Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Geloplasma Solution for Infusion (Polyolefine/Freeflex Bag)

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Modified liquid gelatin*	
amount expressed as anhydrous gelatin	3.0000 g
Sodium chloride	0.5382 g
Magnesium chloride hexahydrated	0.0305 g
Potassium chloride	0.0373 g
Sodium (S)-lactate solution	
amount expressed as sodium lactate	0.3360 g

per 100 ml of solution for infusion

* partially hydrolysed and succinylated

For the full list of excipients, see section 6.1.

Ionic formula

Sodium = 150 mmol/l
Potassium = 5 mmol/l
Magnesium = 1.5 mmol/l
Chloride = 100 mmol/l
Lactate = 30 mmol/l

Total osmolality : 295 mOsm/kg
pH : 5.8 to 7.0

3 PHARMACEUTICAL FORM

Solution for infusion.
Clear and colourless to slightly yellowish solution.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Emergency treatment of states of shock:
- hypovolaemic shock resulting from : haemorrhage, dehydration, capillary leak, burns;
- vasoplegic shock of traumatic, surgical, septic or toxic origin.

Treatment of relative hypovolaemia associated with hypotension in the context of vasoplegia related to the effects of hypotensive drugs, notably during anesthesia.

4.2 Posology and method of administration

Posology
Dosage volume and rate of administration depend upon the individual patient status, circumstances and response to vascular replacement.
Modified liquid gelatin is given by IV infusion (drip infusion). The infusion rate can be increased using a pump.
The dose and infusion rate depend upon the patient's needs and blood volume to be replaced and haemodynamic status of the patient.
The dose administered is 500 to 1000 ml on average (1 to 2 bags), sometimes more.

As a general rule, in adults and children weighing more than 25 kilos, 500 ml (1 bag) is administered at an appropriate rate depending on the status of the patient. The infusion rate can be increased in case of severe haemorrhage.
If there is blood/fluid loss in excess of 1.5 litres in the adult (i.e. greater than 20% of blood volume) blood should usually be administered as well as GELOPLASMA, solution for infusion. The haemodynamic, haematological and coagulation system should be monitored.

Paediatric population
See above.

Method of administration
The solution is administered intravenously only.

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);
- predominantly extracellular hyperhydration;
- hyperkalemia;
- metabolic alkalosis;
- end of pregnancy (during labor/delivery): see section 4.6.

4.4 Special warnings and precautions for use

Warnings
This solution must not be given by intramuscular injection.
This solution may cause metabolic alkalosis because of the presence of lactate ions.
This liquid gelatin solution must not be infused at the same time as blood or its derivatives (packed cells, plasma and plasma fractions) but using two separate infusion systems.
Determination of blood group, irregular antigens and any laboratory blood tests are possible in patients who have received up to 2 litres of liquid gelatin, though interpretation is hampered by haemodilution and it may be preferred to draw the sample for these tests before the infusion of liquid gelatin.
Because of the possibility of allergic (anaphylactic/anaphylactoid) reactions, appropriate monitoring of patient is necessary.

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 innards 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.
Hepatic impairment
This solution may not have its alkalinizing action in patients with impaired liver function since lactate metabolism may be impaired.

This medicine contains 5 mmol of potassium per litre. Patients with reduced kidney function or patients on controlled potassium diet should take into consideration this information.
This medicine contains 150 mmol of sodium per litre. Patients on controlled sodium diet should take into consideration this information.
Precautions
Use of this solution requires clinical and laboratory monitoring of the patient's status:
- blood pressure, and possibly central venous pressure;
- urine output;
- haematocrit and electrolytes.

Especially in the following situations:
- congestive heart failure;
- pulmonary functional impairment;
- severely impaired renal function;
- oedema with water/salt retention;
- circulatory overload;

- treatment with corticosteroids and their derivatives.
- major coagulation disturbances

The haematocrit should not fall below 25%; in elderly patients it should not fall below 30%. Blood coagulation disorders caused by dilution of coagulation factors should be avoided.
If more than 2,000 to 3,000 ml of GELOPLASMA, solution for infusion, are infused pre-and intra-operatively, it is recommended that the serum protein concentration be checked post-operatively, especially if there are signs if tissue oedema.

4.5 Interaction with other medicinal products and other forms of interactions

Concomitant use of other substances by IV administration is inadvisable, since the pharmacokinetics of constituents of mixtures have not been studied.
Since this solution contains potassium, it is preferable to avoid using potassium and medicinal products that may cause hyperkalemia (e.g. potassium sparing diuretics, ACE inhibitors).

4.6 Fertility, pregnancy and lactation

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

No embryotoxic effect has, however, hitherto been observed, but there is a risk of severe anaphylactic/anaphylactoid reactions, with consequential foetal and neonatal distress secondary to maternal hypotension.
Due to this possible allergic reaction, this medicinal product must not be given to pregnant women at the end of pregnancy.
As with all drugs, the benefits and risks of use should be assessed in the light of the patient's condition: under these circumstances this preparation should only be prescribed when the potential advantage outweighs the potential risk to the foetus. It should not be used for the prophylaxis of hypovolemia during delivery with analgesia or epidural anaesthesia; however it can be used to treat hypovolemia when plasma volume replacement is needed during pregnancy.
Breast-feeding
It is unknown whether this product/metabolites are excreted in human milk. A risk to the newborns/infants cannot be excluded.
Fertility
There are no data on the effects of GELOPLASMA, solution for infusion, on human or animal fertility.

4.7 Effects on ability to drive and use machines

Not relevant.

4.8 Undesirable effects

The undesirable effects are divided into system organ class and frequency according to the following convention: 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).
Undesirable effects observed during the infusion of this product are:

	Rare **≥1/10,000 to <1/1,000**	**Very rare** **< 1/10,000**
Immune system disorders	Anaphylactic shock (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)	
Skin and subcutaneous tissue disorders	Allergic skin reaction	
Vascular disorders		Hypotension
Cardiac disorders		Slowing of heart rate

Respiratory,thoracic and mediastinal disorders		Respiratory difficulties
General disorders and administration site conditions		Fever, chills

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 the national reporting system.
For Ireland via the 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

Higher doses may cause circulatory overload with a significant fall in haematocrit and plasma proteins.
Increased pressure in the pulmonary circulation leads to leakage of fluid into the extravascular space and may cause pulmonary oedema.
If overdose occurs, stop the infusion and give a fast acting diuretic.
In case of overdose, the patient should be treated symptomatically and electrolytes should be monitored.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: BLOOD SUBSTITUTES AND PLASMA PROTEIN FRACTIONS. ATC Code: B05AA
Modified liquid gelatin in ionic solution similar to that of extracellular fluid, to be used for vascular filling and restoration of water/electrolyte balance.
This solution enables:
- restoration of blood volume, volume by volume, without plasma expansion due tointravascular transfer of interstitial fluids;
- haemodilution with lowering of blood viscosity and improvement of the microcirculation;
- rehydration of the extravascular sector.

This solution contributes in the restoration of ionic balance and the correction of acidosis.
Liquid gelatin also slightly increases urine output.
Liquid gelatin can be used alone, without any need for transfusion, to cover blood loss of 10 to 20% of total blood volume, and substituted for blood for any infusion of limited volume (about 500 ml).
It does not interfere with the determination of blood groups and is neutral regarding clotting mechanisms.
In the presence of heavy bleeding, alternate administration of blood and liquid gelatin ensures adequate haemodilution (restoration of blood volume and maintenance of oncotic pressure).

5.2 Pharmacokinetic properties

The distribution and elimination of modified liquid gelatin administered by intravenous infusion depends upon many factors: particle size, molecular weight, electric charge, volume administered, rate of administration, etc. The presence of low molecular weight substances explains the action on the kidney and increased urine output.

This modified gelatin solution ensures effective vascular filling for four to five hours after its infusion.

Modified liquid gelatin is eliminated quickly (75% in 24 hours), essentially via the kidney.

5.3 Preclinical safety data

Preclinical safety data are limited and provide no additional information.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium hydroxide
Succinic anhydride as succinic acid
Hydrochloric acid, concentrated
Water for injections

6.2 Incompatibilities

Physical chemical incompatibility with certain antibiotics (chlortetracycline, amphotericin B (IV), oxytetracycline, vancomycin).

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

6.3 Shelf life

2 years for **free***flex*bags.
Once opened: use immediately.

6.4 Special precautions for storage

Do not store above 25°C.
Do not freeze.
Do not store in a refrigerator.

6.5 Nature and contents of container

20 x 500 ml Freeflex bag® (polyolefine), with overwrap.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Aseptic handling of the solution must be ensured

Check that the container is intact and the solution clear before use.
Discard any container which is damaged or from which fluid has been removed.
The residual volume of solution left after infusion must never be used again later.

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

7 MARKETING AUTHORISATION HOLDER

Fresenius Kabi Deutschland GmbH
Else-Kroener Strasse 1
Bad Homburg v.d.H 61352
Germany

8 MARKETING AUTHORISATION NUMBER

PA2059/008/002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 10 September 2010

10 DATE OF REVISION OF THE TEXT

August 2018