Peroxide value (*2.5.5, Method A*): maximum 10.0.

Saponification value (*2.5.6*): 130 to 140, determined on 2.0 g.

Oleic acid (*2.4.22, Method A*): minimum 60.0 per cent in the fatty acid fraction of the substance.

Water (*2.5.12*): maximum 1.0 per cent, determined on 1.00 g.

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

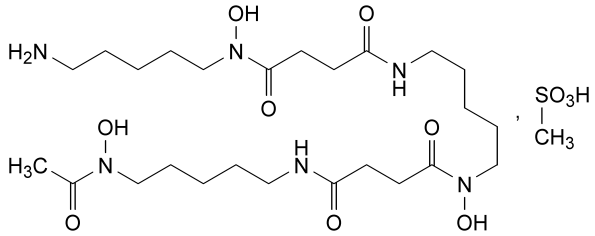
STORAGE

Protected from light.

01/2008:0896

DEFEROXAMINE MESILATE

Deferoxamini mesilas



$C_{26}H_{52}N_6O_{11}S$ M_r 657

[138-14-7]

DEFINITION

N'-[5-[[4-[[5-(Acetylhydroxyamino)pentyl]amino]-4-oxobutanoyl]hydroxyamino]pentyl]-*N*-(5-aminopentyl)-*N*-hydroxybutanediamide methanesulfonate.

Content: 98.0 per cent to 102.0 per cent (anhydrous substance).

PRODUCTION

The production method must be evaluated to determine the potential for formation of alkyl mesilates, which is particularly likely to occur if the reaction medium contains lower alcohols. Where necessary, the production method is validated to demonstrate that alkyl mesilates are not detectable in the final product.

CHARACTERS

Appearance: white or almost white powder.

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

IDENTIFICATION

First identification: A, D.

Second identification: B, C, D.

A. Infrared absorption spectrophotometry (*2.2.24*).

Preparation: discs.

Comparison: *deferoxamine mesilate CRS.*

If the spectra obtained show differences, dissolve the substance to be examined and the reference substance separately in *ethanol (96 per cent) R*, evaporate to dryness and record new spectra using the residues.

B. Dissolve about 5 mg in 5 ml of *water R*. Add 2 ml of a 5 g/l solution of *trisodium phosphate dodecahydrate R* and 0.5 ml of a 25 g/l solution of *sodium naphthoquinonesulphonate R*. A brownish-black colour develops.

C. Solution A obtained in the Assay is brownish-red. To 10 ml of solution A add 3 ml of *ether R* and shake. The organic layer is colourless. To 10 ml of solution A add 3 ml of *benzyl alcohol R* and shake. The organic layer is brownish-red.

D. Dissolve 0.1 g in 5 ml of *dilute hydrochloric acid R*. Add 1 ml of *barium chloride solution R2*. The solution is clear. In a porcelain crucible, mix 0.1 g with 1 g of *anhydrous sodium carbonate R*, heat and ignite over a naked flame. Allow to cool. Dissolve the residue in 10 ml of *water R*, heating if necessary, and filter. The filtrate gives reaction (a) of sulphates (*2.3.1*).

TESTS

Solution S. Dissolve 2.5 g in *carbon dioxide-free water R* prepared from *distilled water R* and dilute to 25 ml with the same solvent.

Appearance of solution. Solution S is clear (*2.2.1*) and not more intensely coloured than reference solution Y_5 (*2.2.2, Method II*).

pH (*2.2.3*): 3.7 to 5.5 for freshly prepared solution S.

Related substances. Liquid chromatography (*2.2.29*). *Prepare the solutions immediately before use, protected from light.*

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

Reference solution (a). Dissolve 10.0 mg of *deferoxamine mesilate CRS* in the mobile phase and dilute to 10.0 ml with the mobile phase.

Reference solution (b). Dilute 1.0 ml of the test solution to 25.0 ml with the mobile phase.

Column:

– *size*: *l* = 0.25 m, Ø = 4.6 mm;

– *stationary phase*: *octadecylsilyl silica gel for chromatography R* (10 µm).

Mobile phase: dissolve 1.32 g of *ammonium phosphate R* and 0.37 g of *sodium edetate R* in 950 ml of *water R*; adjust to pH 2.8 with *phosphoric acid R* (about 3-4 ml) and add 55 ml of *tetrahydrofuran R*.

Flow rate: 2 ml/min.

Detection: spectrophotometer at 220 nm.

Injection: 20 µl.

Run time: 3 times the retention time of deferoxamine.

System suitability: reference solution (a):

– *resolution*: minimum 1.0 between the peak with a relative retention time of about 0.8 and the principal peak.

Limits:

– *impurity A*: not more than the area of the principal peak in the chromatogram obtained with reference solution (b) (4.0 per cent);

– *total*: not more than 1.75 times the area of the principal peak in the chromatogram obtained with reference solution (b) (7.0 per cent);

– *disregard limit*: 0.02 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.08 per cent).

Chlorides (*2.4.4*): maximum 330 ppm.

Dilute 2 ml of solution S to 20 ml with *water R*.

Sulphates (*2.4.13*): maximum 400 ppm.

Dilute 5 ml of solution S to 20 ml with *distilled water R*.

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

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

Water (*2.5.12*): maximum 2.0 per cent, determined on 1.000 g.

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

Bacterial endotoxins (*2.6.14*): less than 0.025 IU/mg, if intended for use in the manufacture of parenteral dosage forms without a further appropriate procedure for the removal of bacterial endotoxins.

ASSAY

Dissolve 0.500 g in 25 ml of *water R*. Add 4 ml of *0.05 M sulphuric acid*. Titrate with *0.1 M ferric ammonium sulphate*. Towards the end of the titration, titrate uniformly and at a rate of about 0.2 ml/min. Determine the end-point potentiometrically (*2.2.20*) using a platinum indicator electrode and a calomel reference electrode. Retain the titrated solution (solution A) for identification test C.

1 ml of *0.1 M ferric ammonium sulphate* is equivalent to 65.68 mg of $C_{26}H_{52}N_6O_{11}S$.

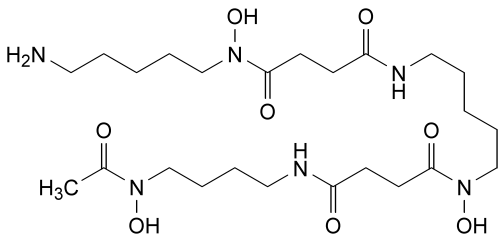
STORAGE

Protected from light, at a temperature of 2 °C to 8 °C. If the substance is sterile, store in a sterile, airtight, tamper-proof container.

IMPURITIES

Specified impurities: A.

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*): *B.*



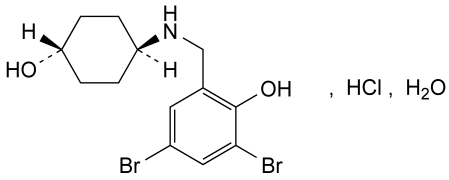
A. *N*′-[5-[[4-[[4-(acetylhydroxyamino)butyl]amino]-4-oxobutanoyl]hydroxyamino]pentyl]-*N*-(5-aminopentyl)-*N*-hydroxybutanediamide (desferrioxamine A_1),

B. other desferrioxamines.

01/2008:2169

DEMBREXINE HYDROCHLORIDE MONOHYDRATE FOR VETERINARY USE

Dembrexini hydrochloridum monohydricum ad usum veterinarium



$C_{13}H_{18}Br_2ClNO_2,H_2O$ M_r 433.6
[52702-51-9]

DEFINITION

trans-4-[(3,5-Dibromo-2-hydroxybenzyl)amino]cyclohexanol hydrochloride monohydrate.

Content: 98.0 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 methanol, slightly soluble in anhydrous ethanol.

IDENTIFICATION

A. Infrared absorption spectrophotometry (*2.2.24*).
Comparison: *dembrexine hydrochloride monohydrate CRS*.

B. It gives reaction (a) of chlorides (*2.3.1*).

TESTS

Related substances. Liquid chromatography (*2.2.29*). *Prepare the solutions immediately before use.*

Test solution. Dissolve 25.0 mg of the substance to be examined in *methanol R* and dilute to 10.0 ml with the same solvent.

Reference solution (a). Dilute 1.0 ml of the test solution to 50.0 ml with *methanol R*. Dilute 1.0 ml of this solution to 10.0 ml with *methanol R*.

Reference solution (b). Dissolve 2.5 mg of *tribromophenol R* (impurity E) in *methanol R* and dilute to 50.0 ml with the same solvent. To 1.0 ml of this solution add 1.0 ml of the test solution and dilute to 10.0 ml with *methanol R*.

Blank solution. Methanol R.

Column:

– *size*: *l* = 0.15 m, Ø = 4.0 mm;
– *stationary phase*: *endcapped octadecylsilyl silica gel for chromatography R* (5 µm);
– *temperature*: 40 °C.

Mobile phase:

– *mobile phase A*: dissolve 1.0 g of *potassium dihydrogen phosphate R* in 900 ml of *water R*, adjust to pH 7.4 with *0.5 M potassium hydroxide* and dilute to 1000 ml with *water R*; mix 80 volumes of this solution with 20 volumes of *methanol R*;
– *mobile phase B*: *methanol R, acetonitrile R* (20:80 *V/V*);