Fleboflex® IV Solutions

0.9% Sodium Chloride Injection, USP, in Fleboflex plastic container

GRIFOLS

icumedical
human connections

The overwrap protects and maintains the sterility of the Fleboflex® container and limits evaporative moisture loss from the primary solution container. The overwrap is transparent to allow visual inspection and has a peelable opening system.

Fleboflex®

0.9% Sodium Chloride Injection, USP, is a sterile, nonpyrogenic solution for fluid and electrolyte replenishment in Fleboflex® plastic container for intravenous administration.

- Fleboflex is a flexible container free of PVC, plasticizers, adhesives, and latex
- The Fleboflex container consists of a polypropylene multilayer film. Polypropylene is a highly compatible material. It is used for the preparation of intravenous mixtures with drugs that have shown their incompatibility with other plastics[1]
- Fleboflex is totally collapsible, lightweight, and transparent
- The Fleboflex container meets the Class VI U.S. Pharmacopeia (USP) testing for plastic containers. These tests confirm the biological safety of the container system

Fleboflex can accept additional solution volume without significant overpressure[2]

Fleboflex mL container format	Additive volume in mL up to a pressure of 50 mbar		
	Minimum	Mean	Maximum
50 mL	79	84	90
100 mL	74	80	88
250 mL	122	128	135
500 mL	164	182	191
1000 mL	131	153	176

Hypersensitivity/infusion reactions, including hypotension, pyrexia, tremor, chills, urticaria, rash, and pruritus have been reported with 0.9% Sodium Chloride Injection, USP. Please see Important Safety Information on page 6 and full Prescribing information on page 7 for 0.9% Sodium Chloride Injection, USP.

Grifols state-of-the-art plastic container

Fleboflex® benefits and features

Can be used with ICU Medical's FleboCap™ for tamper evidence and tamper deterrence.

Designed for safe and easy handling

- Designed with rounded upper and lower corners that guarantee handling without accidental punctures
- Integrated eyelet support for easy and safe handling of the container during the infusion

Highly compatible material

- The solution is only in contact with polypropylene. Both the multilayer film and the inner membranes of the medication and outlet ports contain only polypropylene
- Polypropylene can be sterilized at a higher temperature as it resists heat better than other olefins[3,4]

Product information

- Inclusion of the National Drug Code
- Inclusion of lot and expiration date

High sealing resistance

- High resistance to pressure cuffs responding satisfactorily to 400 mmHg pressure for 72 hours[2]

Grifols port system

- Medication and outlet ports designed with rigid and long tubes to avoid perforation due to needle insertion
- Safe attachment of the infusion set due to its internal membrane
- No parts of the cover have to be removed/broken in order to access the outlet port

FAQs

Condensation vs leaks

Condensation in the product overwrap is not a defect.

The overwrap serves as a moisture barrier. The presence of some small droplets of water in the overwrap is normal.

After removing the overwrap, check for minute leaks by squeezing the inner container firmly. If leaks are found, discard solution as sterility may be impaired.

Horizontal marks on the container

The marks on the container are not a product defect.

This appearance is a normal aspect of the Grifols sterilization process. During steam sterilization, the overwrapped product is placed on stainless steel racks. These racks have openings to allow steam to flow over the product and through the chamber. For this reason, following the sterilization, the container shows the horizontal markings due to contact with the surface of the racks. The marks on the container have no impact on the safety, efficacy, or function of the product and will gradually fade over time.

Opacity of the plastic

Some opacity of the plastic may be observed due to moisture absorption during the sterilization process. This is normal and does not affect the solution quality or safety. The opacity will diminish gradually.

Administration set and Fleboflex® outlet port

The Fleboflex outlet port has an internal membrane to ensure its integrity and correct adhesion of the administration set. The Fleboflex outlet port has been designed and tested in accordance with ISO 15747 “Plastic containers for intravenous injections.”

Please see Important Safety Information on page 6 and full Prescribing Information on page 7 for 0.9% Sodium Chloride Injection, USP.

Important Safety Information

Sodium Chloride Injection, USP is indicated as a source of water and electrolytes. 0.9% Sodium Chloride Injection, USP is also indicated for use as a priming solution in hemodialysis procedures.

Warnings

Hypersensitivity

Hypersensitivity and infusion reactions, including hypotension, pyrexia, tremor, chills, ur-ticaria, rash, and pruritus have been reported with 0.9% Sodium Chloride Injection, USP. Stop the infusion immediately if signs or symptoms of a hypersensitivity reaction de-velop, such as tachycardia, chest pain, dyspnea and flushing. Appropriate therapeutic countermeasures must be instituted as clinically indicated.

Electrolyte Imbalances

Fluid Overload

Depending on the volume and rate of infusion, and the patient's underlying clini-cal condition, the intravenous administration of Sodium Chloride Injection, USP can cause fluid disturbances such as overhydration/hypervolemia and congested states, including pulmonary congestion and edema.

Avoid 0.9% Sodium Chloride Injection, USP in patients with or at risk for fluid and/or solute overloading. If use cannot be avoided, monitor fluid balance, electrolyte con-centrations, and acid base balance, as needed and especially during prolonged use.

Hyponatremia

Sodium Chloride Injection, USP may cause hyponatremia. Hyponatremia can lead to acute hyponatremic encephalopathy characterized by headache, nausea, seizures, lethargy, and vomiting. Patients with brain edema are at particular risk of severe, irreversible and life-threatening brain injury. Avoid Sodium Chloride Injection, USP in patients with or at risk for hyponatremia. If use cannot be avoided, monitor serum sodium concentrations.

Hypernatremia

Hypernatremia may occur with Sodium Chloride Injection, USP. Conditions that may increase the risk of hypernatremia, fluid overload and edema (central and peripheral), include 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); and pre-eclampsia. Avoid Sodium Chloride Injection, USP in patients with, or at risk for, hypernatremia. If use cannot be avoided, monitor serum sodium concentrations.

Precautions

Patients with Severe Renal Impairment

Administration of Sodium Chloride Injection, USP in patients with or at risk of severe renal impairment, may result in hypernatremia and/or fluid overload. Avoid Sodium Chloride Injection, USP in patients with severe renal impairment or conditions that may cause sodium and/or potassium retention, fluid overload, or edema. If use can-not be avoided, monitor patients with severe renal impairment for development of these adverse reactions.

Drug Interactions

Other Products that Affect Fluid and/or Electrolyte Balance

Administration of Sodium Chloride Injection, USP to patients treated concomitantly with drugs associated with sodium and fluid retention may increase the risk of hypernatremia and volume overload. Avoid use of Sodium Chloride Injection, USP in patients receiving such products, such as corticosteroids or corticotropin. If use can-not be avoided, monitor serum electrolytes, fluid balance and acid-base balance.

Lithium

Renal sodium and lithium clearance may be increased during administration of 0.9% Sodium Chloride Injection, USP. Monitor serum lithium concentrations during con-comitant use.

Other Drugs that Increase the Risk of Hyponatremia

Administration of Sodium Chloride Injection, USP in patients treated concomitantly with medications associated with hyponatremia may increase the risk of developing hyponatremia.

Avoid use of Sodium Chloride Injection, USP in patients receiving products, such as diuretics, and certain antiepileptic and psychotropic medications. Drugs that increase the vasopressin effect reduce renal electrolyte free water excretion and may also increase the risk of hyponatremia following treatment with intravenous fluids. If use cannot be avoided, monitor serum sodium concentrations.

Pregnancy

Sodium Chloride Injection, USP should be given during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Lactation

It is not known whether this drug is present in human milk. Because many drugs are present in human milk, caution should be exercised when Sodium Chloride Injection, USP is administered to a nursing woman.

Pediatric Use

Closely monitor plasma electrolyte concentrations in pediatric patients who may have impaired ability to regulate fluids and electrolytes. In very low birth weight infants, excessive or rapid administration of Sodium Chloride Injection, USP may result in increased serum osmolality and risk of intracerebral hemorrhage.

Children (including neonates and older children) are at increased risk of developing hyponatremia as well as for developing hyponatremic encephalopathy.

Geriatric Use

Geriatric patients are at increased risk of developing electrolyte imbalances. Sodium Chloride Injection, USP is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function.

Adverse Reactions

The following adverse reactions have been reported in the post-marketing experi-ence during use of 0.9% Sodium Chloride Injection, USP and include the following: General disorders and administration site conditions (Infusion site erythema, injection site streaking, burning sensation, and infusion site urticaria), Hypersensitvity reac-tions: (Hypotension, pyrexia, tremor, chills, urticaria, rash, and pruritus), Metabolism and nutrition disorders (Hypernatremia, hyponatremia, hyperchloremic metabolic aci-dosis) and Nervous System Disorders (Hyponatremic encephalopathy).

Please see a Grifols representative for full Prescribing Information for 0.9% Sodium Chloride Injection, USP.

References

1. Sastri V. (2010). Commodity Thermoplastics: Polyvinyl Chloride, Polyolefins, Cycloolefins and Polystyrene. 10.1016/B978-0-323- 85126-8.00002-3 **2.** Grifols data on file **3.** Maddah, Hisham. (2016). Polypropylene as a Promising Plastic: A Review. 2163-1352. 2016. 1-11. 10.5923/j.ajps.20160601.01 **4.** ELECTROCOME, s.l. POLIETILENO - PE. Accessed May 15, 2024 https://www.electrocome.com/p-1-38/POLIETILENO---PE.htm

FULL PRESCRIBING INFORMATION
0.9% Sodium Chloride Injection, USP
in FLEBOFLEX and FLEBOFLEX LUER Plastic Container

DESCRIPTION
Sodium Chloride Injection, USP is a sterile, nonpyrogenic solution for fluid and electrolyte replenishment in single dose containers for intravenous administration. It contains no antimicrobial agents. The pH ranges from 4.5 to 7.0. Composition, osmolarity, and ionic concentration are shown below:

0.9% Sodium Chloride Injection, USP contains 9 g/L Sodium Chloride, USP (NaCl) with an osmolarity of 308 mOsmol/L (calc). It contains 154 mEq/L sodium and 154 mEq/L chloride.

The FLEBOFLEX and FLEBOFLEX LUER plastic containers are fabricated from latex-free polyolefins or polypropyl- ene plastic materials. The solution contact materials do not contain PVC, DEHP, or other plasticizers. The amount of water that can permeate from inside the container into the overwrap is insufficient to affect the solution signif- icantly. The suitability of the container materials has been established through biological evaluations, which have shown the containers pass Class VI U.S. Pharmacopeia (USP) testing for plastic containers. These tests confirm the biological safety of the container systems.

CLINICAL PHARMACOLOGY
Sodium Chloride Injection, USP has value as a source of water and electrolytes. It is capable of inducing diuresis depending on the clinical condition of the patient.

INDICATIONS AND USAGE
Sodium Chloride Injection, USP is indicated as a source of water and electrolytes.

0.9% Sodium Chloride Injection, USP is also indicated for use as a priming solution in hemodialysis procedures.

CONTRAINDICATIONS
None known.

WARNINGS
Hypersensitivity
Hypersensitivity and infusion reactions, including hypotension, pyrexia, tremor, chills, urticaria, rash, and pruritus have been reported with 0.9% Sodium Chloride Injection, USP.

Stop the infusion immediately if signs or symptoms of a hypersensitivity reaction develop, such as tachycardia, chest pain, dyspnea and flushing. Appropriate therapeutic countermeasures must be instituted as clinically in- dicated.

Electrolyte Imbalances
Fluid Overload
Depending on the volume and rate of infusion, and the patient's underlying clinical condition, the intravenous administration of Sodium Chloride Injection, USP can cause fluid disturbances such as overhydration/hypervolemia and congested states, including pulmonary congestion and edema.

Avoid 0.9% Sodium Chloride Injection, USP in patients with or at risk for fluid and/or solute overloading. If use cannot be avoided, monitor fluid balance, electrolyte concentrations, and acid base balance, as needed and especially during prolonged use.

Hyponatremia
Sodium Chloride Injection, USP may cause hyponatremia. Hyponatremia can lead to acute hyponatremic enceph- alopathy characterized by headache, nausea, seizures, lethargy, and vomiting. Patients with brain edema are at particular risk of severe, irreversible and life-threatening brain injury.

The risk of hospital-acquired hyponatremia is increased in patients with cardiac or pulmonary failure, and in patients with non-osmotic vasopressin release (including SIADH) treated with high volume of Sodium Chloride Injection, USP.

The risk for hyponatremia is increased in pediatric patients, elderly patients, postoperative patients, those with psychogenic polydipsia, and in patients treated with medications that increase the risk of hyponatremia (such as diuretics, certain antiepileptic and psychotropic medications). See Drug Interactions.

Patients at increased risk for developing complications of hyponatremia such as hyponatremic encephalopathy, include pediatric patients, women (in particular pre-menopausal women), patients with hypoxemia, and patients with underlying central nervous system disease. Avoid Sodium Chloride Injection, USP in patients with or at risk for hyponatremia. If use cannot be avoided, monitor serum sodium concentrations.

Rapid correction of hyponatremia is potentially dangerous with risk of serious neurologic complications. Brain adaptations reducing risk of cerebral edema make the brain vulnerable to injury when chronic hyponatremia is too rapidly corrected, which is known as osmotic demyelination syndrome (ODS). To avoid complications, monitor serum sodium and chloride concentrations, fluid status, acid-base balance, and signs of neurologic complications.

Hypernatremia
Hypernatremia may occur with Sodium Chloride Injection, USP. Conditions that may increase the risk of hyper- natremia, fluid overload and edema (central and peripheral), include 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); and pre-eclampsia. Certain medications such as corticosteroids or corticotropin, may also increase risk of sodium and fluid retention, see Drug Interactions.

Avoid Sodium Chloride Injection, USP in patients with, or at risk for, hypernatremia. If use cannot be avoided, monitor serum sodium concentrations.

Rapid correction of hypernatremia is potentially dangerous with risk of serious neurologic complications. Exces- sively rapid correction of hypernatremia is also associated with a risk for serious neurologic complications such as osmotic demyelination syndrome (ODS) with risk of seizures and cerebral edema.

PRECAUTIONS
Patients with Severe Renal Impairment
Administration of Sodium Chloride Injection, USP in patients with or at risk of severe renal impairment, may result in hypernatremia and/or fluid overload (see WARNINGS). Avoid Sodium Chloride Injection, USP in patients with severe renal impairment or conditions that may cause sodium and/or potassium retention, fluid overload, or edema. If use cannot be avoided, monitor patients with severe renal impairment for development of these adverse reactions.

Drug Interactions
Other Products that Affect Fluid and/or Electrolyte Balance
Administration of Sodium Chloride Injection, USP to patients treated concomitantly with drugs associated with sodium and fluid retention may increase the risk of hypernatremia and volume overload. Avoid use of Sodium Chloride Injection, USP in patients receiving such products, such as corticosteroids or corticotropin. If use cannot be avoided, monitor serum electrolytes, fluid balance and acid-base balance.

Lithium
Renal sodium and lithium clearance may be increased during administration of 0.9% Sodium Chloride Injection, USP. Monitor serum lithium concentrations during concomitant use.

Other Drugs that Increase the Risk of Hyponatremia
Administration of Sodium Chloride Injection, USP in patients treated concomitantly with medications associated with hyponatremia may increase the risk of developing hyponatremia.

Avoid use of Sodium Chloride Injection, USP in patients receiving products, such as diuretics, and certain antiepi- leptic and psychotropic medications. Drugs that increase the vasopressin effect reduce renal electrolyte free water excretion and may also increase the risk of hyponatremia following treatment with intravenous fluids. If use cannot be avoided, monitor serum sodium concentrations.

Pregnancy
There are no adequate and well controlled studies with Sodium Chloride Injection, USP in pregnant women and animal reproduction studies have not been conducted with this drug. Therefore, it is not known whether Sodium Chloride Injection, USP can cause fetal harm when administered to a pregnant woman. Sodium Chloride Injection, USP should be given during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Lactation
It is not known whether this drug is present in human milk. Because many drugs are present in human milk, caution should be exercised when Sodium Chloride Injection, USP is administered to a nursing woman.

Pediatric Use
The use of Sodium Chloride Injection, USP in pediatric patients is based on clinical practice. (See DOSAGE AND ADMINISTRATION). Closely monitor plasma electrolyte concentrations in pediatric patients who may have impaired ability to regulate fluids and electrolytes. In very low birth weight infants, excessive or rapid administration of Sodium Chloride Injection, USP may result in increased serum osmolality and risk of intracerebral hemorrhage.

Children (including neonates and older children) are at increased risk of developing hyponatremia as well as for developing hyponatremic encephalopathy.

Geriatric Use
Geriatric patients are at increased risk of developing electrolyte imbalances. Sodium Chloride Injection, USP is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Therefore, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

Consider monitoring renal function in elderly patients.

ADVERSE REACTIONS
Post-Marketing Adverse Reactions
The following adverse reactions have been identified during post approval use of Sodium Chloride Injection, USP. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

The following adverse reactions have been reported in the post-marketing experience during use of 0.9% Sodium Chloride Injection, USP and include the following:

General disorders and administration site conditions: Infusion site erythema, injection site streaking, burning sen- sation, and infusion site urticaria.

Hypersensitvity reactions: Hypotension, pyrexia, tremor, chills, urticaria, rash, and pruritus.

Metabolism and nutrition disorders: Hypernatremia, hyponatremia, hyperchloremic metabolic acidosis.

Nervous System Disorders: Hyponatremic encephalopathy.

If an adverse reaction does occur, discontinue the infusion, evaluate the patient, institute appropriate therapeutic countermeasures and save the remainder of the fluid for examination if deemed necessary.

OVERDOSAGE
Excessive administration of 0.9% Sodium Chloride Injection, USP can cause hypernatremia. Hypernatremia can lead to CNS manifestations, including seizures, coma, cerebral edema and death.

Excessive administration of Sodium Chloride Injection, USP can cause fluid overload (which can lead to pulmonary and/or peripheral edema).See WARNINGS and ADVERSE REACTIONS.

When assessing an overdose, any additives in the solution must also be considered. The effects of an overdose may require immediate medical attention and treatment.

Interventions include discontinuation of Sodium Chloride Injection, USP administration, dose reduction, and other measures as indicated for the specific clinical constellation (e.g., monitoring of fluid balance, electrolyte concen- trations and acid base balance).

DOSAGE AND ADMINISTRATION
Important Administration Instructions
- Sodium Chloride Injection, USP is intended for intravenous administration using sterile equipment.
- Do not connect flexible plastic containers in series in order to avoid air embolism due to possible residual air contained in the primary container.
- Set the vent to the closed position on a vented intravenous administration set to prevent air embolism.
- Use a dedicated line without any connections to avoid air embolism.
- Do not pressurize intravenous solutions contained in flexible plastic containers to increase flow rates in order to avoid air embolism due to incomplete evacuation of residual air in the container.
- Prior to infusion, visually inspect the solution for particulate matter and discoloration. The solution should be clear and there should be no precipitates. Do not administer unless solution is clear, and container is undamaged.

Dosing Information
The choice of product, dosage, volume, rate, and duration of administration is dependent upon the age, weight and clinical condition of the patient and concomitant therapy, and administration should be determined by a physician experienced in intravenous fluid therapy.

Introduction of Additives
Additives may be incompatible.

Evaluate all additions to the plastic container for compatibility and stability of the resulting preparation. Consult with a pharmacist, if available.

If, in the informed judgment of the physician, it is deemed advisable to introduce additives, use aseptic technique. Mix thoroughly when additives have been introduced. After addition, if there is a discoloration and/or the appear- ance of precipitates, insoluble complexes or crystals, do not use. Do not store solutions containing additives. Discard any unused portion.

HOW SUPPLIED
The available sizes of 0.9% Sodium Chloride Injection, USP are shown below:

Size (mL)	NDC
Fleboflex bags:	
50 (115 units in one carton)	76297-001-11
50 (115 units in one carton)	76297-001-11
100 (70 units in one carton)	76297-001-21
250 (28 units in one carton)	76297-001-31
500 (20 units in one carton)	76297-001-01
1000 (10 units in one carton)	76297-001-41
Fleboflex Luer bags:	
50 (90 units in one carton)	76297-001-51
100 (50 units in one carton)	76297-001-61
250 (32 units in one carton)	76297-001-71
500 (24 units in one carton)	76297-001-81
1000 (10 units in one carton)	76297-001-91

Exposure of pharmaceutical products to heat should be minimized. Avoid excessive heat. It is recommended the product be stored at 20° to 25°C (68° to 77°F); excursions are permitted between 15° to 30°C (59° to 86°F). [see USP Controlled Room Temperature.] Store unit in moisture barrier overwrap. Brief exposure up to 40°C (104°F) does not adversely affect the product.

DIRECTIONS FOR USE OF FLEBOFLEX AND FLEBOFLEX LUER PLASTIC CONTAINER
For Information on Risk of Air Embolism – see DOSAGE AND ADMINISTRATION.

To Open
Peel off the overwrap and remove solution container. Visually inspect the container. If the outlet port protector is damaged, detached, or not present, discard container as solution path sterility may be impaired. Some opacity of the plastic due to moisture absorption during the sterilization process may be observed. This is normal and does not affect the solution quality or safety. The opacity will diminish gradually. Check for minute leaks by squeezing inner bag firmly. If leaks are found, discard solution as sterility may be impaired. If supplemental medication is desired, follow directions below.

Preparation for Administration
1. Suspend container from eyelet support.
2. Fleboflex bags: Remove plastic protector from outlet port at bottom of container. Fleboflex Luer bags: Break the twist-off administration port by means of torsion.
3. Attach administration set. Refer to complete directions accompanying set.

To Add Medication
Additives may be incompatible.

To add medication before solution administration
1. Prepare medication site.
2. Fleboflex bags: Using syringe with 19 to 22 gauge needle, puncture resealable medication port and inject. Fleboflex Luer bags: Using syringe or vial, connect to the needle-free medication port and inject.
3. Mix solution and medication thoroughly.

To add medication during solution administration
1. Close clamp on the set.
2. Prepare medication site.
3. Fleboflex bags: Using syringe with 19 to 22 gauge needle, puncture resealable medication port and inject. Fleboflex Luer bags: Using syringe or vial, connect to the needle-free medication port and inject.
4. Remove container from intravenous pole and/or turn to an upright position.
5. Mix solution and medication thoroughly.
6. Return container to in-use position and continue administration.

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- Personalized instructional materials

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Refer to the Directions for Use of Fleboflex and Fleboflex Luer Plastic Containers in the full Prescribing Information

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