B BRAUN
SHARING EXPERTISE

PRESCRIPTION | PATIENT ACCESS | PREPARATION | APPLICATION | DISCHARGE MANAGEMENT

Sterofundin® ISO

Balance your Infusion Therapy

Balanced Solution Characteristics

There is a growing body of evidence indicating that balanced fluids improve the acid-base status and preserve a strong ion difference.

Surgery

The patients who received buffered fluids had an acid-base status that was more normal than those who received non buffered fluids. Overall, buffered fluids are a safe and effective alternative to non-buffered fluids in patients undergoing surgery.[1]

"The administration of an unbalanced crystalloid solution in vascular surgery patients in our study was associated with poor patient outcomes."[2]

Critically ill patients

"Among critically ill adults with sepsis, resuscitation with balanced fluids was associated with a lower risk of in-hospital mortality."[3]

Benefits of Sterofundin® ISO at a glance

- Isotonic to prevent undesired fluid shifts
- Contains all relevant electrolytes of the plasma – including calcium
- Contains metabolizable anions – lactate free

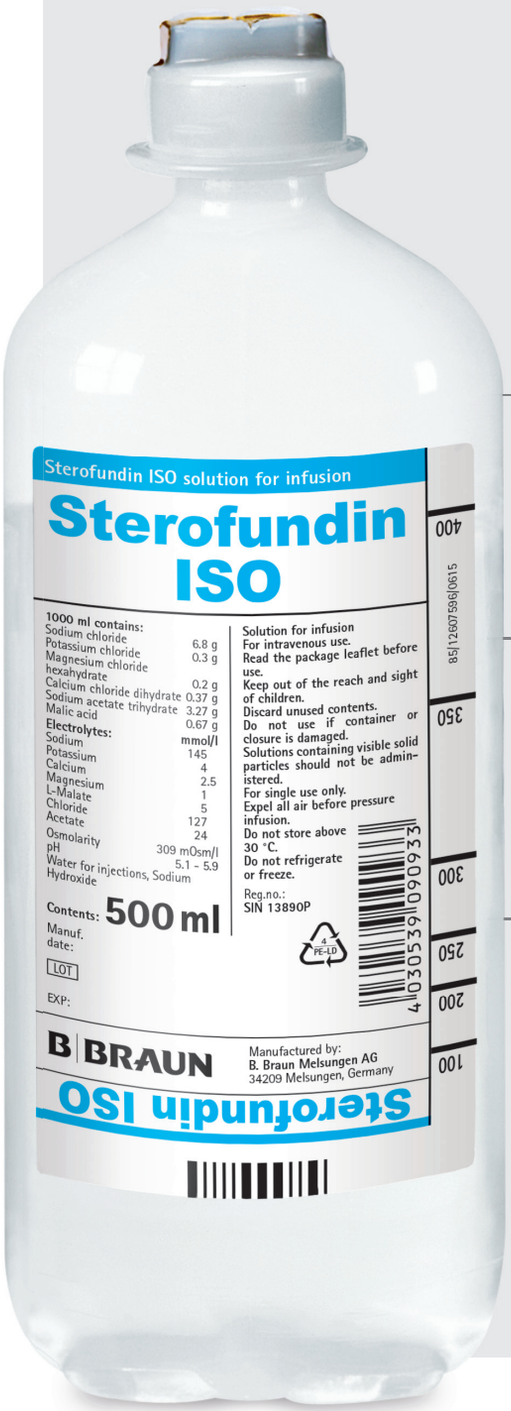
Sterofundin® ISO – isotonic and plasma adapted

	Kations				Anions				Osmolality mOsmol/kg H_2O
	Na^+	K^+	Ca^{2+}	Mg^{2+}	Cl^-	HCO_3	Acetate	Malate	
Plasma	142	4.5	2.5	1.25	103	24			290
Sterofundin® ISO	145	4	2.5	1	127		24	5	290
NaCl 0.9 %	154				154				290

Fluid & Volume Therapy

According to guidelines

Recent literature and guidelines suggest to use balanced electrolyte solutions rather than 0.9 % saline for fluid resuscitation.



German Society for Anesthesiology and Intensive Care:

Recommendations Guideline for Intravascular Volume Therapy in Adults

Balanced crystalloid isotonic electrolyte solution must be used for peri-interventional volume substitution & for critically ill ICU patients (GOR* A).

Isotonic NaCl must not be used as peri-interventional volume substitute and in intensive care medicine (GOR* A).[4]

German Society for Trauma Surgery:

Recommendations Guideline Polytrauma – Recommendations for Volume Therapy

Balanced crystalloid isotonic electrolyte solution should be used (GOR* B).[5]

Expert Panel Pediatrics, Germany:

Perioperative intravenous fluid therapy in children: Guidelines from the Association of the Scientific Medical Societies in Germany

Perioperative fluid therapy: Consensus-based recommendation. A balanced isotonic electrolyte solution should be used for fluid therapy.[6]

Ministry of Health, Malaysia:

Management of Dengue Infection in Adults (Third edition 2015)

Hyperchloremia, caused by the administration of large volumes of 0.9 % sodium chloride solution (chloride concentration of 154 mmol/l), may cause metabolic acidosis with normal lactate levels and present as a normal anion gap metabolic acidosis. If serum chloride levels increase, change the fluid to balanced solution such as Sterofundin® ISO or Hartmann's. This improves chloride-related acidosis.[7]

* GOR = Grade of Recommendation

Sterofundin® ISO

Contains malate and acetate – lactate free

The purpose of using balanced solutions is based on two principles:

1. Reducing the chloride content and its detrimental effects, while providing a plasma-like ionic content.
2. Increasing bicarbonate and pH by metabolism of bicarbonate precursors.[8]

Considering the use of lactate in balanced solutions

Although lactated infusion solutions such as Ringer's lactate are frequently applied, a number of considerations argue against the use of lactate:

- Lactate solutions may interfere with the diagnostic use of lactate as a maker of hypoxia.[9]
- Lactate is primarily metabolized in the liver, whereas acetate is metabolized in other organs including the muscles, brain, myocardium, and renal cortex.
- Malate is ubiquitously metabolized, no negative side effects known.[10]
- Acetate buffered crystalloid solutions do have a favorable influence on microcirculation.[11]

Acetate is metabolized regardless of liver function and may be the most efficient bicarbonate precursor.[8]

Acetate, malate, lactate, and gluconate are anions used in balanced solutions. However, gluconate is not considered to be a relevant bicarbonate precursor.[8]

Recommendations Guideline for Intravascular Volume Therapy in Adults

As they do not influence diagnostic criteria, balanced infusions containing acetate or malate instead of lactate may be integrated into the treatment algorithm for volume substitution in peri-interventional and critically ill patients (GOR* 0).[4]

Recommendations Guideline Polytrauma – Recommendations for volume therapy

Balanced solutions with acetate or malate may be used (GOR* 0).[5]

* GOR = Grade of Recommendation

Sterofundin® ISO

Balanced base excess

> *The BE_{pot} of a solution should be in the range of - 10 to 10 mmol/l* [13]

Acid-base balance

Infusion solutions without bicarbonate might cause dilutional acidosis. Adding the right concentration of metabolizable anions helps to prevent this complication.

BE_{pot} is an indicator to measure the influence of an infusion solution on the acid-base status. The BE_{pot} of a solution should be in the range of -10 to 10 mmol/l.

Sterofundin® ISO contains acetate and malate which are both precursors of bicarbonate. The potential base excess of the solution is 5 mmol/l which helps to correct acidosis.

Low chloride versus base excess

The combination of chloride and base excess is important. In the context of infusion solutions "balanced" means as physiological as possible. In the order of importance a solution should be assessed by:

1. The BE_{pot}
2. In-vivo Osmolality of 290 +/- 10 mosm/kg H_2O
3. The electrolyte pattern (Na^+, K^+, Cl^- including Ca^{2+} concentrations). [12]

- Sterofundin® ISO has a reduced chloride content compared to NS (127 versus 154 mmol/l)
- Sterofundin® ISO has a balanced base excess (+5 mmol/l)
- Other balanced solutions have a comparatively high amount of metabolizable anions and therefore a higher BE_{pot} which could have an impact on the acid-base metabolism of the patient (= alkalizing effect).

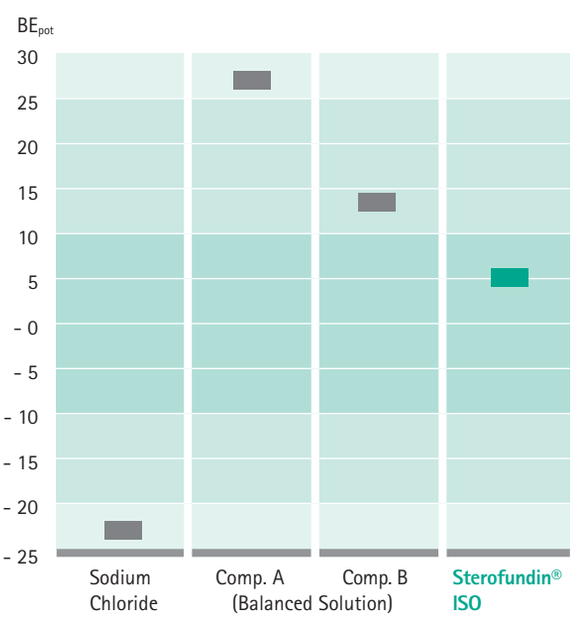


FIGURE 1 | BE_{pot} of Sodium Chloride, Competitor A, Competitor B, and Sterofundin® ISO

B. Braun Fluid Therapy Concept According to S3* Guidelines [4]

Infusion solutions substitute fluid and volume loss

DEHYDRATION (FLUID LOSS)

Administration of isotonic and plasma-adapted crystalloid solutions

Sterofundin® ISO

BLOOD LOSS (VOLUME LOSS)

Peri-interventionally	ICU
Balanced crystalloid: Sterofundin® ISO Balanced colloid: Gelaspan®, Tetraspan®	Balanced crystalloid: Sterofundin® ISO

CONTROL OF VOLUME THERAPY

Peri-interventionally	ICU
If Crystalloids are not considered sufficient	If Crystalloids are not considered sufficient
Balanced colloid: Gelaspan®, Tetraspan®	Balanced colloid: Gelaspan®

*S3 = formalized methodical development of the guideline (outcome analysis); national guideline (highest degree of guidelines)

For reference see S3 Guidelines for intravascular volume therapy in adults [4]

Product Information

Sterofundin® ISO solution for infusion

COMPOSITION
1,000 ml of 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
L-Malic acid	0.67 g
Electrolyte concentrations	
Sodium	145.0 mmol/l
Potassium	4.0 mmol/l
Magnesium	1.0 mmol/l
Calcium	2.5 mmol/l
Chloride	127.0 mmol/l
Acetate	24.0 mmol/l
Malate	5.0 mmol/l

Excipients
Water for injections, Sodium hydroxide (for pH adjustment)

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

CONTRAINDICATIONS
- Hypervolaemia
- Severe congestive cardiac failure
- Renal failure with oliguria or anuria
- Severe general oedema
- Hyperkalaemia
- Hypercalcaemia
- Metabolic alkalosis

Special warnings
Monitoring of the serum electrolytes, fluid balance, and pH is necessary.

UNDESIRABLE EFFECTS
Undesirable effects are listed according to their frequency terms used in this section:

Rare:	≥ 1/10,000 to < 1/1,000
Not known:	Cannot be estimated from the available data

Signs of overdose may occur.

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

Gastrointestinal disorders
Rare: Although oral magnesium salts stimulate peristalsis, paralytic ileus has been rarely reported after intravenous infusion of magnesium sulphate.

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

WARNINGS
Keep out of the sight and reach of children.
Do not reconnect partially used containers. Discard unused contents. Do not use if container or closure is damaged. Solutions containing visible solid particles should not be administered.

For single use only.

(Expel all air before pressure infusion.)[1]
1. For polyethylene plastic bottles only

MARKETING AUTHORIZATION HOLDER
B. Braun Melsungen AG, 34209 Melsungen, Germany

Last revision: 09/2014

Prescription only

Not all products are registered and approved for sale in all countries or regions. Indications of use may also vary by country and region. Please contact your country representative for product availability and information.

Gelaspan® solution for infusion

COMPOSITION
1,000 ml solution contain:

Succinylated gelatine (= modified fluid gelatine) (Molecular weight, weight average: 26,500 Dalton)	40.00 g
Sodium chloride	5.55 g
Sodium acetate trihydrate	3.27 g
Potassium chloride	0.30 g
Calcium chloride dihydrate	0.15 g
Magnesium chloride hexahydrate	0.20 g
Electrolyte concentrations	
Sodium	151 mmol/l
Chloride	103 mmol/l
Potassium	4 mmol/l
Calcium	1 mmol/l
Magnesium	1 mmol/l
Acetate	24 mmol/l

Excipients
Sodium hydroxide (for pH adjustment), Hydrochloric acid, diluted (for pH-adjustment), Water for injections

THERAPEUTIC INDICATIONS
Gelaspan® is a colloidal plasma volume substitute in an isotonic, fully balanced electrolyte solution for:
- Prophylaxis and treatment of imminent or manifest relative or absolute hypovolaemia and shock

CONTRAINDICATIONS
- Hypersensitivity to the active substance or to any of the excipients.
- Hypervolaemia
- Hyperhydration
- Hyperkalaemia

Special warnings
Gelaspan® should be administered with caution to patients with a history of allergic diseases, e.g. asthma. Gelatine preparations for volume replacement may rarely cause allergic (anaphylactic/anaphylactoid) reactions of varying degrees of severity. In order to detect the occurrence of an allergic reaction as early as possible, the first 20 – 30 ml should be infused slowly and the patient should be under careful observation especially at the beginning of the infusion. In case of an allergic reaction, the infusion must be stopped immediately and appropriate treatment given.

UNDESIRABLE EFFECTS
Undesirable effects are listed according to their frequency terms used in this section:

Uncommon:	≥ 1/1,000 to < 1/100
Rare:	≥ 1/10,000 to < 1/1,000
Very rare:	< 1/10,000

Immune system disorders
Rare: Anaphylactoid reactions, all grades.
Very rare: Severe anaphylactoid reactions

Cardiac disorders
Very rare: Tachycardia

Vascular disorders
Very rare: Hypotension

Respiratory, thoracic and mediastinal disorders
Very rare: Respiratory difficulties

Skin and subcutaneous tissue disorders
Rare: Allergic skin reactions

General disorders and administration site conditions
Uncommon: Mild transient increase of body temperature.
Very rare: Fever, chills

WARNINGS
Keep out of the sight and reach of children.
For single use only. Discard unused contents.
Only to be used if solution is clear, particle free and container and closure are undamaged.
Use immediately after first opening.
Expel all air before starting pressure infusion

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Product Information & Literature

Tetraspan® 60 mg/ml solution for infusion / Tetraspan® 100 mg/ml solution for infusion

COMPOSITION
1,000 ml of solution for infusion contain:

	Tetraspan® 60 mg/ml	Tetraspan® 100 mg/ml
Hydroxyethyl starch (HES)	60.0 g	100.0 g
Molar substitution:	0.42	0.42
Average molecular weight:	130,000 Da	130,000 Da
Sodium chloride	6.25 g	6.25 g
Potassium chloride	0.30 g	0.30 g
Calcium chloride dihydrate	0.37 g	0.37 g
Magnesium chloride hexahydrate	0.20 g	0.20 g
Sodium acetate trihydrate	3.27 g	3.27 g
L-Malic acid	0.67 g	0.67 g
Electrolyte concentration:		
Sodium	140 mmol/l	140 mmol/l
Potassium	4.0 mmol/l	4.0 mmol/l
Calcium	2.5 mmol/l	2.5 mmol/l
Magnesium	1.0 mmol/l	1.0 mmol/l
Chloride	118 mmol/l	118 mmol/l
Acetate	24 mmol/l	24 mmol/l
L-Malate	5.0 mmol/l	5.0 mmol/l

Excipients
Sodium hydroxide (for pH adjustment), Water for injection

THERAPEUTIC INDICATIONS
Tetraspan® is a solution for infusion for treatment of hypovolaemia due to acute blood loss when crystalloids alone are not considered sufficient.

CONTRAINDICATIONS
Hypersensitivity to the active substances or to any of the other excipients.
- Sepsis, burns, renal impairment or renal replacement therapy
- Intracranial or cerebral haemorrhage
- Critically ill patients (typically admitted to the intensive care unit)
- Hyperhydration
- Pulmonary oedema
- Dehydration
- Hyperkalaemia
- Severe hypernatraemia or severe hyperchloraemia
- Severely impaired hepatic function
- Congestive heart failure
- Severe coagulopathy
- Organ transplant patients

SPECIAL WARNINGS
Haemodynamic monitoring is required for volume and dose control. HES solutions should only be used when crystalloids alone are not sufficient. The use of HES must be discontinued at the first sign of renal injury, monitoring of renal function is recommended. Serum electrolytes and fluid balance should be monitored closely, volume overload must be avoided. Caution is to be exercised when treating patients with impaired hepatic function or in patients with blood coagulation disorders. Severe haemodilution must also be avoided in hypovolaemic patients. In case of repeated administration monitoring of blood coagulation parameters is recommended and the therapy must be discontinued at the first sign of coagulopathy. Sufficient fluid intake must be ensured.

Elderly patients, who are more likely to suffer from cardiac insufficiency and renal impairment, should be closely monitored during treatment and the dosage should be carefully adjusted.

Pediatric population: Due to limited data in children it is recommended not to use HES products in this population.

UNDESIRABLE EFFECTS
General
The most common side effects observed are directly related to the therapeutic effect of starch solutions and the volume given, i.e. dilution of the blood as a result of the filling of the intravascular space without administering blood components at the same time. Coagulation factor dilution can also occur.

Undesirable effects are listed according to their frequencies as follows:

Very common:	≥ 1/10
Common:	≥ 1/100 to < 1/10
Uncommon:	≥ 1/1,000 to < 1/100
Rare:	≥ 1/10,000 to < 1/1,000
Very rare:	< 1/10,000
Not known:	Cannot be estimated from the available data

Blood and lymphatic system disorders
Very common: Decreased haematocrit, reduced concentration of plasma proteins
Common: Dilution of coagulation factors, prolongation of bleeding time and aPTT, reduced level of FVIII/vWF complex[1]

Hepatobiliary disorders
Not known: Hepatic injury

Immune system disorders
Rare: Anaphylactic/Anaphylactoid reactions of various degrees
(see "Anaphylactic/Anaphylactoid reactions" below)

Renal and urinary disorders
Not known: Renal injury

General disorders and administration site conditions
Uncommon: Itching which responds poorly to any therapy[2]

Investigations
Very common: Increased serum α-amylase levels[3]

(1) Effects occur after administration of relatively large volumes of Hydroxyethyl starch and can affect blood coagulation.

(2) This itching can occur several weeks after the end of the starch infusions and can persist for months. The probability of this undesirable effect has not been sufficiently studied for Tetraspan 60 mg/ml.

(3) This effect is a result of the formation of an amylase complex of Hydroxyethyl starch with delayed renal and extrarenal elimination. This should not be misinterpreted as evidence of a pancreatic disorder.

Anaphylactic/Anaphylactoid reactions
After administration of Hydroxyethyl starch, anaphylactic/anaphylactoid reactions of various degrees can occur which are not dose-dependent. Therefore, all patients receiving starch infusion should be monitored closely for anaphylactic/anaphylactoid reactions. In the event of an anaphylactic/anaphylactoid reaction, the infusion should be discontinued immediately and the usual acute treatment initiated.

WARNINGS
Keep out of the sight and reach of children.
For single use only. Discard unused contents. Use immediately after first opening.
Use only if solution is clear and the container and closure are undamaged.
Expel all air before starting pressure infusion.

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Notes

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