SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Sodium Chloride Intravenous Infusion BP 0.9% w/v

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1000 ml of solution contains:

Sodium Chloride	9.0g

For the full list of excipients, see section 6.1

3. PHARMACEUTICAL FORM

A sterile non-pyrogenic intravenous infusion for administration to human beings.

4. CLINICAL PARTICULARS

4.1. Therapeutic Indications

Sodium Chloride Intravenous Infusion BP 0.9% w/v is of value as a source of water and electrolytes and is indicated for replenishing fluid and for restoring and maintaining the concentrations of sodium and chloride ions.

It is also of value in the treatment of poisoning, by aiding excretion.

It may also be used as a vehicle for the reconstitution and administration of intravenous medications.

4.2 Posology and method of administration

Posology

Adults, older people and children:
Doses may be expressed in terms of mEq or mmol of sodium, mass of sodium, or mass of sodium salt (1 g NaCl = 394 mg, 17.1 mEq or 17.1 mmol of Na and Cl).

Fluid balance, serum electrolytes and acid-base balance should be monitored before and during administration, with particular attention to serum sodium in patients with increased non-osmotic vasopressin release (syndrome of inappropriate antidiuretic hormone secretion, SIADH) and in patients co-medicated with vasopressin agonist drugs, due to the risk of hospital acquired hyponatraemia (see sections 4.4, 4.5 and 4.8). Monitoring of serum sodium is particularly important for hypotonic fluids.
Sodium Chloride 0.9% intravenous infusion has a tonicity of 308 mOsm/l (approx.)
The infusion rate and volume depend on age, weight, clinical condition condition (e.g. burns, surgery, head-injury, infections), and concomitant therapy should be determined by the consulting physician experienced in paediatric intravenous fluid therapy (see sections 4.4. and 4.8).

Recommended dosage

The recommended dosage for treatment of isotonic extracellular dehydration and sodium depletion is:

- For adults: 500 ml to 3 litres/24h
- For babies and children: 20 to 100 ml per 24h and per kg of body weight, depending of the age and the total body mass.

The recommended dosage when used as a vehicle or diluent ranges from 50 to 250 ml per dose of medicinal product to be administered.

When Sodium Chloride 0.9 % is used as a diluent for injectable preparations of other drugs, the dosage and the infusion rate will also be dictated by the nature and the dose regimen of the prescribed drug.

Method of administration

The solution is for administration by intravenous infusion through a sterile and non-pyrogenic administration set, using aseptic technique. The equipment should be primed with the solution in order to prevent air entering the system.

The product should be inspected visually for particulate matter and discoloration prior to administration. Do not administer unless solution is clear, free from visible particles and the seal is intact.

Do not remove unit from overwrap until ready for use. The inner bag maintains the sterility of the solution. Administer immediately following the insertion of infusion set.

Do not connect flexible plastic containers in series in order to avoid air embolism due to possible residual air contained in the primary container. Pressurizing intravenous solutions contained in flexible plastic containers to increase flow rates can result in air embolism if the residual air in the container is not fully evacuated prior to administration. Use of a vented

intravenous administration set with the vent in the open position could result in air embolism. Vented intravenous administration sets with the vent in the open position should not be used with flexible plastic containers.

Additives may be introduced before infusion or during infusion through the injection site.

For information on incompatibilities and preparation of the product (with additives), please see sections 6.2 and 6.6.

4.3. Contra-Indications

This product must be used with caution in patients with an impaired ability to handle sodium such as organic heart disease especially with a history of congestive heart failure, patients with renal insufficiency, cirrhosis of the liver, cardiopulmonary diseases or patients receiving salt retaining steroids.

When used in conjunction with cell separator procedures, the solution is contraindicated in those patients where adequate anticoagulation cannot be achieved.

4.4 Special warnings and precautions for use

Fluid balance/renal function

Use in patients with (severe) renal impairment

Sodium Chloride 0.9% should be administered with particular caution to patients with or at risk of severe renal impairment. In such patients administration of Sodium Chloride 0.9% may result in sodium retention. (See "Use in patients at risk for sodium retention, fluid overload and oedema" below, for additional considerations.)

Risk of fluid and/or solute overload and electrolyte disturbances

Depending on the volume and rate of infusion, intravenous administration of Sodium Chloride 0.9% can cause:

- Fluid and/or solute overload resulting in overhydration/hypervolemia and, for example, congested states, including central and peripheral oedema.
- Clinically relevant electrolyte disturbances and acid-base imbalance.

In general, the risk of dilutional states (retention of water relative to sodium) is inversely proportional to the electrolyte concentrations of Sodium Chloride 0.9% and its additions. Conversely, the risk of solute overload causing congested states (retention of solute relative to water) is directly proportional to the electrolyte concentrations of Sodium Chloride 0.9% and its additions.

Special clinical monitoring is required at the beginning of any intravenous infusion. Clinical evaluation and periodic laboratory determinations may be necessary to monitor changes in fluid balance, electrolyte concentrations, and acid-base balance during prolonged parenteral therapy or whenever the condition of the patient or the rate of administration warrants such evaluation.

High volume infusion must be used under specific monitoring in patients with cardiac or pulmonary failure and in patients with non-osmotic vasopressin release (including SIADH), due to the risk of hospital-acquired hyponatraemia (see below).

Hyponatraemia

Patients with non-osmotic vasopressin release (e.g. in acute illness, pain, post-operative stress, infections, burns, and CNS diseases), patients with heart-, liver- and kidney diseases and patients exposed to vasopressin agonists (see section 4.5) are at particular risk of acute hyponatraemia upon infusion of hypotonic fluids.

Acute hyponatraemia can lead to acute hyponatraemic encephalopathy (cerebral oedema) characterized by headache, nausea, seizures, lethargy and vomiting. Patients with cerebral oedema are at particular risk of severe, irreversible and life-threatening brain injury.

Children, women in the fertile age and patients with reduced cerebral compliance (e.g. meningitis, intracranial bleeding, cerebral contusion and brain oedema) are at particular risk of the severe and life-threatening brain swelling caused by acute hyponatraemia.

Use in patients at risk for sodium retention, fluid overload and oedema
Sodium Chloride 0.9% should be used with particular caution, if at all, in patients with or at risk for:

- Hypernatraemia. Rapidly correcting hypernatraemia once adaptation has occurred may lead to cerebral oedema, potentially resulting in seizures, permanent brain damage, or death.
- Hyperchloraemia
- Metabolic acidosis, which may be worsened by prolonged use of this product, especially in patients with renal impairment.
- Hypervolaemia such as congestive heart failure and pulmonary oedema may be precipitated, particularly in patients with cardiovascular disease.
- Iatrogenic hyperchloraemic metabolic acidosis (e.g., during intravenous volume resuscitation)
- Conditions that may cause sodium retention, fluid overload and oedema (central and peripheral), such as patients with
    - primary hyperaldosteronism,
    - secondary hyperaldosteronism, associated with, for example,
        - hypertension,
        - congestive heart failure,
        - liver disease (including cirrhosis),
        - renal disease (including renal artery stenosis, nephrosclerosis) or pre-eclampsia.

Medications that may increase the risk of sodium and fluid retention, such as corticosteroids

Infusion reactions
Symptoms of unknown aetiology which can appear to be hypersensitivity reactions have been reported very rarely in association with infusion of Sodium Chloride 0.9 %. These have been characterized as hypotension, pyrexia, tremor, chills, urticaria, rash and pruritus. Stop the infusion immediately if signs or symptoms of these reactions develop. Appropriate therapeutic countermeasures should be instituted as clinically indicated.

Specific patient groups
The consulting physician should be experienced in this product's use and safety in these special populations that are especially sensitive to rapid changes in serum sodium levels.
Rapid correction of hyponatraemia and hypernatremia is potentially dangerous (risk of serious neurologic complications). See section "*Hyponatraemia/hypernatraemia*" above.
Paediatric population

Plasma electrolyte concentrations should be closely monitored in the paediatric population as this population may have impaired ability to regulate fluids and electrolytes. Repeated infusions of sodium chloride should therefore only be given after determination of the serum sodium level.

Geriatric population
When selecting the type of infusion solution and the volume/rate of infusion for a geriatric patient, consider that geriatric patients are generally more likely to have cardiac, renal, hepatic, and other diseases or concomitant drug therapy.

For information on preparation of the product and additives, please see section 6.6.

As with any prolonged intravenous infusion, venous irritation and thrombophlebitis may occur at the injection site.
When used in conjunction with cell separator procedures, there is a risk of air embolism or haemolysis. A donor should not be subjected to this procedure more frequently than once in a 48 hour period, twice in 7 days or 24 times a year.

4.5 Interaction with other medicinal products and other forms of interaction

Drugs leading to an increased vasopressin effect

The below listed drugs increase the vasopressin effect, leading to reduced renal electrolyte free water excretion and may increase the risk of hospital acquired hyponatraemia following inappropriately balanced treatment with i.v. fluids (see sections 4.2, 4.4 and 4.8).

- Drugs stimulating vasopressin release include: Chlorpropamide, clofibrate, carbamazepine, vincristine, selective serotonin reuptake inhibitors, 3.4-methylenedioxy-N-methamphetamine, ifosfamide, antipsychotics, narcotics
- Drugs potentiating vasopressin action include: Chlorpropamide, NSAIDs, cyclophosphamide
- Vasopressin analogues include: Desmopressin, oxytocin, terlipressin

Other medicinal products increasing the risk of hyponatraemia also include diuretics in general and antiepileptics such as oxcarbazepine.
Caution is advised in patients treated with lithium. Renal sodium and lithium clearance may be increased during administration of Sodium Chloride 0.9%. Administration of Sodium Chloride 0.9% may result in decreased lithium levels.

Corticoids/Steroids and carbenoxolone, are associated with the retention of sodium and water (with oedema and hypertension). See Section 4.4 Special warnings and precautions for use.

4.6 Fertility, pregnancy and lactation

There are no adequate data from the use of Sodium Chloride 0.9% in pregnant or lactating women. The physician should carefully consider the potential risks and benefits for each specific patient before administering Sodium Chloride 0.9%.

Sodium Chloride 0.9% should be administrated with special caution for pregnant women during labour particularly as to serum-sodium if administered in combination with oxytocin (see sections 4.4, 4.5 and 4.8).

Caution is advised with patients with pre-eclampsia (See Section 4.4. Special warnings and precautions for use).

When a medicinal product is added, the nature of the drug and its use during pregnancy and lactation has to be considered separately.

4.7 Effects on ability to drive and use machines

No studies have been conducted on the influence of Sodium Chloride 0.9% on the ability to operate an automobile or other heavy machinery.

4.8 Undesirable effects

The following adverse reactions have been reported in post-marketing experience. The frequency of the adverse drug reactions listed in this section cannot be estimated from the available data.

System Organ Class (SOC)	Adverse reactions (Preferred Term)	Frequency
Nervous system disorders	Tremor Acute hyponatraemic encephalopathy*	Not known
Metabolism and nutrition disorders	Hospital acquired hyponatraemia*	Not known
Vascular disorders	Hypotension	Not known
Skin and subcutaneous tissue disorders	Urticaria Rash Pruritus	Not known
General disorders and administration site conditions:	Infusion site reactions, such as • Infusion site erythema, • Injection site streaking, Burning sensation, • Infusion site urticaria • Pyrexia • Chills	Not known

*Hospital acquired hyponatraemia may cause irreversible brain injury and death, due to development of acute hyponatraemic encephalopathy, frequency unknown (see sections 4.2. 4.4, 4.5).

The following adverse reactions have not been reported with this product but may occur:

- Hypernatraemia (eg. when administered to patients with nephrogenic diabetes insipidus or high nasogastric output)
- Hyperchloremic metabolic acidosis
- Hyponatraemia, which may be symptomatic. Hyponatraemia may occur when normal free water excretion is impaired. (eg SIADH or postoperative)

General adverse effects of sodium excess are described in section 4.9 Overdose.

Additives

When Sodium Chloride 0.9% is used as a diluent for injectable preparations of other drugs, the nature of additives will determine the likelihood of any other undesirable effect.

If an adverse event occurs the patient should be evaluated and appropriate counter measures be started, if needed the infusion should be stopped. The remaining part of the solution should be kept for investigation if deemed necessary.

When used in conjunction with cell separator procedures, reactions commonly experienced in routine blood collection such as syncope, vomiting and hyperventilation may occur. Individuals donating for the first time may be predisposed to these symptoms due to psychological factors. Reactions unique to apheresis collection procedures may also occur.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme.

Website: www.mhra.gov.uk/yellowcard

4.9 Overdose

General adverse effects of sodium excess in the body include nausea, vomiting, diarrhea, abdominal cramps, thirst, reduced salivation and lacrimation, sweating, fever, tachycardia, hypertension, renal failure, peripheral and pulmonary oedema, respiratory arrest, headache, dizziness, restlessness, irritability, weakness, muscular twitching and rigidity, convulsions, coma, and death.

An excessive volume of Sodium Chloride 0.9% may lead to hypernatraemia (which can lead to CNS manifestations, including seizures, coma, cerebral oedema and death) and sodium overload (which can lead to central and/or peripheral oedema) and should be treated by an attending specialised physician.

Excess chloride in the body may cause a loss of bicarbonate with an acidifying effect.

When Sodium Chloride 0.9% is used as a diluent for injectable preparations of other drugs, the signs and symptoms of over infusion will be related to the nature of the additives being used. In the event of accidental over infusion, treatment should be discontinued and the patient should be observed for the appropriate signs and symptoms

related to the drug administered. The relevant and supportive measures should be provided as necessary.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic Properties

Not applicable.

5.2. Pharmacokinetic Properties

Not applicable.

5.3. Pre-clinical Safety Data

Not applicable.

6. PHARMACEUTICAL PARTICULARS

6.1. List of Excipients

Hydrochloric Acid	*Ph.Eur.*	*QS*
Water for Injection	*Ph.Eur.*	*QS*
Sodium Hydroxide	*BP*	*QS*

6.2 Incompatibilities

As with all parenteral solutions compatibility of the additives with the solution must be assessed before addition. In the absence of compatibility studies, this solution must not be mixed with other medicinal products. Those additives known to be incompatible should not be used.

See section 6.6 for further instructions on the use of the product with additives

6.3 Shelf life

1000ml, 500ml, 250ml, 150ml - the shelf life is 24 months providing the unit has not been opened.

50ml and 100ml with Reconstitution Device (also referred to as MiniBag Plus) the shelf life is 9 months providing the unit has not been opened.

6.4. Special Precautions for Storage

Storage temperature should not exceed 25°C.

6.5 Nature and contents of container

The solution is supplied in a plastic Viaflex container fabricated from PVC. The bag is sized to contain either 50ml, 100ml, 150ml, 250ml, 500ml or 1000ml and is sealed in a plastic overpouch.

The 250ml containers may also incorporate a pre-attached polycarbonate reconstitution device (also referred to as MiniBag Plus).

The 50 and 100ml containers incorporate a pre attached polycarbonate reconstitution device (also referred to as MiniBag Plus).

6.6 Special precautions for disposal

Please see section 4.2 for information regarding the method of administration.

Before adding a drug, verify it is soluble and stable in water at the pH range of the Sodium Chloride 0.9% Intravenous Infusion solution. Additives may be introduced before infusion or during infusion through the injection site.

It is the responsibility of the physician to judge the incompatibility of an additive medication with the Sodium Chloride 0.9% Intravenous Infusion solution by checking for eventual colour change and/or eventual precipitate, insoluble complexes or crystals apparition. The Instructions for Use of the medication to be added must be consulted.

The solution for infusion should be visually inspected prior to use.

Use only if the solution is clear, without visible particles and if the container is undamaged.

Administer immediately following the insertion of infusion set.

Do not remove unit from overwrap until ready for use.

The inner bag maintains the sterility of the product. Do not use plastic containers in series connections. Such use could result in air embolism due to residual air being drawn from the primary container before the administration of the fluid from the secondary container is completed. Pressurizing intravenous solutions contained in flexible plastic containers to increase flow rates can result in air embolism if the residual air in the container is not fully evacuated prior to administration.

The solution should be administered with sterile equipment using an aseptic technique. The equipment should be primed with the solution in order to prevent air entering the system.

Additives may be introduced before infusion or during infusion through the re-sealable medication port. When additive is used, verify isotonicity prior to parenteral administration. Thorough and careful aseptic mixing of any additive is mandatory. Solutions containing additives should be used immediately and not stored.

Adding medication or using an incorrect administration technique might cause the appearance of fever reactions due to the possible introduction of pyrogens. In case of adverse reaction, infusion must be stopped immediately.

Discard after single use.
Discard any unused portion.
Do not reconnect partially used bags.

Preparation for Administration
VIAFLEX

The VIAFLEX container has an outlet port designed for an administration set with a short single connector. If an administration set with a combined air inlet/fluid path connector has to be used, ensure the air inlet tube is always clamped off.

1. **Opening**
   a. Remove the protective overpouch by tearing down from notch and remove container.
   b. Carefully straighten hanger and ports, if necessary.
   c. Squeeze container and inspect for minute leaks and examine solution for visible particles or cloudiness by viewing along seam.
   d. Discard unit if leaks, particles or cloudiness are evident.

2. Preparation for administration
Use sterile material for preparation and administration.
   a. Suspend container from base eyelet support.
   b. Use an aseptic technique to prepare the administration set.
   c. Remove blue protector from outlet port and insert set connector well into port.
   d. Prime set and regulate administration as required.
   e. If administration set becomes blocked do not pump contents back into container but replace equipment.
   f. Discard any unused portion and equipment after use. Do not store or reconnect partly used containers.

3. Techniques for injection of additive medications

The VIAFLEX container has a second port with a self-sealing rubber medication port designed for the addition of medication using a syringe. This is the only port for adding medication. Warning: Additives may be incompatible.
To add medication before administration

a. Swab the medication port with the appropriate anti-bacterial fluid in line with current recommended practice and procedure.
b. Using a syringe with a 20 – 22 gauge needle, puncture re-sealable medication port and inject. Do not leave the syringe and needle in the port once the medication has been injected.
c. Shake and squeeze the VIAFLEX container so that the solution and medication are thoroughly mixed. For high density medications such as potassium chloride, squeeze both ports while upright and invert the container several times while shaking and squeezing to ensure thorough mixing.
Caution: Do not store bags containing added medications.

To add medication during administration

a. Close clamp on the set.
b. Disinfect medication port.
c. Using a syringe with a 20 – 22 gauge needle, puncture re-sealable medication port and inject.
d. Remove container from IV pole and/or turn to an upright position.
e. Evacuate both ports by tapping gently while the container is in an upright position.
f. Mix solution and medication thoroughly.
g. Return container to in use position, re-open the clamp and continue administration.

Cautions

a. Do not vent.
b. Do not administer unless the solution is clear and container undamaged.
c. Do not use in series connections as this could result in air embolism due to residual air being drawn from the primary container before administration of fluid from the secondary container is completed.
d. Discontinue infusion if adverse reaction occurs.
e. Rapid infusion may be harmful.
f. It is recommended that the intravenous administration set be replaced at least once every 24 hours. Details of the use of the set can be recorded – record labels are available from Baxter Healthcare Ltd.

4. In-use shelf life

Chemical and physical stability of any additive medication at the pH of the Sodium chloride 0.9 Infusion in the VIAFLEX container should be established prior to use.

From a microbiological point of view, the diluted product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user, and would normally not be longer than 24 hours at 2 to 8°C, unless reconstitution has taken place in controlled and validated aseptic conditions.

5. Incompatibilities of additive medications

WARNING: Additives may be incompatible. The introduction of additives to any solution, regardless of type of container, requires special attention to assure that no incompatibilities result.

While some incompatibilities are readily observed, it is important to be aware that subtle physical, chemical and pharmacological incompatibilities can occur. The medical literature, the additive package insert and other available sources of information should be reviewed for a more thorough understanding of possible incompatibility problems.

If, in the informed judgment of the physician, it is deemed advisable to introduce additives into this solution, aseptic technique must be employed.

It is recommended that medication is added only under Pharmaceutical supervision.
Do not add medication before hanger and ports have been straightened and the container inspected.
Do not store solutions with added medication. Before adding a drug, verify it is soluble and stable in water at the pH of the Sodium chloride 0.9 Infusion.

Those additives known to be incompatible should not be used.

Preparation for Administration
MINIBAG PLUS

The Minibag Plus Container is a standard diluent container with an integral closed system transfer device (CSTD) drug vial adaptor. It allows for drug admixture after connection to a single dose powder or liquid (up to 10 mL) drug vial having a 20 mm closure. A breakaway seal in the tube between the vial adaptor and the container is broken to allow transfer of the diluent into the vial and reconstitution of the drug.

During the vial docking process, vapor and drug powder in the vial are contained within the container/vial system.

Once the vial has been docked to the vial adaptor, the Minibag Plus is designed to prevent ingress of micro-organisms and limit escape of drug powder and vapour from the reconstituted drugs, minimising environmental and user exposure

The reconstituted drug is then transferred from the vial into the container diluent and mixed to result in an admixture for delivery to the patient.

Do not remove unit from overwrap until ready for use. The overwrap is a moisture barrier. The inner bag maintains the sterility of the product.

1. To open, tear overwrap down side at slit and remove solution container. Straighten hanger and ports and inspect for minute leaks by squeezing inner bag firmly. Check to ensure seals are intact and blue frangible is not leaking. If leaks are found discard unit as sterility or function may be impaired.

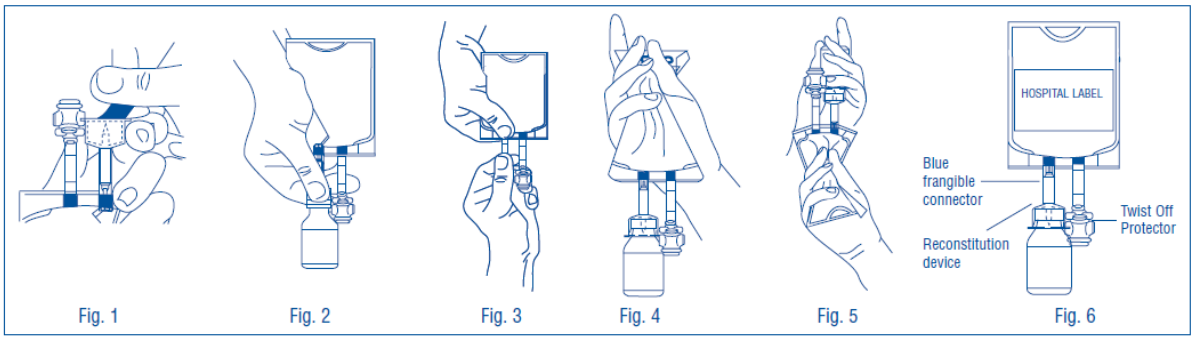
2. Remove protective cover of drug vial and swab with appropriate disinfectant.

3. Observing aseptic technique, peel back the foil cover from end of reconstitution device. Fig. 1.

4. Place the drug vial on a flat surface. Hold the reconstitution device with your thumb and index finger and push the device over the drug vial, puncturing the stopper and locking in place. Fig. 2.

5. Just prior to administration, break blue frangible connector. Grip top of blue frangible connector between thumb and forefinger of one hand. Grip base of frangible with thumb and forefinger of other hand. Break frangible seal by bending 90° in one direction then 180° in the opposite direction. Fig. 3.

6. For liquid drug vials proceed directly to Step 8. For powder drug vials position the drug vial below the Minibag Plus and squeeze the Minibag Plus to transfer solution thereby partially filling the vial approximately 1/2 full. Fig. 4.
7. Keep the reconstitution device attached to the drug vial. Agitate the vial gently to dissolve the drug in the vial
8. Invert the drug vial above the Minibag Plus. Squeeze the Minibag Plus to force air into the vial, then release the pressure on the Minibag Plus by relaxing your hand and allowing the reconstituted drug to flow back into the Minibag Plus container. Repeat procedure until vial is empty of all drug. Fig. 5.
9. Immediately prior to administration, examine solution for any visible particles.
10. Label the Minibag Plus according to hospital procedures. Fig. 6.
11. Do not detach drug vial from reconstitution device at any time



Preparation for Administration

Minibag Plus containers have an outlet port designed for an administration set with a single connector. If an administration set with a combined air inlet/fluid path connector has to be used, ensure the air inlet tube is always clamped off.

1. Suspend container from D-shaped hanger.
2. Using aseptic technique prepare administration set.
3. Remove the protector from the administration port as follows:

   a. with one hand, grip the wings of the blue protector below the fracture zone (a)

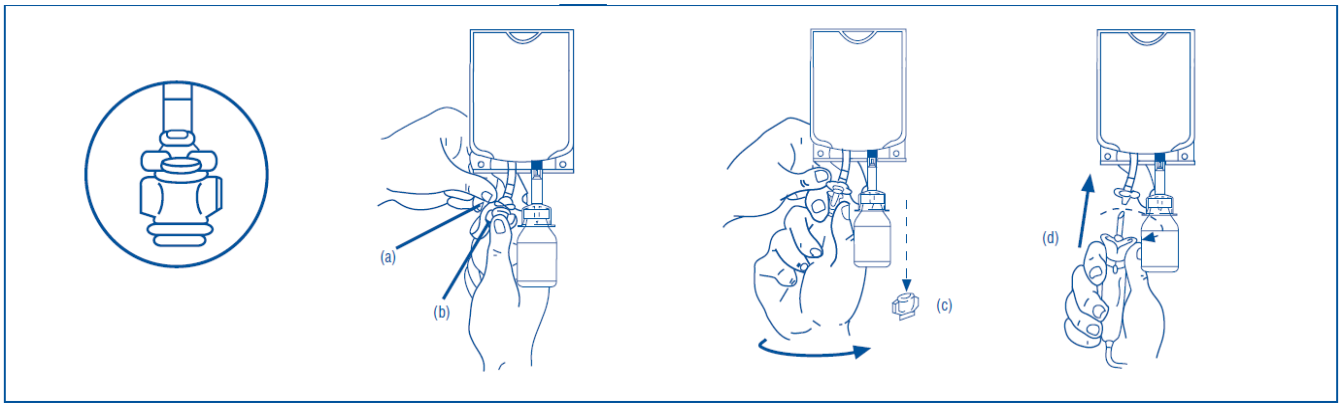
   b. with the other hand, grip the wings above the fracture zone (b)

   c. remove the upper section of the protector with one twisting movement (c)

   d. insert the set connector well into the port (d)

4. Prime set and regulate administration as required. If administration set becomes blocked do not pump contents back into container but replace equipment.

5. Discard any unused portion and equipment after use. Do not store or reconnect partly used containers.



7. MARKETING AUTHORISATION HOLDER

Baxter Healthcare Ltd.
Caxton Way
Thetford
Norfolk
IP24 3SE

8 MARKETING AUTHORISATION NUMBER(S)

PL 00116/5057R

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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10 DATE OF REVISION OF THE TEXT

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