

SUMMARY OF PRODUCT CHARACTERISTICS

Product Summary

1. TRADE NAME OF THE MEDICINAL PRODUCT

RescueFlow*, solution for infusion

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1000 ml contains

<u>Active substances</u>	<u>Quantity</u>
Dextran 70 for injection	60 g
Sodium chloride	75 g

For excipients, see 6.1.

pH 3.5 to 7.0.

3. PHARMACEUTICAL FORM

Solution for infusion (clear, colourless).

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications

Initial treatment of hypovolemia with hypotension induced by traumatic injury.

4.2 Posology and Method of Administration

RescueFlow is administered as a single 250 ml dose intravenously, as the initial treatment after primary stabilisation of respiration and bleeding. RescueFlow should be given by rapid i.v. infusion (a full dose in two to five minutes). Treatment with RescueFlow should be followed by immediate administration of isotonic fluids, dosed according to the needs of the patient.

4.3 Contra-indications

Known hypersensitivity to the active substances or to any of the excipients.

Pregnancy at term (see section 4.6).

4.4 Special Warnings and Special Precautions for Use

Attention should be paid to haemostatic competence in patients on concomitant treatment with drugs known to affect coagulation. The amount of dextran 70 contained in RescueFlow (15 g) will not per se affect haemostasis, since changes in haemostatic variables only occur at doses above 1.5 g dextran /kg bodyweight. Aggressive fluid resuscitation can, however, dilute blood clotting factors to such an extent that a bleeding diathesis occurs.

As RescueFlow is a potent volume expander, caution should be exercised in patients with compromised cardiac function.

In patients with diabetes mellitus having severe hyperglycaemia with hyperosmolality, hypertonic solutions should be used with caution. If this condition is known or suspected other forms of fluid treatment should be considered.

Pretreatment with hapten dextran (Promit, Promiten) has been shown to reduce the risk of hypersensitivity reactions during dextran usage. In the clinical trials performed to document RescueFlow for the initial treatment of trauma induced hypotension, no such pretreatment was given. The potentially higher risk for anaphylactic reactions with this procedure should be observed and weighed against the expected benefit to the patient.

4.5 Interaction with other Medicaments and other forms of Interaction

None known. However, see 4.4.

4.6 Pregnancy and Lactation

There is no clinical experience with RescueFlow during pregnancy. In animal studies, effects on the foetus have been observed with dextran 70 (see 5.3). The relevance of these data for humans is unknown.

Anaphylactic reactions in the mother in connection with parturition have been observed to cause anoxia in the foetus. Foetal death and neurological sequelae has occurred in connection with the use of infusion fluids containing dextran 40 without pre-injection of hapten dextran (Promit, Promiten).

RescueFlow should therefore not be administered to pregnant women at term or in association with delivery.

Lactation:

It is not known to what extent RescueFlow passes into breast milk. In view of the active substances, its use in lactating mothers is not considered to pose any risk to the child.

4.7 Effects on Ability to Drive and Use Machines

Not applicable.

4.8 Undesirable Effects

No undesirable effects have been attributed to RescueFlow in the clinical trauma trials. Local pain close to the site of infusion has been observed in healthy volunteers. It was attenuated by gentle massage distal to the infusion site. See Section 4.4 regarding the risk for anaphylactic reactions to dextrans and the use of hapten dextran.

4.9 Overdose

Not applicable. RescueFlow 250 ml is administered as a single dose.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

ATC: B05A A05

Both dextran 70 and sodium chloride contribute to the effect of RescueFlow on intravascular volume. Water, primarily from the intracellular compartment, is rapidly shifted into the vascular compartment by the hypertonic component, 7.5% NaCl. The effect of the hypertonic component subsides rapidly due to extravasation of sodium and chloride. The dextran component remains in the circulation for much longer and contributes to a prolonged duration of the volume effect. The increase of intravascular volume provided by 250 ml of RescueFlow has been found to be two to three times the infused volume, similar to the increase in volume resulting from intravenous administration of three litres of crystalloid solution.

Statistically significant overall survival benefit of RescueFlow compared to standard of care was not demonstrated in the clinical trials. In subgroup analyses treatment benefits were observed for patients with severe injuries such as penetrating injury requiring surgery and for patients requiring intensive care.

5.2 Pharmacokinetic Properties

The pharmacokinetic properties of sodium chloride and dextran 70, respectively, are not affected by simultaneous infusion. After infusion of RescueFlow, plasma sodium increases by 9 to 12 mmols returning to normal in less than four hours. Dextran 70 has a plasma half-life of 6 to 8 hours. Dextran molecules below the threshold for glomerular filtration (molecular size less than 50 000 D) are excreted in the urine unaltered while larger molecules are taken up by the RES where they are degraded to glucose by endogenous dextranases.

5.3 Preclinical Safety Data

In acute and subacute toxicology studies of RescueFlow and its active components, doses 4 to 5 times the clinical dose, on a body weight basis, have resulted in toxic effects such as disorientation, inactivity, vomiting, increased salivation and a few cases of lethality, mainly due to the hypertonic sodium chloride component.

In studies in pregnant rabbits and mice in which 6 % dextran 70 was administered during the period of organogenesis, delayed ossification was observed in the foetuses of both species after daily doses two and six times higher than that contained in one unit of RescueFlow to man. In mice there was also an increase in the incidence of exencephaly. It is not known whether the hypertonic component could enhance this effect. There are no studies covering the last trimester of gestation.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Hydrochloric acid
Sodium hydroxide
Water for injections

6.2 Incompatibilities

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

6.3 Shelf Life

2 years

6.4 Special Precautions for Storage

No special precautions for storage.

6.5 Nature and Contents of Container

Plastic bags of PVC, 6 x 250 ml and 12 x 250 ml. The bag is provided with a twist-off connector and a PVC tube.

6.6 Instruction for Use/Handling

No special requirements.

Administrative Data

7. MARKETING AUTHORISATION HOLDER

BioPhausia AB

SE – 741 74 UPPSALA

Sweden

8. MARKETING AUTHORISATION NUMBER

PL 15135/0007

9. DATE OF FIRST AUTHORISATION/RENEWAL OF AUTHORISATION

17 September 1999

10. DATE OF (PARTIAL) REVISION OF THE TEXT

13 March 2002

Vitaline Pharmaceuticals UK Ltd
Chiltern House
Unit P Howland Road
Thame Oxon
OX9 3GQ