

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE FINISHED PHARMACEUTICAL PRODUCT

DNS-SSP (Sodium Chloride 0.9 % w/v and Glucose 5% w/v Solution for Infusion BP)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 1,000 ml contains:

Sodium Chloride BP-0.9% w/v (9g/l)

Glucose Anhydrous 5.0% w/v (50g/l)

Water for Injection BP to Q.S

3. PHARMACEUTICAL FORM

Solution for Infusion, free from visible particles. Osmolarity: 585 mosm/l (approx) & pH: 3.5 to 6.5

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Sodium Chloride 0.9 % w/v and Glucose 5% w/v solution is indicated for Treatment of sodium depletion, extracellular dehydration or hypovolaemia in cases where supply of water and carbohydrates is required due to restriction of the intake of fluids and electrolytes by normal routes.

4.2. Posology and method of administration

The choice of the specific sodium chloride and glucose concentration, dosage, volume, rate and duration of administration depends on the age, weight, clinical condition of the patient and concomitant therapy. It should be determined by a physician. For patients with electrolyte and glucose abnormalities and for paediatric patients, consult a physician experienced in intravenous fluid therapy. Rapid correction of hyponatraemia and hypernatraemia is potentially dangerous (risk of serious neurologic complications).

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

The recommended dosage is: 500 ml to 3 L/24h

Administration rate:

The infusion rate is usually 40 ml/kg/24h and should not exceed the patient's glucose oxidation capacities in order to avoid hyperglycaemia. Therefore the maximum acute administration rate is 5 mg/kg/min.

Paediatric population

The dosage varies with weight:

- 0-10 kg body weight: 100 ml / kg / 24 h
- 10-20 kg body weight: 1000 ml + (50 ml/ kg over 10 kg) / 24h

- > 20 kg body weight: 1500 ml + (20 ml/ kg over 20 kg) / 24h.

The infusion rate should not exceed the patient's glucose oxidation capacities in order to avoid hyperglycemia.

Therefore the maximum acute administration rate is 10-18 mg/kg/min depending on 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.

Sodium chloride 0.9% w/v and Glucose 5% w/v solution is isotonic and hyperosmolar, due to the glucose content. It has an approximate osmolarity of 585 mOsmol/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. Do not administer unless the solution is clear and the 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.

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. Vented intravenous administration sets with the vent in the open position should not be used with flexible plastic containers.

Additives may be introduced before or during infusion through the resalable 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.

Monitoring:

Fluid balance and the concentrations of glucose and electrolytes (especially sodium) in plasma must be monitored during administration. Electrolyte supplementation may be indicated according to the clinical needs of the patient.

4.3. Contraindications

The solution is contraindicated in patients presenting with:

- Known hypersensitivity to the product,

- Extracellular hyperhydration or hypervolaemia,
- Fluid and sodium retention,
- Severe renal insufficiency (with oliguria/anuria),
- Uncompensated cardiac failure,
- Hypernatraemia or hyperchloraemia,
- 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

Hypokalaemia

The infusion of Sodium chloride 0.9% w/v and Glucose 5% w/v solution may result in hypokalaemia. Close clinical monitoring may be warranted in patients with or at risk for hypokalaemia, 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 agonists or insulin).

Sodium retention, fluid overload and oedema

Sodium chloride 0.9% w/v and Glucose 5% w/v solution should be used with particular caution in,

- Patients with metabolic acidosis
- Patients at risk of
 - ✓ Hypernatraemia
 - ✓ Hyperchloraemia
 - ✓ Hypervolaemia
- Patients with conditions that may cause sodium retention, fluid overload and oedema (central and peripheral), such as;
 - o Primary hyperaldosteronism,
 - o Secondary hyperaldosteronism associated with, for example, hypertension,
- congestive heart failure,
- liver disease (including cirrhosis),
- renal disease (including renal artery stenosis, nephrosclerosis)

o Pre-eclampsia.

Patients taking medications that may increase the risk of sodium and fluid retention, such as corticosteroids.

Hyperosmolality, serum electrolytes and water imbalance

Depending on the volume, rate of infusion, the patient's underlying clinical condition and capability to metabolize glucose, administration of Sodium chloride 0.9% w/v and Glucose 5% w/v solution can cause:

- Hyperosmolality, osmotic diuresis and dehydration
- Electrolyte disturbances such as;
 - o hyponatraemia (see “Sodium imbalance” below)
 - o hypokalaemia (see above)
 - o hypophosphataemia,
 - o hypomagnesaemia,
- Acid-base imbalance
- Overhydration/hypervolaemia and, for example, congested states, including central (e.g. pulmonary congestion) and peripheral oedema.
- An increase in serum glucose concentration is associated with an increase in serum osmolality. Osmotic diuresis associated with hyperglycaemia can result in or contribute to the development of dehydration and in electrolyte losses.

Sodium imbalance

Sodium chloride 0.9% w/v and Glucose 5% w/v solution should be used with particular caution in patients with; or at risk for hyponatraemia, for example:

- children
- elderly patients
- women
- postoperatively
- persons with psychogenic polydipsia

Hyponatraemia can lead to headache, nausea, seizures, lethargy, coma, cerebral oedema, and death. Acute symptomatic hyponatraemic encephalopathy is considered a medical emergency.

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.

Hyperglycaemia

Rapid administration of glucose solutions may produce substantial hyperglycaemia and 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 0.9% w/v and Glucose 5% w/v solution 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.
- New-borns.

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
- 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 0.9% w/v and Glucose 5% w/v solution 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 hemorrhage, 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.

- Hyponatraemia can lead to headache, nausea, seizures, lethargy, coma, cerebral oedema 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 0.9% w/v and Glucose 5% w/v solution should not be administered simultaneously with blood through the same administration set because of the possibility of pseudo agglutination or haemolysis.

Geriatric use

When selecting 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

Both the glycaemic and effects on water and electrolyte balance should be taken into account when administering Sodium chloride 0.9% w/v and Glucose 5% w/v solution to patients treated with other substances that affect glycaemic control, or fluid and/or electrolyte balance.

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 agonists or insulin, whom increase the risk of hypokalaemia.

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.

Fertility

There is no information on the effects of Sodium chloride 0.9% w/v and Glucose 5% w/v solution on fertility.

Lactation

Sodium chloride 0.9% w/v and Glucose 5% w/v solution 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 0.9% w/v and Glucose 5% w/v solution 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	hypernatraemia, hyperglycaemia,	Not known
Vascular disorders	phlebitis	Not known
Skin and subcutaneous tissue	rash, pruritus	Not known

disorders		
General disorders and administration site conditions	injection site reactions including: pyrexia chills infusion site pain infusion site vesicles	Not known

4.9. Overdose

Excess administration of Sodium chloride 0.9% w/v and Glucose 5% w/v solution 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).
- Hypernatraemia especially in patients with renal impairment.
- Fluid overload (which can lead to central and/or peripheral oedema).

A clinically significant overdose of Sodium chloride 0.9% w/v and Glucose 5% w/v solution may, therefore, constitute a medical emergency.

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

Interventions include discontinuation of Sodium chloride 0.9% w/v and Glucose 5% w/v solution 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 0.9% w/v and Glucose 5% w/v is an isotonic and hyperosmolar solution of sodium chloride and glucose.

The pharmacodynamic properties of this 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 an important role in neurotransmission and cardiac electrophysiology, and also in 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 principal source of energy in cellular metabolism. The glucose in this solution provides a caloric intake of 200kcal/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 neurones; it is very slow in the bone. Sodium is predominantly excreted by the kidneys, but (as described earlier) there is extensive renal reabsorption. 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 bottle 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 0.9% w/v and Glucose 5% w/v solution.

As guidance, the following medications are incompatible with the Sodium Chloride 0.9 % w/v & Glucose 5% w/v solution (non-exhaustive listing):

- Ampicillin sodium
- Mitomycin
- Amphotericin B
- Erythromycin lactobionate

Those additives known to be incompatible should not be used. Because of the presence of glucose,

Sodium chloride 0.9% w/v and Glucose 5% w/v solution should not be administered simultaneously with blood through the same administration set because of the possibility of pseudoagglutination or haemolysis.

6.3. Shelf life

3 years

6.4. Special precautions for storage

Store below 30° C. Protect from light. Do not refrigerate or freeze

6.5. Nature and contents of container

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. The bag size is 1000 ml.

Outer carton contents: 12 bags of 1,000 ml per one carton.

6.6. Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

Discard any unused portion, must not be used in series connections. Hold the bottle in vertical position & insert I.V set.

Not to be used if container found leaking or solution is hazy or contains visible solid particles.

7. MARKETING AUTHORISATION HOLDER

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8. NUMBER(S) IN THE NATIONAL REGISTER OF FINISHED PHARMACEUTICAL PRODUCTS

07147/07353/NMR/2019

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

25/02/2022

10. DATE OF REVISION OF THE TEXT

25/08/2023