Professional Information for Medicines for Human Use

SCHEDULING STATUS

S3

1. NAME OF THE MEDICINE

GELASPAN 4 %

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1000 mL of GELASPAN 4% solution for infusion contains:

Succinylated gelatine (= modified fluid gelatine)	40,0 g
(Molecular weight, weight average: 26500 Dalton)	
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

For the full list of excipients see section 6.1.

3. PHARMACEUTICAL FORM

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Solution for infusion

Clear, and straw coloured, practically free from particles.

Theoretical osmolarity: 284 mosmol/L

pH: 7,4 ± 0,3

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

GELASPAN 4 % is a colloidal plasma volume substitute in an isotonic, fully balanced electrolyte solution for:

- Treatment of relative or absolute hypovolaemia and shock
- Prophylaxis and treatment 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

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 4 % (see 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 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.

In severe, acute situations, GELASPAN 4 % may be infused rapidly by pressure infusion, 500 mL can be administered in 5 – 10 min, until signs of hypovolaemia are relieved.

Paediatric population

The safety and efficacy of GELASPAN 4 % in children has not yet been completely established. Therefore, no recommendation on a posology can be made. GELASPAN 4 % 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 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 section 4.4.).

Method of administration

Intravenous use

In the special case of rapid infusion under external pressure which may be necessary in emergency situations, before starting the infusion, all air must be removed from containers, and

the infusion set before the solution is administered, as otherwise there is a risk of producing air embolism during the infusion.

GELASPAN 4 % should be administered with caution to patients with hypernatraemia and states of dehydration.

Serum electrolytes and fluid balance controls are required.

Electrolytes are to be replaced as required.

Clinical-chemical parameters may be influenced so that laboratory results are higher than expected: blood sedimentation rate, specific gravity of the urine, unspecific protein determinations (e. g. with the Biuret method).

Special care and adaptation of the dosage is recommended in patents with blood clotting disturbances, renal insufficiency and chronic liver disease.

There are no contraindications to the use of GELASPAN 4 % in the elderly. There is insufficient data to establish safety and efficacy in children.

4.3. Contraindications

GELASPAN 4 % is contraindicated in:

- Known hypersensitivity to gelatine-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
- Severe blood clotting disorders
- Contraindicated in children under 1 year of age.

4.4. Special warnings and precautions for use

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Do not use unless the solution is clear and free from particles.

Do not use if the container is damaged or has been previously opened.

GELASPAN 4 % can cause anaphylactoid/ anaphylactic reactions of varying severity. Ranging from benign skin symptoms (urticarial) through flushing of the face and neck to the much less frequently occurring ones. Fall in blood pressure, shock, bronchospasm, cardiac or respiratory arrest. Such reactions can occur both in conscious and anaesthetised patients. Patients receiving GELASPAN 4 % have to be carefully observed in case of potential anaphylactoid/ anaphylactic reactions.

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 should not be used in these patients (see section 4.3).

In case of an allergic reaction, the infusion must be stopped immediately, and appropriate treatment given.

GELASPAN 4 % should only be administered with caution to patients:

- at risk of circulatory overload e.g., patients with right or left ventricular insufficiency, hypertension, pulmonary oedema or renal insufficiency with oligo- or anuria
- with severely impaired renal function
- severe hypernatraemia
- severe hyperchloraemia
- with oedema with water/ salt retention
- with major blood coagulation disorders
- of advanced age as these are more prone to develop disorders such as cardiac or renal insufficiency

- severe hypercalcaemia
- in case of pre-existing hyperkalaemia, caution should be exercised

As with all colloids, GELASPAN 4 % should only be used if hypovolaemia cannot 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 cardio circulatory problems.

Check of serum electrolyte concentrations, acid base balance and water balance are necessary, in particular in patients with hypernatremia, hypochloraemia or impairment of renal function.

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 4 %, the haematocrit and electrolytes must be monitored under circumstances.

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.

GELASPAN 4 % must not be infused through the same infusion line as blood or blood products (packed cells, plasma and plasma fractions).

Paediatric population:

There is insufficient experience with the use of GELASPAN 4 % in children.

Clinical-chemical parameters may be influenced so that laboratory results are higher than expected: blood sedimentation rate, specific gravity of the urine, unspecific protein determinations (e. g. with the Biuret method).

4.5. Interaction with other medicines and other forms of interaction.

Mixing with other medicines may produce incompatibilities.

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

Potassium sparing diuretics, ACE inhibitors, non-steroidal anti-inflammatory medicines, cyclosporine, tacrolimus or suxamethonium can increase the serum potassium level. The concomitant administration of potassium containing solutions are these medicines may lead to severe hyperkalaemia, which may in turn lead to cardia arrhythmia.

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 is no adequate data from the use of GELASPAN 4 % in pregnant women. Studies in animals are insufficient with respect to reproductive toxicity (see section 5.3). Due to the limited data available and the possibility of severe anaphylactic/ anapylactoid reactions with consecutive foetal and neonatal distress, the use of GELASPAN 4 % solutions during pregnancy should be restricted to emergency situations.

Breastfeeding

There is no or limited data regarding the excretion of succinylated gelatine in mother’s milk, but because of its high molecular weight it is not expected that the milk will contain relevant amounts. 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 4 %.

Fertility

There is no data on the effect of GELASPAN 4 % on human or animal fertility. However, because of the nature of its constituents it is considered unlikely that GELASPAN 4 % will affect fertility.

4.7. Effects on Ability to Drive and Use Machines

GELASPAN 4 % has no or negligible influence on the ability to drive and use machines.

4.8. Undesirable Effects

(a) Summary of the safety profile

As with other colloidal plasma substitutes, side effects can occur during and after the use of GELASPAN 4 %. These will usually involve anaphylactic/ anaphylacoid reactions of varying severity**.**

(b) Tabulated list of adverse reactions

System Organ Class	**Frequency Category**
Immune system disorders	
Anaphylactic/ anaphylactoid reactions up to shock. In the event of an anaphylactoid reaction, the infusion must be discontinued immediately and the usual emergency treatment given.	Less frequent
Cardiac disorders	
Tachycardia	Less frequent
Vascular disorders	
Hypotension	Less frequent
General disorders and administration site conditions	
Fever, chills	Less frequent

Gastro-intestinal disorders	
Nausea, vomiting, abdominal pain	Frequency unknown
Investigations	
Oxygen saturation decreased	Frequency unknown
Blood and lymphatic system disorders	
Decreased haematocrit and reduced concentration of plasma proteins. Relatively large doses of GELASPAN 4 % result in dilution of coagulation factors and can therefore affect blood coagulation. Prothombin time can be increased and activated partial throboplastin time (aPTT) can be prolonged after administration of large doses of GELASPAN 4 %. (See section 4.4).	Frequent

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 to SAHPRA via the '**6.04 Adverse Drug Reactions Reporting Form'**. Found under SAHPRA's publications: https://primaryreporting.who-umc.org/ZA

4.9. Overdose

Symptoms

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 is e.g., headache, dyspnoea, and jugular vein congestion.

Treatment

Treatment is symptomatic and supportive.

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 with monitoring of electrolytes.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Class of Medicine: A.8.4 Plasma Expanders

ATC code: BO5A A06, gelatine agents

GELASPAN 4 % is a 40,0 mg/ mL solution of succinylated gelatine (also known as modified fluid gelatine) with an average molecular weight of 25 000 Daltons (weight average) in a plasma-adapted, 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. GELASPAN 4 % does not interfere with the determination of blood groups.

Mechanism of action

The colloid-osmotic pressure of the solution determines the extent of its initial volume effect. The duration of the effect depends on the clearance of colloid mainly by renal excretion. Since the volume effect of GELASPAN 4 % is equivalent to the administered amount of solution, GELASPAN 4 % is a plasma substitute, not a plasma expander. The solution also restores the extravascular compartment and does not cause fluid shifts into the intracellular space. GELASPAN 4 % contributes in the restoration of electrolyte balance and the correction of acidosis. GELASPAN 4 % 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 4 % 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 increases without dehydrating the extravascular space.

5.2. Pharmacokinetic properties

GELASPAN 4 % has a volume effect of approximately 3-4 hours. It is predominately excreted in the urine, only a very small amount in the faeces and only about 1 % of the amount infused is metabolised.

Distribution

After infusion, GELASPAN 4 % is rapidly distributed in the intravascular compartment.

Biotransformation/ elimination

Most of the infused GELASPAN 4 % 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 in the liver and secondly are excreted via kidney.

Pharmacokinetics in special clinical situations.

The plasma half time of GELASPAN 4 % may be prolonged in patients on haemodialysis (GFR <0,5 mL/ min), however no accumulation of gelatine is observed. GELASPAN 4 % minimises the risks of dilutional acidosis and rebound alkalosis as observed with lactate containing solutions infused to patients with liver diseases. GELASPAN 4 % contains acetate and is lactate free. Therefore, it can also be indicated in hypovolaemic patients with liver disease.

5.3. Preclinical Safety Data

Non-clinical data for the individual components of GELASPAN 4 % 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.

There are no studies on the mutagenic and carcinogenic potential of gelatine.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Sodium hydroxide (for pH adjustment)

Hydrochloric acid (for pH-adjustment)

Water for injections

6.2. Incompatibilities

Mixing with other medicines may produce incompatibilities. Only mixtures of known compatibility should be prepared.

6.3. Shelf life

24 months at 25 °C

6.4. Special precautions for storage

Store at or below 25 °C.

Do not use after expiry date.

Do not freeze.

Do not use unless the solution is clear and free from particles or if the container is damaged or has been previously opened.

Discard any unused portion.

Keep in original packaging until required for use.

6.5. Nature and contents of container

- Ecoflac plus (Polyethylene plastic container), content 500 mL available in packs of 10 x 500 mL.

- Ecobags® with an injection port and a connection port for infusion. These ports are sealed by polypropylene caps with halogen-butyl rubber stoppers, content of 500 mL. available in packs of 20 x 500 mL.

6.6. Special precautions for disposal and other handling

This product is supplied in single use containers for single use only. Unused contents of an opened container must be discarded and not be stored for later use.

7. NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION

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8. REGISTRATION NUMBER

46/8.4/0203

9. DATE OF FIRST AUTHORISATION

25 January 2022

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25 July 2024