Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Gelaspan Solution for Infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1000 ml solution contain:

Succinylated gelatine (= modified fluid gelatine) (Molecular weight, weight average: 26 500 Dalton)	40.0g
Sodium chloride	5.55g
Sodium acetate trihydrate	3.27g
Potassium chloride	0.30g
Calcium chloride dihydrate	0.15g
Magnesium chloride hexahydrate	0.20g

Electrolyte concentrations

Sodium	151 mmol/1
Chloride	103 mmol/l
Potassium	4 mmol/l
Calcium	1 mmol/l
Magnesium	1 mmol/l
Acetate	24 mmol/l

Excipients:
For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for infusion
Clear, colourless or slightly yellowish solution

Theoretical osmolarity: 284 mosmol/l
pH: 7.4 ± 0.3

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Gelaspan is a colloidal plasma volume substitute in an isotonic, fully balanced electrolyte solution for:

- Treatment of relative or absolute hypovolaemia and shock
- Prophylaxis of hypotension
    - caused by relative hypovolaemia during induction of epidural or spinal anaesthesia
    - due to imminent significant blood loss in a surgical setting
- Procedures involving extracorporeal circulation as a component of priming fluid in combination with crystalloid solutions (e.g. heart-lung machine)

4.2 Posology and method of administration

As with all colloids, Gelaspan should only be used if hypovolaemia can not be sufficiently treated with crystalloids alone. In severe hypovolaemia colloids are usually applied in combination with crystalloids.

Volume overload due to overdose or too rapid infusion must always be avoided. The dosage must be adjusted carefully, particularly in patients with pulmonary or cardiocirculatory problems.

Posology
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 can be applied.

Adults
In adults, 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 (see 4.4).

Maximum dose:
The maximum daily dose is determined by the degree of haemodilution. Care must be taken to avoid a decrease of haemoglobin or the haematocrit below critical values.

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:
Up to the first 20 ml of solution should be infused slowly in order to detect anaphylactic/ anaphylactoid reactions as early as possible (see also section 4.4).

In severe, acute situations, Gelaspan may be infused rapidly by pressure infusion, 500 ml can be administered in 5-10 minutes, until signs of hypovolaemia are relieved.

Paediatric population
The safety and efficacy of Gelaspan in children have not yet been completely established. Therefore, no recommendation on a posology can be made. Gelaspan should only be administered to these patients if the expected benefits clearly outweigh potential risks. In those cases the patient's prevailing clinical condition should be taken into account and the therapy should be monitored especially carefully. (See also section 4.4.)

Elderly patients
Caution should be exercised in patients suffering from further diseases like cardiac insufficiency or renal insufficiency that are frequently associated with advanced age (see also section 4.4).

Method of administration
Intravenous use
Before rapid infusion, Gelaspan may be warmed to not more than 37°C.

In case of pressure infusion, which might be necessary in vital emergencies, all air must be removed from the container and the infusion set before the solution is administered. This is to avoid the risk of air embolism that might otherwise be associated with the infusion.

4.3 Contraindications

- hypersensitivity to gelatin containing solutions 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 (mammal meat) and offal (see section 4.4)
- hypervolaemia
- hyperhydration
- acute congestive cardiac failure

4.4 Special warnings and precautions for use

Anaphylactic/ anaphylactoid reactions
Modified fluid gelatine solutions should be administered with caution to patients with a history of allergic diseases, e.g. asthma.

Modified fluid gelatine solutions 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 ml should be infused slowly and the patient should be under careful observation especially at the beginning of the infusion. For symptoms of anaphylactoid reactions, see section 4.8.

Due to possible cross-reactions involving the allergen galactose-alpha-1,3-galactose (alpha-Gal), the risk of sensitization and consequent anaphylactic reaction to gelatin-containing solutions could be highly increased in patients with history of allergy to red meat (mammal meat) and offal and/or 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 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 oligo- or anuria.
- with severely impaired renal function
- with severe hypernatraemia
- with severe hyperchloraemia
- with oedema with water/salt retention
- 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, i.e. potassium-sparing diuretics, ACE inhibitors, non-steroidal anti-inflammatory agents, cyclosporine, tacrolimus or suxamethonium. The concomitant administration of potassium-containing solutions and these drugs may lead to severe hyperkalaemia, which may in turn lead to cardiac arrhythmia.
- of advanced age (elderly patients) as these are more prone to develop disorders such as cardiac or renal insufficiency

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 impairment of renal function. Gelaspan contains supraphysiological concentration of sodium (151 mmol/L).

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

The haemodynamic, haematological and coagulation system should be monitored.

During compensation of severe blood losses by infusions of large amounts of Gelaspan, 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 4.2, "Maximum dose".

Incompatibility
Gelaspan must not be infused through the same infusion line together with blood or blood products (packed cells, plasma and plasma fractions).

Paediatric population
There is no sufficient experience with the use of Gelaspan in children. Therefore Gelaspan should only be administered to these patients if the expected benefits clearly outweigh potential risks. (See also section 4.2)

Influence on laboratory tests
Laboratory blood tests (blood group or irregular antibodies) are possible after Gelaspan infusions. Nevertheless it is recommended to draw blood samples before the infusion of Gelaspan in order to avoid hampered interpretation of results.

Gelaspan may have an influence on the following clinical-chemical tests, leading to falsely high 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 interactions

Caution should be exercised in patients concurrently taking or receiving medicinal products that can cause sodium retention (e.g. corticosteroids, non-steroidal anti-inflammatory agents) as concomitant administration may lead to oedema.

Administration of potassium can reduce the therapeutic effect of cardiac glycosides.
ACTH, corticosteroids and loop diuretics can increase the renal elimination of potassium.

4.6 Fertility, pregnancy and lactation

Pregnancy
There are no or limited amount of data from the use of Gelaspan in pregnant women. Animal studies are insufficient with respect to reproductive toxicity (see section 5.3).

Due to the limited data available and the possibility of severe anaphylactic/anaphylactoid reactions with consecutive foetal and neonatal distress due to maternal hypotension, the use of modified fluid gelatin solutions during pregnancy should be restricted to emergency situations.

Breastfeeding
It is unknown whether Gelaspan/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 mother's milk is expected following the use of Gelaspan. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from Gelespan therapy taking into account the benefit of breast feeding for the child and the benefit of therapy for the woman.

Fertility
There are no data on the effect of Gelaspan on human or animal fertility. However, because of the nature of its constituents it is considered unlikely that Gelaspan will affect fertility.

4.7 Effects on ability to drive and use machines

Gelaspan has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

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)

Summary of the safety profile
Adverse drug reactions can occur during and after the use of Gelaspan. These will usually involve anaphylactic/anaphylactoid reactions of varying severity (see also sections 4.3 and 4.4, notably for hypersensitivity to galactose-α-1,3-galactose (alpha-Gal) and allergy to red meat and offal).

Tabulated list of adverse reactions
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

Gastro intestinal disorders
Unknown: Nausea, vomiting, abdominal pain

Investigations
Unknown: Oxygen saturation decreased

Blood and lymphatic system disorders
Very common:
Decreased haematocrit and reduced concentration of plasma proteins.
Common (depending on the administered dose):
Relatively large doses of Gelaspan 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 after administration of large doses of Gelaspan (see section 4.4).

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

Moderate anaphylactoid reactions include:
Dyspnoea, stridor, wheeze, nausea, vomiting, dizziness (presyncope), diaphoresis, chest or throat tightness, or abdominal pain.

Severe anaphylactoid reactions include:
Cyanosis or $SaO_2 \leq 92\%$ at any stage, hypotension (systolic blood pressure < 90 mmHg in adults), confusion, collapse, loss of consciousness or incontinence.

In the event of an anaphylactoid reaction, the infusion must be discontinued immediately and the usual acute treatment given.

Paediatric population
There are no data relating to a special pattern or incidence of adverse reactions in paediatric patients.

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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; e-mail: medsafety@hpra.ie

4.9 Overdose

Symptoms
Overdose of Gelaspan may cause hypervolaemia and circulatory overload with a significant fall 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 are e.g. headache, dyspnoea, and jugular vein congestion.

Treatment
In case circulatory overload appears the infusion must be stopped and a rapid-acting diuretic should be given. If an overdose occurs, the patient should be treated symptomatically and electrolytes should be monitored with monitoring of electrolytes.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmaco-therapeutic group
Blood substitutes and plasma protein fractions
ATC code: B05A A06, gelatine agents.

Mechanisms of action
Gelaspan is a 40 mg/ml solution of succinylated gelatine (also known as modified fluid gelatine) with an average molecular weight of 26 500 Dalton (weight average) 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 modified fluid gelatine was found to be between 80 and 100% of the infused volume with a volume effect over 4-5 hours.

The colloid-osmotic pressure of the solution determines its initial volume effect. The duration of the effect depends on the clearance of the colloid mainly by renal excretion. Since the volume effect of Gelaspan is equivalent to the administered amount of solution, Gelaspan is a plasma substitute, not a plasma expander. The solution also restores the extravascular compartment, and does not disturb the electrolyte balance of the extracellular space.

Gelaspan contributes in the restoration of electrolyte balance and the correction of acidosis. Gelaspan 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.

Pharmacodynamic effect:
Gelaspan 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 without dehydrating the extravascular space.

Paediatric population
No studies have been performed in the paediatric population with Gelaspan. Therefore, the efficacy and safety of Gelaspan in the paediatric population cannot be assessed.

5.2 Pharmacokinetic properties

Distribution
After infusion, Gelaspan is rapidly distributed in the intravascular compartment.

Biotransformation/elimination
Most of the infused modified fluid gelatine 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 are first degraded proteolytically and secondly are excreted via kidneys.

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

5.3 Preclinical safety data

No additional concerns identified.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium hydroxide (for pH adjustment),
Hydrochloric acid, diluted (for pH-adjustment),
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*

Polyethylene containers "Ecoflac plus": 2 years
Plastic bags "Ecobag" (non-PVC): 2 years

- *After first opening the container*

The infusion should commence immediately after connecting the container to the giving set.

- *After admixture of an additive*

Not applicable (see section 6.2)

6.4 Special precautions for storage

Do not store above 25 °C. Do not freeze.

6.5 Nature and contents of container

Gelaspan is supplied in:

- Bottles of low-density polyethylene "Ecoflac plus", contents: 500 ml available in packs of 10 × 500 ml
- Plastic bags "Ecobag" (non-PVC), sealed with halogenbutyl rubber stoppers contents: 500 ml available in packs of 20 × 500 ml

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements for disposal

The product is supplied in containers for single use only. Unused contents of an opened container must be discarded.

Only to be used if solution is clear and free of precipitate and the container undamaged.

Use immediately after connecting container to the giving set.

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

7 MARKETING AUTHORISATION HOLDER

B. Braun Melsungen AG
Carl-Braun-Straße 1
34212 Melsungen
Germany

8 MARKETING AUTHORISATION NUMBER

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 9th September 2011
Date of last renewal: 18th May 2016

10 DATE OF REVISION OF THE TEXT

June 2021