ISOPLEX 4% W/V SOLUTION FOR INFUSION
(Succinylated gelatin)

PL 13538/0017

UKPAR

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ISOPLEX 4% W/V SOLUTION FOR INFUSION
(Succinylated gelatin)
PL 13538/0017

LAY SUMMARY

The Medicines and Healthcare products Regulatory Agency (MHRA) granted IS Pharmaceuticals Limited a Marketing Authorisation (licence) for the medicinal product Isoplex 4% w/v Solution for Infusion (PL 13538/0017) on 7th July 2008. This is a prescription-only medicine (POM).

Plasma is the fluid component of blood in which the red cells and white cells are carried. Isoplex is a temporary plasma substitute solution containing succinylated gelatin 4%w/v. Isoplex is administered directly into a vein via a drip tube (intravenous infusion).

You will be given Isoplex if you have lost blood or body fluids because of bleeding, injury, surgery, burns or infection. It takes time for your body to replace the blood or body fluids that you have lost. Isoplex can help maintain the volume of fluid in your blood vessels during that time. Isoplex is not intended to provide nutrition nor replace blood components such as red cells which carry oxygen or white cells which fight infection; Isoplex can only replace lost fluid volume.

Isoplex can be used for the treatment of initial blood loss during pregnancy.

This application is a duplicate of a previously granted application for Volpex (PL 13538/0015), held by IS Pharmaceuticals Limited. The test and reference products are identical.

No new or unexpected safety concerns arose from this application and it was therefore judged that the benefits of using Isoplex 4% w/v Solution for Infusion outweigh the risk, hence a Marketing Authorisation has been granted.
ISOXPEX 4% W/V SOLUTION FOR INFUSION
(Succinylated gelatin)

PL 13538/0017

SCIENTIFIC DISCUSSION

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INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the MHRA granted IS Pharmaceuticals Limited a Marketing Authorisation for the medicinal product Isoplex 4% w/v Solution for Infusion (PL 13538/0017) on 7th July 2008. The product is a prescription-only medicine (POM).

The application was submitted as a simple abridged application according to article 10c of Directive 2001/83/EC (as amended), cross-referring to Volpex (PL 13538/0015, IS Pharmaceuticals Limited), approved on 1st July 2002. Volpex had been approved as a generic medicinal product of Gelofusine (PL 03551/0042), held by B Braun Melsungen AG, and originally granted to B Braun Melsungen AG as PL 12100/0001 on 1st November 1993.

No new data were submitted nor was it necessary for this simple application, as the data are identical to that of the previously granted cross-reference product. As the cross-reference product was granted prior to the introduction of current legislation, no PAR was generated for it.

Isoplex 4% w/v Solution for Infusion contains succinylated gelatin (modified fluid gelatin) 4% w/v in water for injections, also containing electrolytes. Isoplex is a colloidal plasma substitute indicated for the initial management of hypovolaemic shock caused by, for example, haemorrhage, acute trauma or surgery, burns, sepsis, peritonitis, pancreatitis or crush injury. Isoplex may also be used in the initial treatment of blood loss during pregnancy where plasma volume replacement is needed.

When used in the treatment of hypovolaemia, Isoplex produces significant increases in blood volume, cardiac output, stroke volume, blood pressure, urinary output and oxygen delivery. Isoplex promotes osmotic diuresis, thereby helping to protect the kidneys from the adverse effects of hypovolaemia. Isoplex is administered intravenously; the volume and rate of infusion will depend on the condition of the patient.
PHARMACEUTICAL ASSESSMENT

LICENCE NUMBER: PL 13538/0017

PROPRIETARY NAME: Isoplex 4% w/v Solution for Infusion

ACTIVE INGREDIENT/S: succinylated gelatin

COMPANY NAME: IS Pharmaceuticals Limited

E.C. ARTICLE: Article 10c of Directive 2001/83/EC (as amended)

LEGAL STATUS: POM

1. INTRODUCTION

This is a simple abridged application, submitted under Article 10c of Directive 2001/83/EC (as amended) for Isoplex 4% w/v Solution for Infusion. The proposed MA holder is ‘IS Pharmaceuticals Limited, Office Village, Chester Business Park, Chester CH4 9QZ, UK’.

The reference product is Volpex (PL 13538/0015), held by IS Pharmaceuticals Limited. The test and reference products are identical.

2. MARKETING AUTHORISATION APPLICATION FORM

2.1 Name(s)

The approved name of the product is Isoplex 4% w/v Solution for Infusion. The product has been named in line with current requirements.

2.2 Strength, pharmaceutical form, route of administration, container and pack sizes

Isoplex 4% w/v Solution for Infusion contains the active ingredient succinylated gelatin 4%. The product is supplied in sterile flexible infusion bags (500 or 1000 ml), which are overwrapped. Each 500ml of Isoplex contains succinylated gelatin 20g in 500ml of water for injections, also containing electrolytes. Each 1000ml of Isoplex contains succinylated gelatin 40g in 1000ml of water for injections, also containing electrolytes. For 500 ml bags, each pack contains 10 units, and for 1000 ml bags, each pack contains 6 units.

The approved shelf-life (2 years) and storage conditions (Do not store above 25°C, Do not freeze or refrigerate) are consistent with the details registered for the cross-reference product.

2.3 Legal status

The product is a POM licensed medicine available on prescription.

2.4 Marketing authorisation holder / Contact Persons / Company

The proposed Marketing Authorisation holder is ‘IS Pharmaceuticals Limited, Office Village, Chester Business Park, Chester CH4 9QZ, UK’.

The QP responsible for pharmacovigilance was stated and their CV included.
2.5 Manufacturers

The proposed manufacturing site is consistent with that registered for the cross-reference product and evidence of GMP compliance has been provided.

2.6 Qualitative and quantitative composition

The proposed composition is consistent with the details registered for the cross-reference product.

2.7 Manufacturing process

The proposed manufacturing process is consistent with the details registered for the cross-reference product and the maximum batch size is stated.

2.8 Finished product / shelf-life specification

The proposed finished product specification is in line with the details registered for the cross-reference product.

2.9 Drug substance specification

The proposed drug substance specification is consistent with the details registered for the cross-reference product.

2.10 TSE Compliance

The only excipient used that contains material of animal or human origin is gelatin. Certificates of suitability have been provided by all the gelatin suppliers stating that the gelatin they provide meets the criteria described in the current version of the monograph ‘Products with risk of transmitting agents of animal spongiform encephalopathies’.

3. EXPERT REPORTS

Satisfactory expert reports and curriculum vitae of experts were provided.

4. PRODUCT NAME & APPEARANCE

See 2.1 for details of the proposed product name. The appearance of the product is consistent with that of the cross-reference product.

5. SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

The approved SmPC is consistent with the details registered for the cross-reference product.
6. **PATIENT INFORMATION LEAFLET (PIL) / CARTON**

**PIL**

The patient information leaflet has been prepared in line with the details registered for the cross-reference product. The approved PIL is satisfactory.

**Labelling**

Colour mock-ups of the labelling have been provided and are satisfactory. The approved artwork is comparable to the artwork registered for the cross-reference product and complies with statutory requirements.

7. **CONCLUSIONS**

The grounds for this application are considered adequate. A Marketing Authorisation was, therefore, granted.
PRECLINICAL ASSESSMENT

The application was submitted as a simple, abridged application, according to Article 10c of Directive 2001/83/EC, as amended.

No new preclinical data have been supplied with this application and none are required for an application of this type. A preclinical expert report has been written by a suitably qualified person and is satisfactory.
CLINICAL ASSESSMENT

The application was submitted as a simple abridged application according to article 10c of Directive 2001/83/EC (as amended).

As this is a duplicate application for PL 13538/0015, no new clinical data have been supplied with the application and none are required.
OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

QUALITY
The data for this application are consistent with that previously assessed for the cross-reference product and as such have been judged to be satisfactory.

PRECLINICAL
No new preclinical data were submitted and none are required for an application of this type.

EFFICACY
This application is identical to the previously granted application for Volpex (PL 13538/0015).

No new or unexpected safety concerns arise from this application.

PRODUCT LITERATURE
The approved SmPC, PIL and labelling are satisfactory and consistent with that for the cross-reference product.

A package leaflet has been submitted to the MHRA along with results of consultations with target patient groups ("user testing"), in accordance with Article 59 of Council Directive 2001/83/EC. The results indicate that the package leaflet is well-structured and organised, easy to understand and written in a comprehensive manner. The test shows that the patients/users are able to act upon the information that it contains.

The approved labelling artwork complies with statutory requirements.

RISK BENEFIT ASSESSMENT
The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. The applicant’s product is identical to the cross-reference product. Extensive clinical experience with succinylated gelatin, and electrolytes, is considered to have demonstrated the therapeutic value of the active substances. The risk: benefit is, therefore, considered to be positive.
ISOLEX 4% W/V SOLUTION FOR INFUSION
(Succinylated gelatin)

PL 13538/0017

STEPS TAKEN FOR ASSESSMENT

1. The MHRA received the marketing authorisation application on 5th March 2007.

2. Following standard checks and communication with the applicant the MHRA considered the application valid on 20th July 2007.

3. Following assessment of the application the MHRA requested further information relating to the quality dossier on 12th May 2008.

4. The applicant responded to the MHRA’s request, providing further information for the quality sections on 7th July 2008.

5. The application was determined on 7th July 2008.
# ISOPLEX 4% W/V SOLUTION FOR INFUSION
(Succinylated gelatin)

**PL 13538/0017**

## STEPS TAKEN AFTER AUTHORISATION

<table>
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<th>Application type</th>
<th>Scope</th>
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<td>25/07/2008</td>
<td>Variation</td>
<td>To change the composition of the electrolyte excipients by adding sodium lactate, potassium chloride and magnesium chloride. The product specification, SPC, labelling and leaflet have been consequentially updated</td>
<td>Application granted 06/08/2008</td>
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SUMMARY OF PRODUCT CHARACTERISTICS

The UK Summary of Product Characteristics (SPC) for Isoplex 4% w/v Solution for Infusion is as follows:

1 NAME OF THE MEDICINAL PRODUCT
Isoplex 4% w/v Solution for Infusion

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Succinylated gelatin (Modified Fluid Gelatin) 4% w/v in Water for Injections, also containing electrolytes.

Electrolytes
- Sodium ion (Na⁺) 145 mmol/litre
- Chloride ion (Cl⁻) 105 mmol/litre
- Lactate ion 25 mmol/litre
- Potassium ion (K⁺) 4 mmol/litre
- Magnesium ion (Mg²⁺) 0.9 mmol/litre

3 PHARMACEUTICAL FORM
Sterile non-pyrogenic solution for infusion.

A clear pale yellow or straw coloured solution contained within a flexible infusion bag

Key Physico-chemical properties:
- Weight average molecular weight (Mw) 30 000 Dalton
- Number average molecular weight (Mn) 20 000 Dalton
- pH 7.4 ± 0.5
- Osmolarity 284 mOsm/litre

4 CLINICAL PARTICULARS

4.1 Therapeutic indications
Isoplex is a colloidal plasma substitute indicated for the initial management of hypovolaemic shock caused by, for example, haemorrhage, acute trauma or surgery, burns, sepsis, peritonitis, pancreatitis or crush injury.

Isoplex may be used in the initial treatment of blood loss during pregnancy where plasma volume replacement is needed.

4.2 Posology and method of administration
Isoplex is administered intravenously; the volume and rate of infusion will depend on the condition of the patient. The rate of administration can be increased by the application of pressure to the container or by adjusting the giving set pump. When given rapidly Isoplex should be warmed to no more than 37°C if possible. In severe acute blood loss, Isoplex may be given rapidly (500ml in 5 - 10 minutes) until signs of hypovolaemia are relieved. When large volumes are given, suitable monitoring should be used to ensure that an adequate haematocrit is maintained (the haematocrit should not be allowed to fall below 25%) and that dilutional effects upon coagulation are avoided. (Expert haematological advice should be sought, especially in cases of massive blood loss).

For massive fluid loss, Isoplex may be used concomitantly with blood, the rate and amount of which depends on the clinical condition of the patient. The haemodynamic status of the patient should be monitored.

If blood is to be given at the same time as Isoplex, it can be given through the same giving set since Isoplex has a negligible calcium content and therefore does not clot blood. Isoplex can also be used to reconstitute packed red cells.
4.3 Contraindications
Isoplex is contra-indicated in patients with a known hypersensitivity to succinylated gelatin.
Lactate containing solutions are contraindicated in patients with liver disease.

4.4 Special warnings and precautions for use
(i) Severe anaphylactic or anaphylactoid reactions have been reported following the intravenous administration of succinylated gelatin. These are rare, having an incidence of between 1 in 6,000 and 1 in 13,000 units. However, they may be more likely to occur if Isoplex is given rapidly to normovolaemic patients, and may be assumed to be more hazardous in patients with known allergic conditions such as asthma.

_Treatment:_ The infusion of Isoplex should be stopped. Further treatment will depend on the severity of the reaction; administration of supplemental oxygen; an alternative infusion fluid; and the parenteral administration of adrenaline (e.g. for adults, 0.5 ml of a 1 in 1,000 solution intramuscularly, repeated every 5 minutes as necessary, or 5 ml of a 1 in 10,000 solution slowly intravenously), and an antihistamine (e.g. chlorpheniramine 10-20mg slowly intravenously) should be considered.

(ii) Caution should be exercised in infusing Isoplex in any patient liable to develop circulatory overload (for example, congestive cardiac failure or renal failure with oliguria or anuria).

_Treatment:_ The infusion of Isoplex should be stopped and the patient treated symptomatically. Electrolytes should be monitored. If necessary, a diuretic can be given to promote fluid loss. Decreased urinary output secondary to shock is not a contraindication unless there is no improvement in urine output after the initial dose of Isoplex.

4.5 Interaction with other medicinal products and other forms of interaction
No interaction studies have been performed

4.6 Pregnancy and lactation
There is very little information available on the use of plasma substitutes in pregnant or lactating women. As with all drugs, the benefits and risks must be assessed.

Isoplex may be used in the initial treatment of blood loss during pregnancy where plasma volume replacement is needed.

4.7 Effects on ability to drive and use machines
Not applicable.

4.8 Undesirable effects
The major undesirable effect risk associated with succinylated gelatin is that of a severe anaphylactic or anaphylactoid reaction, the occurrence and treatment of which is discussed in “4.4 Special warnings and precautions for use”.

A list of rare undesirable effects that have been associated with the administration of succinylated gelatin is given beneath;

_Rare effects ( > 1 in 10,000 to < 1 in 1,000)_

*Immune system disorders*
- Anaphylactic reaction
- Anaphylactoid reaction

*Nervous system disorders*
- Tremor
Cardiac disorders
Tachycardia

Vascular disorders
Hypotension
Hypertension

Respiratory, thoracic and mediastinal disorders
Wheezeing
Dyspnoea
Hypoxia

Skin and subcutaneous tissue disorders
Urticarial reactions
Sweating

General disorders and administration site conditions
Chills
Pyrexia

4.9 Overdose
An overdose of Isoplex may give rise to circulatory overload and electrolyte imbalance (see Section 4.4 Special warnings and precautions for use).

5 PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties
Pharmacotherapeutic group : Gelatin agents ; ATC code B05A A 06

Isoplex is a colloidal plasma substitute. When used in the treatment of hypovolaemia, Isoplex produces significant increases in blood volume, cardiac output, stroke volume, blood pressure, urinary output and oxygen delivery.

Isoplex promotes osmotic diuresis, thereby helping to protect the kidneys from the adverse effects of hypovolaemia.

5.2 Pharmacokinetic properties
The half-life of Isoplex is about 4 hours, with the majority of the dose administered being eliminated by renal excretion within 24 hours.

5.3 Preclinical safety data
There are no preclinical data of relevance to the prescriber, which are additional to those already included in other sections of the SmPC.

6 PHARMACEUTICAL PARTICULARS
6.1 List of excipients
Sodium chloride
Sodium lactate
Potassium chloride
Magnesium chloride
Sodium hydroxide/hydrochloric acid
Water for injection

Isoplex contains no preservatives
6.2 **Incompatibilities**

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

Isoplex does not interfere with blood grouping or cross-matching.

6.3 **Shelf life**

The shelf life for Isoplex 500ml and 1000ml is 2 years.

6.4 **Special precautions for storage**

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

6.5 **Nature and contents of container**

Isoplex is supplied in sterile flexible infusion bags (500 or 1000 ml), which are overwrapped.

For 500 ml bags, each pack contains 10 units.
For 1000 ml bags, each pack contains 6 units

6.6 **Special precautions for use and disposal**

Do not use unless container is free of particles. Do not use if moisture is present between the container and the overwrap, or if the overwrap is damaged. Do not use if the container is not intact before breaking the seal. Check for leaks by squeezing the container before use. For single dose use only. Discard any unused solution immediately after initial use. Do not reconnect any partially used containers.
UKPAR Isoplex 4% w/v Solution for Infusion

PRODUCT INFORMATION LEAFLET

Patient Information Leaflet
Isoplex
4% w/v Solution for Infusion
(sucrylated gelatin)

Read all of this leaflet carefully
• Keep this leaflet. You may need to read it again.
• If you have further questions, please ask your doctor or nurse.

In this leaflet:
1. What is Isoplex and what does it do?
2. Before being given Isoplex
3. How much Isoplex to use and for how long?
4. Possible side effects
5. Storing Isoplex
6. Further Information

1. What is Isoplex and what does it do?
Isoplex is a temporary plasma substitute solution containing sucrylated gelatin 4% w/v (plasma is the fluid component of blood which the red cells and white cells are carried). Isoplex is administered directly into a vein via a drip tube (intravenous infusion).

You will be given Isoplex if you have lost blood or body fluids because of bleeding, injury, surgery, burns or infection. It takes time for your body to replace the blood or body fluids that you have lost. Isoplex can help maintain the volume of fluid in your blood vessels during that time. Isoplex is not intended to provide nutrition or replace blood components such as red cells which carry oxygen or white cells which fight infection; Isoplex can only replace lost fluid volume.

Isoplex can be used for the treatment of initial blood loss during pregnancy.

2. Before being given Isoplex
Do not allow Isoplex to be given to you if you know that you are allergic (hypersensitive) to sucrylated gelatin.

Always tell your doctor or nurse if you are suffering or have suffered from the following conditions:
• Heart failure
• Kidney (renal) failure
• Liver disease

Please inform your doctor or nurse if you are taking, or have recently taken any other medicine, including those medicines obtained without a prescription.

Please ask your doctor or nurse for advice if you are pregnant or breastfeeding.

3. How much Isoplex to use and for how long?
You will be given Isoplex via a drip tube which is inserted into a vein. It is unlikely that you will ever have to use Isoplex yourself. Infusion fluids are mainly intended to be given by your doctor or nurse.

Your doctor or nurse will work out how often you should have Isoplex and how much Isoplex should be used. The amount given will depend on your individual needs. You might also be given other infusion fluids or products made from blood, or a blood transfusion.

For infusion, the usual dose rates are:
For Adults: 500–1500 ml/hour
For Children: 150–1500 ml/hour
For Elderly: As Adults

Each container of Isoplex is designed to last only a few hours at a time; most of the sucrylated gelatin is passed out of the body in less than 12 hours. For this reason, you may be given more Isoplex when your doctor or nurse thinks this is necessary. In time, your body will make up the blood or body fluids that you have lost.

4. Possible side effects
Like all medicines Isoplex can cause side effects, although not everybody gets them.

Faintly (between 1 in 1,000 and 1 in 10,000 people), patients may experience an allergic-like reaction to Isoplex. Tell your doctor or nurse immediately if you notice any of the following:
• Swelling of your face, mouth or throat
• Changes in your breathing, e.g. fast breathing, difficulty breathing out, wheezing
• Changes in the way your heart beats, e.g. fast beating
• Changes in your blood pressure, e.g. feeling dizzy or faint, headache
• Changes in your body temperature, e.g. chills, fever, sweating
• Abnormal feelings in your skin, including itching, rash, swelling or any other changes to your skin
• Shaking of your arms and/or legs

If you suffer from any of these side effects, or any other undesired effect, please inform your doctor or nurse immediately.

5. Storing Isoplex
Isoplex should not be used if:
• the container shows any sign of leakage
• the solution is cloudy
• the solution is NOT a clear pale yellow or straw color
• particles are visible within the container
• the date of use is after the last day of the month of the expiry date, which is stated on the infusion bag in the format YYYYMM

Please inform your doctor or nurse immediately if you believe that any of the above situations have occurred.

6. Further Information
The active substance in Isoplex is sucrylated gelatin (4% w/v), 500ml and 1000ml bags of Isoplex contain 20g and 40g of sucrylated gelatin respectively. The other ingredients are sodium chloride, sodium lactate, potassium chloride, magnesium chloride, sodium bicarbonate, hydrochloric acid, and water for injection.

Isoplex is a clear pale yellow or straw coloured solution for infusion which is supplied in 500ml and 1000ml flexible plastic containers (infusion bags).

The Marketing Authorisation Holder for Isoplex is IS Pharmaceuticals Limited, Office Village, Chester Business Park, Chester, CH1 9QZ, United Kingdom

The Manufacturer of Isoplex is Schering-Plough Pharma KG, Hannover-Lindenhofstrasse 105 b, 30469 Hannover, Germany

Leaflet printed:
ISOLEX is a Registered Trademark of IS Pharmaceuticals Ltd.
LABELLING

500ml pack

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**Isoplex® 500 ml**

4% w/v Solution for Infusion

Sterile, apyrogenic plasma substitute for intravenous infusion

**Composition:**
Each 500 ml of Isoplex® contains Succinylated gelatin (Modified Fud Gelatin) 20 g in 500 ml of Water for Injections.
Also contains sodium chloride, sodium lactate, potassium chloride, magnesium chloride, sodium hydroxide and hydrochloric acid.

**Electrolytes:**
- **Cations:**
  - 72.5 mmol Na⁺ / 500ml
  - 2 mmol K⁺ / 500ml
  - 0.45 mmol Mg²⁺ / 500ml

- **Anions:**
  - 52.5 mmol Cl⁻ / 500ml
  - 12.5 mmol Lactate⁻ / 500ml

**Osmolarity:** 284 mOsm / litre

**Weight average-molecular weight:** 30,000 Da

**Number average-molecular weight:** 20,000 Da

**pH:** 7.4

**Cautions:**
1. For use under medical supervision.
2. Do not store above 25°C. Do not freeze or refrigerate.
3. Do not use unless container is free of particles.
4. Do not use if moisture is present between the container and the overwrap, or if the overwrap is damaged.
5. Do not use if the container is not intact before breaking the seal.
6. Check for leaks by squeezing the container before use.
7. For Single Dose Use Only. Discard any unused solution immediately after initial use.
8. Do not vent. Read instruction leaflet before use.
9. Discontinue administration if adverse reaction occurs.

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**Marketing Authorisation Holder and Distributor:** IS Pharmaceuticals Limited
Chester CH4 9DZ UK

**PL 13538/0017**

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**BATCH No:**

**EXPIRY DATE:**
UKPAR Isoplex 4% w/v Solution for Infusion

1000ml pack

Isoplex®

4% w/v Solution for Infusion
Sterile, pyrogenic plasma substitutes for intravenous infusion

Composition:
Each 1000 ml of Isoplex® contains succinylated gelatin (Modified Fluid Gelatin) 40 g in 1000 ml of Water for Injections. Also contains sodium chloride, sodium lactate, potassium chloride, magnesium chloride, sodium hydroxide and hydrochloric acid.

Electrolytes:
Cations:
- 145 mmol Na⁺/1000ml
- 4 mmol K⁺/1000ml
- 0.9 mmol Mg²⁺/1000ml
- 105 mmol Cl⁻/1000ml
- 25 mmol Lactate⁻/1000ml

Anions:

Osmolarity:
284 mOsm/litre

Weight average-molecular weight:
30,000 Da

Number average-molecular weight:
20,000 Da

pH:
7.4

Cautions:
1. For use under medical supervision.
2. Do not store above 25°C. Do not freeze or refrigerate.
3. Do not use unless container is free of particules.
4. Do not use if moisture is present between the container and the overwrap, or if the overwrap is damaged.
5. Do not use if the container is not intact before breaking the seal.
6. Check for leaks by squeezing the container before use.
7. For single dose use only. Discard any unused solution immediately after initial use.
8. Do not vent. Read instruction leaflet before use.
9. Discontinue administration if adverse reaction occurs.
10. Keep out of the reach of children.

PL 13538/0017

Marketing Authorisation Holder and Distributor: I8 Pharmaceuticals Limited
Chester CH4 8QZ UK

BATCH No: EXPIRY DATE: