SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Sodium Chloride 0.45% Solution for Infusion Baxter

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active ingredient: Sodium Chloride 0.45% w/v (4.500 g/l)

Each ml contains 4.5 mg sodium chloride.

	Na^+	Cl^-
mmol/l	77	77
mEq/l	77	77

154 mOsm/l (approx.)
pH: 4.5 – 7.0

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for infusion.
Clear solution, free from visible particles.

4. CLINICAL PARTICULARS

4.1. THERAPEUTIC INDICATIONS

Sodium Chloride 0.45% Solution for Infusion is indicated for supply of water and electrolytes.

4.2. POSOLOGY AND METHOD OF ADMINISTRATION

Note : Do not administer unless solution is clear and seal is intact

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever solution or container permit. Use of a final filter is recommended during administration of all parenteral solutions, where possible .

All injections in plastic containers are intended for intravenous administration using sterile equipment. It is recommended that intravenous administration apparatus be replaced at least once every 24 hours.

Additives may be incompatible- see updated literature.
If additives are introduced to the solution use an aseptic technique and mix thoroughly.

Do not store solutions containing additives.

Dosage is depended upon the age, weight and clinical condition of the patient, as well as laboratory determinations.
Method of Administration:
The equipment should be primed with the solution to prevent air entering the system.
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.

Adding other medication or using an incorrect administration technique might cause the appearance of fever reactions due to the possible introduction of pyrogens. If an adverse event occurs the patient evaluated and appropriate countermeasures started. If needed the infusion should be stopped.

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

4.3. CONTRAINDICATIONS

The solution is contra-indicated in patient presenting:
- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.
- Hyponatraemia, hypochloraemia,
- Extracellular hyperhydration or hypervolaemia,
- Severe renal insufficiency (with oliguria/anuria),
- Fluid and sodium retention,
- Uncompensated cardiac failure,
- General oedema and ascitic cirrhosis.

The contra-indications related to the added medicinal product should be considered.

4.4. SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Electrolyte balance
Hyponatraemia/Hypernatraemia
The infusion of solutions with sodium concentrations <0.9% may result in hyponatraemia.

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. The risk for hyponatraemia is increased, for example,

- in children
- in elderly patients
- in women
- in patients with hypoxemia
- in patients with underlying central nervous system disease
- postoperatively
- in persons with psychogenic polydipsia

in patients treated with medications that increase the risk of hyponatraemia (such as certain antiepileptic and psychotropic medications).
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.

Acute symptomatic hyponatraemic encephalopathy is considered a medical emergency.
Hyponatraemia should be corrected at a calculated rate to prevent hyponatraemic encephalopathy.

Rapid correction of hyponatraemia and hypernatremia is potentially dangerous (risk of serious neurologic complications). Rapidly correcting hypernatremia once adaptation has occurred may lead to cerebral oedema, potentially resulting in seizures, permanent brain damage, or death.

Dosage, rate, and duration of administration should be determined by a physician experienced in intravenous fluid therapy.

Fluid balance/renal function
Use in patients with moderate renal impairment
The product should be administered with particular caution to patients with moderate renal impairment. In such patients administration of Sodium Chloride 0.45% Solution for Infusion may result in sodium retention.

Risk of fluid and/or solute overload and electrolyte disturbances
Depending on the volume and rate of infusion, intravenous administration of Sodium Chloride 0.45% Solution for Infusion can cause

- Fluid and/or solute overload resulting in over hydration/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 is inversely proportional to the electrolyte concentrations in the solution and additions. The risk of solute overload causing congested states is directly proportional to the electrolyte concentration in the solution and its additions.

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.

Use in patients at risk for sodium retention, fluid overload and oedema
Sodium Chloride 0.45% Solution for Infusion should be used with particular caution, if at all, in patients with or at risk for:

- Hypervolemia

- 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 parenteral infusion of Sodium Chloride. 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 only be given after determination of serum sodium level.

The infusion of hypotonic fluids together with the non-osmotic secretion of ADH may result in hyponatraemia. Hyponatraemia can lead to headache, nausea, seizures, lethargy, coma, cerebral oedema and death, therefore acute symptomatic hyponatraemic encephalopathy is considered a medical emergency.

Geriatric population

In older people, the risk for hyponatraemia is increased. 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.

Other warnings

Osmolarity

Sodium Chloride 0.45% Solution for Infusion is hypotonic with an osmolarity of approximately 154 mOsmol/L.

Administration *with blood products*

Do not mix or administer Sodium Chloride 0.45% Solution for Infusion through the same administration set with whole blood or cellular blood components.

During long-term infusion, the doctor can decide to give you an appropriate nutritive supply.
As with all parenteral solutions, compatibilities should be checked when additives are used (see section 6.2).

4.5. INTERACTIONS WITH OTHER MEDICINAL PRODUCTS AND OTHER FORMS OF INTERACTION

Interaction related to the presence of sodium:
Corticoids/Steroids and carbenoxolone, which are associated with the retention of sodium and water (with oedema and hypertension), see section 4.4 special warnings and precautions for use.

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 decreased in the presence of hyponatraemia. Administration of Sodium Chloride 0.45% Solution for Infusion may result in increased lithium levels.

4.6. PREGNANCY AND LACTATION

There are no adequate data from the use Sodium Chloride 0.45% Solution for Infusion in pregnant or lactating women. The physician should carefully consider the potential risks and benefits for each specific patient before administering Sodium Chloride 0.45% Solution.

Sodium Chloride 0.45% Solution for Infusion should be administrated with special caution for pregnant women during labour particularly as to serum-sodium if administered in combination with oxytocin (see section 4.4, 4.5 and 4.8).

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

4.7. EFFECTS ON THE ABILITY TO DRIVE AND USE MACHINES

There is no information on the effects of Sodium Chloride 0.45% Solution for Infusion on the ability to operate an automobile or other heavy machinery

4.8. UNDESIRABLE EFFECTS

the following undesirable effects have been reported to have occurred during or following infusion of Sodium Chloride 0.45% Solution for Infusion.

System Organ Class	Symptoms (LLT terms MedDRA)
Metabolism and nutrition disorders	Overhydration* (associated or not with polyuria) in patients with cardiac disorder or pulmonary oedema Asymptomatic electrolyte disturbance Hyponatraemia Hospital acquired hyponatraemia**
Nervous system disorders	Acute hyponatraemic encephalopathy**
Cardiac disorders	Heart failure in patients with cardiac disorder or pulmonary oedema
Vascular disorders	Thrombophlebitis* Venous thrombosis*
General disorders and administration site conditions	Fever* Injection site pain* Injection site reaction* Injection site phlebitis* Injection site irritation* Injection site infection* Extravasation*

The frequency of the adverse drug reactions listed in this section cannot be estimated from the available data

* Adverse reactions associated with the technique of administration

**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:

- Hyperchloraemic metabolic acidosis
- Infusion reactions, including hypotension, tremor, chills, urticaria, rash, and pruritus.

Adverse reactions may be associated to the medicinal products added to the solution; the nature of the additive will determine the likelihood of any other undesirable effects.

If an adverse event occurs the patient should be evaluated and appropriate countermeasures started, if needed the infusion should be stopped.

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. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form: https://sideeffects.health.gov.il/

4.9. OVERDOSE

An excessive volume of Sodium Chloride 0.45% Solution for Infusion may lead to:

- hypo- and hypernatremia (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).

See also section 4.4.

Excessive administration of chloride salts may cause a loss of bicarbonate with an acidifying effect. When Sodium Chloride 0.45% Solution for Infusion is used as a diluent for injectable preparations of other medicinal products, 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

Pharmacotherapeutic group "Electrolyte solutions", ATC code B05XA03.

Sodium Chloride 0.45% Solution for Infusion is a hypotonic solution, with an approximate osmolarity of 154 mOsm/l.

The pharmacodynamic properties of the solution are those of the sodium and chloride ions in maintaining the fluid and electrolyte balance. Ions, such as sodium, circulate through the cell membrane, using various mechanisms of transport, among which is the sodium pump (Na-K-ATPase). Sodium plays an important role in neurotransmission and cardiac electrophysiology, and also in renal function.
Chloride is mainly an extracellular anion. Intracellular chloride is in high concentration in red blood cells and gastric mucosa. Reabsorption of chloride follows reabsorption of sodium.

When medication is added to Sodium Chloride 0.45% Solution for Infusion, the overall pharmacodynamics of the solution will depend on the nature of the medicinal product used.

5.2. PHARMACOKINETIC PROPERTIES

Sodium and Chloride are mainly distributed in blood and extracellular compartiments (Na^+: 142 mmol/l – Cl^-: 103 mmol/l).

Sodium is predominantly excreted by the kidney with a renal reabsorption.
Small amounts of sodium are lost in the faeces and sweat at the skin level.

When medication is added to Sodium Chloride 0.45% Solution for Infusion, the overall pharmacokinetics of the solution will depend on the nature of the medicinal product used.

5.3. PRECLINICAL SAFETY DATA

Preclinical safety data of this solution for infusion in animals are not relevant since its constituents are physiological components of animal and human plasma.

Toxic effects are not to be expected under the condition of clinical application.

The safety of potential additives should be considered separately.

6. PHARMACEUTICALS PARTICULARS

6.1. LIST OF EXCIPIENTS

Water for Injections

6.2. INCOMPATIBILITIES

Incompatibility of the medicinal product to be added to the solution in Viaflo container must be assessed before addition. Those additives known to be incompatible should not be used.

In the absence of compatibility studies, this solution must not be mixed with other medicinal products. See section 6.6 for further instructions on the use of the product with additives.

6.3. SHELF LIFE

500 ml bags: The expiry date of the product is indicated on the packaging materials

In-use shelf-life: From a microbiological point of view, the diluted product must 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.

6.4. SPECIAL PRECAUTIONS FOR STORAGE

No special storage conditions. Recommended to store at room temperature.

6.5. NATURE AND CONTENTS OF CONTAINERS

The bags known as Viaflo are composed of polyolefin/polyamide co-extruded plastic (PL 2442).

The bags are overwrapped with a protective plastic pouch composed of polyamide/polypropylene.

Bag size: 500 ml

6.6. SPECIAL PRECAUTIONS FOR DISPOSAL AND OTHER HANDLING

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 0.45% Solution for Infusion (pH 4.5 to 7.0). Additives may be introduced before infusion or during infusion through the injection site.

It is the responsibility of the healthcare professional to judge the incompatibility of an additive medication with the Sodium Chloride 0.45% Solution for Infusion, by checking for eventual colour

change and/or eventual appearance of precipitate, insoluble complexes or crystals. The instruction for use of the medicinal product to be added must be consulted.

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.

Discard after single use.

Discard any unused portion.

Do not reconnect partially used bags.

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

1. Opening

a. Remove the Viaflo container from the overpouch just before use.
b. Check for minute leaks by squeezing inner bag firmly. If leaks are found, discard solution, as sterility may be broken.
c. Check the solution for clarity and absence of foreign matters. If solution is not clear or contains foreign matters, discard the solution.

2. Preparation for administration

Use sterile material for preparation and administration.

a. Suspend container from eyelet support.
b. Remove plastic protector from outlet port at bottom of container:
   - grip the small wing on the neck of the port with one hand,
   - grip the large wing on the cap with the other hand and twist,
   - the cap will pop off.
c. Use an aseptic method to set up the infusion.
d. Attach administration set. Refer to complete directions accompanying set for connection, priming of the set and administration of the solution.

3. Techniques for injection of additive medications

Warning: Additives may be incompatible.

To add medication before administration

a. Disinfect medication site.
b. Using syringe with 19 (1.10 mm) to 22 (0.70 mm) gauge needle, puncture resealable medication port and inject.
c. Mix solution and medication thoroughly. For high-density medication such as potassium chloride, tap the ports gently while ports are upright and mix.

   Caution: Do not store bags containing added medications.

To add medication during administration

a. Close clamp on the set.
b. Disinfect medication site.

c. Using syringe with 19 (1.10 mm) to 22 (0.70 mm) gauge needle, puncture resealable 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.

7. REGISTRATION HOLDER

Teva Israel Ltd. 124 Dvora HaNevi'a St.,
Tel Aviv 6944020 Israel

8. REGISTRATION NUMBER

164-05-35828-00

9. MANUFACTURER

Bieffe Medital S.A.,
Sabinanigo, Spain

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