balance

1.5 % glucose

1.25 mmol/l calcium

Package Insert

balance 1.5% glucose, 1.25 mmol/l calcium, solution for peritoneal dialysis

1. NAME OF THE MEDICINAL PRODUCT

STAY SAFE BALANCE 1.5% glucose 1.25 mmol/L calcium peritoneal dialysis solution bag

Further denominated as *balance* 1.5% glucose, 1.25 mmol/l calcium

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

balance 1.5% 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:

Calcium chloride dihydrate	0.3675 g
Sodium chloride	11.279 g
Magnesium chloride hexahydrate	0.2033 g
Glucose monohydrate (anhydrous glucose)	33.0 g (30.0 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:

Calcium chloride dihydrate	0.1838 g
Sodium chloride	5.640 g
Sodium (S)-lactate solution (sodium (S)-lactate)	7.85 g (3.925 g)
Magnesium chloride hexahydrate	0.1017 g
Glucose monohydrate (anhydrous glucose)	16.5 g (15.0 g)

Ca^{2+}	1.25 mmol
Na^{+}	134 mmol
Mg^{2+}	0.5 mmol
Cl^{-}	100.5 mmol
(S)-Lactate	35 mmol
Glucose	83.2 mmol

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for peritoneal dialysis

Double chamber bag containing clear and colourless aqueous solutions

For the ready-to-use solution:

Theoretical osmolarity 356 mOsm/l

pH ≈ 7.0

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

End-stage (decompensated) chronic renal failure of any origin which can be treated with peritoneal dialysis.

4.2 Posology and method of administration

Posology

This solution is indicated exclusively for intraperitoneal use.

The mode of therapy, frequency of administration, and dwell time required will be specified by the attending physician.

Continuous ambulatory peritoneal dialysis (CAPD)

Adults:

Unless otherwise prescribed, 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.

If dilation pain 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 patients who tolerate larger volumes, a volume of 2500-3000 ml solution per exchange may be given.

Paediatric population:

In children the solution volume per exchange should be prescribed according to age and body surface area (BSA).

For initial prescription, the volume per exchange should be 600-800 ml/m² BSA with 4 (sometimes 3 or 5) exchanges per day. It can be increased up to 1000-1200 ml/m² BSA depending on tolerance, age and residual renal function.

There are no special dosage recommendations for the elderly.

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.

Peritoneal dialysis is a long-term therapy involving repeated administrations of single solutions.

balance 1.5% glucose, 1.25 mmol/l calcium contains 15 g glucose in 1000 ml solution.

Method and duration of administration

Before performing peritoneal dialysis at home the patient must be trained appropriately, must practice 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.

Dialysis using the prescribed doses should be performed daily and should be continued for as long as renal function substitution therapy is required.

Continuous ambulatory peritoneal dialysis (CAPD): *stay•safe*® bag

The solution bag is first warmed up to body temperature. For details see section 6.6.

The appropriate dose is infused in the peritoneal cavity using a peritoneal catheter over 5 - 20 minutes. Depending on physician's instructions, the dose should dwell in the peritoneal cavity for 2 to 10 hours (equilibrium time), and then be drained.

Depending on the required osmotic pressure, *balance* 1.5% glucose, 1.25 mmol/l calcium can be used sequentially with other peritoneal dialysis solutions with higher glucose content (i.e. with higher osmolarity).

4.3 Contraindications

For this specific peritoneal dialysis solution

balance 1.5% glucose, 1.25 mmol/l calcium must not be used in patients with lactic acidosis, severe hypokalaemia and severe hypocalcaemia.

For 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, severe abdominal burns, bowel perforation,
- extensive inflammatory conditions of the abdominal skin (dermatitis),
- inflammatory bowel diseases (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 the peritoneal dialysis, the attending physician will have to decide on how to proceed.

4.4 Special warnings and precautions for use

The solution for peritoneal dialysis must not be used for intravenous infusion.

This solution may only be administered after careful benefit-risk assessment in:

- 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 an adequate enteral supply of calcium, by calcium-containing phosphate binders and/or vitamin D, is not possible.
- loss of electrolytes due to vomiting and/or diarrhoea (a temporary change to a peritoneal dialysis solution containing potassium might then become necessary).

MAL

0875480_05_jd_ETW_Korr02.indd 15 23.06.2025 13:34:47

- patients receiving digitalis therapy: Regular monitoring of the serum potassium level is mandatory (see section 4.5). Severe hypokalaemia may necessitate the use of a potassium-containing dialysis solution together with dietary counselling.
- patients with large polycystic kidneys.

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.

Regular monitoring of the following parameters is recommended:

- body weight for the early recognition of over- and dehydration,
- 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.

The effluent should be checked for clarity and volume. Turbidity and/or abdominal pain are indicators of peritonitis.

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

Elderly

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

4.5 Interaction with other medicinal products and other forms of interaction

The use of this peritoneal dialysis solution can lead to a loss of efficacy of other medicinal products if these are dialysable through the peritoneal membrane. A dose adjustment might be necessary.

A distinct reduction of the serum potassium level can increase the frequency of digitalis-associated adverse reactions. Potassium levels must be monitored particularly closely during concurrent digitalis therapy (see section 4.4).

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

In diabetic patients the daily dose of insulin or oral hypoglycaemic medicinal products must be adjusted to take account of the increased glucose load.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no or limited amount of data from the use of *balance* solutions in pregnant women. Data from animal studies are lacking (see section 5.3). When considering peritoneal dialysis as a possible therapy during pregnancy, the benefit of therapy should be weighed against the potential risks and complications for mother and child.

Breastfeeding

The components of *balance* are excreted in human milk. With adequate therapy, however, no adverse effects are expected in the child. A temporary interruption of breastfeeding may be considered, taking into account the benefit of breastfeeding for the child and the benefit of therapy for the mother.

Fertility

There are no clinical data available on the possible effects on fertility. In therapeutic use, however, no effects are expected on fertility.

4.7 Effects on ability to drive and use machines

balance 1.5% glucose, 1.25 mmol/l calcium has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

balance 1.5% glucose, 1.25 mmol/l calcium is an electrolyte solution the composition of which is similar to blood. In addition the solution has a neutral pH which is similar to the physiological pH value.

Possible adverse reactions may result from the peritoneal dialysis itself or may be induced by the peritoneal dialysis solution.

The adverse drug reactions are ranked under the headings of reporting frequency, using the following convention:

very common	≥1/10
common	≥1/100 to <1/10
uncommon	≥1/1000 to <1/100
rare	≥1/10000 to <1/1000
very rare	<1/10000
not known	cannot be estimated from the available data

Potential adverse reactions of the peritoneal dialysis solution

Endocrine disorders

- Secondary hyperparathyroidism with potential disturbances of the bone metabolism (not known)

Metabolism and nutrition disorders

- Increased blood sugar levels (common)
- Hyperlipidaemia (common)
- Increase in body weight due to the continuous uptake of glucose from the peritoneal dialysis solution (common)

Cardiac and vascular disorders

- Tachycardia (uncommon)
- Hypotension (uncommon)
- Hypertension (uncommon)

Respiratory, thoracic and mediastinal disorders

- Dyspnoea (uncommon)

Renal and urinary disorders

- Electrolyte disturbances, e.g. hypokalaemia (very common)
- Hypocalcaemia (uncommon)

General disorders

- Dizziness (uncommon)
- Oedema (uncommon)
- Disturbances in hydration (uncommon) indicated either by a rapid decrease (dehydration) or increase (overhydration) in body weight. Severe dehydration might occur when using solutions of higher glucose concentration.

Potential adverse reactions of the treatment mode

Infections and infestations

- Peritonitis (very common) 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 cell count.
- Skin exit site and tunnel infections (very common). In case of skin exit site and tunnel infections the attending physician should be consulted as soon as possible.
- Sepsis (very rare)

Respiratory, thoracic and mediastinal disorders

- Shoulder pain (common)
- Dyspnoea caused by the elevated diaphragm (not known)

Gastrointestinal disorders

- Hernia (very common)
- Abdominal distension and sensation of fullness (common)
- Diarrhoea (uncommon)
- Constipation (uncommon)
- Encapsulating peritoneal sclerosis (not known)

General disorders and administration/catheter site conditions

- Redness, oedema, exudations, crusts and pain at the catheter exit site (very common)
- In- and outflow disturbances of the dialysis solution (common)
- General malaise (not known)

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. Healthcare professionals are asked to report any suspected adverse reactions via national health authority.

4.9 Overdose

No emergency situations in connection with overdose have been reported.

Any excess of dialysis solution infused in the peritoneal cavity can easily be drained into the drainage bag. In case of too frequent exchanges dehydration and/or electrolyte disturbances might result 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 hyper- or dehydration and electrolyte disturbances.

The most likely consequence of an overdosage with *balance* 1.5% glucose, 1.25 mmol/l calcium is dehydration.

Underdosage, interruption of treatment or discontinuation of treatment may lead to life-threatening hyperhydration 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.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Peritoneal dialytics, hypertonic solutions

ATC code: B05D B

balance 1.5% glucose, 1.25 mmol/l calcium is a lactate-buffered, glucose-containing electrolyte solution indicated for intraperitoneal administration for the treatment of end-stage renal failure of any origin by continuous ambulatory peritoneal dialysis (CAPD).

The characteristic of continuous ambulatory peritoneal dialysis (CAPD) is the more or less continuous presence of usually 2 litres of dialysis solution 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 a semi-permeable membrane allowing the exchange of solutes and water between the 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 intraperitoneal substances and fluid exchange.

0875480_05_jd_ETW_Korr02.indd 16 23.06.2025 13:34:47

The calcium concentration of this dialysis solution is 1.25 mmol/l, which has 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 phosphate, 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 in *balance* 1.5% glucose, 1.25 mmol/l calcium. 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.

After 4 hours the ultrafiltrate averages 100 ml with a 1.5%, 400 ml with a 2.3%, and 800 ml with a 4.25% glucose solution. During the dialysis period of six hours 60 to 80% of dialysate glucose is absorbed.

Lactate used as the buffering agent is almost completely absorbed after a 6 hour dwell time. In patients with a normal hepatic function lactate is rapidly metabolised demonstrated by normal values of intermediate metabolites.

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

It has been estimated that a typical CAPD schedule of three 1.5 % and one 4.25 % glucose containing solutions per day with a calcium concentration of 1.25 mmol/l would remove up to 160 mg calcium per day enabling a higher oral intake of calcium containing medicinal products and vitamin D without the risk of hypercalcaemia.

5.3 Preclinical safety data

No preclinical toxicity studies with *balance* 1.5% glucose, 1.25 mmol/l calcium have been carried out. The electrolytes and glucose included in *balance* are physiological components in human plasma. Thus, no toxic effects are expected to occur as long as the indications, contraindications and dosage recommendations are adequately observed.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Water for injections
Hydrochloric acid
Sodium hydroxide
Sodium hydrogen carbonate

6.2 Incompatibilities

Because of the risk of incompatibility and of contamination medicinal products must only be added when prescribed by a physician.

This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.

6.3 Shelf life

Shelf life as packed for sale: 2 years.

Shelf life of the ready-to-use solution prepared as described in section 6.6 and without any additional medicinal products: Chemical and physical in-use stability has been demonstrated for 24 hours at 20 °C.

6.4 Special precautions for storage

Do not store below 4 °C.

6.5 Nature and contents of container

Double chamber bag:

Lactate solution : glucose-based electrolyte solution = 1:1

Double chamber bag system consisting of a non-PVC double chamber solution bag which is wrapped in a protective bag, both made of multi layer polyolefine-based foils.

stay•safe®:

The *stay•safe®* system contains the double chamber bag system, a tubing system made of polyolefines, a system connector (DISC) with a rotable switch (polypropylene) and a drainage bag, also made of polyolefine-based multi layer film.

Pack sizes:

stay•safe®
4 bags each containing 2000 ml
4 bags each containing 2500 ml

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements for disposal.

For single use only. Any unused portion of the solution is to be discarded.

***stay•safe®* system** for continuous ambulatory peritoneal dialysis (CAPD):

The solution bag is first warmed up to body temperature. For bags with a volume up to 3000 ml this should be done using an appropriate bag warmer. The heating time depends on bag volume and the used bag warmer (for a 2000 ml bag with a starting temperature of 22 °C usually 120 min.). The temperature control is done automatically and is set to 39 °C ± 1 °C. More detailed information can be obtained from the operating instructions of the bag warmer. Use of microwaves is not recommended due to the risk of local overheating.

1. Preparation of the solution

◗ Check the warmed solution bag (label, expiry date, clearness of the solution, bag and overwrap not damaged, integrity of peel seams). ◗ Place the bag on a solid surface. ◗ Open the overwrap of the bag and the packaging of the disinfection cap. ◗ Wash your hands with an antimicrobial washing lotion. ◗ Roll up the bag, which is lying on the outer wrapping foil, from one of the side edges until the middle seam opens. The solutions in the two chambers are mixed automatically. ◗ Now roll up the bag from the upper edge until the peel seam of the lower triangle is completely open. ◗ Check whether all peel seams are completely open. ◗ Check whether the solution is clear and that the bag is not leaking.

2. Preparation of the bag exchange

◗ Hang the solution bag in the upper hole of the infusion pole, unroll the tubing line of the solution bag, and place the DISC into the organizer. After unrolling the tubing line to the drainage bag, hang the drainage bag in the lower hole of the infusion pole. ◗ Place catheter connector into one of the two inserts of the organizer. ◗ Place the new disinfection cap into the other free insert. ◗ Disinfect your hands and remove the protection cap of the DISC. ◗ Connect catheter connector to the DISC.

3. Outflow

◗ Open the clamp on the extension. The outflow starts. ◗ Position ●

4. Flush

◗ After completion of outflow flush fresh solution into the drainage bag (approx. 5 seconds). ◗ Position ●●

5. Inflow

◗ Start inflow by turning the control switch to ◗ Position ○◑●

6. Safety step

◗ Close the catheter extension by introducing the PIN into the catheter connector. ◗ Position ●●●●

7. Disconnection

◗ Remove protection cap from the new disinfection cap and screw it onto the old one. ◗ Screw the catheter connector off the DISC and screw the catheter connector to the new disinfection cap.

8. Closure of the DISC

◗ Close the DISC with the open end of the used disinfection cap, which has remained in the right hole of the organizer.

9. Check the drained dialysate for clarity and weight **and** if the effluent is clear **discard it.**

See also section 4.2.

Handling

The ready-to-use solution should be used immediately, but if this is not possible within a maximum of 24 hours after mixing (see also section 6.3).

Plastic containers may occasionally be damaged during transport or storage. This can result in a contamination with growth of microorganisms in the dialysis solution. 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. Damaged bags or bags with cloudy content should never be used.

This solution must only be used if the solution for dialysis is clear and the container undamaged.

The overwrap should only be removed before administration.

Do not use before the two solutions have been mixed.

Aseptic conditions must be maintained during dialysate exchange in order to reduce the risk of infection.

Addition of medication to the peritoneal dialysis solution:

Medicinal products must be added under aseptic conditions only when medically prescribed. Because of the risk of incompatibility between the dialysis solution and the added medicinal products only the following medicinal products may be added up to the mentioned concentration if indicated by the attending physician: heparin 1000 I.U./l, insulin 20 I.U./l, vancomycin 1000 mg/l, teicoplanin 400 mg/l, cefazolin 500 mg/l, ceftazidime 250 mg/l, gentamicin 8 mg/l. After thorough mixing and checking for the absence of any turbidity or particles the peritoneal dialysis solution must be used immediately (no storage).

MAL

7. PRODUCT REGISTRATION HOLDER

Fresenius Medical Care Malaysia Sdn. Bhd.,
Second Floor, Axis Technology Centre,
Lot 13, Jalan 51A/225,
46100 Petaling Jaya, Selangor, Malaysia

8. MARKETING AUTHORISATION NUMBER(S)

MAL09011449AZ

9. DATE OF REVISION OF THE TEXT

May 2025

0875480_05_jd_ETW_Korr02.indd 17 23.06.2025 13:34:47