Solutions for peritoneal dialysis are 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 parenteral use (3.2.1 and 3.2.2).

Several formulations are used. The concentrations of the components per litre of solution are usually in the following range:

<table>
<thead>
<tr>
<th>Component</th>
<th>Expression in mmol</th>
<th>Expression in mEq</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium</td>
<td>125 - 150</td>
<td>125 - 150</td>
</tr>
<tr>
<td>Potassium</td>
<td>0 - 4.5</td>
<td>0 - 4.5</td>
</tr>
<tr>
<td>Calcium</td>
<td>0 - 2.5</td>
<td>0 - 5.0</td>
</tr>
<tr>
<td>Magnesium</td>
<td>0.25 - 1.5</td>
<td>0.50 - 3.0</td>
</tr>
<tr>
<td>Acetate and/or lactate</td>
<td>30 - 60</td>
<td>30 - 60</td>
</tr>
<tr>
<td>and/or hydrogen carbonate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chloride</td>
<td>90 - 120</td>
<td>90 - 120</td>
</tr>
<tr>
<td>Glucose</td>
<td>25 - 250</td>
<td></td>
</tr>
</tbody>
</table>

See the information section on general monographs (cover pages)
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 such as metabisulphite salts 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 sulphate 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 Y1, (2.2.2, Method I).

pH (2.2.3). The pH of the solution is 5.0 to 6.5. If the solution contains hydrogen carbonate, the pH is 6.5 to 8.0.

Hydroxymethylfurfural. To a volume of the solution 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 and 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 min to 3 min is not greater than that of a standard prepared at the same time in the same manner using a solution containing 10 µg of hydroxymethylfurfural R in the same volume as the solution to be examined. If the solution contains hydrogen carbonate, use as the standard a solution containing 20 µg of hydroxymethylfurfural R.

Aluminium (2.4.17). Take 400 ml, adjust to pH 6.0 and add 10 ml of acetate buffer solution pH 6.0 R. The solution complies with the limit test for aluminium (15 µg/l). Use as the reference solution a mixture of 3 ml of aluminium standard solution (2 ppm Al) R, 10 ml of acetate buffer solution pH 6.0 R and 9 ml of water R. To prepare the blank use a mixture of 10 ml of acetate buffer solution pH 6.0 R and 10 ml of water R.

Particulate contamination. Carry out the test for sub-visible particles (2.9.19) using 50 ml of solution.

<table>
<thead>
<tr>
<th>Particles larger than</th>
<th>10 µm</th>
<th>25 µm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximum number of particles per millilitre</td>
<td>25</td>
<td>3</td>
</tr>
</tbody>
</table>

Extractable volume (2.9.17). The solution complies with the test prescribed for parenteral infusions.

Sterility (2.6.7). The solution complies with the test for sterility.

Bacterial endotoxins (2.6.14): less than 0.25 IU/ml.

Pyrogens (2.6.18). 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, determined by atomic absorption spectrometry (2.2.23, Method II).

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.

Measure the absorbance at 589.0 nm using a sodium hollow-cathode lamp as source of radiation and an air-propane or an air-acetylene flame.

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

Measure the absorbance at 766.5 nm, using a potassium hollow-cathode lamp as source of radiation and an air-propane or an air-acetylene flame.

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

Measure the absorbance at 422.7 nm using a calcium hollow-cathode lamp as source of radiation and an air-propane or an air-acetylene flame.

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

Measure the absorbance at 285.2 nm using a magnesium hollow-cathode lamp as source of radiation and an air-propane or an 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 to 50 ml with water R and accurately measured volume of the solution to be examined containing the equivalent of about 60 mg of chloride. Add 5 ml of dilute nitric acid R, 25.0 ml of 0.1 M silver nitrate and 2 ml of dibutyl phthalate R. Shake.
Using 2 ml of ferric ammonium sulphate solution R2 as indicator, titrate with 0.1 M ammonium thiocyanate until a reddish-yellow colour is obtained.

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 two 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. Then 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 two 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 NaHCO₃.

**Lactate and hydrogen carbonate**: 95.0 per cent to 105.0 per cent of the content of lactates and/or hydrogen carbonates stated on the label. Examine by liquid chromatography (2.2.29).

**Test solution. 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 indicated on the label.

R

The chromatographic procedure may be carried out using:

- a column 0.30 m long and 7.8 mm in internal diameter packed with cation exchange resin R (9 µm),
- as mobile phase at a flow rate of 0.6 ml/min 0.005 M sulphuric acid previously degassed with helium R,
- a differential refractometer detector, maintaining the temperature of the column at 85 °C.

Inject in duplicate 20 µl of test solution and 20 µl of each reference solution. When the chromatograms are recorded in the prescribed conditions, the peaks elute in the following order: lactates then hydrogen carbonates.

Determine the concentration of lactates 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 anhydrous glucose). 95.0 per cent to 105.0 per cent of the content of glucose stated on the label. Transfer a volume of 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 cupric-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 sulphuric acid R. Titrate with 0.1 M sodium thiosulphate 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 anhydrous glucose (C₆H₁₂O₆), by means of Table 0862.3:

<table>
<thead>
<tr>
<th>Volume of 0.1 M sodium thiosulphate (ml)</th>
<th>Anhydrous glucose (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>19.8</td>
</tr>
<tr>
<td>9</td>
<td>22.4</td>
</tr>
<tr>
<td>10</td>
<td>25.0</td>
</tr>
<tr>
<td>11</td>
<td>27.6</td>
</tr>
<tr>
<td>12</td>
<td>30.3</td>
</tr>
<tr>
<td>13</td>
<td>33.0</td>
</tr>
<tr>
<td>14</td>
<td>35.7</td>
</tr>
<tr>
<td>15</td>
<td>38.5</td>
</tr>
<tr>
<td>16</td>
<td>41.3</td>
</tr>
</tbody>
</table>

**STORAGE**

Store at a temperature not below 4 °C.

**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 solution is to be discarded.

01/2005:0629

**PERPHENAZINE**

Perphenazinum

C₂₁H₂₆ClN₃OS \( M_r \) 404.0

**DEFINITION**

Perphenazine contains not less than 99.0 per cent and not more than the equivalent of 101.0 per cent of 2-[4-[[3-(2-chlorophenothiazin-10-yl)propyl]piperazin-1-yl]ethyl] ethanol, calculated with reference to the dried substance.