SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Sodium chloride 0.33% and Glucose 5% Baxter.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Glucose (as monohydrate) 50 g/L
Sodium chloride 3.3 g/L

Each mL contains 50 mg glucose (as monohydrate) and 3.3 mg sodium chloride.

mmol/L: Na^+: 56 Cl^-: 56

390 mOsm/L (approx.)
pH: 3.5-6.5

Nutritional value: approximately 840 KJ/L (200 Kcal/L).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for infusion.
Clear solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

A source of water, electrolytes and calories.

4.2 Posology and method of administration

Posology

The choice of the specific sodium chloride and glucose concentration, dosage, volume, duration and rate of administration depend on the age, weight, clinical condition of the patient and concomitant therapy. These should be determined by a physician. For patients with electrolyte and glucose abnormalities and for pediatric patients, consult a physician experienced in intravenous fluid therapy.

Fluid balance, serum glucose, serum sodium and other electrolytes should be monitored before and during administration, especially in patients with increased non-osmotic vasopressin release (syndrome of inappropriate antidiuretic hormone secretion, SIADH) and in patients co-medicated with vasopressin agonists due to the risk of hyponatremia.

Monitoring of serum sodium is particularly important when administering physiologically hypotonic solutions. Sodium chloride 0.33% and Glucose 5% Baxter may become extremely hypotonic after administration due to glucose metabolization in the body (see sections 4.4, 4.5 and 4.8).

Rapid correction of hyponatremia and hypernatremia is potentially dangerous (risk of serious neurologic complications). Electrolyte supplementation may be indicated according to the clinical needs of the patient.

Adults, older patients and adolescents (age 12 years and over):

The recommended dosage is: 500 mL to 3 liters every 24 hours

Administration rate:

The infusion rate is usually 40 mL/kg/24 h and should not exceed the patient's glucose oxidation capacities in order to avoid hyperglycemia. Therefore, the maximum dosage is 5 mg/kg/min.

Pediatric population

- The dosage varies with weight: from 0 to 10 kg body weight: 100 mL/kg/24 h
- from 10 to 20 kg body weight: 1000 mL + (50 mL/kg over 10 kg)/24 h
- > 20 kg body weight: 1500 mL + (20 mL/kg over 20 kg)/24 h.

The infusion rate varies with weight:

- from 0 to 10 kg body weight: 6 – 8 mL/kg/h
- from 10 to 20 kg body weight: 4 – 6 mL/kg/h
- > 20 kg body weight: 2 – 4 mL/kg/h

The infusion rate should not exceed the patient's glucose oxidation capacities in order to avoid hyperglycemia. Therefore, the maximum dosage is 10-18 mg/kg/min, depending on the age and the total body mass.

For all patients, a gradual increase of flow rate should be considered when starting administration of glucose-containing products.

Method of administration

The administration is performed by intravenous infusion.

Precautions to be taken into consideration before handling or administering the medicinal product.

Parenteral medicinal products should be inspected visually for particulate matter and discoloration prior to administration.
Do not administer unless the solution is clear and the container is intact. Administer immediately following the insertion of the infusion set.

Do not remove the bag from the overpouch until immediately prior to use. The inner bag maintains the sterility of the product.

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.

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. This type of intravenous administration set with the vent in the open position should not be used with flexible plastic vessels.

Additives may be introduced before or during infusion through the injection port of the container.

When additives are used, verify tonicity of 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.

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

4.3 Contraindications

The solution is contraindicated in patients with:

- Hypersensitivity to the active substances or to any of the components of the medicinal product Listed in section 6.1
- Extracellular hyperhydration or hypervolemia
- Fluid and sodium retention
- Severe renal failure (with oliguria/anuria)
- Uncompensated cardiac failure
- Hyponatremia
- Hypochloremia
- General edema or ascitic cirrhosis

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

4.4 Special warnings and precautions for use

Glucose-containing solutions for intravenous infusion are usually isotonic. In the body, however, glucose-containing solutions 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 hyponatremia.

Hyponatremia:

Patients with non-osmotic vasopressin release (e.g., in acute illness, pain, postoperative 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 hyponatremia upon infusion of hypotonic solutions.

Acute hyponatremia can lead to acute hyponatremic encephalopathy (cerebral edema) characterized by headache, nausea, convulsions, lethargy and vomiting. Patients with cerebral edema are at particular risk of severe, irreversible and life-threatening brain damage.

Children, women of childbearing potential and patients with reduced cerebral compliance (e.g., meningitis, intracranial hemorrhage and brain contusion) are at particular risk of severe and life-threatening cerebral edema caused by acute hyponatremia.

Sodium retention, fluid overload and edema

Sodium chloride 0.33% and Glucose 5% Baxter should be used with particular caution, in:

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

Hypopotassemia

Sodium chloride 0.33% and Glucose 5% Baxter may result in hypopotassemia. This medicinal product should be used with particular caution in patients with or at risk for hypopotassemia.
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 with aggravation of hypopotassemia
- persons with increased gastrointestinal losses (for example, diarrhea, vomiting)
- prolonged low potassium diet
- persons with primary hyperaldosteronism
- patients treated with medicinal products that increase the risk of hypopotassemia (for example, diuretics, beta-2 agonists or insulin)

Hypo- and hyperosmolality, serum electrolytes and fluid imbalance

Depending on the volume and rate of infusion and depending on the patient's underlying clinical condition and capability to metabolize glucose, administration of Sodium chloride 0.33% and Glucose 5% Baxter can cause:

- Hypo-osmolality
- Hyperosmolality, osmotic diuresis and dehydration
- Electrolyte disturbances such as
  - hyponatremia (see above),

  - hypopotassemia (see above),
  - hypophosphatemia,
  - hypomagnesemia,
- Overhydration/hypervolemia and, for example, congested states, including central (e.g., pulmonary congestion) and peripheral edema.

Clinical evaluations 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.

Hyperglycemia

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

To reduce the risk of hyperglycemia-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 failure or in the presence of sepsis, trauma or shock),
- severe malnutrition (risk of precipitating a refeeding syndrome, see below),
- thiamine deficiency, for example, 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 0.33% and Glucose 5% Baxter should be used with caution include:
- patients with ischemic stroke. Hyperglycemia has been implicated in increasing cerebral ischemic brain damage and impairing recovery after ischemic strokes.
- patients with severe traumatic brain injury (in particular during the first 24 hours following the trauma). Early hyperglycemia has been associated with poor outcomes in patients with severe traumatic brain injury.
- Newborns (See Pediatric glycemia-related complications).

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

Hypersensitivity reactions

- Hypersensitivity/infusion reactions, including anaphylaxis/anaphylactoid reactions, have been reported with glucose solutions (see section 4.8).
- The infusion must be stopped immediately if any signs or symptoms of a suspected hypersensitivity reaction develop, and appropriate therapeutic measures must be instituted as clinically indicated.

Solutions containing glucose should be used with caution in patients with known allergy to corn or corn products (see section 4.3).

Refeeding syndrome

Refeeding severely undernourished patients may result in a refeeding syndrome that is characterized by a 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 failure

Sodium chloride 0.33% and Glucose 5% Baxter should be administered with particular caution to patients at risk of severe renal failure. In such patients, administration of the solution may result in sodium retention and fluid overload.

Pediatric population

Pediatric glycemia-related complications

The infusion rate and volume depend on the age, weight, clinical and metabolic conditions of the patient, concomitant therapy, and should be determined by a physician experienced in pediatric therapy with solutions for intravenous infusion.

- Newborns, especially those born premature and with low birth weight, are at increased risk of developing hypoglycemia or hyperglycemia, and therefore, they need close monitoring during treatment with intravenous glucose solutions to ensure adequate glycemic control, in order to avoid potential long-term adverse effects.
- Hypoglycemia in the newborn can cause, e.g.:
  - prolonged convulsions,
  - coma and
  - brain damage.
- Hyperglycemia has been associated with:
  - brain injury, including intraventricular hemorrhage,
  - late-onset bacterial and fungal infection,
  - retinopathy of prematurity,
  - necrotizing enterocolitis,
  - increased oxygen requirements,
  - prolonged length of hospital stay and
  - death.

Pediatric hyponatremia-related complications

- Children (including newborns and older children) are at increased risk of developing hypo-osmotic hyponatremia as well as for developing hyponatremic encephalopathy.
- The infusion of hypotonic fluids together with the non-osmotic secretion of ADH may result in hyponatremia.
- Hyponatremia can lead to headache, nausea, convulsions, lethargy, coma, cerebral edema and death; therefore, acute symptomatic hyponatremic encephalopathy is considered a medical emergency.
- In the pediatric population, plasma electrolyte concentrations should be closely monitored.
- Rapid correction of hyponatremia is potentially dangerous (risk of serious neurologic complications). The dosage, frequency and duration of administration should be determined by a physician experienced in pediatric therapy with solutions for intravenous infusion.

Blood

Sodium chloride 0.33% and Glucose 5% Baxter should not be administered simultaneously with blood through the same infusion set, because hemolysis and clot formation can occur.

Geriatric use

When selecting the type of infusion solution and the volume and rate of infusion for a geriatric patient, it must be taken into account that such patients are generally more likely to have cardiac, renal, hepatic and other diseases or concomitant therapies.

4.5 Interaction with other medicinal products and other forms of interaction

Baxter has not performed interaction studies.

Both the glycemic effects and the effects on water and electrolyte balance should be taken into account when using Sodium chloride 0.33% and Glucose 5% Baxter in patients treated with other substances that affect glycemic control or fluid and/or electrolyte balance.

Medicinal products leading to an increased vasopressin effect

The below-listed medicinal products increase the vasopressin effect, leading to reduced renal electrolyte-free water excretion and increased risk of hospital-acquired hyponatremia following inappropriately balanced treatment with solutions for intravenous infusion (see sections 4.2, 4.4 and 4.8).

- Medicinal products stimulating vasopressin release, e.g.: Chlorpropamide, clofibrate, carbamazepine, vincristine, selective serotonin reuptake inhibitors, 3,4-methylenedioxy-N-methamphetamine, ifosfamide, antipsychotics, narcotics.
- Medicinal products potentiating vasopressin action, e.g.: Chlorpropamide, NSAIDs, cyclophosphamide.
- Vasopressin analogues, e.g.: Desmopressin, oxytocin, terlipressin.

Other medicinal products known to increase the risk of hyponatremia 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 edema and hypertension).
- diuretics, beta-2 agonists or insulin, which increase the risk of hypopotassemia.
- certain antiepileptic and psychotropic medicinal products that increase the risk of hyponatremia.

4.6 Fertility, pregnancy and lactation

Pregnancy
Intrapartum intravenous glucose infusion may result in fetal insulin production, with an associated risk of fetal hyperglycemia and metabolic acidosis, as well as rebound neonatal hypoglycemia.

Sodium chloride 0.33% and Glucose 5% Baxter should be administered with special caution for pregnant women during labor particularly if administered in combination with oxytocin due to the risk of hyponatremia (see sections 4.4, 4.5 and 4.8).

Fertility
There is no information on the effects of Sodium chloride 0.33% and Glucose 5% Baxter on fertility.

Breastfeeding
Sodium chloride 0.33% and Glucose 5% Baxter can be used during breastfeeding.

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 0.33% and Glucose 5% Baxter on the ability to drive or use 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, with the exception of "hyponatremia" in the pediatric population, for which there are references to literature on clinical trials.

The frequency of adverse reactions is based on the recommended frequency scale: Very common (≥ 1/10); Common (≥ 1/100 to < 1/10), Uncommon (≥ 1/1,000 to < 1/100), Rare (≥ 1/10,000 to < 1/1,000), Very rare (< 1/10,000), and not known (cannot be estimated from the available data).

Tabulated list of adverse reactions associated with these solutions

System Organ Class	Adverse reactions (Preferred Terms)	Frequency
Metabolism and nutrition disorders	Hypervolemia Hyponatremia Electrolyte imbalance Hospital-acquired hyponatremia**	Very common Unknown Unknown Not known
Nervous system disorders	Hyponatremic encephalopathy**	Not known
Cardiac disorders	Heart failure	Unknown
Immune system disorders	Anaphylactic reaction* Hypersensitivity*	Unknown
Renal and urinary disorders	Polyuria	Unknown

Tabulated list of adverse reactions associated with the administration method (for example, intravenous administration)

System Organ Class	Adverse reactions (Preferred Terms)	Frequency
Metabolism and nutrition disorders	Hypervolemia	Unknown
Vascular disorders	Vein damage Superficial thrombophlebitis	Unknown
General disorders and administration site conditions	Pyrexia Chills Injection site infection Injection site pain Injection site reaction Injection site phlebitis Extravasation	Unknown

* Potential manifestation in patients with allergy to corn (see section 4.4)
** Hospital-acquired hyponatremia may cause irreversible brain damage and death due to development of acute hyponatremic encephalopathy (see sections 4.2 and 4.4).

For all patients, a gradual increase of flow rate should be considered when starting administration of glucose-containing products.

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 0.33% and Glucose 5% Baxter can cause:

- Hyperglycemia, adverse effects on water and electrolyte balance, and corresponding complications. For example, severe hyperglycemia and severe dilutional hyponatremia, and their complications, can be fatal.
- Hyponatremia (which can lead to CNS manifestations, including convulsions, coma, cerebral edema and death).
- Fluid overload (which can lead to central and/or peripheral edema).
- 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 0.33% and Glucose 5% 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 0.33% and Glucose 5% Baxter is a hypotonic and hyperosmolar solution of glucose and sodium chloride.

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

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 a very 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. Reabsorption of chloride follows reabsorption of sodium.
Glucose is the main source of energy in cellular metabolism. The glucose in this solution provides a caloric intake of 200 kcal/L.

5.2 Pharmacokinetic properties

The pharmacokinetic properties of this solution are those of its components (glucose, sodium and chloride).
After injection of radiosodium (^{24}Na), 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 neurons; it is very slow in the bone. Sodium is predominantly excreted by the kidneys, but there is also extensive renal reabsorption. Small amounts of sodium are lost in the feces 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 human and animal plasma.

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

The safety of additives should be considered separately.

6 . PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Water for injections

6.2 Incompatibilities

Incompatibility of the medicinal products to be added with the solution in the 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 medicinal product, verify it is soluble and stable in water at the pH of Sodium chloride 0.33% and Glucose 5% Baxter solution for infusion (pH: 3.5 – 6.5).

As guidance, the following medicinal products are incompatible with Sodium chloride 0.33% and Glucose 5% Baxter (non-exhaustive listing):

- Ampicillin sodium
- Mitomycin
- Amphotericin B
- Erythromycin lactobionate
- Human insulin

Do not use medicinal products known to be incompatible.

Because of the presence of glucose, Sodium chloride 0.33% and Glucose 5% Baxter should not be administered simultaneously with whole blood through the same infusion set because of the possibility of hemolysis and agglutination.

6.3 Shelf life

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

6.4 Special precautions for storage

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

- The plastic bags known as Viaflo are composed of polyethylene (PE), polypropylene (PP) and polyamide (PA).
- Module port system contains two ports (medication port and administration port) with membrane. The port system is made of polyethylene (PE).
- The bags are overwrapped with a protective plastic pouch composed of transparent polyamide/polypropylene used as secondary packaging to protect each Viaflo bag.

The bag size is 1000 mL.
Outer carton contents: 10 bags of 1000 mL

6.6 Special precautions for disposal and other handling

Discard after single use.
Discard partially used containers.
Do not reconnect partially used bags.

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

1-Opening

a. Remove the Viaflo bag 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 solution for clarity and absence of foreign matter. If solution is not clear or contains foreign matter, discard the solution.

2-Preparation for administration

Use sterile material for preparation and administration.

a. Suspend container from the eyelet support at the bottom.
b. Remove plastic protector from outlet port 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 directions accompanying set for connection, priming of the set and administration of the solution.

3-Techniques for injection of additives

Warning: Additives may be incompatible.

To add medication before administration:

a. Disinfect medication site.
b. Using syringe with 19-gauge 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 medication.

To add medication during administration:

a. Close clamp on the set.

b. Disinfect medication site.

c. Using syringe with 19-gauge 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 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. MANUFACTURER

Bieffe Medital S.A., Spain
Sabinanigo (Huesca), Spain

8. LISENCE HOLDER

Baxter Healthcare Distribution Ltd,
34 Jerusalem St., Ra'anana Israel

9. REGISTRATION NUMBER

172-06-36115-00

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