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 gelatine	40.0 mg
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 any of the constituents of the solution,
- elevated plasma volumes (hypervolaemia),
- hyperhydratation,
- hyperkalaemia,
- severe heart failure,
- recent myocardial infarction,
- severe clotting disorders,
- severe renal failure.

4.4 Special warnings and precautions for use

Gelaspan 4% B.Braun should be administered with caution to patients with a history of allergic diseases, e.g.asthma.
Gelatin preparations for volume replacement may rarely cause anaphylactoid reactions of varying degrees of severity. In order to detect the occurrence of an anaphylactoid reaction as early as possible, the first 20 – 30 ml should be infused slowly and under careful observation of the patient. (Details of symptoms of anaphylactoid reactions and emergency measures, see section «Undesirable effects»).

Gelaspan 4% B.Braun should only be administered 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.
- patients having oedema with water/salt retention
- dehydration states
- hypernatraemia
- clotting disorders
- chronic liver disease.

Gelaspan 4% B.Braun must not be infused through the same infusion line together with blood or blood products (packed cells, plasma and plasma fractions), two separated infusion lines have to be used.
Checks of serum electrolyte concentrations and water balance are necessary, in particular in patients with hypernatraemia, hypokalaemia, dehydration, or impairment of renal function.
In cases of massive blood loss and a corresponding massive infusion 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 those situations the dilution effect on coagulation factors should be observed, especially in patients with existing disorders of haemostasis.
Because the product does not substitute lost plasma protein, it is advisable to check the plasma protein concentrations, see also section «Dosage/administration» under «Maximum Dosage».

Pediatric population
There is no sufficient experience with the use of Gelaspan 4% B.Braun in children. Therefore, Gelaspan 4% B.Braun should be used in children only after careful benefit-risk assessment, and with careful monitoring. (see also section «Posology/Administration»).
This pharmaceutical product contains 4 mmol potassium in 1 liter solution. This must be kept in mind for patients suffering from renal failure or following a diet with controlled intake of potassium.
This pharmaceutical product contains 151 mmol sodium in 1 liter solution. This must be kept in mind for patients following a diet with controlles intake of sodium.
Laboratory blood tests (blood group or irregular antigens) are possible after Gelaspan 4% B.Braun infusions.
Nevertheless it is recommended to draw blood samples before the infusion of Gelaspan 4% B.Braun in order to avoid hampered interpretation of results.

4.5 Interaction with other medicinal products and other forms of interaction

Considerations should be given to the concomitant administration of medicinal products that can cause potassium- or sodium retention.

4.6 Fertility, pregnancy and lactation

Controlled studies have been carried out neither in animals nor in pregnant or lactating women.
Because of possible anaphylactoid reactions with consecutive foetal- and neonatal distress due to maternal hypotension, the medicinal product should only be administered during pregnancy, if the indication is imperative, and solely if the potential benefit is greater than the foetal risk.
It is not known whether Gelaspan 4% B.Braun passes into breast milk. Sufficient experience with application during the breast-feeding period is not available.

4.7 Effects on ability to drive and use machines

No relevant studies have been conducted.

4.8 Undesirable effects

The only potentially serious adverse reactions are the anaphylactoid reaction described below. However, severe
reactions are very rare.

System Organ Class	Uncommon (≥ 1/1.000, < 1/100)	Rare (≥ 1/10.000, < 1/1.000)	Very rare (< 1/10.000)
Immune system disorders		Anaphylactoid reactions, all grades*	Anaphylactoid reactions severity garde III and IV*
Cardiac disorders			Tachycardia
Vascular disorders			Hypotension
Respiratory, thoracic and mediastinal disorders			Respiratory difficulties
Skin and subcutaneous tissue disorders		Allergic skin reactions*	
General disorders and administration site conditions	Mild transient increase of body temperature		

* Anaphylactoid reactions of severity grade I – II include:

pruritus, local erythema, paresthesia, headache, face and neck flush, urticaria, oedema of the mucous membranes, tachycardia, hypotension, dyspnoea, cough, dizziness, nausea, vomiting.
Anaphylactoid reactions of severity grade III – IV include:
severe dyspnoea, bronchial spasm, severe blood pressure-drop, shock, cardiac and respiratory arrest.
In the event of an anaphylactoid reaction, the infusion must be discontinued immediately and the usual acute treatment given.

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

Overdose or too rapid infusion of Gelaspan 4% B.Braun may cause hypervolaemia and circulatory overload with consecutive impairment of heart and lung function. Symptoms of circulatory overload are e.g. headache, dyspnoea, and jugular vein congestion.
In case of circulatory overload the infusion must be stopped and a fast acting diuretic should be given.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

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

Gelaspan 4% B.Braun is a 4 % w/v solution of succinylated gelatine (also known as modified fluid gelatine) with
an average molecular weight of 30 000 Dalton (weight average) in a plasma–adapted, isotonic
electrolyte solution. The negative charges introduced into the molecule by succinylation lead to an expansion of the molecule, thus rendering it markedly more voluminous than unsuccinylated protein chains of the same molecular weight.
The measured initial volume effect of Gelaspan 4% B.Braun is about 100% of the infused volume with a sufficient volume effect over 4 – 5 hours.

Therapeutic effect
Gelaspan 4% B.Braun substitutes intra- and extravascular volume deficits caused by losses of blood, plasma and interstitial fluid. Thus the mean arterial pressure, the left-ventricular end-diastolic pressure, the cardiac stroke volume, the cardiac index, the oxygen supply, the microcirculation and the diuresis are increased.

Mechanism of action
The colloid-osmotic pressure of the solution determines the extent of its initial effect. The duration of the effect depends on the clearance of the colloid by re-distribution and excretion. The volume effect of Gelaspan 4% B.Braun is equivalent to the administered amount of solution. Gelaspan 4% B.Braun is a plasma substitute, not a plasma expander. The solution also restores the extravascular compartment, does not disturb the electrolyte balance of the extracellular space. Gelaspan 4% B.Braun is isotonic, it therefore does not cause fluid shifts into the intracellular space as caused by hypotonic solutions. Gelaspan 4% B.Braun contributes in the restoration of electrolyte balance and the correction of acidosis. Gelaspan 4% B.Braun is lactate free and can be used in patients with liver diseases. As a precursor of bicarbonate the solution contains acetate which is metabolisable in all organs and muscles.

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 Gelaspan 4% B.Braun is excreted via the kidneys. Only a minor amount is excreted in faeces and not more than about 1 % is metabolised. The smaller molecules are excreted directly by glomerular filtration while the larger molecules first are degraded proteolytically in the liver and then excreted via the kidneys. The proteolytic metabolism is so adaptable that even under the condition of renal insufficiency no accumulation of Gelaspan 4% B.Braun is observed.

Pharmacokinetics in special clinical situations
The plasma half-life time of Gelaspan 4% B.Braun may be prolonged in patients on haemodialysis (GFR < 0.5 ml/min). Gelaspan 4% B.Braun minimizes the risks of dilutional acidosis and rebound alkalosis as observed with lactate containing solutions infused to patients with liver diseases. Gelaspan 4% B.Braun contains acetate and is lactate free. It therefore can also be indicated in hypovolaemic patients with liver disease.

5.3 Preclinical safety data

The maximum dose of the product is limited by its volume and dilution effects, not by any intrinsic toxicological properties.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

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

6.2 Incompatibilities

The pharmaceutical product Gelaspan 4% B.Braun should generally not be mixed with other infusion solutions.
Keep out of the reach of children.

6.3 Shelf life

Unopened

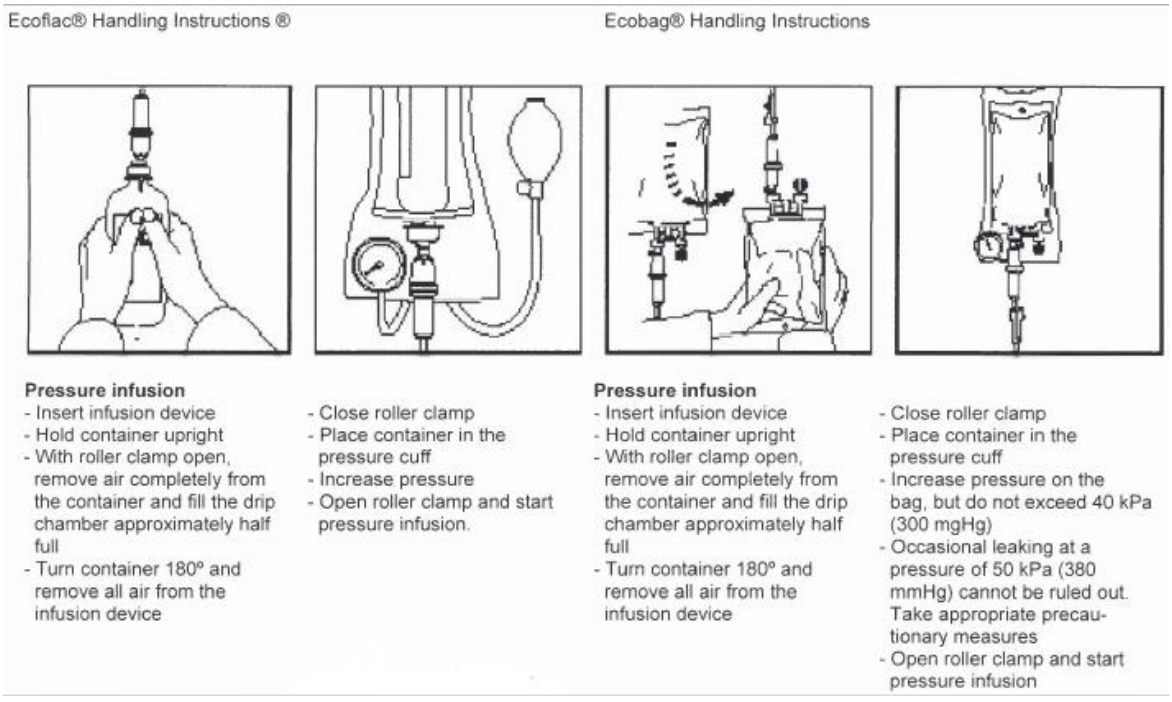
The expiry date of the product is indicated on the packaging materials.

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.

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. See the section «Warnings and precautions for use» as well as the illustrations («Handling Instructions»).



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 MARKETING AUTHORISATION HOLDER

Lapidot Medical Import and Marketing Ltd.
Hashita 8, Industrial Zone, Caesarea 3088900.

9 MARKETING AUTHORISATION NUMBER

166-12-35586

Approved in April 2021