Baxter

Sodium Chloride 0.3 % and Glucose 3.3%

Solution for Infusion Baxter

1. NAME OF THE MEDICINAL PRODUCT

Sodium Chloride 0.3 % and Glucose 3.3% Solution for Infusion Baxter

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Sodium Chloride: 3.0 g/l (0.3% w/v)

Glucose (as monohydrate): 33.0 g/l (3.3% w/v)

Each ml contains 33 mg glucose (as monohydrate) and 3 mg sodium chloride.

mmol/l:	Na+: 51	Cl-:51
mEq/l:	Na+: 51	Cl-:51

Nutritional value: approximately 544Red kJ/l (or 132 kcal/l)

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for infusion.

Clear solution, free from visible particles.

Osmolarity: 285 mOsm/l (approx)

pH: 3.5 to 6.5

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

A source of water supply, electrolytes and calories.

4.2 Posology and method of administration

As directed by a physician. Dosage is dependent upon the age, weight, and clinical condition of the patient as well as laboratory determinations.

The dosage and constant infusion rate of intravenous Sodium Chloride 0.3 % and Glucose 3.3% Solution for Infusion Baxter must be selected with caution in pediatric patients, particularly neonates and low weight infants, because of the increased risk of hyperglycemia/ hypoglycemia.

The infusion rate and volume depends on the age, weight, clinical and metabolic conditions of the patient, concomitant therapy, and should be determined by the consulting physician experienced in pediatric intravenous fluid therapy.

Sodium Chloride 0.3 % and Glucose 3.3% Solution for Infusion Baxter is hypotonic and isoosmolar, due to the glucose content. It has an approximate osmolarity of 285 mOsm/l.

Precautions to be taken before manipulating or administering the product

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit.

Do not administer unless solution is clear and seal is intact.

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.

All injections in plastic containers are intended for intravenous administration using sterile equipment and aseptic technique.

The equipment should be primed with the solution in order to prevent air entering the system. 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. 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 incompatible. Complete information is not available. Those additives known to be incompatible should not be used. Consult with pharmacist, if available. If, in the informed judgment of the physician, it is deemed advisable to introduce additives, use aseptic technique.

Additives may be introduced before or during infusion through the resealable medication port. When additive is used, verify tonicity prior to parenteral administration. Hyperosmolar solutions may cause venous irritation and phlebitis. Thus, any hyperosmolar solution is recommended to be administered through a large central vein, for rapid dilution of the hyperosmotic solution.

Mix thoroughly when additives have been introduced. Do not store solutions containing additives.

For further information on the product with additives, please see sections 6.2, 6.3 and 6.6.

4.3 Contraindications

The solution is contraindicated in patients presenting with:

- Hypersensitivity to the active substance or to any of the excipients listed in section 6.1
- Extracellular hyperhydration or hypervolaemia

- Fluid and sodium retention
- Severe renal insufficiency (with oliguria/anuria)
- Uncompensated cardiac failure
- Hyponatraemia or hypochloraemia
- General oedema and ascitic cirrhosis

Clinically significant hyperglycaemia The solution is also contraindicated in case of uncompensated diabetes, other known glucose intolerances (such as metabolic stress situations), hyperosmolar coma or hyperlactataemia.

4.4 Special warnings and precautions for use

Glucose intravenous infusions are usually isotonic solutions. In the body, however, glucose containing fluids can become extremely physiologically hypotonic due to rapid glucose metabolization (see section 4.2).

Depending on the tonicity of the solution, the volume and rate of infusion and depending on a patient's underlying clinical condition and capability to metabolize glucose, intravenous administration of glucose can cause electrolyte disturbances most importantly hypo- or hyperosmotic hyponatraemia.

Hyponatraemia

The infusion of solutions with sodium concentrations <0.9% may result in hyponatraemia.

Close clinical monitoring may be warranted.

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 (brain oedema) characterized by headache, nausea, seizures, lethargy and vomiting. Patients with brain 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, and cerebral contusion) are at particular risk of the severe and life-threatening brain swelling caused by acute hyponatraemia

Sodium retention, fluid overload and oedema

Sodium Chloride 0.3 % and Glucose 3.3% Solution for Infusion Baxter should be used with particular caution, in:

- Patients with conditions that may cause sodium retention, fluid overload and oedema (central and peripheral), such as
  - Primary hyperaldosteronism,
  - Secondary hyperaldosteronism associated with, for example,
    - hypertension,
    - congestive heart failure,
    - liver disease (including cirrhosis),
    - renal disease (including renal artery stenosis, nephrosclerosis)
  - Pre-eclampsia.
- Patients taking medications that may increase the risk of sodium and fluid retention, such as corticosteroids

Hypokalaemia

The infusion of Sodium Chloride 0.3 % and Glucose 3.3% Solution for Infusion Baxter may result in hypokalaemia. This medicine should be used with particular caution in patients with or at risk for hypokalemia. Close clinical monitoring may be warranted in, for example:

- persons with metabolic alkalosis
- persons with thyrotoxic periodic paralysis, administration of intravenous glucose has been associated in aggravating hypokalaemia
- persons with increased gastrointestinal losses (e.g., diarrhea, vomiting)
- prolonged low potassium diet
- persons with primary hyperaldosteronism
- patients treated with medications that increase the risk of hypokalaemia (e.g. diuretics, beta-2 agonist, or insulin)

Hypo- and hyperosmolality, serum electrolytes and water imbalance

Depending on the volume and rate of infusion and depending on a patient's underlying clinical condition and capability to metabolize glucose, intravenous administration of Sodium Chloride 0.3 % and Glucose 3.3% Solution for Infusion Baxter can cause:

- Hypo-osmolality
- Hyperosmolality, osmotic diuresis and dehydration
- Electrolyte disturbances such as
  - hyponatraemia (see above),
  - hypokalaemia (see above),
  - hypophosphataemia,
  - hypomagnesaemia,
- Overhydration/hypervolaemia and, for example, congested states, including central (e.g., pulmonary congestion) and peripheral oedema.

Clinical evaluation and periodic laboratory determinations may be necessary to monitor hanges 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.

Hyperglycaemia

Rapid administration of glucose solutions may produce substantial hyperglycaemia and a hyperosmolar syndrome. In order to avoid hyperglycaemia the infusion rate should not exceed the patient's ability to utilize glucose.

To reduce the risk of hyperglycaemia-associated complications, the infusion rate must be adjusted and/or insulin administered if blood glucose levels exceed levels considered acceptable for the individual patient.

Intravenous glucose should be administered with caution in patients with, for example:

- impaired glucose tolerance (such as in diabetes mellitus, renal impairment, or in the presence of sepsis, trauma or shock),
- severe malnutrition (risk of precipitating a refeeding syndrome, see below),
- thiamine deficiency, e.g., in patients with chronic alcoholism (risk of severe lactic acidosis due to impaired oxidative metabolism of pyruvate),
- water and electrolyte disturbances that could be aggravated by increased glucose and/or free water load

Other groups of patients in whom Sodium Chloride 0.3 % and Glucose 3.3% Solution for Infusion Baxter should be used with caution include:

- patients with ischemic stroke. Hyperglycaemia has been implicated in increasing cerebral ischemic brain damage and impairing recovery after acute ischemic strokes.
- patients with severe traumatic brain injury (in particular during the first 24 hours following the trauma). Early hyperglycaemia has been associated with poor outcomes in patients with severe traumatic brain injury.
- Newborns (see Paediatric glycaemia-related issues).

Prolonged intravenous administration of glucose and associated hyperglycaemia may result in decreased rates of glucose-stimulated insulin secretion.

Hypersensitivity Reactions

Hypersensitivity/infusion reactions, including anaphylaxis, have been reported (see section 4.8).

- Stop the infusion immediately if signs or symptoms of hypersensitivity/infusion reactions develop. Appropriate therapeutic countermeasures must be instituted as clinically indicated.

Solutions containing glucose should be used with caution in patients with known allergy to corn or corn products.

Refeeding syndrome

Refeeding severely undernourished patients may result in the refeeding syndrome that is characterized by the shift of potassium, phosphorus and magnesium intracellularly as the patient becomes anabolic. Thiamine deficiency and fluid retention may also develop. Careful monitoring and slowly increasing nutrient intake while avoiding overfeeding can prevent these complications.

Severe renal impairment

Sodium Chloride 0.3 % and Glucose 3.3% Solution for Infusion Baxter should be administered with particular caution to patients at risk of (severe) renal impairment. In such patients, administration may result in sodium retention and/or fluid overload.

Paediatric use

The infusion rate and volume depends on the age, weight, clinical and metabolic conditions of the patient, concomitant therapy, and should be determined by a physician experienced in paediatric intravenous fluid therapy.

Paediatric glycaemia-related issues

- Newborns, especially those born premature and with low birth weight, are at increased risk of developing hypo- or hyperglycaemia. Close monitoring during treatment with intravenous glucose solutions is needed to ensure adequate glycaemic control, in order to avoid potential long term adverse effects.
- Hypoglycaemia in the newborn can cause, e.g.,
  - prolonged seizures,
  - coma and
  - cerebral injury.
- Hyperglycaemia has been associated with
  - cerebral injury, including intraventricular haemorrhage,
  - late onset bacterial and fungal infection,
  - retinopathy of prematurity,
  - necrotizing enterocolitis,
  - increased oxygen requirements,
  - prolonged length of hospital stay and
  - death.

Paediatric hyponatraemia-related issues

- Children (including neonates and older children) are at increased risk of developing hyponatraemia as well as for developing hyponatraemic encephalopathy.
- 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 edema and death; therefore, acute symptomatic hyponatraemic encephalopathy is considered a medical emergency.
- Plasma electrolyte concentrations should be closely monitored in the paediatric population.
- Rapid correction of hyponatraemia is potentially dangerous (risk of serious neurologic complications). Dosage, rate, and duration of administration should be determined by a physician experienced in paediatric intravenous fluid therapy.

Blood

Sodium Chloride 0.3 % and Glucose 3.3% Solution for Infusion Baxter should not be administered simultaneously with blood through the same administration set because of the possibility of pseudoagglutination or haemolysis.

Geriatric use

When selecting the type of infusion 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.

4.5 Interaction with other medicinal products and other forms of interaction

No studies have been conducted by Baxter.

Both the glycaemic and effects on water and electrolyte balance should be taken into account when

administering Sodium Chloride 0.3 % and Glucose 3.3% Solution for Infusion Baxter to patients treated with other substances that affect glycaemic control or fluid and/or electrolyte balance.

Drugs leading to an increased vasopressin effect The below listed drugs increase the vasopressin effect, leading to reduced renal electrolyte free water excretion and 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, e.g.: Chlorpropamide, clofibrate, carbamazepine, vincristine, selective serotonin reuptake inhibitors, 3.4-methylenedioxy-Nmethamphetamine, ifosfamide, antipsychotics, narcotics
- Drugs potentiating vasopressin action, e.g.: Chlorpropamide, NSAIDs, cyclophosphamide
- Vasopressin analogues, e.g.: 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 and can result in decreased lithium levels.
- corticosteroids, which are associated with the retention of sodium and water (with oedema and hypertension).
- diuretics, beta-2 agonist, or insulin, whom increase the risk of hypokalemia
- certain anti-epileptic and psychotropic medications that increase the risk of hyponatraemia.

4.6 Fertility, pregnancy and lactation

Pregnancy

Intrapartum maternal intravenous glucose infusion may result in foetal hyperglycaemia and metabolic acidosis as well as rebound neonatal hypoglycaemia due to foetal insulin production.

Sodium Chloride 0.3 % and Glucose 3.3% Solution for Infusion Baxter should be administrated with special caution for pregnant women during labour particularly if administered in combination with oxytocin due to the risk of hyponatraemia (see section 4.4, 4.5 and 4.8).

Fertility

There is no information on the effects of Sodium Chloride 0.3 % and Glucose 3.3% Solution for Infusion Baxter on fertility

Lactation

Sodium Chloride 0.3 % and Glucose 3.3% Solution for Infusion Baxter can be used during breast-feeding.

The potential risks and benefits for each specific patient should be carefully considered before administration.

4.7 Effects on ability to drive and use machines

There is no information on the effects of Sodium Chloride 0.3 % and Glucose 3.3% Solution for Infusion Baxter 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, listed by MedDRA System Organ Class (SOC), then where feasible, by Preferred Term in order of severity.

Frequencies cannot be estimated from the available data as all listed adverse reactions are based on spontaneous reporting

System Organ Class	Adverse reactions (Preferred terms)	Frequency
Immune system disorders	*anaphylactic reaction*, hypersensitivity**	Not known
Metabolism and nutrition disorders	hyponatraemia, hyperglycaemia, hospital acquired hyponatraemia**	Not known
Nervous system disorders	hyponatraemic encephalopathy**	Not known
Vascular disorders	phlebitis	Not known
Skin and subcutaneous tissue disorders	rash pruritus	Not known
General disorders and administration site conditions	injection site reactions including: pyrexia chills infusion site pain infusion site vesicles	Not known

** Potential manifestation in patients with allergy to corn, see section 4.4*

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

Adverse reactions may be associated to the medicinal product(s) added to the solution; the nature of the additive will determine the likelihood of any other adverse reactions.

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

Excess administration of Sodium Chloride 0.3 % and Glucose 3.3% Solution for Infusion Baxter can cause:

- Hyperglycaemia, adverse effects on water and electrolyte balance, and corresponding complications. For example, severe hyperglycaemia and severe dilutional hyponatraemia, and their complications, can be fatal.
- Hyponatraemia (which can lead to CNS manifestations, including seizures, coma, cerebral oedema and death).
- Fluid overload (which can lead to central and/or peripheral oedema).
- See also sections 4.4 and 4.8

When assessing an overdose, any additives in the solution must also be considered.

Clinically significant overdose of Sodium Chloride 0.3 % and Glucose 3.3% Solution for Infusion Baxter may therefore, constitute a medical emergency.

Interventions include discontinuation of administration, dose reduction, administration of insulin and other measures as indicated for the specific clinical constellation.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties

Pharmacotherapeutic group “Electrolytes with carbohydrates”, ATC code: “B05BB02”.

Sodium Chloride 0.3 % and Glucose 3.3% Solution for Infusion Baxter is a hypotonic and isoosmolar solution of sodium chloride and glucose.

The pharmacodynamic properties of Sodium Chloride 0.3 % and Glucose 3.3% Solution for Infusion Baxter are those of its components (sodium chloride and glucose).

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.

Chloride is mainly an extracellular anion. Intracellular chloride is in high concentration in red blood cells and gastric mucosa. Re-absorption of chloride follows re-absorption of sodium.

Glucose is the principal source of energy in cellular metabolism. The glucose in this solution provides a caloric intake of 132 kcal/l.

5.2 Pharmacokinetic Properties

The pharmacokinetic properties of this solution are those of its components (sodium, chloride and glucose).

After injection of radiosodium (24Na), the half -life is 11 to 13 days for 99% of the injected Na and one year for the remaining 1%. The distribution varies according to tissues: it is fast in muscles, liver, kidney, cartilage and skin; it is slow in erythrocytes and neurones; it is very slow in the bone. Sodium is predominantly excreted by the kidneys, but (as described earlier) there is extensive renal re-absorption. Small amounts of sodium are lost in the faeces and sweat.

The two main metabolic pathways of glucose are gluconeogenesis (energy storage) and glycogenolysis (energy release). Glucose metabolism is regulated by insulin.

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. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Water for Injections

6.2 Incompatibilities

Incompatibility of the medicinal product to be added with the solution in the Viaflo container must be assessed before addition.

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

The instructions for use of the medicinal product to be added must be consulted.

Before adding a drug, verify it is soluble and stable in water at the pH of Sodium Chloride 0.3 % and Glucose 3.3% Solution for Infusion Baxter (see section 3).

As guidance, the following medications are incompatible with the Sodium Chloride 0.3 % and Glucose 3.3% Solution for Infusion Baxter (non-exhaustive listing):

- Ampicillin sodium
- Mitomycin
- Erythromycin lactobionate
- Human insulin

Those additives known to be incompatible should not be used.

Because of the presence of glucose, Sodium Chloride 0.3 % and Glucose 3.3% Solution for Infusion Baxter should not be administered simultaneously with blood through the same administration set because of the possibility of pseudoagglutination or haemolysis.

6.3 Shelf life

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

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

From a physico-chemical viewpoint, solution containing additives should be used immediately unless Chemical

and physical in-use stability has been established.

From a microbiological point of view, solutions containing additives 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.

6.4 Special precautions for storage

Store below 25°C.

6.5 Nature and contents of container

The plastic bags known as Viaflo are composed of Polypropylene (PP), Polyamide (PA) and Polyethylene (PE).

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

The bag size is: 500 and 1000 ml.

Outer carton contents: 20 bags of 500ml
10 bags of 1000ml

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Discard after single use.

Discard any unused portion.

Do not reconnect partially used bags.

For method of administration and precautions to be taken before handling or administering the medicinal product, please see also section 4.2.

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 impaired.
   c. Check the solution for limpidity 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 to 22 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. See section 6.3.

To add medication during administration

   a. Close clamp on the set.
   b. Disinfect medication site.
   c. Using syringe with 19 to 22-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 (Pharmaceutical) Ltd.

124 Devora Hanevia st., Tel Aviv 6944020

8. REGISTRATION NUMBERS

165-52-35950-00

9. MANUFACTURER

Bieffe Medital S.A., Sabinanigo, Spain

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