Lead (*2.4.10*): maximum 0.5 ppm.

Nickel (*2.4.15*): maximum 1 ppm.

Water (*2.5.12*): maximum 7.0 per cent, determined on 0.3 g. As solvent, use a mixture of 20 mL of *anhydrous methanol R* and 20 mL of *formamide R* at 50 ± 5 °C.

ASSAY

Liquid chromatography (*2.2.29*) as described in the test for related substances with the following modification.

Injection: test solution and reference solution (a).

Calculate the percentage content of isomalt (1,1-GPM and 1,6-GPS) from the declared content of 1,1-GPM and 1,6-GPS in *isomalt CRS*.

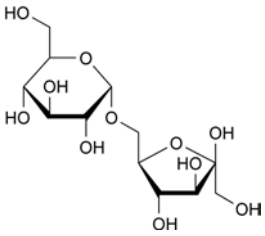
LABELLING

The label states the percentage content of 1,6-GPS and 1,1-GPM.

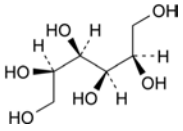
IMPURITIES

Specified impurities: *B, C.*

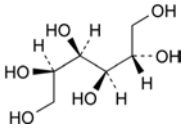
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph *Substances for pharmaceutical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



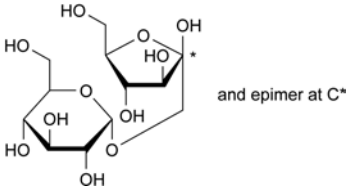
A. 6-*O*-α-D-glucopyranosyl-β-D-*arabino*-hex-2-ulofuranose (isomaltulose),



B. D-mannitol,



C. D-glucitol (D-sorbitol),

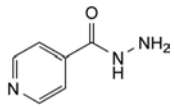


D. 1-*O*-α-D-glucopyranosyl-D-*arabino*-hex-2-ulofuranose (trehalulose).

01/2008:0146
corrected 6.0

ISONIAZID

Isoniazidum



$C_6H_7N_3O$ M_r 137.1
[54-85-3]

DEFINITION

Isoniazid contains not less than 99.0 per cent and not more than the equivalent of 101.0 per cent of pyridine-4-carbohydrazide, calculated with reference to the dried substance.

CHARACTERS

A white or almost white, crystalline powder or colourless crystals, freely soluble in water, sparingly soluble in alcohol.

IDENTIFICATION

First identification: A, B.

Second identification: A, C.

A. Melting point (*2.2.14*): 170 °C to 174 °C.

B. Examine by infrared absorption spectrophotometry (*2.2.24*), comparing with the spectrum obtained with *isoniazid CRS*.

C. Dissolve 0.1 g in 2 mL of *water R* and add 10 mL of a warm 10 g/L solution of *vanillin R*. Allow to stand and scratch the wall of the test tube with a glass rod. A yellow precipitate is formed, which, after recrystallisation from 5 mL of *alcohol (70 per cent V/V) R* and drying at 100 °C to 105 °C, melts (*2.2.14*) at 226 °C to 231 °C.

TESTS

Solution S. Dissolve 2.5 g in *carbon dioxide-free water R* and dilute to 50 mL with the same solvent.

Appearance of solution. Solution S is clear (*2.2.1*) and not more intensely coloured than reference solution BY_7 (*2.2.2, Method II*).

pH (*2.2.3*). The pH of solution S is 6.0 to 8.0.

Hydrazine and related substances. Examine by thin-layer chromatography (*2.2.27*), using *silica gel* GF_{254} *R* as the coating substance.

Test solution. Dissolve 1.0 g of the substance to be examined in a mixture of equal volumes of *acetone R* and *water R* and dilute to 10.0 mL with the same mixture of solvents.

Reference solution. Dissolve 50.0 mg of *hydrazine sulfate R* in 50 mL of *water R* and dilute to 100.0 mL with *acetone R*. To 10.0 mL of this solution add 0.2 mL of the test solution and dilute to 100.0 mL with a mixture of equal volumes of *acetone R* and *water R*.

Apply separately to the plate 5 µL of each solution and develop over a path of 15 cm using a mixture of 10 volumes of *water R*, 20 volumes of *acetone R*, 20 volumes of *methanol R* and 50 volumes of *ethyl acetate R*. Allow the plate to dry in air and examine in ultraviolet light at 254 nm. Any spot in the chromatogram obtained with the test solution, apart from the principal spot, is not more intense than the spot in the chromatogram obtained with the reference solution (0.2 per cent). Spray the plate with *dimethylaminobenzaldehyde solution R1*. Examine in daylight. An additional spot, corresponding to hydrazine, appears in the chromatogram obtained with the reference solution. Any corresponding spot in the chromatogram obtained with the test solution is not more intense than the spot corresponding to hydrazine in the chromatogram obtained with the reference solution (0.05 per cent).

Heavy metals (*2.4.8*). 2.0 g complies with limit test C for heavy metals (10 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 1.00 g by drying in an oven at 105 °C.

Sulfated ash (*2.4.14*). Not more than 0.1 per cent, determined on 1.0 g.

ASSAY

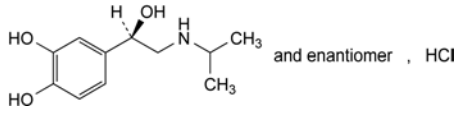
Dissolve 0.250 g in *water R* and dilute to 100.0 mL with the same solvent. To 20.0 mL of the solution add 100 mL of *water R*, 20 mL of *hydrochloric acid R*, 0.2 g of *potassium bromide R* and 0.05 mL of *methyl red solution R*. Titrate dropwise with *0.0167 M potassium bromate*, shaking continuously, until the red colour disappears.

1 mL of *0.0167 M potassium bromate* is equivalent to 3.429 mg of $C_6H_7N_3O$.

01/2011:1332

ISOPRENALINE HYDROCHLORIDE

Isoprenalini hydrochloridum



$C_{11}H_{18}ClNO_3$ M_r 247.7
[51-30-9]

DEFINITION

(1*RS*)-1-(3,4-Dihydroxyphenyl)-2-[(1-methylethyl)amino]ethanol hydrochloride.

Content: 98.0 per cent to 101.5 per cent (dried substance).

CHARACTERS

Appearance: white or almost white, crystalline powder.

Solubility: freely soluble in water, sparingly soluble in ethanol (96 per cent), practically insoluble in methylene chloride.

IDENTIFICATION

First identification: B, C, E.

Second identification: A, C, D, E.

A. Melting point (*2.2.14*): 165 °C to 170 °C, with decomposition.

B. Infrared absorption spectrophotometry (*2.2.24*).

Comparison: *isoprenaline hydrochloride CRS*.

C. Optical rotation (see Tests).

D. To 0.1 mL of solution S (see Tests) add 0.05 mL of *ferric chloride solution R1* and 0.9 mL of *water R*. A green colour is produced. Add dropwise *sodium hydrogen carbonate solution R*. The colour becomes blue then red.

E. To 0.5 mL of solution S add 1.5 mL of *water R*. The solution gives reaction (a) of chlorides (*2.3.1*).

TESTS

Prepare the solutions immediately before use.

Solution S. Dissolve 2.5 g in *carbon dioxide-free water R* and dilute to 25.0 mL with the same solvent.

Appearance of solution. Solution S is clear (*2.2.1*) and not more intensely coloured than reference solution B_7 or BY_7 (*2.2.2, Method II*).

pH (*2.2.3*): 4.3 to 5.5.

Mix 5 mL of solution S and 5 mL of *carbon dioxide-free water R*.

Optical rotation (*2.2.7*): – 0.10° to + 0.10°, determined on solution S.

Related substances. Liquid chromatography (*2.2.29*).

Test solution. Dissolve 50.0 mg of the substance to be examined in the mobile phase and dilute to 10.0 mL with the mobile phase.

Reference solution (a). Dilute 1.0 mL of the test solution to 100.0 mL with the mobile phase. Dilute 5.0 mL of this solution to 10.0 mL with the mobile phase.

Reference solution (b). Dissolve 2.5 mg of *orciprenaline sulfate CRS* in the mobile phase and dilute to 100.0 mL with the mobile phase.

Reference solution (c). To 5.0 mL of reference solution (a) add 5.0 mL of reference solution (b).

Column:

– *size*: *l* = 0.125 m, Ø = 4.0 mm;

– *stationary phase*: *octadecylsilyl silica gel for chromatography R* (5 µm).

Mobile phase: *methanol R*, 11.5 g/L solution of *phosphoric acid R* (5:95 *V/V*).

Flow rate: 1.0 mL/min.

Detection: spectrophotometer at 280 nm.

Injection: 20 µL of the test solution and reference solutions (a) and (c).

Run time: 7 times the retention time of isoprenaline.

Relative retention with reference to isoprenaline (retention time = about 3 min): orciprenaline = about 1.5; impurity A = about 1.8. If necessary, adjust the concentration of methanol in the mobile phase.

System suitability: reference solution (c):

– *resolution*: minimum 3.0 between the peaks due to isoprenaline and orciprenaline.

Limits:

– *impurity A*: not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (0.5 per cent);

– *unspecified impurities*: for each impurity, not more than 0.2 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.10 per cent);

– *total*: 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 principal peak in the chromatogram obtained with reference solution (a) (0.05 per cent).

Loss on drying (*2.2.32*): maximum 1.0 per cent, determined on 1.000 g by drying *in vacuo* at 15-25 °C for 4 h.

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

ASSAY

In order to avoid overheating in the reaction medium, mix thoroughly throughout and stop the titration immediately after the end-point has been reached.

Dissolve 0.150 g in 10 mL of *anhydrous formic acid R* and add 50 mL of *acetic anhydride R*. Titrate with *0.1 M perchloric acid*, determining the end-point potentiometrically (*2.2.20*).

1 mL of *0.1 M perchloric acid* is equivalent to 24.77 mg of $C_{11}H_{18}ClNO_3$.

STORAGE

In an airtight container, protected from light.

IMPURITIES

Specified impurities: A.