NEW ZEALAND DATA SHEET

1. STAY SAFE BALANCE, Dialysis solution

stay•safe balance 1.5% glucose 1.25 mmol/L calcium peritoneal dialysis solution

stay•safe balance 2.3% glucose 1.25 mmol/L calcium peritoneal dialysis solution

stay•safe balance 4.25% glucose 1.25 mmol/L calcium peritoneal dialysis solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

stay•safe balance ready-to-use solution is available in a number of different strengths in various calcium ranges. ***stay•safe balance*** 1.5%/2.3%/4.25% glucose, 1.25 mmol/L calcium is delivered in a double chamber bag. One chamber contains the alkaline lactate solution, the other chamber contains the acidic glucose-based electrolyte solution. Mixing of both solutions by opening the middle seam between the two chambers results in the neutral ready-to-use solution.

BEFORE RECONSTITUTION

1 litre of acidic glucose based electrolyte solution contains:

	stay•safe balance 1.5% glucose, 1.25 mmol/L calcium	*stay •safe balance* 2.3% glucose, 1.25 mmol/L calcium	*stay •safe balance* 4.25% glucose, 1.25 mmol/L calcium
Calcium chloride dihydrate	0.3675 g	0.3675 g	0.3675 g
Sodium chloride	11.279 g	11.279 g	11.279 g
Magnesium chloride hexahydrate	0.2033 g	0.2033 g	0.2033 g
Glucose monohydrate (anhydrous glucose)	33.0 g (30.0 g)	50.0 g (45.46 g)	93.5 g (85.0 g)

1 litre of alkaline lactate solution contains:
Sodium (S)-lactate solution 15.69 g
(sodium (S)-lactate 7.85 g)

AFTER RECONSTITUTION

1 litre of the neutral ready-to-use solution contains:

	stay•safe balance 1.5% glucose, 1.25 mmol/L calcium	*stay•safe balance* 2.3% glucose, 1.25 mmol/L calcium	*stay•safe balance* 4.25% glucose, 1.25 mmol/L calcium
Calcium chloride dihydrate	0.1838 g	0.1838 g	0.1838 g
Sodium chloride	5.640 g	5.640 g	5.640 g
Sodium (S)-lactate	3.925 g	3.925 g	3.925 g
Magnesium chloride hexahydrate	0.1017 g	0.1017 g	0.1017 g

Glucose monohydrate (anhydrous glucose)	16.5 g (15.0 g)	25.0 g (22.73 g)	46.75 g (42.5 g)
Ca^{2+}	1.25 mmol	1.25 mmol	1.25 mmol
Na^{+}	134 mmol	134 mmol	134 mmol
Mg^{2+}	0.5 mmol	0.5 mmol	0.5 mmol
Cl^{-}	100.5 mmol	100.5 mmol	100.5 mmol
(S)-Lactate	35 mmol	35 mmol	35 mmol
Glucose	83.2 mmol	126.1 mmol	235.8 mmol
Theoretical osmolarity	356 mOsm	399 mOsm	509 mOsm
pH ≈	7.0	7.0	7.0

For the full list of excipients, see Section 6.1 List of excipients.

3. PHARMACEUTICAL FORM

Dialysis solution.

stay•safe balance is a double chamber bag containing clear and colourless aqueous solutions.

4. CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

For use as a peritoneal dialysis solution in the management of end-stage renal disease.

4.2 DOSE AND METHOD OF ADMINISTRATION

Dose

stay•safe balance **solutions are indicated exclusively for intraperitoneal use.**

For use in one patient, on one occasion only. Does not contain antimicrobial preservatives.

The mode of therapy, frequency of administration and dwell time required will be specified by the attending physician. Unless otherwise advised, patients will receive an infusion of 2000 mL solution per exchange four times a day. After a dwell time between 2 and 10 hours, the solution will be drained. Adjustment of dosage, volume and number of exchanges will be necessary for individual patients.

Dose adjustment

If pain due to abdominal distension occurs at the commencement of peritoneal dialysis, the solution volume per exchange should be temporarily reduced to 500 – 1500 mL. In large patients and if residual renal function is lost, an increased volume of dialysis solution will be necessary. In these patients or in patients who will tolerate larger volumes, a volume of 2500 mL – 3000 mL solution per exchange may be given.

In children, the solution volume per exchange should be reduced according to age, height and body weight. The usual dose is 30 – 40 mL/Kg body weight per exchange. There are no special dosage adjustments necessary for elderly patients.

Peritoneal dialysis solutions with a high glucose concentration (2.3% or 4.25%) are used when the body weight is above the desired dry weight. The withdrawal of fluid from the body increases

in relation to the glucose concentration of the peritoneal dialysis solution. These solutions should be used cautiously to handle the peritoneal membrane with care, to prevent dehydration and in order to keep the glucose burden as low as possible.

See Section 4.4 Special warnings and precautions for use for recommended regular monitoring.

Method of administration

Dialysis using the prescribed doses should be performed daily. Peritoneal dialysis is a long-term therapy involving repeated administrations of single solutions. Before performing peritoneal dialysis at home, the patient must be trained appropriately, must practise the technique and be shown to be proficient. Peritoneal dialysis should be continued for as long as renal function substitution therapy is required.

The solution bag is warmed up to body temperature. For patients using ***stay•safe balance*** solutions, the heating will be performed with a heating plate. A microwave oven must **not** be used due to the risk of overheating.

The solutions in the two chambers must be mixed just before use. The mixed solution should be used immediately, but within a maximum of 24 hours after mixing. Do not use before mixing.

For that purpose, pressure must be exerted on one solution chamber by rolling up the bag from one of the side edges until the middle seam opens. Due to the design of the bag the pressure will first open the middle seam allowing the mixture of both solutions by creating one single chamber. Then a renewed pressure by rolling up the bag from the upper edge breaks the seam of the solution free outflow part ensuring that only mixed solution can be infused over 5 to 20 minutes through the peritoneal dialysis catheter into the peritoneal cavity.

Depending on the required osmotic pressure, ***stay•safe balance*** solutions with lower or higher glucose content can be used sequentially.

4.3 CONTRAINDICATIONS

Solution for peritoneal dialysis must not be used for intravenous infusion.

stay•safe balance 1.5% glucose, 1.25 mmol/L calcium and ***stay•safe balance*** 2.3% glucose, 1.25 mmol/L calcium:
Must not be used in patients with lactic acidosis, severe hypokalaemia, or severe hypocalcaemia

stay•safe balance 4.25% glucose, 1.25 mmol/L calcium:
Must not be used in patients with lactic acidosis, severe hypokalaemia, severe hypocalcaemia, hypovolaemia, or arterial hypotension

Peritoneal dialysis in general

Peritoneal dialysis should not be commenced if any of the following are present:

- Recent abdominal surgery or injury, a history of abdominal operations with fibrous adhesions, abdominal burns, bowel perforations.
- Extensive inflammatory conditions of the abdominal skin (dermatitis)

- Inflammatory bowel disease (Crohn's disease, ulcerative colitis, diverticulitis)
- Peritonitis
- Internal or external abdominal fistula
- Umbilical, inguinal or other abdominal hernia
- Intra-abdominal tumours
- Ileus
- Pulmonary disease (especially pneumonia)
- Sepsis
- Extreme hyperlipidaemia
- In rare cases of uraemia, which cannot be managed by peritoneal dialysis
- Cachexia and severe weight loss, particularly in cases where ingestion of adequate protein is not guaranteed
- Patients who are physically or mentally incapable of performing peritoneal dialysis as instructed by the physician

If any of the above mentioned disorders develops during treatment with peritoneal dialysis, the attending physician will have to decide how to proceed.

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Encapsulating peritoneal sclerosis is considered to be a known, rare complication of peritoneal dialysis therapy which can infrequently lead to fatal outcome.

Before performing peritoneal dialysis at home, the patient must be trained appropriately, must practise the technique and be shown to be proficient. The training should be performed by qualified personnel. The attending physician must ensure that the patient masters the handling techniques sufficiently before being discharged to carry out peritoneal dialysis at home. In case of any problems or uncertainty, the attending physician should be contacted. Peritoneal dialysis should be continued for as long as renal function substitution therapy is required (Section 4.2 Dose and method of administration).

The effluent should be checked for clarity and volume. Turbidity, which may or may not be accompanied by abdominal pain, or abdominal pain alone are indicators of peritonitis.

A loss of proteins, amino acids, and water soluble vitamins occurs during peritoneal dialysis. To avoid deficiencies, an adequate diet or supplementation should be ensured. The transport characteristics of the peritoneal membrane may change during long term peritoneal dialysis primarily indicated by a loss of ultrafiltration. In severe cases peritoneal dialysis must be stopped and haemodialysis commenced.

Use with caution in the following circumstances

stay•safe balance solutions should only be administered after careful benefit-risk assessment in:

- Loss of electrolytes due to vomiting and/or diarrhoea (a temporary change to a peritoneal dialysis solution containing potassium may then become necessary)
- Digitalis therapy: regular monitoring of the serum potassium level is mandatory. Severe hypokalaemia may necessitate the use of potassium-containing dialysis

solution together with dietary counselling.

- Patients with large polycystic kidneys

stay•safe balance solutions containing 1.25 mmol/L calcium

- Patients with hyperparathyroidism: Therapy should include the administration of calcium containing phosphate binders and/or vitamin D to ensure adequate enteral calcium supply.
- Hypocalcaemia. It may be necessary to use a peritoneal dialysis solution with a higher calcium concentration either temporarily or permanently in case adequate enteral supply of calcium, by calcium-containing phosphate binders and /or vitamin D, is not possible.

Regular monitoring of the following parameters is recommended

- Body weight for the early recognition of over- or underhydration
- Serum sodium, potassium, calcium, magnesium, phosphate, acid base status, blood gases and blood proteins
- Serum creatinine and urea
- Parathormone and other indicators of bone metabolism
- Blood sugar
- Residual renal function in order to adapt the peritoneal dialysis

Check the following before use

Plastic containers may occasionally be damaged during transport or storage. This can result in a contamination with growth of microorganisms in the dialysis solutions. Thus all containers should be carefully inspected for damage prior to connection of the bag and prior to use of the peritoneal dialysis solution. Any damage, even minor, to connectors at the closure, container welds and corners must be noted because of possible contamination. Inspect the integrity of the middle seam. Damaged bags or bags with cloudy content should never be used.

The solution must only be used if the solution for dialysis is clear and the container undamaged. Any unused portion of the solution is to be discarded. The overwrap should only be removed before administration. Do not use before mixing. The solutions in the two chambers should be mixed just before use. The mixed solution should be used immediately, but within a maximum of 24 hours after mixing. Aseptic conditions must be maintained during dialysate exchange in order to reduce the risk of infection.

Use in diabetic patients

The daily dose of insulin or oral hypoglycaemic medicinal products should be adjusted to take account of the increased glucose load in patients with diabetes. Blood glucose levels should be checked regularly.

Use in the elderly

The increased risk of hernia should be considered in elderly patients prior to the start of peritoneal dialysis.

Paediatric population

In children, the dialysate volume should be reduced in accordance with age, height and body weight (see Section 4.2 Dose and method of administration).

Effects on laboratory tests

None reported.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

The use of peritoneal dialysis solutions can lead to a loss of efficacy of other medicinal products if these are dialyzable through the peritoneal membrane. A dose adjustment may be necessary.

A distinct reduction in serum potassium level can increase the frequency of digitalis associated adverse reactions. Potassium levels must be monitored particularly closely during concurrent digitalis therapy.

The concurrent administration of calcium containing medicinal products or vitamin D may cause hypercalcaemia when using solutions of high calcium concentration.

The use of diuretic agents may help maintain residual diuresis, but may also result in water and electrolyte imbalances.

4.6 FERTILITY, PREGNANCY AND LACTATION

Pregnancy

There is no adequate data from the use of ***stay•safe balance*** solutions in animal studies or in pregnant women. The safe use of this product during pregnancy has therefore not been determined. Peritoneal dialysis should be performed during pregnancy only after careful weighing of the potential risks and benefits to mother and foetus.

Breast-feeding

The safe use of ***stay•safe balance*** solutions during lactation has not been determined.

Fertility

No information available.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

stay•safe balance solutions have no or negligible influence on the ability to drive or use machinery.

4.8 UNDESIRABLE EFFECTS

Possible adverse reactions may result from the peritoneal dialysis technique or may be induced by the peritoneal dialysis solution. Very common adverse reactions of peritoneal dialysis are peritonitis and skin exit site infections. Other adverse reactions are less frequent.

Potential adverse reactions of the peritoneal dialysis solutions:

Endocrine disorders

Secondary hyperparathyroidism with potential disturbances of the bone metabolism

when using solutions of low calcium concentration.

Metabolism and nutrition disorders

Increased blood sugar levels, hyperlipidaemia, hypoproteinaemia, increase in body weight due to the continuous uptake of glucose from the peritoneal dialysis solution.

Cardiac and vascular disorders

Tachycardia, hypotension, hypertension.

Respiratory, thoracic and mediastinal disorders

Dyspnoea.

Renal and urinary disorders

Electrolyte disturbances, e.g. hypokalaemia, hypocalcaemia when using solutions of lower calcium concentration.

General disorders and administration site conditions

Dizziness, oedema, disturbances in hydration indicated either by a rapid decrease (dehydrations) or increase (overhydration) in body weight. Severe dehydration may occur when using solutions of higher glucose concentration and can cause low blood pressure, increase heart rate, dizziness and muscle cramps. Overhydration can cause increased body weight, high blood pressure, swollen legs and shortness of breath.

Potential adverse reactions of the treatment mode:

Infections and infestations

Peritonitis, skin exit site and tunnel infections, in very rare cases sepsis.

Peritonitis is indicated by a cloudy effluent. Later, abdominal pain, fever and general malaise may develop or, in very rare cases, sepsis. The patient should seek medical advice immediately. The bag with the cloudy effluent should be closed with a sterile cap and assessed for microbiological contamination and white blood count.

In cases of skin exit site and tunnel infections, the attending physician should be consulted as soon as possible.

Respiratory, thoracic and mediastinal disorders

Dyspnoea caused by elevated diaphragm, shoulder pain.

Gastrointestinal disorders

Diarrhoea, constipation, hernia, abdominal distension and sensation of fullness, encapsulating peritoneal sclerosis.

General disorders and administration/catheter site conditions

General malaise, redness, oedema, exudations, crusts and pain at the catheter exit site.

Peritoneal dialysis procedure related disorders

Inflow and outflow disturbances of the dialysis solution.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://pophealth.my.site.com/carmreportnz/s/

4.9 OVERDOSE

No emergency situations in connection with overdose have been reported.

Excessive inflow of dialysis solution is easily drained into an empty bag. However, if the bag exchanges have been carried out too frequently or too rapidly, states of dehydration and/or electrolyte disturbances can occur which necessitate immediate medical attention. If an exchange has been forgotten, then the attending physician or dialysis centre in charge should be contacted.

Incorrect balancing can lead to overhydration or dehydration and electrolyte disturbances. The most likely consequence of an Overdosage with ***stay•safe balance*** solutions is dehydration. Underdosage, interruption of treatment or discontinuation of treatment may lead to life-threatening overhydration with peripheral oedema and cardiac decompensation and/or other symptoms of uraemia, which may endanger life. The generally accepted rules for emergency care and intensive therapy must be applied. The patient may require immediate haemodialysis.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764766).

5. PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of action

stay•safe balance solutions are lactate-buffered, glucose containing electrolyte solutions indicated for intraperitoneal administration for the treatment of end-stage renal failure of any origin. The characteristic of continuous ambulatory peritoneal dialysis (CAPD) is the more or less continuous presence of usually two litres of dialysis solutions in the peritoneal cavity. This dialysis solution is replaced by fresh solution three to five times a day.

The basic principle behind every peritoneal dialysis technique is the use of the peritoneum as the semi-permeable membrane allowing the exchange of solutes and water between blood and the dialysis solution by diffusion and convection according to their physico-chemical properties.

The electrolyte profile of the solution is basically the same as that of physiological serum, although it has been adapted (e.g. the potassium content) for use in uraemic patients to enable renal function substitution therapy by means of the intraperitoneal substances and fluid exchange. Dialysis solutions containing low calcium concentration (1.0 mmol/L and 1.25 mmol/L) have been shown to reduce the risk of hypercalcaemia during concomitant treatment with calcium containing phosphate binders and/or vitamin D. Substances which are normally eliminated with the urine, like uraemic waste products, such as urea and creatinine, inorganic phosphorus, uric acid, other solutes and water, are removed from the body into the dialysis solution. The fluid balance can be maintained by the administration of different glucose-concentrations in the

solution, effecting the fluid removal (ultrafiltration). Metabolic acidosis secondary to end-stage renal failure is counterbalanced by the presence of lactate in the solution. The complete metabolism of lactate results in the generation of bicarbonate.

5.2 PHARMACOKINETIC PROPERTIES

Uraemic waste products (e.g. urea, creatinine, uric acid), inorganic phosphate and electrolytes like sodium, potassium, calcium and magnesium are removed from the body to the dialysis solution by diffusion and/or convection.

Glucose in the dialysate is used as an osmotic agent. It is slowly absorbed, reducing the diffusion gradient between dialysis solution and extracellular fluid. The ultrafiltration is maximal at the beginning of the dwell time, reaching a peak after about two to three hours. Later absorption starts with a progressive loss of ultrafiltrate. During a dialysis period of six hours, 60%-80% of dialysate glucose is absorbed.

The transfer of calcium depends on the glucose concentration in the dialysis solution, the effluent volume and serum calcium concentration, and the lower the calcium concentration in the dialysis solution, the higher the calcium transfer from the patient to the dialysate.

5.3 PRECLINICAL SAFETY DATA

No carcinogenic or mutagenic studies with ***stay•safe balance*** solutions have been carried out.

6. PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Water for injections
Sodium hydroxide
Sodium bicarbonate
Hydrochloric acid

6.2 INCOMPATIBILITIES

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

6.3 SHELF LIFE

Shelf life as packed for sale: 2 years.

The expiry date can be found on the packaging.

Shelf life of the ready to use solution

The ready to use solution should be used immediately, but within a maximum of 24 hours after mixing.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 25 ˚C. Do not refrigerate.

6.5 NATURE AND CONTENTS OF CONTAINER AND SPECIAL EQUIPMENT FOR USE AND ADMINISTRATION

The ***stay•safe balance*** system consists of a double chamber solution bag, a tubing system, a system connector with a rotating switch and a drainage bag. The system is presented with a clear protective overwrap.

stay•safe balance is available in cartons containing flexible, non-PVC bags: 6 bags of 1500 mL, 4 bags of 2000 mL, 4 bags of 2500 mL and 4 bags of 3000 mL .

Not all pack sizes may be marketed.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

Any unused medicine or waste material should be disposed of in accordance with local requirements.

6.7 PHYSICOCHEMICAL PROPERTIES

Chemical structure
Not applicable.

CAS number
Not applicable

7. MEDICINE SCHEDULE

General sale

8. SPONSOR

Maxx Pharma NZ Limited

Level 4, 21 Queen Street

Auckland 1010

NEW ZEALAND

medical@maxxpharma.com.au

Telephone 0800 437 202

9. DATE OF FIRST APPROVAL

17 October 2002

10. DATE OF REVISION

31 January 2025

SUMMARY TABLE OF CHANGES

Section Changed	Summary of new information
2	Correction of an error in the units of the active ingredients Ca^{2+}, Na^{+}, Mg^{2+}, Cl^{-}, (S)-lactate and glucose after reconstitution from "mmol/L" to "mmol". Correction of an error in the units for theoretical osmolarity after reconstitution from "mOsm/L" to "mOsm".
4.3	Removal of the contraindications "severe dehydration" and "hypotonia" for clarity.
4.9	Revision to the instruction in the event a patient forgets an exchange from reducing the swell times of the next bags to contacting the attending physician or dialysis centre in charge for advice.
6.3	Editorial change – update to the wording of the shelf-life for clarity, and addition of information regarding the product expiry date.
6.5	Editorial change – update to the wording for clarity.
6.7	Editorial change – update to the heading format for "Chemical structure" and "CAS number".
8	Updated Sponsor Details

Version 3.0