allow to stand until separation of the layers is obtained. Transfer the clear upper layer to a suitable tube, add 5 g of *anhydrous sodium sulphate R*, close the tube and allow to stand for 30 min. Filter and evaporate the filtrate to dryness on a water-bath. Dissolve 50 mg of the residue in 25 ml of *ether R*.

Reference solution. Dissolve 50 mg of *ricinoleic acid R* in *methylene chloride R* and dilute to 25 ml with the same solvent.

Plate: *TLC octadecylsilyl silica gel plate R*.

Mobile phase: *methylene chloride R, glacial acetic acid R, acetone R* (10:40:50 *V/V/V*).

Application: 2 µl.

Development: over a path of 8 cm.

Drying: in a current of cold air.

Detection: spray with an 80 g/l solution of *phosphomolybdic acid R* in *2-propanol R* and heat at 120 °C for 1-2 min.

Results: the principal spot in the chromatogram obtained with the test solution is similar in position and colour to the principal spot in the chromatogram obtained with the reference solution.

D. Place about 2 g of the substance to be examined in a test-tube and add 0.2 ml of *sulphuric acid R*. Close the tube using a stopper fitted with a glass tube bent twice at right angles. Heat the tube until white fumes appear. Collect the fumes in 1 ml of *mercuric chloride solution R*. A white precipitate is formed and the fumes turn a filter paper impregnated with *alkaline potassium tetraiodomercurate solution R* black.

TESTS

Solution S. Dissolve 5.0 g in *carbon dioxide-free water R* and dilute to 50 ml with the same solvent.

Appearance of solution. Solution S is not more opalescent than reference suspension III (*2.2.1*) and not more intensely coloured than reference solution BY_5 (*2.2.2, Method II*). If intended for use in the manufacture of parenteral dosage forms, solution S is not more intensely coloured than reference solution BY_6 (*2.2.2, Method II*).

Alkalinity. Dissolve 2.0 g in a hot mixture of 10 ml of *water R* and 10 ml of *ethanol (96 per cent) R*. Add 0.1 ml of *bromothymol blue solution R1*. Not more than 0.5 ml of *0.1 M hydrochloric acid* is required to change the colour of the indicator to yellow.

Acid value (*2.5.1*): maximum 2.0, determined on 5.0 g.

Hydroxyl value (*2.5.3, Method A*). See Table 1082.-1.

Iodine value (*2.5.4*): 25 to 35.

Saponification value (*2.5.6*). See Table 1082.-1.

Table 1082.-1

Ethylene oxide units per molecule (nominal value)	Hydroxyl value	Saponification value
30 - 35	65 - 82	60 - 75
50	48 - 68	38 - 52

Residual ethylene oxide and dioxan (*2.4.25*): maximum 1 ppm of residual ethylene oxide and 10 ppm of residual dioxan.

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

12 ml of solution S, filtered if necessary, complies with test A. Prepare the reference solution using *lead standard solution (1 ppm Pb) R*.

Water (*2.5.12*): maximum 3.0 per cent, determined on 2.000 g.

Total ash (*2.4.16*): maximum 0.3 per cent, determined on 2.0 g.

STORAGE

Protected from light.

LABELLING

The label states:

– the amount of ethylene oxide reacted with castor oil (nominal value),

– where applicable, that the substance is suitable for use in the manufacture of parenteral dosage forms.

01/2008:2052

MACROGOL 15 HYDROXYSTEARATE

Macrogoli 15 hydroxystearas

DEFINITION

Mixture of mainly monoesters and diesters of 12-hydroxystearic (12-hydroxyoctadecanoic) acid and macrogols obtained by ethoxylation of 12-hydroxystearic acid. The number of moles of ethylene oxide reacted per mole of 12-hydroxystearic acid is 15 (nominal value). It contains free macrogols.

CHARACTERS

Appearance: yellowish, waxy mass.

Solubility: very soluble in water, soluble in ethanol (96 per cent), insoluble in liquid paraffin.

It solidifies at about 25 °C.

IDENTIFICATION

A. Thin-layer chromatography (*2.2.27*).

Test solution. To 1.0 g add 100 ml of a 100 g/l solution of *potassium hydroxide R* and boil under a reflux condenser for 30 min. Acidify the warm solution with 20 ml of *hydrochloric acid R* and cool to room temperature. Shake the mixture with 50 ml of *ether R* and allow to stand until a separation of the layers is visible. Separate the clear upper layer, add 5 g of *anhydrous sodium sulphate R*, wait for 30 min, filter and evaporate to dryness on a water-bath. Dissolve 50 mg of the residue in 25 ml of *ether R*.

Reference solution. Dissolve 50 mg of *12-hydroxystearic acid R* in 25 ml of *methylene chloride R*.

Plate: *TLC octadecylsilyl silica gel plate R*.

Mobile phase: *methylene chloride R, glacial acetic acid R, acetone R* (10:40:50 *V/V/V*).

Application: 2 µl.

Development: over 2/3 of the plate.

Drying: in a current of cold air.

Detection: spray with a 80 g/l solution of *phosphomolybdic acid R* in *2-propanol R* and heat at 120 °C for 1-2 min.

Results: the principal spot in the chromatogram obtained with the test solution is similar in position and colour to the principal spot in the chromatogram obtained with the reference solution.

B. Dissolve 15.0 g in 50 ml of *water R*. The viscosity (*2.2.9*) has a maximum of 20 mPa·s.

C. Free macrogols (see Tests).

TESTS

Appearance of solution. The solution is not more opalescent than reference suspension III (*2.2.1*) and not more intensely coloured than reference solution B_6 or BY_6 (*2.2.2, Method II*).

Dissolve 2.0 g in *water R* and dilute to 20 ml with the same solvent.

Acid value (*2.5.1*): maximum 1.0, determined on 2.0 g.

Hydroxyl value (*2.5.3, Method A*): 90 to 110.

Iodine value (*2.5.4, Method A*): maximum 2.0.

Peroxide value (*2.5.5, Method A*): maximum 5.0.

Saponification value (*2.5.6*): 53 to 63.

Free macrogols. Size-exclusion chromatography (*2.2.30*).

Test solution. Dissolve 1.20 g of the substance to be examined in the mobile phase and dilute to 250.0 ml with the mobile phase.

Reference solution (a). Dissolve about 0.4 g of *macrogol 1000 R* in the mobile phase and dilute to 250.0 ml with the mobile phase.

Reference solution (b). Dilute 50.0 ml of reference solution (a) to 100.0 ml with the mobile phase.

Precolumns (2):

- *size*: *l* = 0.125 m, Ø = 4 mm;
- *stationary phase*: spherical *octadecylsilyl silica gel for chromatography R* (5 µm) with a pore size of 10 nm.

Column:

- *size*: *l* = 0.30 m, Ø = 7.8 mm;
- *stationary phase*: *hydroxylated polymethacrylate gel R* (6 µm) with a pore size of 12 nm.

Connect both precolumns to the column using a 3-way valve and switch the mobile phase flow according to the following programme:

- 0-114 s: precolumn 1 and column;
- 115 s to the end: precolumn 2 and column;
- 115 s to 7 min: flow back of precolumn 1.

Mobile phase: *water R, methanol R* (2:8 *V/V*).

Flow rate: 1.1 ml/min.

Detection: refractometer.

Injection: 50 µl.

Calculate the percentage content of free macrogols using the following expression:

$$\frac{A_1 \times m_2 \times 200}{m_1 \times (A_2 + 2A_3)}$$

m_1 = mass of the substance to be examined in the test solution, in grams;

m_2 = mass of *macrogol 1000 R* in reference solution (a), in grams;

A_1 = area of the peak due to free macrogols in the substance to be examined in the chromatogram obtained with the test solution;

A_2 = area of the peak due to macrogol 1000 in the chromatogram obtained with reference solution (a);

A_3 = area of the peak due to macrogol 1000 in the chromatogram obtained with reference solution (b).

Limit:

- *free macrogols*: 27.0 per cent to 39.0 per cent.

Ethylene oxide and dioxan (*2.4.25*): maximum 1 ppm of ethylene oxide and maximum 50 ppm of dioxan.

Nickel (*2.4.31*): maximum 1 ppm.

Water (*2.5.12*): maximum 1.0 per cent, determined on 2.00 g.

Total ash (*2.4.16*): maximum 0.3 per cent, determined on 1.0 g.

STORAGE

In an airtight container.

01/2008:1124
corrected 6.0

MACROGOL LAURYL ETHER

Macrogoli aether laurilicus

DEFINITION

Mixture of ethers of mixed macrogols with fatty alcohols, mainly $C_{12}H_{26}O$. It contains a variable amount of free $C_{12}H_{26}O$ and it may contain free macrogols. The number of moles of ethylene oxide reacted per mole of $C_{12}H_{26}O$ is 3 to 23 (nominal value).

CHARACTERS

- Macrogol lauryl ether with 3 to 5 units of ethylene oxide per molecule.

  Appearance: colourless liquid.

  Solubility: practically insoluble in water, soluble or dispersible in alcohol, practically insoluble in light petroleum.

- Macrogol lauryl ether with 9 to 23 units of ethylene oxide per molecule.

  Appearance: white or almost white, waxy mass.

  Solubility: soluble or dispersible in water, soluble in alcohol, practically insoluble in light petroleum.

IDENTIFICATION

A. It complies with the test for hydroxyl value (see Tests).

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

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

D. Dissolve or disperse 0.1 g in 5 ml of *alcohol R*, add 10 ml of *dilute hydrochloric acid R*, 10 ml of *barium chloride solution R1* and 10 ml of a 100 g/l solution of *phosphomolybdic acid R*. A precipitate is formed.

TESTS

Appearance of solution. The solution is not more intensely coloured than reference solution BY_5 (*2.2.2, Method II*).

Dissolve 5.0 g in *alcohol R* and dilute to 50 ml with the same solvent.

Alkalinity. Dissolve 2.0 g in a hot mixture of 10 ml of *water R* and 10 ml of *alcohol R*. Add 0.1 ml of *bromothymol blue solution R1*. Not more than 0.5 ml of *0.1 M hydrochloric acid* is required to change the colour of the indicator to yellow.

Acid value (*2.5.1*): maximum 1.0, determined on 5.0 g.