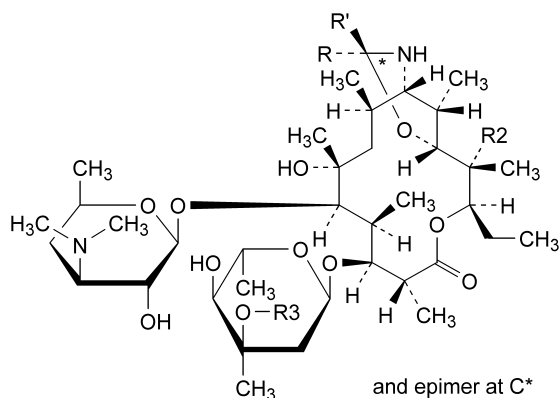


- A. (9*S*)-9-amino-9-deoxyerythromycin,  
 B. R = H: (9*S*)-9-amino-3-de(2,6-dideoxy-3-*C*-methyl-3-*O*-methyl- $\alpha$ -*L*-ribo-hexopyranosyl)-9-deoxyerythromycin,

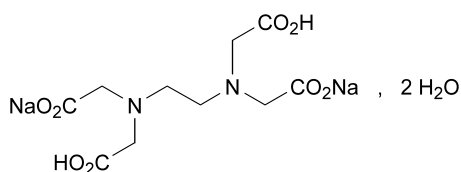


- C. R = CH<sub>2</sub>-O-CH<sub>2</sub>-CH<sub>2</sub>-O-CH<sub>3</sub>, R' = H, R<sub>2</sub> = H, R<sub>3</sub> = CH<sub>3</sub>: (9*S*)-9,11-[imino[(1*RS*)-2-(2-methoxyethoxy)ethylidene]oxy]-9-deoxy-11,12-dideoxyerythromycin (dirithromycin B),  
 D. R = CH<sub>2</sub>-O-CH<sub>2</sub>-CH<sub>2</sub>-O-CH<sub>3</sub>, R' = H, R<sub>2</sub> = OH, R<sub>3</sub> = H: (9*S*)-9,11-[imino[(1*RS*)-2-(2-methoxyethoxy)ethylidene]oxy]-3'-*O*-demethyl-9-deoxy-11-deoxyerythromycin (dirithromycin C),  
 E. R = CH<sub>3</sub>, R' = CH<sub>3</sub>, R<sub>2</sub> = OH, R<sub>3</sub> = CH<sub>3</sub>: 9,11-[imino[(1-methylethylidene)oxy]-9-deoxy-11-deoxyerythromycin.

01/2008:0232

## DISODIUM EDETATE

### Dinatrii edetas

C<sub>10</sub>H<sub>14</sub>N<sub>2</sub>Na<sub>2</sub>O<sub>8</sub>·2H<sub>2</sub>OM<sub>r</sub> 372.2

#### DEFINITION

Disodium dihydrogen (ethylenedinitrilo)tetraacetate dihydrate.

Content: 98.5 per cent to 101.0 per cent.

#### CHARACTERS

Appearance: white or almost white, crystalline powder.

Solubility: soluble in water, practically insoluble in ethanol (96 per cent).

#### IDENTIFICATION

First identification: A, B, D.

Second identification: B, C, D.

A. Infrared absorption spectrophotometry (2.2.24).

Preparation: discs.

Comparison: disodium edetate CRS.

B. Dissolve 2 g in 25 ml of water R, add 6 ml of lead nitrate solution R, shake and add 3 ml of potassium iodide solution R. No yellow precipitate is formed. Make alkaline to red litmus paper R by the addition of dilute ammonia R2. Add 3 ml of ammonium oxalate solution R. No precipitate is formed.

C. Dissolve 0.5 g in 10 ml of water R and add 0.5 ml of calcium chloride solution R. Make alkaline to red litmus paper R by the addition of dilute ammonia R2 and add 3 ml of ammonium oxalate solution R. No precipitate is formed.

D. It gives the reactions of sodium (2.3.1).

#### TESTS

**Solution S.** Dissolve 5.0 g in carbon dioxide-free water R and dilute to 100 ml with the same solvent.

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

**pH (2.2.3):** 4.0 to 5.5 for solution S.

**Impurity A.** Liquid chromatography (2.2.29). Carry out the test protected from light.

**Solvent mixture.** Dissolve 10.0 g of ferric sulphate pentahydrate R in 20 ml of 0.5 M sulphuric acid and add 780 ml of water R. Adjust to pH 2.0 with 1 M sodium hydroxide and dilute to 1000 ml with water R.

**Test solution.** Dissolve 0.100 g of the substance to be examined in the solvent mixture and dilute to 25.0 ml with the solvent mixture.

**Reference solution.** Dissolve 40.0 mg of nitrilotriacetic acid R in the solvent mixture and dilute to 100.0 ml with the solvent mixture. To 1.0 ml of the solution add 0.1 ml of the test solution and dilute to 100.0 ml with the solvent mixture.

**Column:**

– size:  $l = 0.10$  m,  $\varnothing = 4.6$  mm,

– stationary phase: spherical graphitised carbon for chromatography R1 (5  $\mu$ m) with a specific surface area of 120 m<sup>2</sup>/g and a pore size of 25 nm.

**Mobile phase:** dissolve 50.0 mg of ferric sulphate pentahydrate R in 50 ml of 0.5 M sulphuric acid and add 750 ml of water R. Adjust to pH 1.5 with 0.5 M sulphuric acid or 1 M sodium hydroxide, add 20 ml of ethylene glycol R and dilute to 1000 ml with water R.

**Flow rate:** 1 ml/min.

**Detection:** spectrophotometer at 273 nm.

**Injection:** 20  $\mu$ l; filter the solutions and inject immediately.

**Run time:** 4 times the retention time of the iron complex of impurity A.

**Retention times:** iron complex of impurity A = about 5 min; iron complex of edetic acid = about 10 min.

*System suitability*: reference solution:

- *resolution*: minimum 7 between the peaks due to the iron complex of impurity A and the iron complex of edetic acid,
- *signal-to-noise ratio*: minimum 50 for the peak due to impurity A.

*Limit*:

- *impurity A*: not more than the area of the corresponding peak in the chromatogram obtained with the reference solution (0.1 per cent).

**Iron (2.4.9)**: maximum 80 ppm.

Dilute 2.5 ml of solution S to 10 ml with *water R*. Add 0.25 g of *calcium chloride R* to the test solution and the standard before the addition of the *thioglycollic acid R*.

**Heavy metals (2.4.8)**: maximum 20 ppm.

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

#### ASSAY

Dissolve 0.300 g in *water R* and dilute to 300 ml with the same solvent. Add 2 g of *hexamethylenetetramine R* and 2 ml of *dilute hydrochloric acid R*. Titrate with 0.1 M *lead nitrate*, using about 50 mg of *xylanol orange triturate R* as indicator.

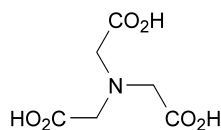
1 ml of 0.1 M *lead nitrate* is equivalent to 37.22 mg of  $C_{10}H_{14}N_2Na_2O_8 \cdot 2H_2O$ .

#### STORAGE

Protected from light.

#### IMPURITIES

*Specified impurities*: A.



A. nitriilotriacetic acid.

01/2008:1509  
corrected 6.0

## DISODIUM PHOSPHATE, ANHYDROUS

Dinatrii phosphas anhydricus

$Na_2HPO_4$   
[7558-79-4]

$M_r$  142.0

#### DEFINITION

*Content*: 98.0 per cent to 101.0 per cent (dried substance).

#### CHARACTERS

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

*Solubility*: soluble in water, practically insoluble in ethanol (96 per cent).

#### IDENTIFICATION

- Solution S (see Tests) is slightly alkaline (2.2.4).
- Loss on drying (see Tests).
- Solution S gives reaction (b) of phosphates (2.3.1).
- Solution S gives reaction (a) of sodium (2.3.1).

#### TESTS

**Solution S**. Dissolve 5.0 g in *distilled water R* and dilute to 100.0 ml with the same solvent.

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

**Reducing substances**. To 10 ml of solution S add 5 ml of *dilute sulphuric acid R* and 0.25 ml of 0.02 M *potassium permanganate* and heat on a water-bath for 5 min. The solution retains a slight red colour.

**Monosodium phosphate**: maximum 2.5 per cent.

From the volume of 1 M *hydrochloric acid* (25 ml) and of 1 M *sodium hydroxide* ( $n_1$  ml and  $n_2$  ml) used in the assay, calculate the following ratio:

$$\frac{n_2 - 25}{25 - n_1}$$

This ratio is not greater than 0.025.

**Chlorides (2.4.4)**: maximum 200 ppm.

Dilute 5 ml of solution S to 15 ml with *dilute nitric acid R*.

**Sulphates (2.4.13)**: maximum 500 ppm.

To 6 ml of solution S add 2 ml of *dilute hydrochloric acid R* and dilute to 15 ml with *distilled water R*.

**Arsenic (2.4.2, Method A)**: maximum 2 ppm, determined on solution S.

**Iron (2.4.9)**: maximum 20 ppm, determined on solution S.

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

12 ml of solution S complies with test A. Prepare the reference solution using 5 ml of *lead standard solution (1 ppm Pb) R* and 5 ml of *water R*.

**Loss on drying (2.2.32)**: maximum 1.0 per cent, determined on 1.000 g by drying in an oven at 105 °C for 4 h.

#### ASSAY

Dissolve 1.600 g ( $m$ ) in 25.0 ml of *carbon dioxide-free water R* and add 25.0 ml of 1 M *hydrochloric acid*. Carry out a potentiometric titration (2.2.20) using 1 M *sodium hydroxide*. Read the volume added at the 1<sup>st</sup> inflexion point ( $n_1$  ml). Continue the titration to the 2<sup>nd</sup> inflexion point (total volume of 1 M *sodium hydroxide* required,  $n_2$  ml).

Calculate the percentage content of  $Na_2HPO_4$  from the following expression:

$$\frac{1420 (25 - n_1)}{m (100 - d)}$$

$d$  = percentage loss on drying.

#### STORAGE

In an airtight container.

01/2008:0602

## DISODIUM PHOSPHATE DIHYDRATE

Dinatrii phosphas dihydricus

$Na_2HPO_4 \cdot 2H_2O$   
[10028-24-7]

$M_r$  178.0

#### DEFINITION

*Content*: 98.0 per cent to 101.0 per cent (dried substance).

#### CHARACTERS

*Appearance*: white or almost white powder or colourless crystals.

*Solubility*: soluble in water, practically insoluble in ethanol (96 per cent).