freeflex®

PACKAGE LEAFLET: INFORMATION FOR THE USER

Volulyte 6%

solution for infusion

Hydroxyethyl starch (HES 130/0.4) in an isotonic electrolyte solution

Read all of this leaflet carefully before you start using this medicine.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What is Volulyte is and what it is used for

Volulyte is a solution for intravenous infusion. It belongs to a group of medicines known as plasma volume substitutes. They work by increasing and maintaining the circulating blood volume for several hours. This helps to keep your blood pressure stable.

Volulyte is used for the treatment and prevention of low blood volumes (hypovolaemia) in adults and children.

2. What you need to know before you take Volulyte

Do not use **Volulyte if you:**
- suffer from severe generalised infection (sepsis)
- have a severe liver disease
- have a known allergy (hypersensitivity) to hydroxyethyl starch
- have a clinical condition where too much fluid in your body is a potential problem, especially if you have too much fluid in your lungs (pulmonary oedema) or if you suffer from a condition in which your heart cannot pump enough blood to other organs of your body (congestive heart failure)
- have pre-existing blood clotting (coagulation) or bleeding disorders
- suffer from kidney failure and you produce little or no urine, if this is not caused by low blood volumes (hypovolaemia)
- receive dialysis treatment
- have a severe increase of potassium, sodium or chloride levels in your blood (severe hyperkalaemia, severe hypernatraemia or severe hyperchloraemia)
- suffer from bleeding in the brain (intracranial bleeding).

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Warnings and precautions
It is important to tell your doctor if you have:
- impairment of your liver function
- problems with your heart or circulation
- blood clotting (coagulation) disorders
- problems with your kidneys

In case of certain serious diseases, your doctor will consider to use salt solutions instead of Volulyte.

Volulyte should be avoided if you have kidney disease and must not be used if you are treated with dialysis.

<u>During treatment by your doctor:</u>
During treatment with Volulyte it is important that:
- sufficient fluid is supplied to you
- your doctor regularly monitors your kidney and liver function, fluid balance and serum electrolytes (the salts dissolved in your blood).

Because of the risk of allergic (anaphylactic/anaphylactoid) reactions, you will be monitored closely to detect early signs of an allergic reaction when you receive this medicine.

Your doctor will adjust the dose of Volulyte carefully in order to prevent fluid overload. This will be done especially if you have problems with your lungs or with your heart or circulation. If necessary you may receive additional salts. In cases of severe lack of fluid (dehydration), your doctor should administer a salt solution first.

If clinically relevant impaired kidney function occurs during therapy, your doctor will stop giving you this medicine. If, for other reasons you are in hospital for long-term, your doctor may need to monitor your kidney function for up to 90 days.

If you are given Volulyte repeatedly or in open heart surgery your doctor will monitor the ability of your blood to clot. In case of a relevant impairment of the ability of your blood to clot, your doctor will stop giving you this medicine.

<u>Children</u>
No clinical trials with the product have been performed in children. However, there is experience in the use of a similar product containing the same hydroxyethyl starch (HES 130/0.4) in 0.9% sodium chloride solution in children.

Your doctor may give the product to children after careful evaluation of advantages and disadvantages.

Your doctor will adapt dosage in children to individual patient needs, taking into account underlying disease, haemodynamics and hydration status.

Other medicines and Volulyte
Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription. To date, Volulyte is not known to have any interactions with other medicines.

Volulyte with food and drink
Volulyte is not known to have any negative effect when given at the same time as food or drink.

Pregnancy and breast-feeding
For Volulyte no clinical data on exposed pregnancies are available.

Your doctor will only give Volulyte after having weighed the benefits versus the potential risk to the baby.

It is not known whether this drug is excreted in human milk. Your doctor will advise you whether to interrupt breast-feeding or not.

Driving and using machines
After receiving Volulyte, your ability to drive a car or operate machinery will not be affected.

3. How to use Volulyte

Volulyte will be given to you by, or under the direct supervision of, your physician, who will closely control the amount of Volulyte given to you.

Mode of administration
You will receive this medicine by infusion into a vein (intravenous drip). The speed of infusion, along with the amount of solution infused, will depend on your specific requirements, the disease for which the product is being used, and by reference to maximum daily dose.

Dosage
Your doctor will decide on the correct dose for you to receive.

The recommended maximum daily dose is up to 50 ml of Volulyte per kg of body weight.

Use in children and adolescents:
Your doctor may give the product to children after careful evaluation of advantages and disadvantages.

If you have received more Volulyte than you should
Your doctor will ensure that you receive the right amount of Volulyte. However, different people need different doses, and if the dose does prove too much for you, your doctor may stop Volulyte immediately and, if necessary, administer a medicine that removes water from the body (diuretic).

If you have any further questions on the use of this product, please ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, Volulyte can cause side effects, although not everybody gets them. If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or nursing staff immediately.

The undesirable effects are defined as follows:

Very common:	may affect more than 1 patient in 10 people
Common:	may affect up to 1 in 10 people
Uncommon:	may affect up to 1 in 100 people
Rare:	may affect up to 1 in 1,000 people
Very rare:	may affect up to 1 in 10,000 people
not known:	frequency cannot be estimated from the available data

Common (may affect up to 1 in 10 people)
- Itching is a known side effect of hydroxyethyl starches when used over long periods of time and at high doses.

- Other effects are associated with the dilution of the blood, which occurs at high dosages, such as prolonged blood clotting time.
- The level of the enzyme serum amylase can rise during administration of hydroxyethyl starch and can interfere with the diagnosis of inflammation of the pancreas (pancreatitis). However, Volulyte does not cause pancreatitis.

Rare (may affect up to 1 in 1,000 people)
- Medicinal products containing hydroxyethyl starch may lead to severe allergic reactions (reddening of the skin, swelling of the throat, and difficult breathing, mild influenza like symptoms, low or high heart rate, fluid in the lungs not caused by heart problems).
- After administration of hydroxyethyl starch disturbances of blood clotting beyond effects caused by dilution of your blood can occur depending on the dose.

5. How to store Volulyte

- Keep this medicine out of the sight and reach of children.
- Do not freeze.
- Do not store above 25 °C.

Do not use Volulyte after the expiry date which is stated on the label. The expiry date refers to the last day of that month.

Your doctor or nurse will ensure that the solution is clear, free from particles, the container undamaged and the overwrap is removed from the polyolefine (**free***flex*) bag before use.

The solution should be used immediately after opening, and any solution remaining after treatment should be discarded. For single use only.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

6. Contents of the pack and other information

What Volulyte contains:

1000 ml solution for infusion contain

The active substances are:

Poly (O-2-hydroxyethyl) starch – Molar substitution: 0.38 – 0.45 – Mean molecular weight (M_w): 130.000 Da (manufactured from waxy maize starch)	60.00 g
Sodium acetate trihydrate	4.63 g
Sodium chloride	6.02 g
Potassium chloride	0.30 g
Magnesium chloride hexahydrate	0.30 g

Electrolytes:	
Na^+	137.0 mmol/l
K^+	4.0 mmol/l
Mg^{++}	1.5 mmol/l
Cl^-	110.0 mmol/l
CH_3COO^-	34.0 mmol/l

Theoretical osmolarity:	286.5 mosm/l
pH:	5.7 – 6,5
Titratable acidity:	< 2.5 mmol NaOH/l

The other ingredients are:
Sodium hydroxide, hydrochloric acid, water for injection.

What Volulyte looks like and contents of the pack
Volulyte is a sterile, clear to slightly opalescent solution, colourless to slightly yellow. It is contained in:
- flexible bags made of polyolefine (**free***flex*)
- in a glass bottle
- in a PE bottle (KabiPac)

All container types are available in 250 ml and 500 ml sizes.

The following information is intended for medicinal or healthcare professionals only:

Volulyte is used for the treatment and prevention of low blood volumes (hypovolaemia) in adults and children. It is not a substitute for red blood cells or coagulation factors in plasma.

Posology and method of administration

Volulyte is administered by intravenous infusion only.

The daily dose and rate of infusion depend on the patient's blood loss, on the maintenance or restoration of haemodynamics and on the haemodilution (dilution effect). Volulyte can be administered repetitively over several days.

The initial 10 to 20 ml should be infused slowly, keeping the patient under close observation due to possible anaphylactic/anaphylactoid reactions.

Adult dose:

Up to 50 ml of Volulyte per kg of body weight per day (equivalent to 3.0 g hydroxyethyl starch, 6.85 mEq sodium and 0.2 mEq potassium per kg of body weight). This dose is equivalent to 3,500 mL Volulyte for a 70 kg patient.

Paediatric use and paediatric dose:

No clinical trials with the product have been performed in paediatric patients (see section 2). However, clinical data on the use of a similar product containing HES 130/0.4 (6%) in 0.9% sodium chloride solution in paediatric patients is available. In one trial newborns and infants < 2 years of age undergoing elective surgery were randomised to receive HES 130/0.4 in 0.9% sodium chloride (N = 41) or 5% albumin (N = 41). The mean dose of HES 130/0.4 in 0.9% sodium chloride administered was 16 ± 9 ml/kg. Administration of this product to children up to 2 years including newborns and infants was safe and well tolerated.

In an additional trial, children from 2–12 years of age undergoing cardiac surgery were randomised to receive HES 130/0.4 in 0.9% sodium chloride (N = 31) or 5% albumin (N = 30). The mean dose administered was 36 ± 11 ml/kg.

The product may be given to children after careful benefit/risk evaluation (in particular in children below one year of age who independently of the product have a potential to develop lactic acidosis) taking into account the disease state, as well as haemodynamic and hydration status.

The dosage in children should be adapted to the individual patient colloid needs, taking into account the disease state, as well as haemodynamics and hydration status.

Special warnings and precautions for use

In critically ill patients, crystalloids should be used primarily, and HES products should only be used, if crystalloids are not sufficient to stabilise the patient, and if the anticipated benefit justifies the risk.

Anaphylactic/anaphylactoid reactions (hypersensitivity, mild influenza-like symptoms, bradycardia, tachycardia, bronchospasm, non-cardiac pulmonary oedema) have been reported with solutions containing hydroxyethyl starch. If a hypersensitivity reaction occurs, administration of the drug should be discontinued immediately and the appropriate treatment and supportive measures should be undertaken until symptoms have resolved.

Avoid use in patients with pre-existing renal dysfunction.

Discontinue use of Volulyte at the first sign of clinically relevant renal injury.

Continue to monitor renal function in hospitalised patients for at least 90 days as use of renal replacement therapy has been recorded up to 90 days after administration of HES products.

Monitor the coagulation status in patients undergoing open heart surgery in association with cardio-pulmonary bypass as excess bleeding has been reported with other HES solutions in this population. Discontinue the use of Volulyte at the first sign of clinically relevant coagulopathy.

Avoid fluid overload; adjust dosage in patients with cardiac or renal dysfunction.

Fluid status and rate of infusion should be assessed regularly during treatment, especially in patients with cardiac insufficiency or severe kidney dysfunction.

In cases of severe dehydration a crystalloid solution should be given first. Generally, sufficient fluid should be administered in order to avoid dehydration.

Particular care must be taken in patients with electrolyte abnormalities.

In metabolic alkalosis and clinical situations where alkalisation should be avoided, saline based solutions like a similar product containing HES 130/0.4 in 0.9% sodium chloride solution should be preferred over alkalising solutions like Volulyte.

Clinical evaluation and periodic laboratory determinations are necessary to monitor fluid balance, serum electrolyte concentrations, kidney function, acid-base balance, and coagulation parameters during prolonged parenteral therapy or whenever the patient's condition warrants such evaluation. Monitor liver function in patients receiving HES products, including Volulyte.

Consideration should be given to the concomitant administration of medicinal products that can cause potassium or sodium retention.

Pregnancy and breast-feeding:
For Volulyte no clinical data on exposed pregnancies are available. The safety of the product in pregnant and breast-feeding women has not been investigated.

There are limited clinical study data available from the use of a single dose of HES 130/0.4 (6%) in 0.9% sodium chloride in pregnant women undergoing caesarean section with spinal anaesthesia. The occurrence of hypotension was significantly lower for HES 130/0.4 (6%) in combination with crystalloid compared to crystalloid control alone (36.6% vs. 55.3%). Overall efficacy evaluation showed significant benefits for HES 130/0.4 (6%) in the prevention of hypotension and in the occurrence of severe hypotension compared to crystalloid control. No negative influence of HES 130/0.4 (6%) in 0.9% sodium chloride on patient safety could be detected; a negative influence on the neonate could also not be detected.

Animal studies with a similar product containing HES 130/0.4 in 0.9% sodium chloride solution do not indicate harmful effects with respect to pregnancy, embryo/foetal development, parturition or postnatal development. No evidence of teratogenicity was seen.

Volulyte should be used during pregnancy only if the potential benefit justifies the potential risk to the foetus.

Information on the use of Volulyte during labour or delivery is unknown with the exception of caesarean section (see above). Use if clearly needed.

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Volulyte is administered to a nursing woman.

How to store Volulyte
For single use only

To be used immediately after the bottle or bag is opened.

Do not use Volulyte after expiry date. Any unused solution should be discarded. Any unused solution should be disposed of in accordance with local requirements.

Use only clear, particle-free solutions and undamaged containers.

Remove the overwrap from the Polyolefine (**free***flex*) bag prior to use.

Do not freeze.

Do not store above 25 °C.

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