*Limit*:

– *sum of the peaks with retention times less than that of the principal peak*: maximum 6.0 per cent.

**Charged variants**. Capillary electrophoresis (*2.2.47*).

*Test solution (a).* Prepare a solution of the substance to be examined containing 1 mg/ml of somatropin.

*Test solution (b).* Mix equal volumes of test solution (a) and the reference solution.

*Reference solution.* Dissolve the contents of a vial of *somatropin CRS* in *water R* and dilute with the same solvent to obtain a concentration of 1 mg/ml.

*Capillary*:

– *material*: uncoated fused silica;

– *size*: effective length = at least 70 cm, Ø = 50 µm.

*Temperature*: 30 °C.

*CZE buffer*: 13.2 g/l solution of *ammonium phosphate R* adjusted to pH 6.0 with *phosphoric acid R* and filtered.

*Detection*: spectrophotometer at 200 nm.

*Set the autosampler to store the samples at 4 °C during analysis.*

*Preconditioning of the capillary*: rinse with *1 M sodium hydroxide* for 20 min, with *water R* for 10 min and with the CZE buffer for 20 min.

*Between-run rinsing*: rinse with *0.1 M sodium hydroxide* for 2 min and with the CZE buffer for 6 min.

*Note: rinsing times may be adapted according to the length of the capillary and the equipment used.*

*Injection*: test solution (a) and the reference solution; under pressure or vacuum, using the following sequence: sample injection for at least 3 s then CZE buffer injection for 1 s.

The injection time and pressure may be adapted in order to meet the system suitability criteria.

*Migration*: apply a field strength of 217 V/cm (20 kV for capillaries of 92 cm total length) for 80 min, using CZE buffer as the electrolyte in both buffer reservoirs.

*Relative migration* with reference to somatropin: deamidated forms = 1.02 to 1.11.

*System suitability*: reference solution:

– the electropherogram obtained is similar to the electropherogram of somatropin supplied with *somatropin CRS*; 2 peaks ($I_1$, $I_2$) eluting prior to the principal peak and at least 2 peaks ($I_3$, $I_4$) eluting after the principal peak are clearly visible.

*Note: peak $I_2$ corresponds to the cleaved form and peak $I_4$ corresponds to the deamidated forms, eluting as a doublet.*

*Limits*:

– *deamidated forms*: maximum 6.5 per cent;

– *any other impurity*: for each impurity, maximum 2.0 per cent;

– *total*: maximum 11.5 per cent.

**Water** (*2.5.32*): maximum 3.0 per cent, unless otherwise justified and authorised.

**Bacterial endotoxins** (*2.6.14*): less than 5 IU/mg.

ASSAY

Size-exclusion chromatography (*2.2.30*) as described in the test for dimer and related substances of higher molecular mass.

Calculate the content of somatropin ($C_{990}H_{1528}N_{262}O_{300}S_7$) from the declared content of $C_{990}H_{1528}N_{262}O_{300}S_7$ in *somatropin CRS*.

STORAGE

In a sterile, airtight, tamper-proof container, at a temperature of 2 °C to 8 °C.

LABELLING

The label states:

– the content of somatropin in the container, in milligrams;

– the composition and volume of the liquid to be added for reconstitution;

– the time within which the reconstituted solution shall be used and the storage conditions during this period;

– the name and quantity of any added substance;

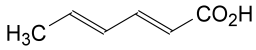
– the storage temperature;

– that the preparation shall not be shaken during reconstitution.

**01/2008:0592**

# SORBIC ACID

## Acidum sorbicum




$C_6H_8O_2$ $M_r$ 112.1
[110-44-1]

DEFINITION

(*E,E*)-Hexa-2,4-dienoic acid.

*Content*: 99.0 per cent to 101.0 per cent (anhydrous substance).

CHARACTERS

*Appearance*: white or almost white, crystalline powder.

*Solubility*: slightly soluble in water, freely soluble in ethanol (96 per cent).

IDENTIFICATION

*First identification: A, C.*

*Second identification: A, B, D.*

A. Melting point (*2.2.14*): 132 °C to 136 °C.

B. Ultraviolet and visible absorption spectrophotometry (*2.2.25*).

*Test solution.* Dissolve 50.0 mg in *water R* and dilute to 250.0 ml with the same solvent. Dilute 2.0 ml of this solution to 200.0 ml with *0.1 M hydrochloric acid.*

*Spectral range*: 230-350 nm.

*Absorption maximum*: at 264 nm.

*Specific absorbance at the absorption maximum*: 2150 to 2550.

C. Infrared absorption spectrophotometry (*2.2.24*).

*Comparison*: *sorbic acid CRS.*

D. Dissolve 0.2 g in 2 ml of *ethanol (96 per cent) R* and add 0.2 ml of *bromine water R*. The solution is decolorised.

TESTS

**Solution S**. Dissolve 1.25 g in *ethanol (96 per cent) R* and dilute to 25 ml with the same solvent.

**Appearance of solution**. Solution S is clear (*2.2.1*) and colourless (*2.2.2, Method II*).

**Aldehydes**: maximum 0.15 per cent, calculated as $C_2H_4O$.

Dissolve 1.0 g in a mixture of 30 ml of *water R* and 50 ml of *2-propanol R*, adjust to pH 4 with *0.1 M hydrochloric acid* or *0.1 M sodium hydroxide* and dilute to 100 ml with *water R*. To 10 ml of this solution add 1 ml of *decolorised fuchsin solution R* and allow to stand for 30 min. Any colour in the solution is not more intense than that in a standard prepared at the same time by adding 1 ml of *decolorised fuchsin solution R* to a mixture of 1.5 ml of *acetaldehyde standard solution (100 ppm $C_2H_4O$) R*, 4 ml of *2-propanol R* and 4.5 ml of *water R*.

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

12 ml of solution S complies with test B. Prepare the reference solution using 5 ml of *lead standard solution (1 ppm Pb) R* and 5 ml of *ethanol (96 per cent) R*.

**Water** (*2.5.12*): maximum 1.0 per cent, determined on 2.000 g.

**Sulphated ash** (*2.4.14*): maximum 0.2 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.1000 g in 20 ml of *ethanol (96 per cent) R*. Using 0.2 ml of *phenolphthalein solution R* as indicator, titrate with *0.1 M sodium hydroxide* until a pink colour is obtained.

1 ml of *0.1 M sodium hydroxide* is equivalent to 11.21 mg of $C_6H_8O_2$.

STORAGE

Protected from light.

**01/2008:1040**

# SORBITAN LAURATE

## Sorbitani lauras

DEFINITION

Mixture usually obtained by partial esterification of sorbitol and its mono- and di-anhydrides with lauric (dodecanoic) acid.

CHARACTERS

*Appearance*: brownish-yellow, viscous liquid.

*Solubility*: practically insoluble, but dispersible in water, miscible with alcohol.

*Relative density*: about 0.98.

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 composition of fatty acids (see Tests).

TESTS

**Acid value** (*2.5.1*): maximum 7.0, determined on 5.0 g.

**Hydroxyl value** (*2.5.3, Method A*): 330 to 358.

**Iodine value** (*2.5.4*): maximum 10.

**Peroxide value** (*2.5.5*): maximum 5.0.

**Saponification value** (*2.5.6*): 158 to 170.

Carry out the saponification for 1 h.

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

Prepare reference solution (a) as indicated in tables 2.4.22.-1 and 2.4.22.-2.

*Composition of the fatty acid fraction of the substance*:

– *caproic acid*: maximum 1.0 per cent,
– *caprylic acid*: maximum 10.0 per cent,
– *capric acid*: maximum 10.0 per cent,
– *lauric acid*: 40.0 per cent to 60.0 per cent,
– *myristic acid*: 14.0 per cent to 25.0 per cent,
– *palmitic acid*: 7.0 per cent to 15.0 per cent,
– *stearic acid*: maximum 7.0 per cent,
– *oleic acid*: maximum 11.0 per cent,
– *linoleic acid*: maximum 3.0 per cent.

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

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 1.5 per cent, determined on 1.00 g.

**Total ash** (*2.4.16*): maximum 0.5 per cent.

STORAGE

Protected from light.

**01/2008:1041**

# SORBITAN OLEATE

## Sorbitani oleas

DEFINITION

Mixture usually obtained by esterification of 1 mole of sorbitol and its mono-and di-anhydrides per mole of oleic (*cis*-9-octadecenoic) acid. A suitable antioxidant may be added.

CHARACTERS

*Appearance*: brownish-yellow, viscous liquid.

*Solubility*: practically insoluble but dispersible in water, soluble in fatty oils producing a hazy solution, miscible with alcohol.

*Relative density*: about 0.99.

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 composition of fatty acids (see Tests).

*Margaric acid*: maximum 0.2 per cent for oleic acid of vegetable origin and maximum 4.0 per cent for oleic acid of animal origin.

TESTS

**Acid value** (*2.5.1*): maximum 8.0, determined on 5.0 g.

**Hydroxyl value** (*2.5.3, Method A*): 190 to 210.

**Iodine value** (*2.5.4*): 62 to 76.

**Peroxide value** (*2.5.5*): maximum 10.0.

**Saponification value** (*2.5.6*): 145 to 160.

Carry out the saponification for 1 h.