Sodium Chloride 0.9% Intravenous Infusion BP

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Sodium Chloride 0.9% Intravenous Infusion BP

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Sodium chloride: 9.0 g/l

Each ml contains 9 mg sodium chloride.

mmol/l: Na^+ : 154 Cl^-: 154.

pH: 4.5 - 7

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 0.9% intravenous infusion is indicated for:

- Treatment of isotonic extracellular dehydration
- Treatment of sodium depletion
- Vehicle or diluent of compatible drugs for parenteral administration.

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).

The dosage, rate and duration of administration is to be individualized as determined by several factors including age, weight, clinical condition, concomitant treatment and in particular the patient's hydration state, clinical and laboratory response to treatment. Fluid balance and plasma electrolyte concentrations must be monitored during treatment.

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. Contraindications

The solution is contra-indicated in patient presenting hypernatraemia or hyperchloraemia.

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

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 hypernatraemia 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.

This medicinal product contains 354 mg sodium per 100 ml, equivalent to 17.7% of the WHO recommended maximum daily intake of 2 g sodium for an adult.

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 4.4 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 section 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 • Vein irritation, injection site streaking, burning sensation • Local pain or reaction, infusion site urticaria • Infection at the site of injection	Not known

	• Venous thrombosis or phlebitis extending from the site of injection, extravasation and hypervolemia • Pyrexia • Chills	

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

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

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

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

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

Pharmacotherapeutic group: "Other IV Solution Additives"
ATC code: B05XX

Sodium Chloride 0.9% intravenous infusion is an isotonic solution, with an approximate osmolarity of 308 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 its renal metabolism.

5.2. Pharmacokinetic properties

Sodium is predominantly excreted by the kidney, but there is extensive renal reabsorption.

Small amounts of sodium are lost in the faeces and sweat.

5.3. Preclinical safety data

The safety of sodium chloride in animals is not relevant in view of its presence as a normal component in animal and human plasma.

6. PHARMACEUTICALS PARTICULARS

6.1. List of excipients

Water for Injection.

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

Shelf life as packaged:

The expiry date of the product is indicated on the packaging materials.

<u>In-use shelf life: Additives</u>.

Chemical and physical stability of any additive at the pH of Sodium Chloride 0.9% Intravenous Infusion in the Viaflo container should be established prior to use.

From a microbiological point of view, the diluted product must be used immediately unless dilution has taken place in controlled and validated aseptic conditions. If not used immediately, in-use storage times and conditions are the responsibility of the user.

6.4. Special precautions for storage

50 and 100 ml bags: Do not store above 30°C.

250, 500 and 1000 ml bags: No special precautions for storage. Recommended to store at room temperature.

6.5 Nature and contents of container

Bag sizes: 50, 100, 250, 500 or 1000 mL

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.

Not all pack sizes may be marketed.

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 0.9% 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 color change and/or eventual precipitate, insoluble complexes or crystals apparition. The Instructions for Use of the medication 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.

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

Instructions for Use

Opening

- Remove the Viaflo container from the overpouch just before use.
- Check for minute leaks by squeezing inner bag firmly. If leaks are found, discard solution, as sterility may be impaired.
- Check solution for limpidity and absence of foreign matter. If solution is not clear or contains foreign matter, discard the solution.

Preparation for administration

Use sterile material for preparation and administration.

- Suspend container from eyelet support.
- 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.
- Use an aseptic method to set up the infusion.
- Attach administration set. Refer to directions of the accompanying set for connection, priming of the set and administration of the solution.

Techniques for injection of additive medications

Warning: Additives may be incompatible.

To add medication before administration

- Disinfect medication site.
- Using syringe with an appropriate needle, puncture resealable medication port and inject.
- 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

- Close clamp on the set.
- Disinfect medication site.
- Using syringe with an appropriate needle, puncture resealable medication port and inject.
- Remove container from IV pole and/or turn to an upright position.
- Evacuate both ports by tapping gently while the container is in an upright position.
- Mix solution and medication thoroughly.
- Return container to in use position, re-open the clamp and continue administration.

7. LICENCE HOLDER AND MANUFACTURER

Licence Holder:

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

Manufacturer:

Baxter Healthcare Ltd.,
Thetford, United Kingdom.

8. REGISTRATION NUMBERS

140.26.30794

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