11.2022

רופא/ה רוקח/ת נכבד/ה,

ברצוננו להודיעך על עדכון בעלון לרופא בעקבות שינוי בתנאי האחסון, עבור התכשיר:

Sterofundin ISO

חומר פעיל :

Sodium chloride	6.80	g
Potassium chloride	0.30	g
Magnesium chloride hexahydrate	0.20	g
Calcium chloride dihydrate	0.37	g
Sodium acetate trihydrate	3.27	g
Malic acid (DAB)	0.67	g

התוויה מאושרת:

Replacement of extracellular fluid losses in the case of isotonic dehydration, where acidosis is present or imminent.

להלן עלון לרופא עם העדכונים (טקסט מסומן ירוק משמעותו עדכון):

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Sterofundin ISO

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1,000 mL Sterofundin ISO solution for infusion contain

Sodium chloride	6.80	g
Potassium chloride	0.30	g
Magnesium chloride hexahydrate	0.20	g
Calcium chloride dihydrate	0.37	g
Sodium acetate trihydrate	3.27	g
Malic acid (DAB)	0.67	g

Electrolyte concentrations:

Na^+	145.0	mmol/L
K^+	4.0	mmol/L
Mg^{2+}	1.0	mmol/L
Ca^{2+}	2.5	mmol/L

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Cl^-	127.0	mmol/L
$Acetate^-$	24.0	mmol/L
$Malate^{2-}$	5.0	mmol/L

Excipient with known effect:
1,000 mL Sterofundin ISO contain 0.2 g sodium hydroxide (0,115 g sodium).

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for infusion.
Clear, colourless aqueous solution

pH: 5.1 - 5.9
Theoretical osmolarity: 309 mosm/L

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Replacement of extracellular fluid losses in the case of isotonic dehydration, where acidosis is present or imminent.

4.2 Posology and method of administration

Posology

Adults, elderly patients, adolescents and children:

The dosage depends on the age, bodyweight, clinical and biological conditions of the patient and the concomitant therapy.

Recommended dosage

The recommended dosage is:
- Adolescents, adults and elderly patients:
  500 mL - 3 L/24 hours, equivalent to 1 - 6 mmol sodium/kg BW/24 hours and 0.03 - 0.17 mmol potassium/kg BW/24 hours
- Infants and children:
  20 mL - 100 mL/kg BW/24 hours, equivalent to 3 - 14 mmol sodium/kg BW/24 hours and 0.08 - 0.40 mmol potassium/kg BW/24 hours.

Infusion rate

The maximum infusion rate depends on the patient's fluid and electrolyte requirements, bodyweight, clinical condition and biological status.

In paediatric patients, the infusion rate is 5 mL/kg BW/h on average, but the value varies with age: 6 - 8 mL/kg BW/h for infants, 4 - 6 mL/kg BW/h for toddlers, and 2 - 4 mL/kg BW/h for children.

Note:
- Infants and toddlers: Age ranges from 28 days - 23 months (a toddler is an infant who can walk.)
- Children: Age ranges from 2 - 11 years

Paediatric population
The safety and efficacy of Sterofundin ISO in newborn infants (below the age of 28 days) has not been established.

Method and duration of administration

For intravenous use as infusion only.

Sterofundin ISO can be infused into peripheral veins (see section 3 for pH and theoretical osmolarity).

If administration is by rapid infusion under pressure, all air must be withdrawn from the plastic container and infusion set prior to infusion, as otherwise there is a risk of producing air embolism during infusion.

Controls:
Fluid balance, plasma electrolyte concentrations and blood pH must be monitored during administration.

Sterofundin ISO may be administered as long as there is an indication for fluid replacement.

4.3 Contraindications

Do not use Sterofundin ISO in cases of:
- Hypersensitivity to the active substances or to any of the excipients listed in section 6.1.
- Hypervolaemia
- Severe congestive cardiac failure
- Severe renal failure with oliguria or anuria
- Severe general oedema
- Hyperkalaemia
- Hypercalcaemia
- Metabolic alkalosis

4.4 Special warnings and precautions for use

High volume infusion must be used under specific monitoring in patients with mild to moderate cardiac or pulmonary failure (for more severe conditions: see section **4.3**).

LAPIDOT MEDICAL

Solutions containing sodium chloride should be administered with caution to patients with:

- mild to moderate cardiac insufficiency, peripheral or pulmonary oedema or extracellular hyperhydration (for more severe conditions: see section **4.3**).
- hypernatraemia, hyperchloraemia, hypertonic dehydration, hypertension, impaired renal function, present or imminent eclampsia, aldosteronism or other conditions or treatments with medicines (e.g. corticoids/steroids) associated with sodium retention (see also section **4.5**).

Solutions containing potassium salts should be administered with caution to patients with cardiac disease or conditions predisposing to hyperkalaemia such as renal or adrenocortical insufficiency, acute dehydration or extensive tissue destruction as occurs with severe burns.

Because of the presence of calcium:

- Care should be taken to prevent extravasation during intravenous infusion
- The solution should be given cautiously to patients with impaired renal function or diseases associated with elevated vitamin D concentrations such as sarcoidosis.
- In case of concomitant blood transfusion, the solution for infusion must not be administered via the same infusion set.

Solutions containing metabolisable anions should be administered cautiously to patients with respiratory impairment.

Monitoring of serum electrolytes, fluid balance and blood pH is necessary.

During long-term parenteral treatment, an adequate nutritive supply must be given to the patient.

This medicinal product contains 145 mmol sodium per 1,000 mL. This must be taken into consideration by patients on a controlled (low-) sodium diet.

4.5 Interaction with other medicinal products and other forms of interaction

Sodium, potassium, calcium and magnesium are present in Sterofundin ISO in the same concentrations as in plasma. Hence, the administration of Sterofundin ISO in accordance with the recommended indications and contraindications does not increase the plasma concentrations of said electrolytes. Should there be a rise in the concentration of any of these electrolytes due to other reasons, the following interactions should be considered:

Sodium
Corticoids/steroids and carbenoxolone are associated with the retention of sodium and water resulting in oedema and hypertension.

Potassium

- Suxamethonium,

– Potassium-sparing diuretics (amiloride, spironolactone, triamterene, alone or in combination),
– Tacrolimus, cyclosporine

may increase the plasma potassium concentration and lead to potentially fatal hyperkalaemia, most notably in patients with existing renal failure, thereby further increasing the hyperkalaemic effect.

Calcium
Hypercalcaemia can potentiate the effect of digitalis glycosides (digitalis cardiotonics) and lead to serious or fatal cardiac arrhythmia.
Vitamin D may induce hypercalcaemia.

4.6 Fertility, pregnancy and lactation

There are no data from the use of Sterofundin ISO in pregnant and lactating women. However, no risks are to be expected in the intended indications when blood volume, electrolyte concentrations and the acid/base balance are carefully monitored (see section **5.3**).

Sterofundin ISO should be used with caution in the event of pregnancy-induced hypertension (pre-eclampsia).

4.7 Effects on ability to drive and use machines

Sterofundin ISO has no influence on the ability to drive and use machines**.**

4.8 Undesirable effects

Side effects may occur as signs of overdose, see section **4.9**.

Definition of frequency terms used in this section:
Rare: (≥ 1/10,000, < 1/1,000)
Not known (cannot be estimated from the available data)

Immune system disorders

Frequency not known: Hypersensitivity reactions characterised by urticaria have been occasionally described after the intravenous administration of magnesium salts.

Gastrointestinal disorders

Although oral magnesium salts stimulate peristalsis, rare cases of paralytic ileus have been reported after intravenous infusion of magnesium sulphate.

General disorders and administration site conditions

Adverse reactions may be associated with the administration technique and include febrile response, infection at the site of injection, local pain or reactions, vein irritation, venous thrombosis or phlebitis extending from the site of injection and extravasation.

Adverse reactions may be associated with the medications added to the solution; the nature of the additive will determine the likelihood of any other undesirable effects.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form (https://sideeffects.health.gov.il).

4.9 Overdose

Overdose or an infusion rate that is too fast may lead to water and sodium overload with a risk of oedema, particularly when renal sodium excretion is impaired. In this case, renal dialysis may be necessary.

Excessive administration of potassium may lead to the development of hyperkalaemia, especially in patients with renal impairment. Symptoms include paraesthesia of the extremities, muscle weakness, paralysis, cardiac arrhythmias, heart block, cardiac arrest and mental confusion. Treatment of hyperkalaemia involves the administration of calcium, insulin (with glucose) and sodium bicarbonate. The use of exchange resins or haemodialysis may be required.

Excessive parenteral administration of magnesium salts leads to hypermagnesaemia, the most important signs of which are loss of deep tendon reflexes and respiratory depression, both due to neuromuscular blockade. Other symptoms of hypermagnesaemia may include: Nausea, vomiting, flushing, thirst, hypotension due to peripheral vasodilatation, drowsiness, confusion, muscle weakness, bradycardia, coma and cardiac arrest.

Excessive administration of chloride salts may cause a loss of bicarbonate with an acidifying effect of the blood.

Excessive administration of compounds, such as acetate and malate, which are metabolised to form bicarbonate, may lead to metabolic alkalosis, especially in patients with impaired renal function. Symptoms may include: Mood changes, tiredness, shortness of breath, muscle weakness and cardiac arrhythmia. Patients with additional hypocalcaemia may develop muscle hypertonicity, twitching and tetany. Treatment of metabolic alkalosis associated with an increase in bicarbonate consists mainly of appropriate correction of the fluid and electrolyte balance.

Excessive administration of calcium salts may lead to hypercalcaemia. Symptoms may include: Anorexia, nausea, vomiting, constipation, abdominal pain, muscle weakness, mental disturbances, polydipsia, polyuria, nephrocalcinosis, renal calculi and, in severe cases, cardiac arrhythmias and coma. Too rapid intravenous injection of calcium salts may also lead to many of the symptoms of hypercalcaemia, as well as to a chalky taste, hot flushes and peripheral vasodilation. Mild asymptomatic hypercalcaemia will usually resolve on discontinuing the administration of calcium and other contributory drugs such as vitamin D. Severe hypercalcaemia is to be treated immediately with loop diuretics, haemodialysis, calcitonin, bisphosphonates or trisodium edetate.

When overdose is related to medications added to the solution for infusion, the signs and symptoms of overdose will be related to the nature of the additive being used. In the event of accidental overdose, treatment should be discontinued and the patient should be observed for the appropriate signs and symptoms related to the drug administered. The relevant symptomatic and supportive measures should be provided as necessary.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Electrolytes
ATC code: B05B B01

This medicinal product is an isotonic electrolyte solution adapted to plasma electrolyte concentrations. It is used to correct extracellular fluid losses (i.e. losses of water and electrolytes in physiological amounts). The supply of this solution is aimed at restoring as well as maintaining normal osmotic conditions in the extracellular and intracellular space.

The anion pattern represents a balanced combination of chloride, acetate and malate, which counteracts metabolic acidosis.

5.2 Pharmacokinetic properties

Absorption

Because the ingredients of Sterofundin ISO are infused intravenously, their bioavailability is 100 %.

Distribution and elimination

Sodium and chloride mainly distribute in the extracellular space, whereas potassium, magnesium and calcium distribute in the intracellular space.

The kidneys are the main route of excretion for sodium, potassium, magnesium and chloride, but small amounts are lost via the skin and intestinal tract. Calcium is excreted in approximately equal amounts in the urine and via intestinal secretion.

During the infusion of acetate and malate, their serum levels rise and appear to reach a steady state. Following termination of the infusion, the acetate and malate concentrations rapidly drop.

The renal excretion of acetate and malate rises during the infusion. However, their metabolism by body tissues is so rapid that only a small fraction appears in the urine.

5.3 Preclinical safety data

No preclinical studies have been conducted with Sterofundin ISO.

There are no preclinical data of relevance to the prescriber additional to those already included elsewhere in this Summary of Product Characteristics.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Water for injections,

sodium hydroxide (to adjust the pH)

6.2 Incompatibilities

Admixture of medicinal products containing carbonates, phosphates, sulphates or tartrates may lead to precipitation.

6.3 Shelf life

- of the medicinal product in the unopened container:The expiry date of the product is indicated on the packaging materials

- of the medicinal product after opening of the container:

From a microbiological point of view, the solution should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 8 ºC unless reconstitution has taken place in controlled and validated aseptic conditions.

6.4 Special precautions for storage

Do not store above 25^{0}C
Do not freeze.

6.5 Nature and contents of container

The solution for infusion is packed in polyethylene plastic bottles.

Polyethylene plastic bottles: 1 x / 10 x 500 mL

6.6 Special precautions for disposal and other handling

For intravenous use only.

For single use only. Discard any unused solution.

Do not reconnect partially used containers.

Do not use if container or closure is damaged. Use only clear solutions free from visible particles.

Use sterile equipment for the infusion and an aseptic technique when connecting the infusion. Prime the infusion equipment with the solution prior to the infusion in order to prevent air entering the system.

For further information, please refer to section **4.2**.

7 MANUFACTURER

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34212 Melsungen, Germany

8 MARKETING AUTHORISATION HOLDER

Lapidot Medical Import and Marketing Ltd.
8 Hashita st., Caesarea Industrial Park 3088900, Israel

9 MARKETING AUTHORISATION NUMBER

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העלון לרופא נשלח למאגר התרופות שבאתר משרד הבריאות www.health.gov.il לצורך העלאתו לאתר וניתן לקבלו מודפס על ידי פניה לבעל הרישום Lapidot Medical Import & Marketing Ltd, רח' השיטה 8, פארק התעשיה קיסריה 3088900 ישראל.

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