.

Reference solution (c). Dissolve 20 mg of *xylometazoline hydrochloride CRS* in 1 mL of test solution (a) and dilute to 5 mL with *methanol R*.

Apply to the plate 5 µL of each solution. Develop over a path of 15 cm using a mixture of 5 volumes of *diethylamine R*, 10 volumes of *methanol R* and 85 volumes of *ethyl acetate R*. Dry the plate in a current of warm air for 15 min. Examine in ultraviolet light at 254 nm. The test is not valid unless the chromatogram obtained with reference solution (c) shows two clearly separated principal spots. Spray with a mixture of equal volumes of a 200 g/L solution of *ferric chloride R* and a 5 g/L solution of *potassium ferricyanide R*. Examine immediately in daylight. Any spot in the chromatogram obtained with test solution (a), apart from the principal spot, is not more intense than the spot in the chromatogram obtained with reference solution (a) (0.5 per cent).

Heavy metals (*2.4.8*). 1.0 g complies with limit test C for heavy metals (20 ppm). Prepare the standard using 2 mL of *lead standard solution (10 ppm Pb) R*.

Loss on drying (*2.2.32*). Not more than 0.5 per cent, determined on 1.000 g by drying in an oven at 105 °C for 3 h.

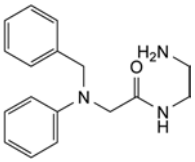
Sulfated ash (*2.4.14*). Not more than 0.1 per cent, determined on the residue obtained in the test for loss on drying.

ASSAY

Dissolve 0.250 g in 100 mL of *alcohol R*. Add 0.1 mL of *phenolphthalein solution R1*. Titrate with *0.1 M alcoholic potassium hydroxide*.

1 mL of *0.1 M alcoholic potassium hydroxide* is equivalent to 30.18 mg of $C_{17}H_{20}ClN_3$.

IMPURITIES



A. *N*-(2-aminoethyl)-2-(benzylphenylamino)acetamide.

01/2008:0209

ANTICOAGULANT AND PRESERVATIVE SOLUTIONS FOR HUMAN BLOOD

Solutiones anticoagulantes et sanguinem humanum conservantes

DEFINITION

Anticoagulant and preservative solutions for human blood are sterile and pyrogen-free solutions prepared with water for injections, filtered, distributed in the final containers and sterilised. The content of sodium citrate ($C_6H_5Na_3O_7,2H_2O$), glucose monohydrate ($C_6H_{12}O_6,H_2O$) or anhydrous glucose ($C_6H_{12}O_6$) and sodium dihydrogen phosphate dihydrate ($NaH_2PO_4,2H_2O$) is not less than 95.0 per cent and not more