

Direction for Use

1. NAME OF THE MEDICINAL PRODUCT

Gelaspan 4% solution for infusion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1000 ml solution contain:

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

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

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:

- Prophylaxis and treatment of hypotension caused by relative hypovolaemia during induction of epidural or spinal anaesthesia or 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. priming of heart-lung machines)
- Acute normovolaemic haemodilution

4.2 Posology and method of administration

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 have to 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.

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.)

Maximum dose:

The maximum daily dose is determined by the degree of haemodilution. Care must be taken to avoid a decrease of the haematocrit below critical values, see section 4.4.

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.

The first 20 – 30 ml of solution should be infused slowly in order to detect anaphylactoid reactions as early as possible. See also sections 4.4 and 4.8.

In shock situations, Gelaspan may be infused rapidly by pressure infusion, 500 ml within 5 – 10 min.

Method of administration

Intravenous use

When given rapidly Gelaspan should be warmed to not more than 37°C if possible.

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.

4.3 Contraindications

Gelaspan must not be used in the following situations:

- hypersensitivity to gelatine solutions or to any of the other ingredients of Gelaspan
- hypervolaemia
- hyperhydration
- hyperkalaemia

4.4 Special warnings and precautions for use

Gelaspan should be administered with caution to patients with a history of allergic diseases, e.g. asthma.

Gelatine preparations for volume replacement 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 – 30 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. In case of an allergic reaction, the infusion must be stopped immediately and appropriate treatment given.

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
- having oedema with water/salt retention
- with major blood coagulation disorders

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

Checks of serum electrolyte concentrations and water balance are necessary, in particular in patients with hypernatraemia, hyperkalaemia or impairment of renal function.

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”.

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 antigens) 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 Interactions with other medicinal products and other forms of interaction

Caution should be exercised in patients concurrently taking or receiving medicinal products that can cause potassium (e.g. potassium, sparing diuretics, ACE inhibitors) or sodium retention.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential

No data available

Contraception in males and females

No data available

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 possible anaphylactoid reactions with consecutive foetal and neonatal distress due to maternal hypotension, the use of Gelaspan should be avoided during pregnancy unless the clinical condition of the woman requires treatment with the medicinal product.

Breastfeeding

There is insufficient information on the excretion of Gelaspan in human or animal milk. A risk to the suckling child cannot be excluded. 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.

4.7 Effects on ability to drive and use machines

Not relevant.

4.8 Undesirable effects

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

	Uncommon ($\geq 1/1,000$ to $< 1/100$)	Rare ($\geq 1/10,000$ to $< 1/1,000$)	Very rare ($< 1/10,000$)
Immune system disorders		Anaphylactoid reactions, all grades*	Severe anaphylactoid reactions *
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		Fever, chills

*

Mild anaphylactoid reactions include:

Generalised oedema, urticaria, periorbital oedema, or angiooedema.

Moderate anaphylactoid reactions include:

Dyspnoea, stridor, wheeze, urticaria, nausea, vomiting, dizziness (presyncope), diaphoresis, chest or throat tightness, or abdominal pain.

Severe anaphylactoid reactions include:

Cyanosis or $\text{SaO}_2 \leq 92\%$ 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 patients:

No special features

4.9 Overdose*Symptoms*

Overdose of Gelaspan may cause hypervolaemia and circulatory overload with a significant fall in haematocrit and plasma proteins. 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 of circulatory overload 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.

5. PHARMACOLOGICAL PROPERTIES**5.1 Pharmacodynamic properties***Pharmaco-therapeutic group*

Blood substitutes and plasma protein fractions

ATC code: B05A A06, gelatine agents.

Gelaspan is a 4 % w/v 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 gelatine of the same molecular weight.

The measured initial volume effect of Gelaspan is about 100% of the infused volume with a sufficient volume effect over 4 – 5 hours.

Gelaspan does not interfere with the determination of blood groups and it is neutral regarding clotting mechanisms.

Therapeutic 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.

Mechanisms of action

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, does not disturb the electrolyte balance of the extracellular space. Gelaspan is isotonic, it therefore does not cause fluid shifts into the intracellular space as caused by hypotonic solutions.

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.

5.2 Pharmacokinetic properties

Distribution

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

Metabolism/elimination

Most of the infused Gelaspan 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 and then excreted via kidneys. The proteolytic metabolism is so adaptable that even under the condition of renal insufficiency no accumulation of Gelaspan is observed.

Pharmacokinetics in special clinical situations

The plasma half-life of Gelaspan may be prolonged in patients on haemodialysis (GFR < 0.5 ml/min). 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

Non-clinical data for the individual components of Gelaspan reveal no special hazard for humans based on conventional studies of single and repeated dose toxicity. There is no or limited non-clinical data available for reproductive toxicity.

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

Sodium hydroxide (for pH adjustment),
Hydrochloric acid (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 30 °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.

7. MARKETING AUTHORISATION HOLDER

Product owner:

B.Braun Medical AG

Seesatz

6204 Sempach – Switzerland

Manufacturing place:

B.Braun Medical AG

9 Route de Sorge

1023 Crissier – Switzerland

8 DATE OF REVISION OF THE TEXT

November 2014