TESTS

Related substances. Liquid chromatography (*2.2.29*).

Test solution. Dissolve 0.20 g of the substance to be examined in *acetonitrile R* and dilute to 20.0 ml with the same solvent. *Prepare the solution immediately before use.*

Reference solution (a). Dissolve 5.0 mg of *triflusal impurity B CRS* in *acetonitrile R* and dilute to 10.0 ml with the same solvent.

Reference solution (b). Dilute 1.0 ml of reference solution (a) to 25.0 ml with *acetonitrile R.*

Reference solution (c). Dissolve 2.5 mg of the substance to be examined in *acetonitrile R,* add 5 ml of reference solution (a) and dilute to 10 ml with *acetonitrile R. Prepare the solution immediately before use.*

Column:
- *size*: *l* = 0.15 m, Ø = 4.0 mm,
- *stationary phase*: *octadecylsilyl silica gel for chromatography R* (4-5 µm).

Mobile phase:
- *mobile phase A*: *acetonitrile R,*
- *mobile phase B*: 0.5 per cent *V/V* solution of *phosphoric acid R,*

Time (min)	Mobile phase A (per cent *V/V*)	Mobile phase B (per cent *V/V*)
0 - 20	20 → 70	80 → 30
20 - 25	70	30
25 - 26	70 → 20	30 → 80
26 - 30	20	80

Flow rate: 1.2 ml/min.

Detection: spectrophotometer at 237 nm.

Injection: 10 µl of the test solution and reference solutions (b) and (c).

Relative retention with reference to triflusal (retention time = about 13 min): impurity A = about 0.3; impurity B = about 1.2; impurity C = about 1.3; impurity D = about 1.6.

System suitability: reference solution (c):
- *resolution*: minimum 3.0 between the peaks due to triflusal and impurity B.

Limits:
- *impurity B*: not more than 1.5 times the area of the corresponding peak in the chromatogram obtained with reference solution (b) (0.3 per cent),
- *total of impurities other than B*: not more than 0.5 times the area of the peak due to impurity B in the chromatogram obtained with reference solution (b) (0.1 per cent),
- *disregard limit*: 0.1 times the area of the peak due to impurity B in the chromatogram obtained with reference solution (b) (0.02 per cent).

Heavy metals (*2.4.8*): maximum 10 ppm.

Dissolve 2.0 g in 12 ml of *alcohol R* and dilute to 20 ml with *water R.* 12 ml complies with limit test B. Prepare the standard using lead standard solution (1 ppm Pb) obtained by diluting *lead standard solution (100 ppm Pb) R* with a mixture of 2 volumes of *water R* and 3 volumes of *alcohol R.*

Loss on drying (*2.2.32*): maximum 0.5 per cent, determined on 1.000 g by drying in a desiccator *in vacuo* over *diphosphorus pentoxide R.*

Sulphated ash (*2.4.14*): maximum 0.1 per cent, determined on 1.0 g in a platinum crucible.

ASSAY

Dissolve 0.200 g in 50 ml of *ethanol R*. Titrate with *0.1 M sodium hydroxide,* determining the end-point potentiometrically (*2.2.20*).

1 ml of *0.1 M sodium hydroxide* is equivalent to 24.82 mg of $C_{10}H_7F_3O_4$.

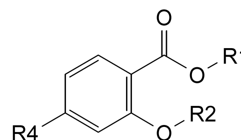
STORAGE

In an airtight container, at a temperature not exceeding 25 °C.

IMPURITIES

Specified impurities: *B.*

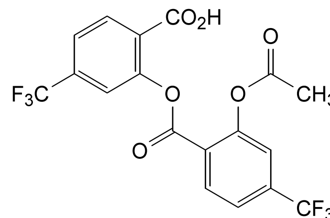
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph *Substances for pharmaceutical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



A. R1 = H, R2 = CO-CH_3, R4 = CO_2H: 2-(acetyloxy)benzene-1,4-dicarboxylic acid (2-acetoxyterephthalic acid),

B. R1 = R2 = H, R4 = CF_3: 2-hydroxy-4-(trifluoromethyl)benzoic acid (4-(trifluoromethyl)salicylic acid),

C. R1 = R2 = CO-CH_3, R4 = CF_3: acetic 2-(acetyloxy)-4-(trifluoromethyl)benzoic anhydride,



D. 2-[[2-(acetyloxy)-4-(trifluoromethyl)benzoyl]oxy]-4-(trifluoromethyl)benzoic acid.

01/2008:0868

TRIGLYCERIDES, MEDIUM-CHAIN

Triglycerida saturata media

DEFINITION

Mixture of triglycerides of saturated fatty acids, mainly of caprylic (octanoic) acid and of capric (decanoic) acid. Medium-chain triglycerides are obtained from the oil extracted from the hard, dried fraction of the endosperm of *Cocos nucifera* L. or from the dried endosperm of *Elaeis guineensis* Jacq.

Content: minimum 95.0 per cent of saturated fatty acids with 8 and 10 carbon atoms.

CHARACTERS

Appearance: colourless or slightly yellowish, oily liquid.

Solubility: practically insoluble in water, miscible with alcohol, with methylene chloride, with light petroleum and with fatty oils.

IDENTIFICATION

First identification: B, C.

Second identification: A, D.

A. Heat 3.0 g under a reflux condenser for 30 min with 50 ml of a mixture of equal volumes of *alcohol R* and *2 M alcoholic potassium hydroxide R*. Reserve 10 ml of the mixture for identification test D. To 40 ml of the mixture add 30 ml of *water R*, evaporate the alcohol and acidify the hot solution with 25 ml of *dilute hydrochloric acid R*. After cooling, shake with 50 ml of *peroxide-free ether R*. Wash the ether layer with 3 quantities, each of 10 ml, of *sodium chloride solution R*, dry over *anhydrous sodium sulphate R* and filter. Evaporate the ether and determine the acid value (*2.5.1*) of the residue, using 0.300 g. The acid value is 350 to 390.

B. It complies with the test for saponification value (see Tests).

C. It complies with the test for composition of fatty acids (see Tests).

D. Evaporate 10 ml of the alcoholic mixture obtained in identification test A to dryness on a water-bath. Transfer the residue into a test-tube, add 0.3 ml of *sulphuric acid R* and close the test-tube with a stopper through which a U-shaped glass tube is inserted. One end of the U-tube is dipped into 3 ml of a 10 g/l solution of *tryptophan R* in a mixture of equal volumes of *sulphuric acid R* and *water R*. Heat the test-tube in a silicone-oil bath at 180 °C for 10 min and collect the liberated fumes in the tryptophan reagent. Heat the tryptophan reagent on a water-bath for 1 min. A violet colour develops.

TESTS

Appearance. The substance to be examined is clear (*2.2.1*) and not more intensely coloured than reference solution Y_3 (*2.2.2, Method I*).

Alkaline impurities. Dissolve 2.00 g in a mixture of 1.5 ml of *alcohol R* and 3.0 ml of *ether R*. Add 0.05 ml of *bromophenol blue solution R*. Not more than 0.15 ml of *0.01 M hydrochloric acid* is required to change the colour of the indicator to yellow.

Relative density (*2.2.5*): 0.93 to 0.96.

Refractive index (*2.2.6*): 1.440 to 1.452.

Viscosity (*2.2.9*): 25 mPa·s to 33 mPa·s.

Acid value (*2.5.1*): maximum 0.2.

Hydroxyl value (*2.5.3, Method A*): maximum 10.

Iodine value (*2.5.4*): maximum 1.0.

Peroxide value (*2.5.5, Method A*): maximum 1.0.

Saponification value (*2.5.6*): 310 to 360.

Unsaponifiable matter (*2.5.7*): maximum 0.5 per cent, determined on 5.0 g.

Composition of fatty acids. Gas chromatography (*2.4.22, Method C*).

Column:

– *material*: fused silica,
– *size*: *l* = 30 m, Ø = 0.32 mm,
– *stationary phase*: *macrogol 20 000 R* (film thickness 0.5 µm),

Carrier gas: *helium for chromatography R*.

Flow rate: 1.3 ml/min.

Temperature:

	Time (min)	Temperature (°C)
Column	0 - 1	70
	1 - 35	70 → 240
	35 - 50	240
Injection port		250
Detector		250

Detection: flame ionisation.

Split ratio: 1:100.

Composition of the fatty acid fraction of the substance:

– *caproic acid*: maximum 2.0 per cent,
– *caprylic acid*: 50.0 per cent to 80.0 per cent,
– *capric acid*: 20.0 per cent to 50.0 per cent,
– *lauric acid*: maximum 3.0 per cent,
– *myristic acid*: maximum 1.0 per cent.

Chromium: maximum 0.05 ppm, if intended for use in parenteral nutrition.

Atomic absorption spectrometry (*2.2.23, Method II*).

Test solution. Dissolve 2.0 g of the substance to be examined in *methyl isobutyl ketone R3* and dilute to 10.0 ml with the same solvent.

Solution A. Dilute 0.100 ml of *chromium liposoluble standard solution (1000 ppm Cr) R* to 10.0 ml with *methyl isobutyl ketone R3*.

Stock solution. Dilute 0.100 ml of solution A to 10.0 ml with *methyl isobutyl ketone R3*.

Reference solutions. Prepare 3 reference solutions by dissolving for each 2.0 g of the substance to be examined in the minimum volume of *methyl isobutyl ketone R3*, adding 0.5 ml, 1.0 ml and 2.0 ml, respectively, of stock solution and diluting to 10.0 ml with *methyl isobutyl ketone R3*.

Source: chromium hollow-cathode lamp.

Wavelength: 357.8 nm.

Atomic generator: graphite furnace.

Carrier gas: *argon R*.

Copper: maximum 0.1 ppm, if intended for use in parenteral nutrition.

Atomic absorption spectrometry (*2.2.23, Method II*).

Test solution. Dissolve 2.0 g of the substance to be examined in *methyl isobutyl ketone R3* and dilute to 10.0 ml with the same solvent.

Solution A. Dilute 0.100 ml of *copper liposoluble standard solution (1000 ppm Cu) R* to 10.0 ml with *methyl isobutyl ketone R3*.

Stock solution. Dilute 0.100 ml of solution A to 10.0 ml with *methyl isobutyl ketone R3*.

Reference solutions. Prepare 3 reference solutions by dissolving for each 2.0 g of the substance to be examined in the minimum volume of *methyl isobutyl ketone R3*, adding 1.0 ml, 2.0 ml and 4.0 ml, respectively, of stock solution and diluting to 10.0 ml with *methyl isobutyl ketone R3*.

Source: copper hollow-cathode lamp.

Wavelength: 324.7 nm.

Atomic generator: graphite furnace.

Carrier gas: *argon R*.

Lead: maximum 0.1 ppm, if intended for use in parenteral nutrition.

Atomic absorption spectrometry (*2.2.23, Method II*).

Test solution. Dissolve 2.0 g of the substance to be examined in *methyl isobutyl ketone R3* and dilute to 10.0 ml with the same solvent.

Solution A. Dilute 0.100 ml of *lead liposoluble standard solution (1000 ppm Pb) R* to 10.0 ml with *methyl isobutyl ketone R3*.

Stock solution. Dilute 0.100 ml of solution A to 10.0 ml with *methyl isobutyl ketone R3*.

Reference solutions. Prepare 3 reference solutions by dissolving for each 2.0 g of the substance to be examined in the minimum volume of *methyl isobutyl ketone R3*, adding 1.0 ml, 2.0 ml and 4.0 ml, respectively, of stock solution and diluting to 10.0 ml with *methyl isobutyl ketone R3*.

Source: lead hollow-cathode lamp.

Wavelength: 283.3 nm.

Atomic generator: graphite furnace coated inside with palladium carbide; calcination is carried out in the presence of oxygen at a temperature below 800 °C.

Carrier gas: *argon R*.

Nickel: maximum 0.2 ppm, if intended for use in parenteral nutrition.

Atomic absorption spectrometry (*2.2.23, Method II*).

Test solution. Dissolve 2.0 g of the substance to be examined in *methyl isobutyl ketone R3* and dilute to 10.0 ml with the same solvent.

Solution A. Dilute 0.100 ml of *nickel liposoluble standard solution (1000 ppm Ni) R* to 10.0 ml with *methyl isobutyl ketone R3*.

Stock solution. Dilute 0.100 ml of solution A to 10.0 ml with *methyl isobutyl ketone R3*.

Reference solutions. Prepare 3 reference solutions by dissolving for each 2.0 g of the substance to be examined in the minimum volume of *methyl isobutyl ketone R3*, adding 1.0 ml, 2.0 ml and 4.0 ml, respectively, of stock solution and diluting to 10.0 ml with *methyl isobutyl ketone R3*.

Source: nickel hollow-cathode lamp.

Wavelength: 232 nm.

Atomic generator: graphite furnace.

Carrier gas: *argon R*.

Tin: maximum 0.1 ppm, if intended for use in parenteral nutrition.

Atomic absorption spectrometry (*2.2.23, Method II*).

Test solution. Dissolve 2.0 g of the substance to be examined in *methyl isobutyl ketone R3* and dilute to 10.0 ml with the same solvent.

Solution A. Dilute 0.100 ml of *tin liposoluble standard solution (1000 ppm Sn) R* to 10.0 ml with *methyl isobutyl ketone R3*.

Stock solution. Dilute 0.100 ml of solution A to 10.0 ml with *methyl isobutyl ketone R3*.

Reference solutions. Prepare 3 reference solutions by dissolving for each 2.0 g of the substance to be examined in the minimum volume of *methyl isobutyl ketone R3*, adding 1.0 ml, 2.0 ml and 4.0 ml, respectively, of stock solution and diluting to 10.0 ml with *methyl isobutyl ketone R3*.

Source: tin hollow-cathode lamp.

Wavelength: 286.3 nm.

Atomic generator: graphite furnace coated inside with palladium carbide.

Carrier gas: *argon R*.

Heavy metals (*2.4.8*): maximum 10 ppm, if intended for use other than parenteral nutrition.

2.0 g complies with limit test D. Prepare the standard using 2 ml of *lead standard solution (10 ppm Pb) R*.

Water (*2.5.12*): maximum 0.2 per cent, determined on 10.00 g.

Total ash (*2.4.16*): maximum 0.1 per cent, determined on 2.0 g.

STORAGE

In a well-filled container, protected from light.

LABELLING

The label states, where applicable, that the substance is intended for use in parenteral nutrition.

01/2008:2032

TRIGLYCEROL DIISOSTEARATE

Triglyceroli diisostearas

DEFINITION

Mixture of polyglycerol diesters of mainly isostearic acid, obtained by esterification of polyglycerol and isostearic acid. The polyglycerol consists mainly of triglycerol.

CHARACTERS

Appearance: clear, yellowish, viscous liquid.

Solubility: practically insoluble in water, miscible with ethanol (96 per cent) and with fatty oils.

IDENTIFICATION

A. Infrared absorption spectrophotometry (*2.2.24*).

Preparation: film between 2 plates of *sodium chloride R*.

Comparison: *triglycerol diisostearate CRS*.

B. Composition of fatty acids (see Tests).

TESTS

Appearance of solution. The solution is not more intensely coloured than reference solution BY_3 (*2.2.2, Method I*).

Mix 10 ml with 10 ml of *ethanol (96 per cent) R*.

Acid value (*2.5.1*): maximum 3.0, determined on 1.0 g.

Hydroxyl value (*2.5.3, Method A*): 180 to 230, determined on 0.25 g.

Iodine value (*2.5.4, Method B*): maximum 3.0.

Peroxide value (*2.5.5, Method B*): maximum 6.0.

Saponification value (*2.5.6*): 128 to 160.

Composition of fatty acids (*2.4.22, Method B*). Use the mixture of calibrating substances in Table 2.4.22.-1.

Composition of the fatty-acid fraction of the substance:

– *sum of the contents of the fatty acids eluting between palmitic acid and stearic acid*: minimum 60.0 per cent;
– *sum of the contents of myristic acid, palmitic acid and stearic acid*: maximum 11.0 per cent.

Water (*2.5.12*): maximum 0.5 per cent, determined on 2.00 g.