Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

ViaSpan Solution for organ preservation

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 l Solution for organ preservation contains:

Poly (0-2-hydroxyethyl) starch 0.40-0.50 MS[1)] (Pentafraction*)	50.0	g/l	
Lactobionic Acid (as Lactone)	35.83	g/l	(105 mmol/l)
Potassium Hydroxide 56 %	14.5	g/l	(100 mmol/l)
Sodium Hydroxide 40 %	3.679	g/l	(27 mmol/l)
Adenosine	1.34	g/l	(5 mmol/l)
Allopurinol	0.136	g/l	(1 mmol/l)
Potassium Dihydrogen Phosphate	3.4	g/l	(25 mmol/l)
Magnesium Sulphate x $7H_2O$	1.23	g/l	(5 mmol/l)
Raffinose x $5H_2O$	17.83	g/l	(30 mmol/l)
Glutathione	0.922	g/l	(3 mmol/l)

[1)]MS = moles hydroxyethyl groups per moles anhydroglucose units
*German Patent Number 3,688,936.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Solution for organ preservation.

Clear, yellow solution. The solution has an approximate osmolality of 320 mosmol/kg, sodium final concentration of 29 mEq/l, potassium concentration of 125 mEq/l and pH of 7.4 at room temperature.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Solution for the preservation of kidney, liver and pancreas. Not for continuous machine perfusion.

4.2 Posology and method of administration

Perfusion and preservation of organs.

ViaSpan is only to be used to prepare Belzer UW Cold Storage Solution. The following can be added aseptically to each litre of ViaSpan immediately before use:
16 mg dexamethasone
40 units of regular insulin
200,000 units of Penicillin G

If desired, an additional 0.922g/l (3 mmol/l) freshly prepared reduced glutathione solution may be added immediately prior to use.

Remove the protective cap from the outlet port of the filter and insert the spike from the administration set into the port with a twisting motion. Open the clamp on the administration set. Remove the twist-off plug from the bag port designated “delivery set port”. Remove the long protective cap from the filter spike and insert with a twisting motion into the “delivery set port”. Hold the administration set vertically above the solution bag, then squeeze solution bag to fill filter and administration set. Close the clamp.

Prior to connection to the organ, the ViaSpan container should be suspended from a sufficient height to allow for a steady stream of solution and to produce flow rates of at least 30 ml/min during flushing. Open the clamp to begin flushing. Flushing should be continued until the organ is uniformly pale and the effluent is relatively clear. One filter should be used per bag, and filters must not be reused.

Suggested minimum volume

In situ aortic flush:	adults, 2 − 4 l children, 50 ml/kg
In situ portal flush (optional):	adult, l l
Ex vivo infusion: Liver (via portal vein and biliary tree)	adults, 1000 − 1200 ml children, 50 ml/kg
Pancreas or kidney:	adults, 300 − 500 ml children, 150 − 250 ml

Additional solution should be dispensed into the container holding the organ until the organ is immersed. Seal the container aseptically. The organ storage container should be maintained within a well-insulated transport container. Melting ice should be used to surround the organ storage container, but should not be used in the container, where the ice could come into direct contact with the organ. Any unused portion of the cold storage solution must be discarded.

Prior to anastomosis and reperfusion before transplantation, the donor organs must be thoroughly flushed, pancreas of approximately 150 grams with 10 − 40 ml lactated Ringer’s solution, kidney of approximately 250 grams with 20 − 70 ml lactated Ringer’s solution to remove the cold storage solution (see section 4.4). In order to minimise residues of solution in the liver, just prior to anastomosis and reperfusion, flush one litre of lactated Ringer’s through the hepatic portal vein.

4.3 Contraindications

Hypersensitivity to the active substances or to any of the excipients or one of the additives: dexamethasone, insulin or penicillin.

4.4 Special warnings and precautions for use

- Not for systemic administration by direct injection or intravenous infusion. Systemic administration of ViaSpan leads to life-threatening side effects.
- Not for *in situ* organ flushing in LIVING donors.
- Prolonged preservation, especially using extended criteria donor organs, may lead to primary dysfunction and affect short-term function and long-term outcome after transplantation.

- The donor organ must be flushed free of the cold storage solution prior to transplantation into the recipient.
- ViaSpan must be filtered prior to use in order to reduce the amount of particles which are present in the preservation solutions (see 4.2 for filtration instructions).

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.

4.6 Fertility, pregnancy and lactation

No animal or clinical studies with ViaSpan have been performed on reproduction toxicity, during pregnancy, lactation or placental place.

4.7 Effects on ability to drive and use machines

Not relevant.

4.8 Undesirable effects

If the cold storage solution is not completely flushed out of the organ with a physiological solution prior to transplantation in the recipient cardiovascular complications (such as bradyarrhythmia, cardiac arrest) may occur due to the potassium and adenosine content (see section 4.2). Sensitivity to one of the drug ingredients in ViaSpan or one of the additives (penicillin, insulin and dexamethasone) may also occur (see section 4.3).

Livers which have been preserved for an extended period may develop progressive clinical complications (including impaired liver function, organ failure, rejection, ischaemic type lesions of the bile ducts). These may lead to deterioration of the prognosis and, in some cases, to the death of the patient. Histologically, ischaemic type lesions and, in some cases mild rejection are observed. To date no causal relationship between these clinical problems and the use of ViaSpan has been demonstrated.

4.9 Overdose

If the donor organ is not flushed free of the cold storage solution as recommended the recipient may experience cardiovascular complications or allergic reactions. (see section 4.2). In this case, the patient should be treated as medically indicated.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic Group: Solution for perfusion and storage of organs (kidney, liver and pancreas), for transplantation, ATC Code: V07AB

ViaSpan has been demonstrated to be an effective preservation solution for livers, kidneys and pancreas in animal and human studies.

Systemic exposure of the patient to this product is not likely. The following contribution of the components of ViaSpan towards the preservation of organs has been either assumed or proven.

Pharmacological Properties

Component	Purpose
Pentafraction	Colloid, reduction of interstitial oedema and endothelial cell swelling
Lactobionic Acid	Impermeant; suppression of hypothermic cell swelling
Potassium Hydroxide	Maintenance of intracellular Na^+/K^+ concentration
Sodium Hydroxide	Maintenance of intracellular Na^+/K^+ concentration
Adenosine	Restoration of high energy phosphate (ATP)
Allopurinol	Inhibition of xanthine oxidase activity and purine metabolism/reduction of O2 free radicals
Potassium Dihydrogen Phosphate	pH buffer Maintenance of intracellular Na^+/K^+ concentration Restoration of high energy phosphate (ATP)
Magnesium Sulphate	Preservation of intracellular Mg^{2+} concentration
Raffinose	Impermeant; suppression of hypothermic cell swelling
Glutathione	Antioxidant Restoration of high energy phosphate (ATP)
Additives	**Purpose**
Penicillin	Bactericidal action
Dexamethasone	Cytoprotective action
Insulin	Promotion of anaerobic energy production

5.2 Pharmacokinetic properties

Pharmacokinetic evaluation on ViaSpan has not been conducted in human or animal transplant recipients since the solution is not intended for systemic administration.

5.3 Preclinical safety data

Carcinogenicity, mutagenicity, and fertility/reproductive toxicity studies as well as acute and chronic animal toxicity studies with ViaSpan have not been performed since the solution is not intended for systemic administration.

In one study involving rat livers, which have been perfused with ViaSpan, it has been reported that the particles in this specific rat model can cause microcirculation disturbances. The relevance of these results for human transplantations, if any, is not known.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium Hydroxide 20% (pH adjuster)
Hydrochloric Acid 14.6% (pH adjuster)
Water for Injection

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned in section 4.2.

6.3 Shelf life

Unopened bag: 1 year

After adding the additives to the solution the cold storage solution should be used immediately for the organ preservation.

6.4 Special precautions for storage

Store the product at 2 − 8°C. Do not freeze. Store in the original container. Do not remove over wrap until immediately prior to use.

6.5 Nature and contents of container

PVC bag containing 1 l solution.
Pack size: Box of 6 bags.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

See also section 4.2.

ViaSpan is packaged in sterile plastic bags which over time will release stearates and palmitates and could result in variable amounts of visible and sub-visible particles.

Remove overwrap immediately prior to use. Check the ViaSpan container for leaks by squeezing the container firmly. If leaks are found, discard solution container. **With the overwrap removed, carefully perform a visual inspection of the solution for particulate matter and do not use if obvious particulate matter, precipitates, or contamination is evident in the solution or if it is discoloured.** Bags which pass visual inspection must be filtered at the time of use with an in-line Pall Blood Transfusion Filter (No SQ40S) as instructed in section 4.2. Only this filter is recommended for use with ViaSpan.

Using the solution at 2 − 8°C the isolated organ is flushed immediately before or after removal from the deceased donor or immediately after removal from the living donor. The solution is then left in the organ vasculature during hypothermic storage and transportation. This solution is to be used for cold storage of the organ and not for continuous machine perfusion. Administration of the solution at the recommended temperatures will effectively cool the organ.

Any unused portion of the cold storage solution must be discarded. Any unused product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

Bristol-Myers Squibb Pharmaceuticals Limited
Swords
County Dublin

8 MARKETING AUTHORISATION NUMBER

PA 2/75/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 3 December 2001

Date of last renewal: 18 July 2010

10 DATE OF REVISION OF THE TEXT

February 2012