The use of Volulyte in critically ill patients, including those with severe sepsis, is associated with an increased risk of death or the need for renal replacement therapy.

1 PRODUCT NAME

VOLULYTE® 6% solution for infusion

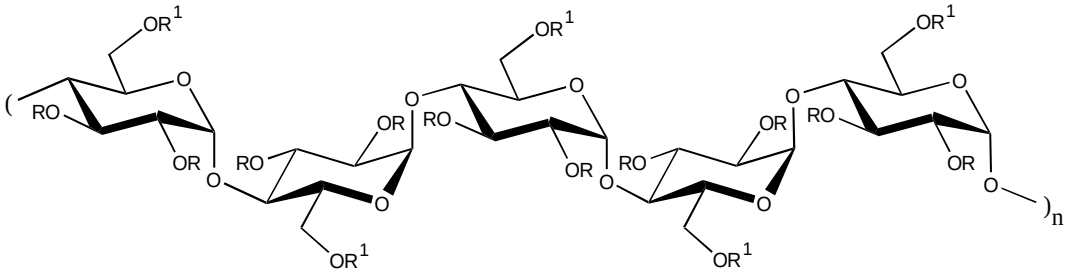
2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Active	Amount(L)
Hydroxyethyl starch 130/0.4	60.0 g
Sodium chloride	6.02 g
Sodium acetate trihydrate	4.63 g
Potassium chloride	0.30 g
Magnesium chloride hexahydrate	0.30 g

Electrolytes	Amount/L
Sodium (Na^+)	137.0 mmol
Potassium (K^+)	4.0 mmol
Magnesium (Mg^{2+})	1.5 mmol
Chloride (Cl^-)	110.0 mmol
Acetate (CH_3COO^-)	34.0 mmol
Titratable acidity:	< 2.5 mmol NaOH/L

For the full list of excipients, see Section 6.1 List of excipients.

Chemical structure



R = -H, $-CH_2CH_2OH$
R^1 = -H, $-CH_2CH_2OH$ or glucose units

Molar substitution: 0.4 (0.38 – 0.45)

Weight average molecular weight: 130,000 ± 20,000 Dalton

Chemical name: Poly (O-2 hydroxyethyl) starch

Active Substance	**CAS number**
Hydroxyethyl Starch 130/0.4	9005-27-0

Hydroxyethyl Starch 130/0.4 is a white to yellowish white, odourless and tasteless, amorphous powder, readily soluble in water at room temperature, soluble in DMSO, practically insoluble in most organic solvents

3 PHARMACEUTICAL FORM

Solution for infusion.
Volulyte (HES 130/0.4 in a balanced electrolyte solution) is a clear to slightly opalescent solution, colourless to slightly yellow.

Osmolality:	approx. 260 - 310 mOsm/kg water
Theoretical osmolarity	286.5mosm/l
pH:	5.7 – 6.5

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Treatment of hypovolaemia due to acute blood loss when crystalloids alone are not considered sufficient. The use of Volulyte is not a substitute for the appropriate use of packed red blood cells or fresh frozen plasma.

4.2 Dose and method of administration

For intravenous infusion.

Use of Volulyte should be restricted to the initial phase of volume resuscitation with a maximum duration of use of 24 hours.

Administration of Volulyte may cause anaphylactic reactions that may manifest as acute hypotension. In all patients, the initial 10-20 mL of Volulyte should be infused slowly, keeping the patient under close observation for anaphylactic/anaphylactoid reactions manifesting as unexpected hypotension, or the development of wheeze or rash, (Please also refer to section 4,.4 and 4.8)

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).

In clinical trials, infusions up to 33 mL/kg/day were most commonly used. There is limited experience with infusions between 33 mL/kg/day and 50 mL/kg/day.

Hepatic and renal monitoring is necessary at higher doses, (Please also refer to section 4.4)

The majority of clinical trial data stem from maximal dose of up to 33mL/kg/day.

Volulyte can be administered repetitively over several days according to the patient's needs. The duration of treatment depends on the duration and extent of hypovolaemia and shock, the haemodynamics and on the haemodilution.

Treatment of children
Data are limited in children. It is therefore recommended not to use HES products in paediatric patients,(please also refer to section 4.4)

Instructions for use/handling
Each container should be used in one patient and on one occasion only. It should be used immediately after the bottle or bag is opened and any unused solution must be discarded. The solution contains no antimicrobial preservatives. Do not use if the solution is not clear or if the container is damaged.

(Please also refer to ***Appendix "SPECIAL HANDLING INSTRUCTIONS"***).

4.3 Contraindications
Volulyte should not be used, if any one or more of the following clinical conditions apply:

- Critically ill patients (typically admitted to intensive care unit), including those with sepsis.Fluid overload (hyperhydration), especially in cases of pulmonary oedema and congestive cardiac failure
- Patients with pre-existing coagulation or bleeding disorders
- Renal failure with oliguria or anuria not related to hypovolaemia
- Patients receiving dialysis treatment
- Intracranial bleeding
- Known hypersensitivity to hydroxyethyl starches
- Patients with severe liver disease
- Patients with severe hyperkalaemia, severe hypernatraemia or severe hyperchloraemia

4.4 Special warnings and precautions for use
Volulyte is not a substitute for red blood cells or coagulation in plasma.

Fluid Overload
Administration of Volulyte may cause fluid overload, resulting in cardiac and pulmonary failure. Administration should be carefully titrated to relevant physiological endpoints. Particular care must be taken in patients with cardiac insufficiency or severe renal dysfunction.

Dehydration

In cases of severe dehydration a crystalloid solution should first be given. Intravenous fluid resuscitation in cases of severe dehydration should be through the use of crystalloid solutions.

Bleeding risk
Volulyte administration may cause coagulopathy, either through a direct effect; or indirectly through the dilution effect. This will increase the risk of bleeding. Administration should be ceased if a coagulopathy develops or excessive bleeding occurs.

Cardiopulmonary bypass
Coagulation status must be closely monitored during cardiopulmonary bypass in patients receiving Volulyte because of the bleeding risk.

Surgery and trauma
There is a lack of robust, long-term safety data in patients undergoing surgical procedures and in patients with trauma. The expected benefit of treatment should be carefully weighed against uncertainty with regard to this long term safety. Other available treatment options should be considered.

Renal function
Avoid use in patients with pre-existing renal dysfunction.

Discontinue use of HES at the first sign of renal injury. A need for renal replacement therapy has been reported up to 90 days after HES administration. Continue to monitor renal function for at least 90 days in any case of deterioration of renal function.

Liver function
Monitor liver function in patients receiving HES products, including Volulyte.

Anaphylactic/anaphylactoid reactions
Regarding the occurrence of anaphylactic/anaphylactoid reactions please refer to" " section 4.8 UNDESIRABLE EFFECTS".

Laboratory Assessments
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.

Use in the elderly
Clinical experience with 6% HES 130/0.4 (including published trials) has included elderly populations, some exclusively with patients of 70 years and above. Dose reduction was not required and safety has been comparable to control treatments (gelatin or albumin) in elderly patients.

Paediatric use
There is lack of robust, long-term safety data in children undergoing surgical procedures. The expected benefit of treatment should be carefully weighed against uncertainty with regard to this long-term safety and informed consent obtained from the patient/parent where possible. Other available treatment options should be considered.

Effects on laboratory tests
No data available.

4.5 Interaction with other medicines and other forms of interactions

No interactions of Volulyte with other drugs or nutritional products are known to date.
Consideration should be given to the concomitant administration of medicinal products that can cause potassium or sodium retention.

Please refer to "section 4.8 "undesirable effects" concerning the concentration of serum amylase which can rise during administration of hydroxyethyl starch and can interfere with the diagnosis of pancreatitis.

4.6 Fertility, pregnancy and lactation

Effects on fertility

HES 130/0.4 10% solution in 0.9% sodium chloride did not impair fertility in male rats at IV doses up to 5 g/kg/day. In female rats, no adverse effects on fertility were observed at doses up to 2.5 g/kg/day. Slight inhibition of ovulation, evident as a decrease in corpora lutea and resulting in a reduced number of fetuses, was observed at a maternotoxic dose of 5 g/kg/day IV.

Use in pregnancy (Category B3)

No clinical data are currently available on the use of Volulyte during pregnancy.

Studies in pregnant rats and rabbits showed that the type of hydroxyethyl starch present in Volulyte was associated with embryo fetal toxicity following IV administration at 5 g/kg/day. The embryo fetal toxicity included resorptions, stillbirths, reduced fetal weight and delayed fetal development, but was only observed in conjunction with maternotoxicity.

Volulyte should not be used during pregnancy, unless the expected therapeutic benefit clearly outweighs the potential risk to the fetus.

Use in lactation

It is not known whether hydroxyethyl starch is excreted in human breast milk. The excretion of hydroxyethyl starch in milk has not been studied in animals.A study in lactating rats showed that the type of hydroxyethyl starch present in Volulyte was associated with decreased postnatal growth and development following IV administration at 5 g/kg/day, a maternotoxic dose. A decision on whether to continue/discontinue breast-feeding or to discontinue/continue therapy with Volulyte should be made taking into account the benefit of breast-feeding to the child and the benefit of Volulyte therapy to the nursing mother.

There are currently no clinical data available on the use of Volulyte 6% in lactating women.

Electrolyte disturbances

Particular care must be taken in patients with severe electrolyte abnormalities like hypermagnesaemia.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. Serum electrolytes should be monitored.

4.7 Effects on ability to drive and use machines

Volulyte has no influence on the ability to drive and use machines.

4.8 Undesirable effects

The undesirable effects are divided into: *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 (<10,000), not known (cannot be estimated from the available data).*

Blood and lymphatic system disorders

Rare (in high dose): With the administration of hydroxyethyl starch disturbances of blood coagulation beyond dilution effects can occur depending on the dosage.

Immune system disorders

Rare: Medicinal products containing hydroxyethyl starch may rarely lead to anaphylactic/anaphylactoid reactions (hypersensitivity, mild influenza-like symptoms, bradycardia, tachycardia, bronchospasm, non-cardiac pulmonary oedema). In the event of an intolerance reaction occurring, the infusion should be discontinued immediately and the appropriate emergency medical treatment initiated.

Skin and subcutaneous tissue disorders

Common (dose dependent): Prolonged administration of high dosages of hydroxyethyl starch may cause pruritus (itching) which is a known undesirable effect of hydroxyethyl starches. The itching may not appear until weeks after the last infusion and may persist for months.

Investigations

Common (dose dependent): The concentration of serum amylase can rise during administration of hydroxyethyl starch and can interfere with the diagnosis of pancreatitis. The elevated amylase is due to the formation of an enzyme-substrate complex of amylase and hydroxyethyl starch subject to slow elimination and must not be considered diagnostic of pancreatitis.

Common (dose dependent): At high dosages the dilution effects may result in a corresponding dilution of blood components such as coagulation factors and other plasma proteins and in a decrease of haematocrit.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://nzphvc.otago.ac.nz/reporting.

4.9 Overdose

As with all volume substitutes, overdose can lead to overloading of the circulatory system (e.g. pulmonary oedema). In this case the infusion should be stopped immediately and if necessary, a diuretic should be administered.

For advice on the management of overdose, contact the national Poison Information Centre on 0800 764 766 (New Zealand).

5 PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Plasma substitutes and plasma protein fractions.
ATC code: B05A A07

5.1 Pharmacodynamic properties

Mechanism of action

Volulyte is an artificial colloid for volume replacement whose effect in intravascular volume expansion and haemodilution depends on the molar substitution by hydroxyethyl groups (0.4), the mean molecular weight (130,000 Da), the concentration (6%), as well as the dosage and infusion rate. HES 130/0.4 contained in Volulyte is derived from waxy maize starch and has a substitution pattern (C_2/C_6 ratio) of approximately 9:1.

Infusion of 500 mL of a similar product containing HES 130/0.4 (6%) in 0.9% sodium chloride solution in 30 minutes in volunteers results in a plateau-like non-expansive volume increase of approximately 100% of the infused volume which lasts for approximately 4 to 6 hours.

Isovolaemic exchange of blood with HES 130/0.4 in 0.9% sodium chloride solution maintains blood volume for at least 6 hours.

Volulyte contains the electrolytes sodium (Na^+), potassium (K^+), magnesium (Mg^{++}), chloride (Cl^-) and acetate (CH_3COO^-) in an isotonic composition. Acetate is a metabolisable anion which is oxidised in different organs and has an alkalising effect.

Volulyte contains a reduced amount of chloride compared to normal saline based solutions and therefore counteracts the development of hyperchloraemic metabolic acidosis, especially when large dose infusions are required or in patients at risk for the development of metabolic acidosis.

In cardiac surgery, chloride levels were statistically significantly lower and base excess levels were seen to be less negative for Volulyte in comparison to HES 130/0.4 (6%) in 0.9% sodium chloride solution. Please also refer to the “CLINICAL TRIALS” section.

Clinical trials

A prospective, randomized, double-blinded, multicentre, parallel group, phase III trial compared the clinical efficacy and safety of two different HES formulations: Volulyte (balanced group) versus a similar product containing 6% HES 130/0.4 in 0.9% sodium chloride solution (saline group) for intra- and post-operative volume therapy in patients undergoing cardiac surgery. Forty-three patients were randomized to Volulyte, 38 were randomized to 6% HES 130/0.4 in 0.9% sodium chloride solution.

The primary objective of the study was to demonstrate therapeutic equivalence between Volulyte and 6% HES 130/0.4 in 0.9% sodium chloride solution regarding the volume of study drug needed for adequate therapy. Consecutive objectives for confirmatory analysis were to show that Volulyte results in lower chloride levels and higher arterial pH than 6% HES 130/0.4 in 0.9% sodium chloride solution.

The volume usage was equivalent in both treatment groups. Volulyte showed statistically significant advantages in terms of lower chloride levels over 6% HES 130/0.4 in 0.9% sodium chloride solution.

Concerning the acid-base balance, there are explicit signs that treatment with Volulyte results in higher arterial pH, indicated by less negative base excess values.

The results for the efficacy variables are shown in the following table:

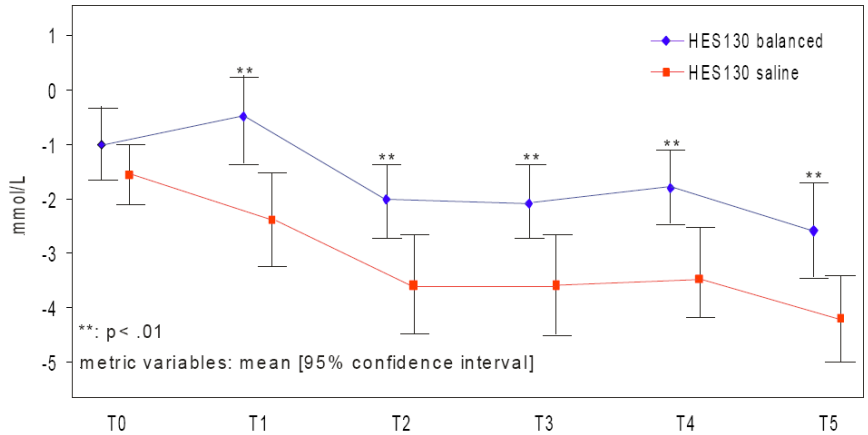
Variable Treatment / Treatment Contrast	Least squares mean	95% confidence interval	p-value
Volume of study drug (mL) administered until 6 hours post surgery			
Volulyte (n = 43)	2391	[2233 ; 2549]	
HES 130 saline (n = 38)	2241	[2075 ; 2408]	
Volulyte - HES 130 saline	150	[-77 ; 377] [a]	0.0015 [a]
Chloride level (mmol/L) at end of surgery			
Volulyte (n = 43)	110.0	[108.8 ; 111.1]	
HES 130 saline (n = 38)	111.8	[110.6 ; 113.0]	
Volulyte - HES 130 saline	-1.8	[-3.5 ; -0.1] [b]	0.0171 [b]
Arterial pH at end of surgery			
Volulyte (n = 43)	7.378	[7.365 ; 7.391]	
HES 130 saline (n = 38)	7.365	[7.352 ; 7.378]	
Volulyte - HES 130 saline	0.013	[-0.005 ; 0.031] [c]	0.0793 [c]

[a] since the confidence interval is entirely between -500 mL and 500 mL, statistically significant equivalence between treatment groups was shown.

[b] since the confidence interval is entirely below 0, the chloride level was shown to be statistically significantly lower for Volulyte than for HES 130/0.4 in 0.9% sodium chloride solution.

[c] since the confidence interval includes 0, statistical significance was not achieved.

The following figure demonstrates the course of the base excess during cardiac surgery:



T0 = after anaesthesia induction (baseline)
T1 = during extracorporeal circulation
T2 = after extracorporeal circulation
T3 = end of surgery
T4 = 1h after arrival at the intensive care unit
T5 = first post-operative morning

For base excess ANCOVA yielded highly significant group differences at all time points after baseline.

The following table shows the treatment contrast of base excess between Volulyte and HES 130/0.4 in 0.9% sodium chloride for different time points:

	Contrast 'Volulyte - HES 130/0.4 in 0.9% sodium chloride'		
Time point	**Least squares mean**	**95% confidence interval**	**p-value[a]**
During extracorporeal circulation (T1)	1.29	[0.64 ; 1.94]	<0.0001
After extracorporeal circulation (T2)	1.05	[0.29 ; 1.81]	0.0037
End of surgery (T3)	1.17	[0.34 ; 2.00]	0.0032
One hour after arrival at the ICU (T4)	1.30	[0.54 ; 2.06]	0.0005
First postoperative morning (T5)	1.50	[0.41 ; 2.60]	0.0039

[a] one-sided p-value for testing superiority of Volulyte over HES130/0.4 in 0.9% sodium chloride (i.e., higher base excess): Since the confidence interval does not include 0, statistically significant superiority of Volulyte was shown at each time point.

Groups were comparable with regard to overall safety.

There is no evidence that the addition of Mg^{2+}, K^+, and $acetate^-$ in the solvent of Volulyte in comparison to saline solutions influences coagulation parameters or bleeding events, as both the measured and calculated red blood cell loss showed no differences between treatment groups in this study.

Please also refer to the "CLINICAL TRIALS" section of the Voluven 6% Product Information. Voluven 6% is a similar product containing HES 130/0.4 in 0.9% sodium chloride solution.

5.2 Pharmacokinetic properties

The pharmacokinetics of hydroxyethyl starch is complex and depends on the molecular weight and mainly on the molar substitution degree and the substitution pattern (C_2/C_6 ratio). When applied intravenously, molecules smaller than the renal threshold (60,000 – 70,000 Da) are readily excreted in the urine, while larger ones are metabolised by plasma α-amylase before the degradation products are renally excreted.

The mean *in vivo* molecular weight of HES 130/0.4 in plasma is 70,000 – 80,000 Da immediately after infusion and remains above the renal threshold throughout the treatment period.

The volume of distribution is about 5.9 litres. Within 30 minutes of infusion the plasma level of HES 130/0.4 (6%) is still 75% of the maximum concentration. After 6 hours the plasma level has decreased to 14%. Following a single dose of 500 mL hydroxyethyl starch plasma levels almost return to baseline levels 24 hours.

Plasma clearance was 31.4 mL/min when 500 ml of HES 130/0.4 (6%) was administered with an AUC of 14.3 mg/mL x h. Plasma half-lives were $t_{1/2\alpha}$ = 1.4 h and $t_{1/2ß}$ = 12.1 h when 500 mL were administered on a single occasion.

Using the same dose (500 mL) in subjects with stable mild to severe renal impairment, the AUC moderately increased by a factor of 1.7 (95% confidence limits 1.44 and 2.07) in subjects with ClCr < 50 mL/min compared to > 50 mL/min. Terminal half life and peak HES concentration were not affected by renal impairment. At ClCr ≥ 30 mL/min, 59% of the drug could be retrieved in the urine, vs 51% at ClCr 15 to 30

mL/min. Plasma levels of HES 130/0.4 returned to baseline levels 24 hours following infusion.

The pharmacokinetics of HES 130/0.4 is very similar following single and multiple dose administration. No significant plasma accumulation occurred even after a daily administration of 500 mL of a 10% solution containing HES 130/0.4 to volunteers over a period of 10 days. Elimination rates in the urine were approximately 70% within 72 hours.

In an experimental model in rats using repetitive doses of 0.7 g/kg BW per day of HES 130/0.4 over 18 days, 52 days after the last administration tissue storage was 0.6% of the total administered dose.

Pharmacokinetic data in patients with hepatic insufficiency or in pediatric or geriatric patients are not available. Effects of gender on the pharmacokinetics of Volulyte 6% have not been studied.

Hydroxyethyl starch (HES) is a derivative of amylopectin, which is a highly branched compound of starch. In humans and animals amylopectin is rapidly hydrolysed by amylase. In order to reduce the metabolic degradation, glucose residues of the amylopectin are reacted with ethylene oxide. The hydroxyethyl groups can be introduced at three positions (C_2, C_3, C_6) of the glucose residues. The degree of substitution and the substitution pattern expressed by the C_2/C_6 ratio determines the enzymatic degradation of HES. Volulyte is characterised by its molar substitution, molecular weight and the C_2/C_6 ratio.

Molecular weight (Mw): The molecular weight indicates the weight average. The Mw of HES 130/0.4 lies between 110,000 and 150,000 Dalton, which corresponds approximately to 609 to 830 partially hydroxyethylated glucose units.

Molar substitution (MS): The ratio of hydroxyethyl groups to glucose units is called the molar substitution (MS). The MS for this substance is 0.4 (range 0.38 – 0.45) and determines the molar ratio of hydroxyethyl ether groups to glucose units.

C_2/C_6 ratio: This parameter gives information about the preferred position of hydroxyethylation and reflects the different intrinsic reactivity of the secondary and the primary alcohol functionality at the respective positions of the glucose ring. The value of the C_2/C_6 ratio should be higher than 8.

5.3 Preclinical safety data

Genotoxicity

In vitro genotoxicity studies revealed no evidence for mutagenicity or clastogenicity for the type of hydroxyethyl starch present in Volulyte. An in vivo chromosomal aberration study in rats was also negative at the tested dose of 5 g/kg/day IV of HES 130/0.4.

Carcinogenicity

The carcinogenic potential of Volulyte has not been investigated in animals.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Excipients	Amount
Sodium hydroxide to adjust pH	q.s
Hydrochloric acid to adjust pH	q.s
Water for injection	q.s

6.2 Incompatibilities

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

6.3 Shelf life

Approved shelf life as packaged for sale:

Freeflex bag 36 months
The product should be used immediately after opening.
For single use only. Discard unused portion.

6.4 Special precautions for storage

Store below 25°C. Do not freeze.

Each container should be used in one patient and on one occasion only. It should be used immediately after the bottle or bag is opened and any unused solution must be discarded. The solution contains no antimicrobial preservatives. Do not use if the solution is not clear or if the container is damaged.

6.5 Nature and contents of container

Polyolefin bag (Freeflex®) with overwrap
All packaging components for the Freeflex®bag are latex- and PVC-free.
Pack sizes

Freeflex® bags with overwrap	250 ml (Cartons of 20/30/35/40 bags)
Freeflex® bags with overwrap	500 mL (Cartons of 15/20 bags)

6.6 Special precautions for disposal and other handling

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

7 MEDICINE SCHEDULE

General Sale Medicine

8 SPONSOR

Fresenius Kabi New Zealand Limited
c/o GNZCC,
HSBC Tower, Level 14,
188 Quay Street, Auckland 1010,
New Zealand.
Freecall: 0800 144 892

9 DATE OF FIRST APPROVAL

Date of publication in the New Zealand Gazette of consent to distribute the medicine:
3 May 2012

10 DATE OF REVISION OF TEXT

27 September 2021

Summary table of changes

Section Changed	Summary of new information
All	Reformat Datasheet as per new Medsafe datasheet form
3	Added Theoretical osmolarity 308 mosm/l
6.3	Added Shelf life data

Section Changed	Summary of new information
6.4	Duplicated statement from section 4.2 "dose and method of administration"concerning storage after opening.
6.5	Added *Freeflex* Bag description and statement
8	New Zealand sponsor address changed
8	NZ address changed to, c/o GNZCC, HSBC Tower, Level 14,188 Quay Street, Auckland 1010, New Zealand.
10	Date of revision changes

APPENDIX: SPECIAL HANDLING INSTRUCTIONS

Method of administration

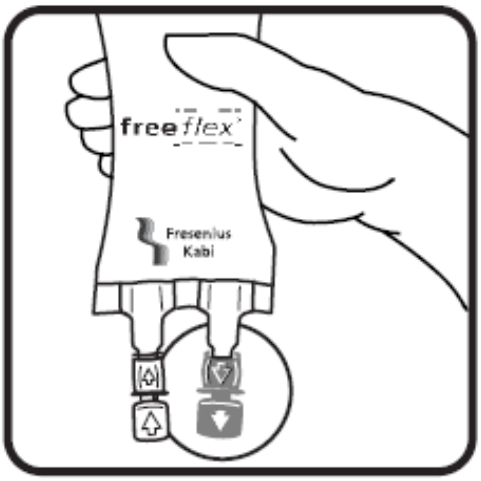
Precautions to be taken before administering product.

Before administering the product in plastic bags to patient, review these directions:

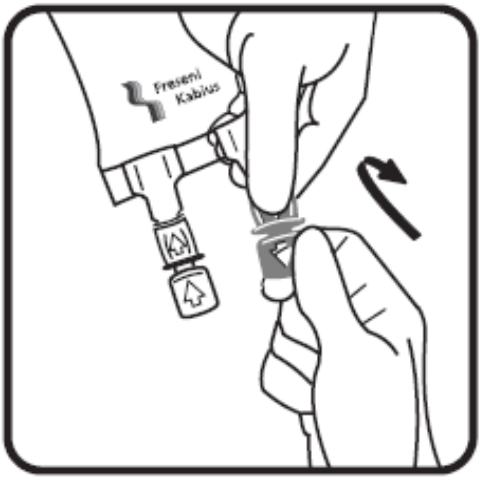
freeflex® IV Solution Container

(1) Check the expiry date and the solution for visible particles or cloudiness, do not use unless the solution is clear. Inspect the container for damage or leakage, if damaged do not use.

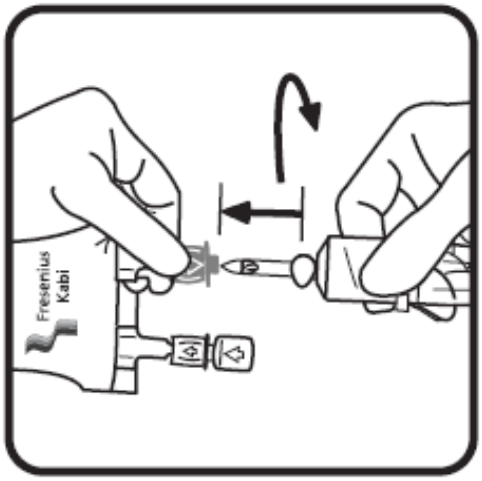
(2) Using the pre-cut corner tabs, peel open and remove the over-wrap.



(3) Identify the blue infusion (administration) port. **Use the BLUE port only to administer solution**. Never use the white port.



(4) Break off the blue tamper-evident cover from the freeflex® blue infusion port.



(5) Close roller clamp. Insert the spike until the clear plastic collar of the port meets the shoulder of the spike. Use a non-vented standard infusion set and close air inlet. Hang the bag on the infusion stand. Press drip chamber to get fluid level. Prime infusion set. Connect and adjust the flow rate.

Warnings

1. Do not remove the freeflex® IV container from its overwrap until immediately before use.
2. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.
3. Do not administer unless the solution is clear, free from particles and the freeflex® IV container is undamaged.
4. Volulyte should be used immediately after insertion of the administration set.
5. Use the BLUE port only to administer solution. Never use the white port.
6. Do not vent.

7. If administered by pressure infusion, air should be withdrawn or expelled from the bag through the medication/administration port prior to infusion.
8. Discontinue the infusion if an adverse reaction occurs.
9. It is recommended that administration sets are changed at least once every 24 hours.
10. For single use only. Discard unused portion.