SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Gelaspan 4% B.Braun

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ml of the solution contains:

Succinylated gelatin	40.00 mg

(Average molecular weight, weight average: 26,500 Dalton). The gelatin is produced from bovine bone.

Sodium chloride	5.55 mg
Sodium acetate trihydrate	3.27 mg
Potassium chloride	0.30 mg
Calcium chloride dihydrate	0.15 mg
Magnesium chloride hexahydrate	0.20 mg

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

pH	7.4±0.3
Theoretical osmolarity:	284 mOsm/l

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for infusion

Clear and straw-coloured, practically free from particles.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Gelaspan 4% B.Braun is a colloidal plasma volume substitute in an isotonic, fully balanced electrolyte solution for Prophylaxis and emergency treatment of imminent or manifest relative or absolute hypovolaemia and shock.

4.2. Posology and method of administration

Posology

Gelaspan 4% B.Braun is administered intravenously.

Dosage and infusion rate are adjusted according to the amount of blood loss and to individual needs for restoration and maintenance of a stable haemodynamic situation, respectively. The dose administered is initially 500 to 1000 ml on average, in case of severe blood loss higher doses have to be applied.
In adults and children weighing over 25 kg, 500 ml is administered at an appropriate rate depending on the haemodynamic status of the patient. In the case of more than 20 per cent blood loss usually blood or blood components should be given in addition to Gelaspan 4% B.Braun.

Pediatric population:
As documented experience regarding the use of Gelaspan 4% B.Braun in children is insufficient, the dosage must be adjusted very carefully according to the patient's prevailing clinical condition and the therapy should be monitored especially carefully (see also section « Special warnings and Precautions for Us».)

Maximum Dose:
The maximum daily dose is determined by the degree of haemodilution. Care must be taken to avoid a decrease the haematocrit below critical values, see section «Special warnings and Precautions for Use».
If necessary, blood or packed red cells must be transfused additionally.
Attention must also be paid to the dilution of plasma proteins (e.g. albumin and coagulation factors), which must be adequately substituted if necessary.

Infusion rate:
The infusion rate depends on the actual haemodynamic situation.
Usually, 500 ml are infused over 30 min. However, the first 20 – 30 ml of solution should be infused slowly in order to detect the occurrence of an anaphylactoid reaction as early as possible. See also sections «Special warnings and Precautions for Use» and «Undesirable Effects».
In shock situations, Gelaspan 4% B.Braun may be infused rapidly by pressure infusion, 500 ml within 5 – 10 min.
The haemodynamic, haematological and coagulation system should be monitored.

Method of Administration
Intravenous use. When given rapidly Gelaspan 4% B.Braun should be warmed to not more than 37°C if possible.
When giving Gelaspan 4% B.Braun by pressure infusion, all air must be removed from containers with air space inside and from the infusion set before the solution is administered.

4.3 Contraindications

Gelaspan 4% B.Braun must not be administered in case of:
- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.,
- Hypersensitivity to galactose-α-1,3-galactose (alpha-gal) or known allergy to red meat (mammalian meat) and offal;
- Hypervolaemia,
- Hyperhydration,

- Hyperkalaemia,
- Acute heart failure.

4.4 Special warnings and precautions for use

Anaphylactic/anaphylactoid reactions
Solutions containing modified fluid gelatins should be administered with caution to patients with a history of allergic diseases, e.g. asthma.
As with all volume substitutes, solutions with modified fluid gelatin 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 20ml should be infused slowly and the patient should be under careful observation particularly at the start of the infusion (For symptoms of anaphylactoid reactions, see section 4.8).

Due to possible cross-reactions with the allergan galactose-alpha-1,3-galactose (alpha-gal), the risk of sensitisation and subsequent anaphylactic reaction to gelatin-containing solutions could be much higher in patients with a history of allergy to red meat (mammalian meat) and offal and/or patients who have tested positive for anti-alpha-gal-IgE antibodies. Gelatin-containing colloidal solutions are contraindicated in these patients (see section 4.3).
In case of an allergic reaction, the infusion must be stopped immediately and appropriate treatment given.

Pre-existing conditions to be considered

Gelaspan 4% B.Braun should be administered only with caution to patients
- at risk due to circulatory overload e.g. patients with congestive heart failure, right or left ventricular insufficiency, hypertension, pulmonary oedema or renal insufficiency with oliguria or anuria.
- with severely impaired renal function
- with oedema with water/salt retention
- with severe hypernatraemia
- with severe hyperchloraemia
- with major blood coagulation disorders
- in case of pre-existing hyperkalaemia, caution should be exercised and the solution should only be administered if it is clear that the benefits outweigh the risks
- taking medicinal products that can increase the serum potassium level (potassium-sparing diuretics, ACE inhibitors, non-steroidal anti-inflammatory agents, cyclosporine, tacrolimus or suxamethonium) can lead to an increased serum potassium level. The concomitant administration of those medicinal products with potassium-containing solutions may lead to severe hyperkalaemia, which may in turn result in cardiac arrhythmia
- of advanced age (elderly patients), as these are more prone to develop disorders such as cardiac or renal insufficiency.

Clinical monitoring

Clinical monitoring should include regular checks of serum electrolyte concentrations, acid-base balance and water balance, in particular in patients with hypernatraemia, hyperchloraemia, hypercalcaemia, hyperkalaemia or impaired renal function. Gelaspan 4% B.Braun contains supraphysiological concentrations of sodium (151 mmol/L).

Electrolytes and fluids should be substituted according to individual requirements if necessary.

The haemodynamic, haematological and coagulation systems must be monitored. During compensation of severe blood losses by infusion of large amounts of Gelaspan 4% B.Braun, haematocrit and electrolytes must be monitored. The haematocrit should not decrease below 25%. In elderly or critically ill patients, it should not fall below 30%.
Likewise in these situations, the dilution effect on coagulation factors should also be observed, especially in patients with existing blood clotting disorders.
Because the product does not substitute lost plasma protein, it is advisable to check the plasma protein concentrations, see also section 4.2, “Maximum Dose”.
Gelaspan 4% B.Braun must not be infused concurrently through the same infusion line with blood or blood products (packed cells, plasma and plasma fractions). Two separate infusion systems must be used.

Pediatric population
There is no sufficient experience with the use of Gelaspan 4% B.Braun in children. Therefore, Gelaspan 4% B.Braun should be administered to these patients only if the expected benefit clearly outweighs the potential risks. (See also section 4.2).

Influence on diagnostic methods
Laboratory blood tests (blood group or irregular antibodies) can be performed after infusion of Gelaspan 4% B.Braun. Nevertheless, drawing of blood tests before the infusion of Gelaspan 4% B.Braun is recommended to avoid complicating the interpretation of the results.
Gelaspan 4% B.Braun may have an influence on the following clinical-chemical tests, leading to false raised values:
– Erythrocyte sedimentation rate,
– Specific gravity of urine,
– Unspecific protein assays, e.g. the Biuret method.

4.5 Interaction with other medicinal products and other forms of interaction

Caution is advised in patients who are concomitantly taking or receiving medicinal products that may cause sodium retention (e.g. corticosteroids, non-steroidal anti-inflammatory drugs), as concomitant administration can lead to oedema.
Administration of potassium may reduce the therapeutic effect of cardiac glycosides.
ACTH, corticosteroids and loop diuretics may increase potassium elimination.

4.6 Fertility, pregnancy and lactation

Pregnancy
There are no or limited amount of data from the use of Gelaspan 4% B.Braun in pregnant women. Animal studies are insufficient with respect to reproductive toxicity: see section 5.3.
Due to limited data available and the possibility of severe anaphylactic/anaphylactoid reactions with consecutive foetal- and neonatal distress caused by maternal hypotension, the use of modified gelatin solutions should be restricted to emergency situations during pregnancy.

Breastfeeding
It is not known whether Gelaspan 4% B.Braun or its metabolites are excreted in human milk. Sodium and chloride are normal constituents of the human body and of food. No significant increase in the content of these electrolytes in breast milk is expected following the use of Gelaspan 4% B.Braun. A decision must be made whether to discontinue breast-feeding or to interrupt/ discontinue Gelaspan 4% B.Braun therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

Fertility
No data are available on the effects of Gelaspan 4% B.Braun on fertility in humans or animals. In view of the nature of its constituents, it is highly improbable, however, that Gelaspan 4% B.Braun has any effect on fertility.

4.7 Effects on ability to drive and use machines

No relevant studies have been conducted. Gelaspan 4% B.Braun has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

The following frequencies are used:
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), frequency not known (cannot be estimated from the available data).

Adverse drug reactions may occur during and after the use of Gelaspan 4% B.Braun. They are usually associated with anaphylactic/anaphylactoid reactions of varying severity (see also sections 4.3 and 4.4, especially with respect to hypersensitivity to galactose-alpha-1,3-galactose (alpha-gal) and allergy to red meat and offal).

Immune system disorders
Rare: Anaphylactic/anaphylactoid reactions up to shock (see section 4.4).

Cardiac disorders
Very rare: Tachycardia.

Vascular disorders
Very rare: Hypotension.

General disorders and administration site conditions

Very rare: Fever, chills.

Gastrointestinal disorders
Not known: Nausea, vomiting, abdominal pain.

Investigations
Not known: Oxygen saturation reduced.

Blood and lymphatic system disorders
Very common: Reduced haematocrit and reduced concentration of plasma proteins.
Common (depending on dose administered): Relatively large doses of Gelaspan 4% B.Braun result in dilution of coagulation factors and can therefore affect blood coagulation. Prothrombin time can be increased and activated partial thromboplastin time (aPTT) can be prolonged. See section 4.4.

Information on particular undesirable effects
Mild anaphylactoid reactions include:
Generalised erythema, urticaria, periorbital oedema, angiooedema.

Moderate anaphylactoid reactions include:
Dyspnoea, stridor, wheezing, nausea, vomiting, dizziness (presyncope), sweating, chest and throat tightness, abdominal pain.

Severe anaphylactoid reactions include:
Cyanosis or $SaO_2 \leq 92\%$, hypotension (systolic blood pressure < 90 mm Hg in adults), confusion, collapse, loss of consciousness or incontinence.
In the event of an anaphylactoid reaction, the infusion must be discontinued immediately and an emergency treatment according to established standards provided.

Children and adolescents
No data are available on patterns or incidence of adverse reactions in children or adolescents.

Reporting 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

Signs and symptoms
Overdose of Gelaspan 4% B.Braun may cause hypervolaemia and circulatory overload with a significant drop in haematocrit and plasma proteins, accompanied by an electrolyte and acid-base imbalance. This may be associated with consecutive impairment of heart and lung function (pulmonary oedema). Symptoms of circulatory overload include e.g. headache, dyspnoea and jugular

vein congestion.

Treatment
With the onset of circulatory overload the infusion must be stopped and a rapid-acting diuretic administered. In the event of an overdose, the patient should be treated symptomatically and electrolytes should be monitored.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

ATC classification
Pharmacotherapeutic group:
Blood substitutes and plasma protein fractions.
ATC code: B05A A06.

Mechanism of action

Gelaspan 4% B.Braun contains 40 mg/ml of gelatin polysuccinate (also known as succinylated or modified fluid gelatin) with an average molecular weight of 26,500 Daltons in a plasma–adapted, balanced isotonic electrolyte solution. The negative charges introduced into the molecule by succinylation cause an expansion of the molecule; the molecular volume is therefore higher than that of unsuccinylated gelatin of the same molecular weight.
In healthy volunteers, the measured initial volume effect of Gelaspan 4% B.Braun was found to be 80% and 100% of the infused volume with a volume effect over 4 – 5 hours.
The colloid osmotic pressure of the solution determines the initial volume effect. The duration of the effect depends on clearance of the colloid, which is mainly by renal excretion.
Since the volume effect of Gelaspan 4% B.Braun is equivalent to the administered amount of solution, Gelaspan 4% B.Braun is a plasma substitute and not a plasma expander.
Gelaspan 4% B.Braun also restores the extravascular compartment and does not disturb the electrolyte balance of the extracellular space.
Gelaspan 4% B.Braun contributes to restoration of the electrolyte balance and the correction of an acidosis. Gelaspan 4% B.Braun is lactate-free and may be administered to patients with hepatic disorders. Acetate was added to the solution as a bicarbonate precursor, which can be metabolised in all organs and muscles.

Pharmacodynamic effect
Gelaspan 4% B.Braun replaces the intra- and extravascular volume deficits caused by losses of blood, plasma and interstitial fluid. Thus mean arterial pressure, left-ventricular end-diastolic pressure, cardiac stroke volume, cardiac index, oxygen supply, microcirculation and diuresis are increased by this medicinal product without dehydrating the extravascular space.

Children and adolescents
No studies have been performed in children and adolescents with Gelaspan 4% B.Braun. Therefore, efficacy and safety of Gelaspan 4% B.Braun in children and adolescents cannot be assessed.

5.2. Pharmacokinetic properties

Distribution
After infusion, Gelaspan 4% B.Braun is rapidly distributed in the intravascular compartment. There is no evidence that Gelaspan 4% B.Braun is stored in the reticulo-endothelial system or elsewhere in the organism.

Metabolism/Elimination
Most of the infused modified fluid gelatin is excreted via the kidneys. Only a minor amount is excreted in faeces and only approx. 1% is metabolised. The smaller molecules are excreted directly by glomerular filtration, while the larger molecules are probably first degraded proteolytically in the liver and then excreted renally.

Pharmacokinetics in special clinical situations
The plasma half-life of Gelaspan 4% B.Braun may be prolonged in haemodialysis patients (GFR < 0.5 ml/min). However, no accumulation of gelatin is observed. Gelaspan 4% B.Braun minimizes the risks of dilutional acidosis and rebound alkalosis as observed with lactate-containing solutions infused in patients with liver diseases. Gelaspan 4% B.Braun contains acetate and is lactate-free. It therefore can also be administered to hypovolaemic patients with liver disease.

5.3 Preclinical safety data

No data available.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Excipients: Sodium hydroxide solution 10N, Hydrochloric acid 20% w/w, Water for injections.

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

Unopened

The expiry date of the product is indicated on the packaging materials.

After first opening
From a microbiological point of view, the product 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 °C.

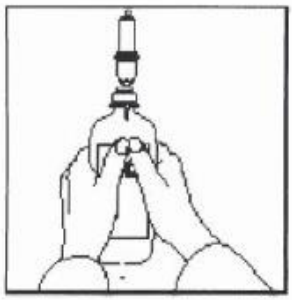
6.4 Special precautions for storage

Store below 25 °C. Do not freeze.

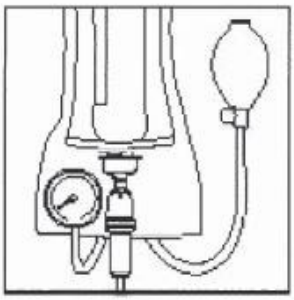
Keep out of the reach of children.

Handling instructions
Use only if the container is undamaged and the solution is clear. For single use only. Discard any leftover solution. If there is an Ecobag container, do not remove the outer packaging until just before use.
When using Gelaspan 4% B.Braun as a pressure infusion in an emergency situation (pressure cuff, infusion pump), it should be heated to body temperature first.

Ecoflac® Handling Instructions ®

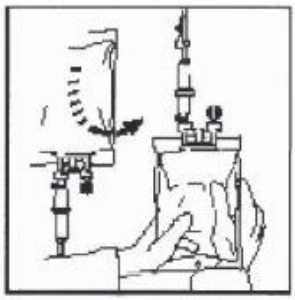


Pressure infusion
- Insert infusion device
- Hold container upright
- With roller clamp open, remove air completely from the container and fill the drip chamber approximately half full
- Turn container 180° and remove all air from the infusion device

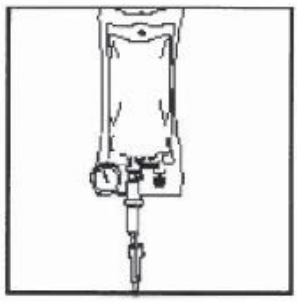


- Close roller clamp
- Place container in the pressure cuff
- Increase pressure
- Open roller clamp and start pressure infusion.

Ecobag® Handling Instructions



Pressure infusion
- Insert infusion device
- Hold container upright
- With roller clamp open, remove air completely from the container and fill the drip chamber approximately half full
- Turn container 180° and remove all air from the infusion device



- Close roller clamp
- Place container in the pressure cuff
- Increase pressure on the bag, but do not exceed 40 kPa (300 mgHg)
- Occasional leaking at a pressure of 50 kPa (380 mmHg) cannot be ruled out. Take appropriate precautionary measures
- Open roller clamp and start pressure infusion

6.5 Nature and contents of container

Pack sizes:
“Ecoflac Plus” bottles: 10 x 500 ml
“Ecobag” bags: 20 x 500 ml
Not all pack sizes may be marketed.

7 MANUFACTURER

B. Braun Medical, AG,
Seesatz 17, 6204 Sempach, Switzerland

8 REGISTRATION HOLDER

Lapidot Medical Import and Marketing Ltd.
8 Hashita St., Industrial Park, Caesarea 3088900, ISRAEL.

9 MARKETING AUTHORISATION NUMBER

166-12-35586-00

Revised in February 2024