Mobile phase:
– *mobile phase A*: *methanol R, water R* (50:50 *V/V*);
– *mobile phase B*: *methanol R*;

Time (min)	Mobile phase A (per cent *V/V*)	Mobile phase B (per cent *V/V*)
0 - 30	71	29
30 - 35	71 → 0	29 → 100
35 - 37	0	100
37 - 38	0 → 71	100 → 29

Flow rate: 1.0 mL/min.
Detection: spectrophotometer at 215 nm.
Injection: 10 µL.
Relative retention with reference to ethambutol (retention time = about 14 min): impurity B = about 1.3.
System suitability: reference solution (b):
– *resolution*: minimum 4.0 between the peaks due to ethambutol and impurity B.
Limits:
– *impurity B*: not more than twice the area of the principal peak in the chromatogram obtained with reference solution (a) (1.0 per cent);
– *unspecified impurities with a relative retention of 0.75 to 1.5 with reference to ethambutol*: for each impurity, not more than 0.2 times the area of the peak due to ethambutol in the chromatogram obtained with reference solution (a) (0.10 per cent);
– *total (impurity B and unspecified impurities with a relative retention of 0.75 to 1.5 with reference to ethambutol)*: not more than twice the area of the principal peak in the chromatogram obtained with reference solution (a) (1.0 per cent);
– *disregard limit*: 0.1 times the area of the peak due to ethambutol in the chromatogram obtained with reference solution (a) (0.05 per cent).

Impurity D (1,2-dichloroethane) (*2.4.24*): maximum 5 ppm.

Heavy metals (*2.4.8*): maximum 10 ppm.
Dissolve 2.0 g in *water R* and dilute to 20 mL with the same solvent. 12 mL of the solution complies with test A. Prepare the reference solution using 10 mL of *lead standard solution (1 ppm Pb) R*.

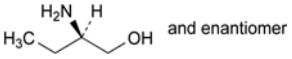
Loss on drying (*2.2.32*): maximum 0.5 per cent, determined on 0.500 g by drying in an oven at 105 °C for 3 h.

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

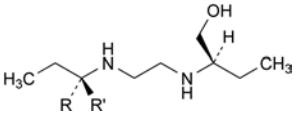
ASSAY
Dissolve 0.200 g in 50 mL of *water R* and add 1.0 mL of *0.1 M hydrochloric acid*. Carry out a potentiometric titration (*2.2.20*), using *0.1 M sodium hydroxide*. Read the volume added between the 2 points of inflexion.
1 mL of *0.1 M sodium hydroxide* is equivalent to 27.72 mg of $C_{10}H_{26}Cl_2N_2O_2$.

STORAGE
In an airtight container.

IMPURITIES
Specified impurities: A, B, D.
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*): *C.*

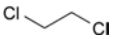


A. 2-aminobutan-1-ol,



B. R = CH_2-OH, R′ = H: (2*R*,2′*S*)-2,2′-(ethylenediimino)-dibutan-1-ol (meso-ethambutol),

C. R = H, R′ = CH_2-OH: (2*R*,2′*R*)-2,2′-(ethylenediimino)dibutan-1-ol ((*R*,*R*)-ethambutol),



D. 1,2-dichloroethane (ethylene chloride).

01/2008:1317

ETHANOL (96 PER CENT)

Ethanolum (96 per centum)

DEFINITION
Content:
– *ethanol* (C_2H_6O; M_r 46.07): 95.1 per cent *V/V* (92.6 per cent *m/m*) to 96.9 per cent *V/V* (95.2 per cent *m/m*) at 20 °C, calculated from the relative density using the alcoholimetric tables (*5.5*);
– *water*.

CHARACTERS
Appearance: colourless, clear, volatile, flammable liquid, hygroscopic.
Solubility: miscible with water and with methylene chloride.
It burns with a blue, smokeless flame.
bp: about 78 °C.

IDENTIFICATION
First identification: A, B.
Second identification: A, C, D.
A. Relative density (see Tests).
B. Infrared absorption spectrophotometry (*2.2.24*).
Comparison: *Ph. Eur. reference spectrum ethanol (96 per cent)*.
C. Mix 0.1 mL with 1 mL of a 10 g/L solution of *potassium permanganate R* and 0.2 mL of *dilute sulfuric acid R* in a test-tube. Cover immediately with a filter paper moistened with a freshly prepared solution containing 0.1 g of *sodium nitroprusside R* and 0.5 g of *piperazine hydrate R* in 5 mL of *water R*. After a few minutes, an intense blue colour appears on the paper and becomes paler after 10-15 min.
D. To 0.5 mL add 5 mL of *water R*, 2 mL of *dilute sodium hydroxide solution R*, then slowly add 2 mL of *0.05 M iodine*. A yellow precipitate is formed within 30 min.

TESTS
Appearance. It is clear (*2.2.1*) and colourless (*2.2.2, Method II*) when compared with *water R*. Dilute 1.0 mL to 20 mL with *water R*. After standing for 5 min, the dilution remains clear (*2.2.1*) when compared with *water R*.

Acidity or alkalinity. To 20 mL add 20 mL of *carbon dioxide-free water R* and 0.1 mL of *phenolphthalein solution R*. The solution is colourless. Add 1.0 mL of *0.01 M sodium hydroxide*. The solution is pink (30 ppm, expressed as acetic acid).

Relative density (*2.2.5*): 0.805 to 0.812.

Absorbance (*2.2.25*): maximum 0.40 at 240 nm, 0.30 between 250 nm and 260 nm and 0.10 between 270 nm and 340 nm. The absorption curve is smooth.

Examine between 235 nm and 340 nm, in a 5 cm cell using *water R* as the compensation liquid.

Volatile impurities. Gas chromatography (*2.2.28*).

Test solution (a). The substance to be examined.

Test solution (b). Add 150 µL of *4-methylpentan-2-ol R* to 500.0 mL of the substance to be examined.

Reference solution (a). Dilute 100 µL of *anhydrous methanol R* to 50.0 mL with the substance to be examined. Dilute 5.0 mL of the solution to 50.0 mL with the substance to be examined.

Reference solution (b). Dilute 50 µL of *anhydrous methanol R* and 50 µL of *acetaldehyde R* to 50.0 mL with the substance to be examined. Dilute 100 µL of the solution to 10.0 mL with the substance to be examined.

Reference solution (c). Dilute 150 µL of *acetal R* to 50.0 mL with the substance to be examined. Dilute 100 µL of the solution to 10.0 mL with the substance to be examined.

Reference solution (d). Dilute 100 µL of *benzene R* to 100.0 mL with the substance to be examined. Dilute 100 µL of the solution to 50.0 mL with the substance to be examined.

Column:

– *material*: fused silica;

– *size*: *l* = 30 m, Ø = 0.32 mm;

– *stationary phase*: *poly[(cyanopropyl)(phenyl)][dimethyl]siloxane R* (film thickness 1.8 µm).

Carrier gas: *helium for chromatography R*.

Linear velocity: 35 cm/s.

Split ratio: 1:20.

Temperature:

	Time (min)	Temperature (°C)
Column	0 - 12	40
	12 - 32	40 → 240
	32 - 42	240
Injection port		200
Detector		280

Detection: flame ionisation.

Injection: 1 µL.

System suitability: reference solution (b):

– *resolution*: minimum 1.5 between the first peak (acetaldehyde) and the second peak (methanol).

Limits:

– *methanol* in the chromatogram obtained with test solution (a): not more than half the area of the corresponding peak in the chromatogram obtained with reference solution (a) (200 ppm *V/V*);

– *acetaldehyde + acetal*: maximum 10 ppm *V/V*, expressed as acetaldehyde.

Calculate the sum of the contents of acetaldehyde and acetal in parts per million (*V/V*) using the following expression:

$$\frac{10 \times A_E}{A_T - A_E} + \frac{30 \times C_E}{C_T - C_E}$$

A_E = area of the acetaldehyde peak in the chromatogram obtained with test solution (a),

A_T = area of the acetaldehyde peak in the chromatogram obtained with reference solution (b),

C_E = area of the acetal peak in the chromatogram obtained with test solution (a),

C_T = area of the acetal peak in the chromatogram obtained with reference solution (c).

– *benzene*: maximum 2 ppm *V/V*.

Calculate the content of benzene in parts per million (*V/V*) using the following expression:

$$\frac{2B_E}{B_T - B_E}$$

B_E = area of the benzene peak in the chromatogram obtained with the test solution (a),

B_T = area of the benzene peak in the chromatogram obtained with reference solution (d).

If necessary, the identity of benzene can be confirmed using another suitable chromatographic system (stationary phase with a different polarity).

– *total of other impurities* in the chromatogram obtained with test solution (b): not more than the area of the peak due to 4-methylpentan-2-ol in the chromatogram obtained with test solution (b) (300 ppm),

– *disregard limit*: 0.03 times the area of the peak corresponding to 4-methylpentan-2-ol in the chromatogram obtained with test solution (b) (9 ppm).

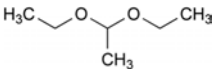
Residue on evaporation: maximum 25 ppm *m/V*.

Evaporate 100 mL to dryness on a water-bath and dry at 100-105 °C for 1 h. The residue weighs a maximum of 2.5 mg.

STORAGE

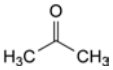
Protected from light.

IMPURITIES



A. 1,1-diethoxyethane (acetal),

B. acetaldehyde,

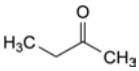


C. propan-2-one (acetone),

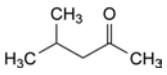
D. benzene,

E. cyclohexane,

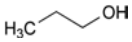
F. methanol,



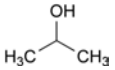
G. butan-2-one (methyl ethyl ketone),



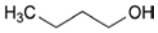
H. 4-methylpentan-2-one (methyl isobutyl ketone),



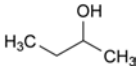
I. propan-1-ol (propanol),



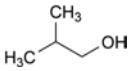
J. propan-2-ol (isopropyl alcohol),



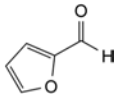
K. butan-1-ol (butanol),



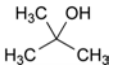
L. butan-2-ol,



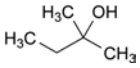
M. 2-methylpropan-1-ol (isobutanol),



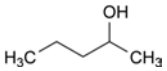
N. furane-2-carbaldehyde (furfural),



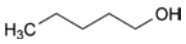
O. 2-methylpropan-2-ol (1,1-dimethylethyl alcohol),



P. 2-methylbutan-2-ol,

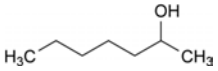


Q. pentan-2-ol,

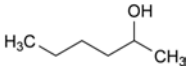


R. pentan-1-ol (pentanol),

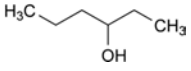
S. hexan-1-ol (hexanol),



T. heptan-2-ol,



U. hexan-2-ol,

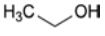


V. hexan-3-ol.

01/2008:1318

ETHANOL, ANHYDROUS

Ethanolum anhydricum



C_2H_6O M_r 46.07

[64-17-5]

DEFINITION

Content: not less than 99.5 per cent *V/V* of C_2H_6O (99.2 per cent *m/m*), at 20 °C, calculated from the relative density using the alcoholimetric tables (*5.5*).

CHARACTERS

Appearance: colourless, clear, volatile, flammable liquid, hygroscopic.

Solubility: miscible with water and with methylene chloride.

It burns with a blue, smokeless flame.

bp: about 78 °C.

IDENTIFICATION

First identification: A, B.

Second identification: A, C, D.

A. Relative density (see Tests).

B. Infrared absorption spectrophotometry (*2.2.24*).

Comparison: *Ph. Eur. reference spectrum of anhydrous ethanol.*

C. Mix 0.1 mL with 1 mL of a 10 g/L solution of *potassium permanganate R* and 0.2 mL of *dilute sulfuric acid R* in a test-tube. Cover immediately with a filter paper moistened with a freshly prepared solution containing 0.1 g of *sodium nitroprusside R* and 0.5 g of *piperazine hydrate R* in 5 mL of *water R*. After a few minutes, an intense blue colour appears on the paper and becomes paler after 10-15 min.

D. To 0.5 mL add 5 mL of *water R*, 2 mL of *dilute sodium hydroxide solution R*, then slowly add 2 mL of *0.05 M iodine*. A yellow precipitate is formed within 30 min.

TESTS

Appearance. It is clear (*2.2.1*) and colourless (*2.2.2, Method II*) when compared with *water R*. Dilute 1.0 mL to 20 mL with *water R*. After standing for 5 min, the dilution remains clear (*2.2.1*) when compared with *water R*.

Acidity or alkalinity. To 20 mL add 20 mL of *carbon dioxide-free water R* and 0.1 mL of *phenolphthalein solution R*. The solution is colourless. Add 1.0 mL of *0.01 M sodium hydroxide*. The solution is pink (30 ppm, expressed as acetic acid).

Relative density (*2.2.5*): 0.790 to 0.793.

Absorbance (*2.2.25*): maximum 0.40 at 240 nm, 0.30 between 250 nm and 260 nm, and 0.10 between 270 nm and 340 nm. The absorption curve is smooth.

Examined between 235 nm and 340 nm in a 5 cm cell using *water R* as the compensation liquid.

Volatile impurities. Gas chromatography (*2.2.28*).

Test solution (a). The substance to be examined.

Test solution (b). Add 150 µL of *4-methylpentan-2-ol R* to 500.0 mL of the substance to be examined.

Reference solution (a). Dilute 100 µL of *anhydrous methanol R* to 50.0 mL with the substance to be examined. Dilute 5.0 mL of the solution to 50.0 mL with the substance to be examined.

Reference solution (b). Dilute 50 µL of *anhydrous methanol R* and 50 µL of *acetaldehyde R* to 50.0 mL with the substance to be examined. Dilute 100 µL of the solution to 10.0 mL with the substance to be examined.

Reference solution (c). Dilute 150 µL of *acetal R* to 50.0 mL with the substance to be examined. Dilute 100 µL of the solution to 10.0 mL with the substance to be examined.

Reference solution (d). Dilute 100 µL of *benzene R* to 100.0 mL with the substance to be examined. Dilute 100 µL of the solution to 50.0 mL with the substance to be examined.

Column:

– *material*: fused silica;
– *size*: *l* = 30 m, Ø = 0.32;
– *stationary phase*: *poly[(cyanopropyl)(phenyl)][dimethyl]siloxane R* (film thickness 1.8 µm).