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Peritoneal Dialysis Solutions

General Notices

(Solutions for Peritoneal Dialysis, Ph. Eur. monograph 0862)

Ph Eur

DEFINITION

Preparations for intraperitoneal use containing electrolytes with a concentration close to the electrolytic composition of plasma. They contain glucose in varying concentrations or other suitable osmotic agents.

Solutions for peritoneal dialysis are supplied in:

— rigid or semi-rigid plastic containers;

— flexible plastic containers fitted with a special connecting device; these are generally filled to a volume below their nominal capacity and presented in closed protective envelopes;

— glass containers.

The containers and closures comply with the requirements for containers for preparations for parenteral administration (*3.2*).

Several formulations are used. The concentrations of the components per litre of solution are usually in the following range (see Table 0862.-1).

Table 0862.-1.

	Concentration (mmol/L)	Concentration (mEq/L)
Sodium	125 - 150	125 - 150
Potassium	0 - 4.5	0 - 4.5
Calcium	0 - 2.5	0 - 5.0
Magnesium	0.25 - 1.5	0.50 - 3.0
Acetate and/or lactate and/or hydrogen carbonate	30 - 60	30 - 60
Chloride	90 - 120	90 - 120
Glucose	25 - 250	

When hydrogen carbonate is present, the solution of sodium hydrogen carbonate is supplied in a container or a separate compartment and is added to the electrolyte solution immediately before use.

Unless otherwise justified and authorised, antioxidants are not added to the solutions.

IDENTIFICATION

According to the stated composition, the solution to be examined gives the following identification reactions (2.3.1):

— potassium: reaction (b);

— calcium: reaction (a);

— sodium: reaction (b);

— chlorides: reaction (a);

— acetates: to 5 mL of the solution to be examined add 1 mL of *hydrochloric acid R* in a test-tube fitted with a stopper and a bent tube, heat and collect a few millilitres of distillate; carry out reaction (b) of acetates on the distillate;

— lactates, hydrogen carbonates: the identification is carried out together with the assay;

— magnesium: to 0.1 mL of *titan yellow solution R* add 10 mL of *water R*, 2 mL of the solution to be examined and 1 mL of *1 M sodium hydroxide*; a pink colour is produced;

— glucose: to 5 mL of the solution to be examined, add 2 mL of *dilute sodium hydroxide solution R* and 0.05 mL of *copper sulfate solution R*; the solution is blue and clear; heat to boiling; an abundant red precipitate is formed.

TESTS

Appearance of solution

The solution is clear (2.2.1) and not more intensely coloured than reference solution Y_4 (2.2.2, *Method I*).

pH (2.2.3)

5.0 to 6.5. If the solution contains hydrogen carbonate, the pH is 6.5 to 8.0.

Hydroxymethylfurfural

Carry out the test only if glucose is added to the preparation. To a volume of the solution to be examined containing the equivalent of 25 mg of glucose, add 5.0 mL of a 100 g/L solution of *p-toluidine R* in *2-propanol R* containing 10 per cent *V/V* of *glacial acetic acid R*, then add 1.0 mL of a 5 g/L solution of *barbituric acid R*. The absorbance (2.2.25) determined at 550 nm after allowing the mixture to stand for 2-3 min is not greater than that of a standard prepared at the same time and in the same manner using a solution containing 10 µg of *hydroxymethylfurfural R* in the same volume as the solution to be examined (400 ppm expressed with reference to the glucose concentration). If the solution contains hydrogen carbonate, use as the standard a solution containing 20 µg of *hydroxymethylfurfural R* (800 ppm expressed with reference to the glucose concentration).

Aluminium

Maximum 10 µg/L.

Atomic absorption spectrometry (2.2.23, *Method I or II*). Use a matrix modifier (for example *nitric acid R* and *magnesium nitrate R* in *water R*) in the same quantity for the test solution, the reference solutions and the blank solution.

Test solution If necessary, dilute the solution to be examined with *water R* to a concentration suitable for the instrument to be used.

Reference solutions. Method I – direct calibration.

Prepare the reference solutions by diluting, for example *aluminium standard solution (10 ppm Al) R* with acidified *water R*.

Reference solutions. Method II – standard additions.

Prepare at least 3 reference solutions in the test solution, in a range spanning the expected aluminium concentration of the test solution, for example by diluting *aluminium standard solution (10 ppm Al) R* with the test solution.

Blank solution *water R*.

Source Aluminium hollow-cathode lamp.

Wavelength 309.3 nm.

Atomisation device Graphite furnace.

Particulate contamination (*2.9.19, Method I*)

Use 50 mL of the solution to be examined.

Extractable volume (*2.9.17*)

The solution complies with the test prescribed for parenteral infusions.

Sterility (*2.6.1*)

The solution complies with the test.

Bacterial endotoxins (*2.6.14*)

Less than 0.05 IU/mL, unless otherwise justified and authorised.

Pyrogens (*2.6.8*)

Solutions for which a validated test for bacterial endotoxins cannot be carried out comply with the test for pyrogens. Inject per kilogram of the rabbit's mass 10 mL of the solution.

ASSAY

Sodium

97.5 per cent to 102.5 per cent of the content of sodium (Na) stated on the label.

Atomic emission spectrometry (*2.2.22, Method I*).

Test solution If necessary, dilute the solution to be examined with *water R* to a concentration suitable for the instrument to be used.

Reference solutions Prepare the reference solutions using *sodium standard solution (200 ppm Na) R*.

Wavelengths 589.0 nm or 589.6 nm (sodium emits as a doublet).

Potassium

95.0 per cent to 105.0 per cent of the content of potassium (K) stated on the label.

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

Test solution If necessary, dilute the solution to be examined with *water R* to a concentration suitable for the instrument to be used. To 100 mL of the solution add 10 mL of a 22 g/L solution of *sodium chloride R*.

Reference solutions Prepare the reference solutions using *potassium standard solution (100 ppm K) R*. To 100 mL of each reference solution add 10 mL of a 22 g/L solution of *sodium chloride R*.

Source Potassium hollow-cathode lamp.

Wavelength 766.5 nm.

Atomisation device Air-propane or air-acetylene flame.

Calcium

95.0 per cent to 105.0 per cent of the content of calcium (Ca) stated on the label.

Atomic absorption spectrometry (2.2.23, Method I).

Test solution If necessary, dilute the solution to be examined with water R to a concentration suitable for the instrument to be used.

Reference solutions Prepare the reference solutions using calcium standard solution (400 ppm Ca) R.

Source Calcium hollow-cathode lamp.

Wavelength 422.7 nm.

Atomisation device Air-propane or air-acetylene flame.

Magnesium

95.0 per cent to 105.0 per cent of the content of magnesium (Mg) stated on the label.

Atomic absorption spectrometry (2.2.23, Method I).

Test solution If necessary, dilute the solution to be examined with water R to a concentration suitable for the instrument to be used.

Reference solutions Prepare the reference solutions using magnesium standard solution (100 ppm Mg) R.

Source Magnesium hollow-cathode lamp.

Wavelength 285.2 nm.

Atomisation device Air-propane or air-acetylene flame.

Total chloride

95.0 per cent to 105.0 per cent of the content of chloride (Cl) stated on the label.

Dilute an accurately measured volume of the solution to be examined containing the equivalent of about 0.68 mEq of chloride with an appropriate volume of water R in order to immerse the electrode. Carry out a potentiometric titration (2.2.20), using 0.1 M silver nitrate. Read the volume added between the 2 points of inflexion.

1 mL of 0.1 M silver nitrate is equivalent to 3.545 mg of Cl.

Acetate

95.0 per cent to 105.0 per cent of the content of acetate stated on the label.

To a volume of the solution to be examined, corresponding to about 0.7 mmol of acetate, add 10.0 mL of 0.1 M hydrochloric acid. Carry out a potentiometric titration (2.2.20), using 0.1 M sodium hydroxide. Read the volume added between the 2 points of inflexion.

1 mL of 0.1 M sodium hydroxide is equivalent to 0.1 mmol of acetate.

Lactate

95.0 per cent to 105.0 per cent of the content of lactate stated on the label.

To a volume of the solution to be examined, corresponding to about 0.7 mmol of lactate, add 10.0 mL of 0.1 M hydrochloric acid. Add 50 mL of acetonitrile R. Carry out a potentiometric titration (2.2.20), using 0.1 M sodium hydroxide. Read the volume added between the 2 points of inflexion.

1 mL of 0.1 M sodium hydroxide is equivalent to 0.1 mmol of lactate.

Sodium hydrogen carbonate

95.0 per cent to 105.0 per cent of the content of sodium hydrogen carbonate stated on the label.

Titrate with 0.1 M hydrochloric acid, a volume of the solution to be examined corresponding to about 0.1 g of sodium hydrogen carbonate, determining the end-point potentiometrically (2.2.20).

1 mL of *0.1 M hydrochloric acid* is equivalent to 8.40 mg of $NaHCO_3$.

Lactate and hydrogen carbonate

95.0 per cent to 105.0 per cent of the content of lactates and hydrogen carbonates stated on the label.

Liquid chromatography (*2.2.29*).

Test solution The solution to be examined.

Reference solution Dissolve in 100 mL of *water for chromatography R* quantities of lactates and hydrogen carbonates, accurately weighed, in order to obtain solutions having concentrations representing about 90 per cent, 100 per cent and 110 per cent of the concentrations stated on the label.

Column:

— *size*: *l* = 0.30 m, Ø = 7.8 mm;

— *stationary phase*: *cation-exchange resin R* (9 µm);

— *temperature*: 60 °C.

Mobile phase *0.005 M sulfuric acid* previously degassed with *helium for chromatography R*.

Flow rate 0.6 mL/min.

Detection Differential refractometer.

Injection 20 µL, twice.

Order of elution Lactates, hydrogen carbonates.

Determine the concentration of lactate and hydrogen carbonates in the test solution by interpolating the peak area for lactate and the peak height for hydrogen carbonate from the linear regression curve obtained with the reference solutions.

Reducing sugars

(expressed as glucose): 95.0 per cent to 105.0 per cent of the content of glucose stated on the label.

Transfer a volume of the solution to be examined containing the equivalent of 25 mg of glucose to a 250 mL conical flask with a ground-glass neck and add 25.0 mL of *cupri-citric solution R*. Add a few grains of pumice, fit a reflux condenser, heat so that boiling occurs within 2 min and boil for exactly 10 min. Cool and add 3 g of *potassium iodide R* dissolved in 3 mL of *water R*. Carefully add, in small amounts, 25 mL of a 25 per cent *m/m* solution of *sulfuric acid R*. Titrate with *0.1 M sodium thiosulfate* using *starch solution R*, added towards the end of the titration, as indicator. Carry out a blank titration using 25.0 mL of *water R*.

Calculate the content of reducing sugars expressed as glucose ($C_6H_{12}O_6$), using Table 0862.-2.

Table 0862.-2.

Volume of *0.1 M sodium thiosulfate* (mL)	Glucose (mg)
8	19.8
9	22.4
10	25.0
11	27.6
12	30.3
13	33.0
14	35.7
15	38.5
16	41.3

STORAGE

At 4 °C or above.

LABELLING

The label states:

— the formula of the solution for peritoneal dialysis, expressed in grams per litre and in millimoles per litre;

— the calculated osmolarity, expressed in milliosmoles per litre;

— the nominal volume of the solution for peritoneal dialysis in the container;

— that the solution is free from bacterial endotoxins, or where applicable, that it is apyrogenic;

— the storage conditions;

— that the solution is not to be used for intravenous infusion;

— that any unused portion of the solution is to be discarded.