Approved Professional Information for BALSOL

SCHEDULING STATUS

S3

1. NAME OF THE MEDICINE

BALSOL solution for infusion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1 000 ml contains:

Sodium chloride	6,0 g
Potassium chloride	0,3 g
Magnesium chloride hexahydrate	0,3 g
Sodium bicarbonate	2,3 g

Sugar free.

Constituents:

Each 1 000 ml contains:

Sodium ion	130 mmol
Potassium ion	4,0 mmol
Magnesium ion	1,5 mmol
Chloride ion	110 mmol
Bicarbonate ion	27 mmol

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for infusion.

Clear, colourless, sterile solution.

Osmolarity (approx.): 273 mOsm/l

pH (approx.): 7,4.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Haemorrhage with or without shock, during and after surgery and to replace extracellular fluid (ECF) losses or shifts and to overcome acidosis.

4.2 Posology and method of administration

Posology:

For haemorrhagic shock:

Initial treatment: one to two litres per 45 to 60 minutes. If response is transient, give 3 to 4 litres BALSOL plus blood.

Central venous pressure monitoring may be necessary.

Haemorrhage without shock:

Depends on severity of blood loss.

During surgery:

Major surgery: 7 to 10 ml per kg per hour

Less traumatic surgery: 3 to 5 ml per kg per hour

General dosage: (Adults): 0,5 to 1 litre per hour. Maximum 3 to 4 litres.

After surgery:

One to two litres if necessary.

To replace ECF losses or shifts:

Depends on the degree of losses or shifts.

Prolonged labour:

Depends on severity of dehydration.

Method of administration:

For intravenous use.

Fluid balance, serum electrolytes and acid-base balance may need to be monitored before and during administration, with particular attention to serum sodium in patients with increased non-osmotic vasopressin release (syndrome of inappropriate antidiuretic hormone secretion, SIADH) and in patients co-medicated with vasopressin agonist medicines, due to the risk of hospital acquired hyponatraemia (see sections 4.4, 4.5 and 4.8).

Monitoring of serum sodium is particularly important for hypotonic fluids.

BALSOL tonicity: 273 mOsm/l.

The infusion rate and volume depend on the age, weight, clinical condition (e.g. burns, surgery, head injury, infections), and concomitant therapy should be determined by the medical practitioner experienced in paediatric intravenous fluid therapy (see sections 4.4. and 4.8).

4.3 Contraindications

- Hypersensitivity to the active ingredients (see section 2) or to any of the excipients of BALSOL listed in section 6.1.
- Fluid overload (hyperhydration).
- Metabolic or respiratory alkalosis.
- Hyperkalaemia.
- Conditions where sodium intake is restricted (e.g. renal failure, hypertension, oedema, congestive heart failure).
- Patients with hyperventilation (risk of acidosis).
- Patients with a history or urinary calculi.
- Patients with co-existent potassium depletion or chloride depletion, hypocalcaemia and hypernatraemia.

4.4 Special warnings and precautions for use

High volume infusions must be used under specific monitoring in patients with cardiac or pulmonary failure, and in patients with non-osmotic vasopressin release (including SIADH), due to the risk of hospital-acquired hyponatraemia (see below).

The patient's clinical status and laboratory parameters (fluid balance, blood and urine electrolytes as well as acid-base balance) must be monitored during use of BALSOL.

Fluid overload caused by overdose should be avoided in general. Particularly for patients with cardiac insufficiency or severe kidney dysfunctions the increased risk of hyperhydration must be taken into consideration; posology must be adapted.

Hyponatraemia: Patients with non-osmotic vasopressin release (e.g. in acute illness, pain, post-operative stress, infections, burns, and CNS diseases), patients with heart-, liver- and kidney diseases and patients exposed to vasopressin agonists (see section 4.5) are at particular risk of acute hyponatraemia upon infusion of hypotonic fluids.
Acute hyponatraemia can lead to acute hyponatraemic encephalopathy (cerebral oedema) characterised by headache, nausea, seizures, lethargy and vomiting. Patients with cerebral oedema are at particular risk of severe, irreversible and life-threatening brain injury.
Children, women in the fertile age and patients with reduced cerebral compliance (e.g. meningitis, intracranial bleeding, cerebral contusion and brain oedema) are at particular risk of the severe and life-threatening brain swelling caused by acute hyponatraemia.
Particular care must be taken in patients with severe electrolyte abnormalities, like hypernatraemia, hypermagnesaemia and hyperchloraemia.

Solutions containing sodium chloride should be administered with caution to patients with hypertension, heart failure, peripheral or pulmonary oedema, impaired renal function, pre-eclampsia, aldosteronism or other conditions or treatment (e.g. corticosteroids) associated with sodium retention (see section 4.5).

Solutions containing magnesium salts should be used with caution in patients with renal impairment, severe heart rate disorders and myasthenia gravis. Patients should be monitored for clinical signs of excess magnesium, particularly when being treated for eclampsia. Administration in the postoperative period after neuromuscular block should be used with caution since magnesium salts can lead to a recurarisation effect (see section 4.5).

When solutions containing sodium bicarbonate are used intravenously, arterial blood gas analysis, in particular arterial/venous blood pH and carbon dioxide levels, should be performed before and during the course of treatment to minimise the possibility of overdosage and resultant alkalosis.

Whenever respiratory acidosis is concomitant with metabolic acidosis, both pulmonary ventilation and perfusion must be adequately supported to get rid of excess CO_2. Administration of sodium bicarbonate to a patient with inadequate minute ventilation can cause worsening of the acidosis.

The treatment of metabolic acidosis must, if possible, be combined with concurrent treatment to combat the primary cause of the acidosis, for example the administration of insulin in uncomplicated diabetes, or blood volume restoration in shock.

Since BALSOL contains potassium, combination with potassium-sparing diuretics is not recommended. Plasma potassium must be particularly closely monitored in patients at risk of hyperkalaemia, e.g. in the presence of severe chronic renal failure (see section 4.5).

Precaution must be taken when using BALSOL in combination with angiotensin-converting enzyme inhibitors, angiotensin II receptor antagonists, suxamethonium, tacrolimus, ciclosporin or in case of severe digitalis intoxication (risk of cardiac symptoms).

Although BALSOL has a potassium concentration similar to the concentration in plasma, it is insufficient to produce a useful effect in case of severe potassium deficiency and therefore it should not be used for this purpose.

Accidental extravascular injection of hypertonic solutions may cause vascular irritation or sloughing. The use of scalp veins should be avoided.

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

4.5 Interaction with other medicines and other forms of interaction

Medicines leading to an increased vasopressin effect:

The below listed medicines increase the vasopressin effect, leading to reduced renal electrolyte free water excretion and may increase the risk of hospital acquired hyponatraemia following inappropriately balanced treatment with i.v. fluids (see sections 4.2, 4.4 and 4.8).

- Medicines stimulating vasopressin release include: chlorpropamide, clofibrate, carbamazepine, vincristine, selective serotonin reuptake inhibitors, 3.4-methylenedioxy-N-methamphetamine, ifosfamide, antipsychotics and narcotics.
- Medicines potentiating vasopressin action include: chlorpropamide, nonsteroidal anti-inflammatory drugs (NSAIDs) and cyclophosphamide.
- Vasopressin analogues include: desmopressin, oxytocin, vasopressin and terlipressin.

Other medicines increasing the risk of hyponatraemia also include diuretics in general and antiepileptics such as oxcarbazepine.

Interactions related to the presence of sodium:

Not recommended combinations (see section 4.4):

Corticosteroids and carbenoxolone are associated with retention of sodium and water (with oedema and hypertension).

Interactions related to the presence of potassium:

The following combinations are not recommended due to an increase in the concentration of potassium in the plasma and may lead to potentially fatal hyperkalaemia, notably in case of renal failure, increasing the hyperkalaemic effects (see section 4.4):

- Potassium-sparing diuretics: amiloride, spironolactone, triamterene alone or in combination.
- Angiotensin-converting enzyme inhibitors (ACE inhibitors) and angiotensin II receptor antagonists.
- Tacrolimus, ciclosporin.
- Suxamethonium.

Interactions related to the presence of magnesium:

Not recommended combinations (see section 4.4):

Competitive and depolarising neuromuscular blockers.

Interactions related to the presence of sodium bicarbonate:

Hypochloraemic alkalosis may occur if sodium bicarbonate is used in conjunction with potassium-depleting diuretics such as bumetanide, ethacrynic acid, furosemide and thiazides.

Concurrent use in patients taking potassium supplements may reduce serum potassium concentration by promoting an intracellular ion shift.

Alkalisation of urine:

Urinary alkalisation will increase the renal clearance of medicines which are acid in nature e.g. tetracyclines (especially doxycycline), acetylsalicylic acid, chlorpropamide, lithium and methenamine. It increases the half-life and duration of action of basic medicines such as quinidine, amphetamines, ephedrine, pseudoephedrine, memantine and flecainide.

Sodium bicarbonate in BALSOL is known to increase renal tubular re-absorption of mecamylamine causing hypotension.

4.6 Fertility, pregnancy and lactation

Safety of BALSOL in pregnancy and lactation has not been established.

BALSOL should be administrated with special caution to pregnant women during labour particularly as

to serum-sodium if administered in combination with oxytocin (see section 4.2). Also see sections 4.4, 4.5 and 4.8.

4.7 Effects on ability to drive and use machines

BALSOL has no influence on the ability to drive and use machines.

4.8 Undesirable effects

Metabolism and nutrition disorders:

Hyperhydration and heart failure in patients with cardiac disorder or pulmonary oedema, oedema due to water/sodium overload.

Alkalosis, hypokalaemia, hypernatremia, hyperosmolarity, hypocalcaemia, hypoglycaemia, paradoxal intracellular acidosis.

Hospital acquired hyponatraemia*, acute hyponatraemic encephalopathy*.

*Hospital acquired hyponatraemia may cause irreversible brain injury and death, due to development of acute hyponatraemic encephalopathy, frequency unknown (see sections 4.2. 4.4, 4.5).

Nervous system disorders:

Intracranial haemorrhage (in neonates), hyperirritability or tetany.

Cardiac disorders:

Deterioration of haemodynamic status associated with volume overload.

General disorders and administration site conditions:

Adverse reactions may be associated with the technique of administration including febrile response, infection at the site of injection, local pain or reaction, vein irritation, venous thrombosis or phlebitis extending from the site of injection and extravasation. Incorrect administration (intra-arterial, paravenous) may cause tissue necrosis.

Investigations:

In high doses the effects of dilution can commonly lead to a similar dilution of components of the blood, e.g. coagulation factors and other plasma proteins, and a decrease of the haematocrit.

Reporting of suspected adverse reactions:

Reporting suspected adverse reactions after authorisation of BALSOL is important. It allows continued monitoring of the benefit/risk balance of BALSOL. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "**6.04 Adverse Drug Reactions Reporting Form**", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose

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 components of BALSOL.
The relevant symptomatic and supportive measures should be provided as necessary, e.g. administration of a diuretic. In oliguric or anuric patients, haemofiltration or dialysis may be necessary in order to remove excessive fluid.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Category and class: A 24 Mineral substitutes, electrolytes.

Pharmacotherapeutic group: Electrolytes.

ATC code: B05BB01.

A balanced electrolyte solution for intravenous use.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Water for injection.

6.2 Incompatibilities

In the absence of compatibility studies, BALSOL should not be mixed with other medicines. Additives may be incompatible.

6.3 Shelf life

Unopened:

24 months.

In use:

To be used immediately after the bag or bottle is opened.

6.4 Special precautions for storage

Store at or below 25 °C.

6.5 Nature and contents of container

1 000 ml polyethylene bottles.

1 000 ml PVC or **free***flex*® bags.

Not all container types may be marketed.

6.6 Special precautions for disposal and other handling

For single use only.

Remove the overwrap from the **free***flex*® bag prior to use.

Do not use unless solution is clear.

Check for minute leaks by squeezing bags.

Destroy any unused portion.

7. HOLDER OF CERTIFICATE OF REGISTRATION

Fresenius Kabi Manufacturing SA (Pty) Ltd

6 Gibaud Road

Korsten

Port Elizabeth 6020

South Africa

8. REGISTRATION NUMBER

H/24/176

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

25 May 1976

10. DATE OF REVISION OF THE TEXT

17 January 2021