IV Solutions

Fleboflex®

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

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

NEXTGEN
PHARMACEUTICALS

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.
- 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

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

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® has drug-container compatibility studies with a selected number of drugs[1]

	Fleboflex®	
	5 °C (41°F)	25 °C (77°F)
Cefotaxime / 0.5 mg/mL in 0.9% SC	10 days	1 day
Cefuroxime / 0.5 mg/mL in 0.9% SC	10 days	1 day
Cyclophosphamide / 2 mL in 0.9% SC	6 days	5 days
Diazepam / 50 µg/mL in 0.9% SC	10 days	4 days
Docetaxel / 0.3 mg/mL in 0.9% SC	7 days	7 days
Doxorubicin / 0.1 mg/mL in 0.9% SC	30 days	15 days
Etoposide / 0.3 mg/mL in 0.9% SC	-	10 days
5-fluorouracil / 3 mg/mL in 0.9% SC	28 days	28 days
Isosorbide Dinitrate / 0.1 mg/mL in 0.9% SC	10 days	10 days
Methylprednisolone / 5 mg/mL in 0.9% SC	10 days	2 days Free Prednisolone > 6.6 %
Morphine / 0.1 mg/mL in 0.9% SC	10 days	10 days
Nitroglycerin / 50 µg/mL in 0.9% SC	10 days	10 days
Ondansetron / 80 µg/mL in 0.9% SC	10 days	10 days
Paclitaxel / 0.3 mg/mL in 0.9% SC	7 days	7 days

0.9% SC: 0.9% Sodium Chloride

[1] The compatibility of additives with Sodium Chloride 0.9% must be checked before adding a medication.

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

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State-of-the-art plastic container

Fleboflex® benefits and features

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.

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.

Designed for a safe and easy handling

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

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.

Guidelines for *Fleboflex*® use

Overwrap removal

The overwrap serves as a moisture barrier. It is intended to limit evaporative moisture loss from the primary solution container.

The overwrap is designed to be opened by pulling apart the two sheets of the overwrap.

The recommended method to remove the overwrap is to peel off sheet by the corner while holding the other sheet at one end and carefully remove the solution container.

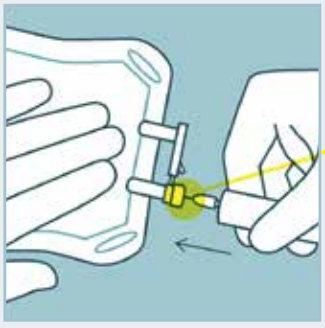
The overwrap should not be removed until product is to be used.

Container inspection

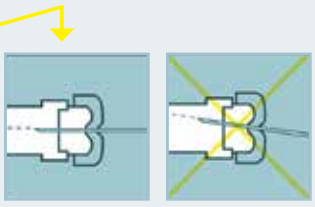
Visually inspect the container for particulate matter and discoloration.
Check for minute leaks by squeezing inner container firmly. **If leaks are found, discard solution as sterility may be impaired**.
If the outlet port protector is damaged, detached, or not present, discard container as solution path sterility may be impaired.

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

To add medication



Prepare medication site.
Using syringe with 19 to 22 gauge needle, securely hold the container and insert the needle through the center of the medication port and inject.

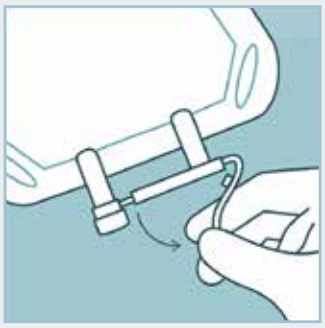


Insert the needle perpendicular to the point of addition.

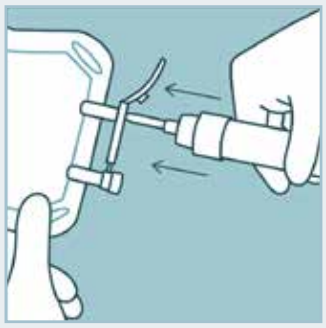
The compatibility of the additives with Sodium Chloride 0.9% must be checked before adding a medication.

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

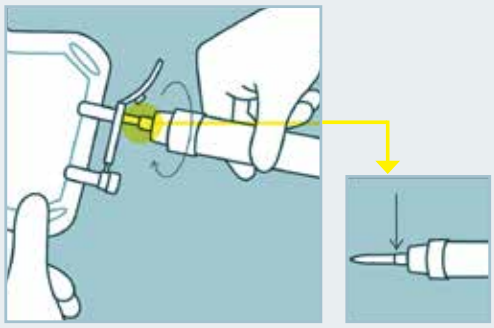
Attach administration set



Suspend the container from eyelet support and remove protector from outlet port at the bottom of the container.

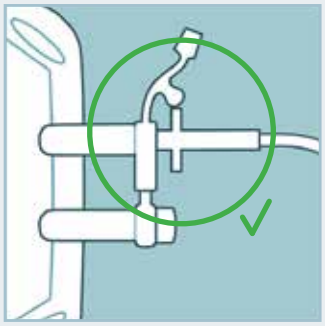


Hold the container properly and attach the administration set.



While advancing through the tube, a slight resistance will gradually appear.

To ensure proper connection and prevent leakage, push the administration set using a rotary motion up to the shoulder of the spike.

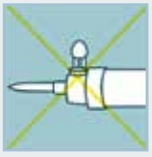


Correctly attached.

Not correctly attached.

Use non-vented administration sets

The Fleboflex® container has been designed to work without venting. No air is required to withdraw the solution. **Air entering through the administration set could slow or even stop the infusion due to air bubbles.**



Administration sets should come without air venting. If vented administration sets are used, **be sure air venting inlet remains closed during the infusion**.

After opening the container, the contents should be used immediately and should not be stored for a subsequent infusion. Do not reconnect any partially used containers. Discard any unused portion.

Do not connect flexible plastic containers in series in order to avoid air embolism due to possible residual air contained in the primary container.

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.

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.

Contraindications

None known.

Warnings and Precautions

Hypersensitivity/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.

Depending on the volume and rate of infusion, the intravenous administration of Sodium Chloride Injection, USP can cause fluid and/or solute overloading resulting in dilution of serum electrolyte concentrations, overhydration/hypervolemia, congested states, pulmonary edema, or acid-base imbalance.

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.

Administer 0.9% Sodium Chloride Injection, USP with particular caution to patients with or at risk for hypernatremia, hyperchloremia, or metabolic acidosis.

Administer Sodium Chloride Injection, USP with particular caution to patients with or at risk for hypervolemia or with conditions that may cause sodium retention, fluid overload and edema, such as patients with primary hyperaldosteronism or secondary hyperaldosteronism (eg, associated with hypertension, congestive heart failure, liver disease [including cirrhosis], renal disease [including renal artery stenosis, nephrosclerosis], or pre-eclampsia).

Administer Sodium Chloride Injection, USP with particular caution to patients with severe renal impairment.

Do not connect flexible plastic containers in series in order to avoid air embolism due to possible residual air contained in the primary container. Such use could result in air embolism due to residual air being drawn from the primary container before 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.

Rapid correction of hypo- and hypernatremia is potentially dangerous (risk of serious neurologic complications). Dosage, rate, and duration of administration should be determined by a physician experienced in intravenous fluid therapy.

Caution must be exercised in the administration of Sodium Chloride Injection, USP to patients treated with drugs that may increase the risk of sodium and fluid retention, such as corticosteroids.

Renal sodium and lithium clearance may be increased during administration of 0.9% Sodium Chloride Injection, USP. Administration of 0.9% Sodium Chloride Injection, USP may result in decreased lithium levels.

Use in Specific Populations

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

Because many drugs are present in human milk, caution should be exercised when Sodium Chloride Injection, USP is administered to a nursing woman.

Plasma electrolyte concentrations should be closely monitored in the pediatric population as this population may have impaired ability to regulate fluids and electrolytes.

This drug 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. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

Adverse Reactions

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: hypersensitivity/infusion reactions, including hypotension, pyrexia, tremor, chills, urticaria, rash, and pruritus.

Also reported are infusion site reactions, such as infusion site erythema, injection site streaking, burning sensation, and infusion site urticarial.

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

0.9 % Sodium Chloride Injection, USP
in FLEBOFLEX 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.
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 plastic container is fabricated from latex-free polyolefins or polypropylene 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 significantly. The suitability of the container materials has been established through biological evaluations, which have shown the container passes Class VI U.S. Pharmacopeia (USP) testing for plastic containers. These tests confirm the biological safety of the container system.

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/infusion reactions, including hypotension, pyrexia, tremor, chills, urticaria, rash, and pruritus have been reported with 0.9% Sodium Chloride Injection, USP and may occur with 0.45% 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 indicated.
Depending on the volume and rate of infusion, the intravenous administration of Sodium Chloride Injection, USP can cause fluid and/or solute overloading resulting in dilution of serum electrolyte concentrations, overhydration/hypervolemia, congested states, pulmonary edema, or acid-base imbalance. The risk of dilutive states is inversely proportional to the electrolyte concentration of the injection. The risk of solute overload causing congested states with peripheral and pulmonary edema is directly proportional to the electrolyte concentrations of the injection.
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.
Administer 0.9% Sodium Chloride Injection, USP with particular caution, to patients with or at risk for hypernatremia, hyperchloremia, or metabolic acidosis.
The infusion of solutions with 0.45% Sodium Chloride Injection, USP may result in hyponatremia. Close clinical monitoring may be warranted. Hyponatremia can lead to headache, nausea, seizures, lethargy, coma, cerebral edema and death. The risk for hyponatremia is increased, for example, in children, elderly, women, postoperatively, in persons with psychogenic polydipsia, and in patients treated with medications that increase the risk of hyponatremia (such as certain antiepileptic and psychotropic medications). The risk for developing hyponatremic encephalopathy is increased, for example, in pediatric patients (≤16 years of age), women (in particular pre-menopausal women), in patients with hypoxemia, and in patients with underlying central nervous system disease. Acute symptomatic hyponatremic encephalopathy is considered a medical emergency.
Administer Sodium Chloride Injection, USP with particular caution, to patients with or at risk for hypervolemia or with conditions that may cause sodium retention, fluid overload and edema; such as patients with primary hyperaldosteronism, or secondary hyperaldosteronism [e.g., associated with hypertension, congestive heart failure, liver disease (including cirrhosis), renal disease (including renal artery stenosis, nephrosclerosis) or pre-eclampsia]. Certain medications may increase risk of sodium and fluid retention, see **Drug Interactions**.
Administer Sodium Chloride Injection, USP with particular caution, to patients with severe renal impairment. In such patients, administration of Sodium Chloride Injection, USP may result in sodium retention.

PRECAUTIONS

General

Do not connect flexible plastic containers in series in order to avoid air embolism due to possible residual air contained in the primary container. Such use could result in air embolism due to residual air being drawn from the primary container before 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.
Do not mix or administer 0.45% Sodium Chloride Injection, USP through the same administration set with whole blood or cellular blood components.
Rapid correction of hypo- and hypernatremia is potentially dangerous (risk of serious neurologic complications). Dosage, rate, and duration of administration should be determined by a physician experienced in intravenous fluid therapy.

Drug Interactions

Caution must be exercised in the administration of Sodium Chloride Injection, USP to patients treated with drugs that may increase the risk of sodium and fluid retention, such as corticosteroids.
Caution is advised in patients treated with lithium. Renal sodium and lithium clearance may be decreased in the presence of hyponatremia. Administration of 0.45% Sodium Chloride Injection, USP may result in increased lithium levels.
Renal sodium and lithium clearance may be increased during administration of 0.9% Sodium Chloride Injection, USP. Administration of 0.9% Sodium Chloride Injection, USP, may result in decreased lithium levels.

Pregnancy

Pregnancy Category C
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.

Nursing Mothers

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**).
Plasma electrolyte concentrations should be closely monitored in the pediatric population as this population may have impaired ability to regulate fluids and electrolytes.
The infusion of hypotonic fluids (0.45% Sodium Chloride Injection, USP) together with the non-osmotic secretion of ADH may result in hyponatremia in patients with acute volume depletion. Hyponatremia can lead to headache, nausea, seizures, lethargy, coma, cerebral edema and death, therefore acute symptomatic hyponatremic encephalopathy is considered a medical emergency.

Geriatric Use

Clinical studies of Sodium Chloride Injection, USP did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, 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.
This drug 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. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

ADVERSE REACTIONS

Post-Marketing Adverse Reactions

The following adverse reactions have been identified during postapproval 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: hypersensitivity/ infusion reactions, including hypotension, pyrexia, tremor, chills, urticaria, rash, and pruritus.
Also reported are infusion site reactions, such as infusion site erythema, injection site streaking, burning sensation, and infusion site urticaria.
The following adverse reactions have not been reported with 0.9% Sodium Chloride Injection, USP but may occur: hypernatremia, hyperchloremic metabolic acidosis, and hyponatremia, which may be symptomatic.
Hyponatremia has been reported for 0.45% Sodium Chloride Injection, USP (see **Pediatric Use** section).
The following adverse reactions have not been reported with 0.45% Sodium Chloride Injection, USP but may occur: hyperchloremic metabolic acidosis, hypersensitivity/infusion reactions (including hypotension, pyrexia, tremor, chills, urticaria, rash, and pruritus), and infusion site reactions (such as infusion site erythema, injection site streaking, burning sensation, infusion site urticaria).
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 0.45% Sodium Chloride Injection, USP may lead to hypo- and hypernatremia, while excessive administration of 0.9% Sodium Chloride Injection, USP may lead to hypernatremia. Both hypo- and hypernatremia can lead to CNS manifestations, including seizures, coma, cerebral edema and death.
Excessive administration of Sodium Chloride Injection, USP may lead to sodium overload (which can lead to central and/or peripheral edema).
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.

DOSAGE AND ADMINISTRATION

All injections in FLEBOFLEX plastic containers are intended for intravenous administration using sterile and nonpyrogenic equipment.
As directed by a physician. Dosage, rate, and duration of administration are to be individualized and depend upon the indication for use, the patient's age, weight, clinical condition, concomitant treatment, and on the patient's clinical and laboratory response to treatment.
When other electrolytes or medicines are added to this solution, the dosage and the infusion rate will also be dictated by the dose regimen of the additions.
Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit. Use of a final filter is recommended during administration of all parenteral solutions, where possible.
Do not administer unless the solution is clear and seal is intact.
Additives may be incompatible with Sodium Chloride Injection, USP. As with all parenteral solutions, compatibility of the additives with the solution must be assessed before addition. Before adding a substance or medication, verify that it is soluble and/or stable in water and that the pH range of Sodium Chloride Injection, USP is appropriate. After addition, check for unexpected color changes and/or the appearance of precipitates, insoluble complexes or crystals.
The instructions for use of the medication to be added and other relevant literature must be consulted. Additives known or determined to be incompatible must not be used. When introducing additives to Sodium Chloride Injection, USP, aseptic technique must be used. Mix the solution thoroughly when additives have been introduced. Do not store solutions containing additives.
After opening the container, the contents should be used immediately and should not be stored for a subsequent infusion. Do not reconnect any partially used containers. Discard any unused portion.

HOW SUPPLIED

The available size of 0.9% Sodium Chloride Injection, USP is shown below:

Size (mL)	NDC
50 (115 units in one carton)	79672-0613-01
100 (70 units in one carton)	79672-0613-02
250 (28 units in one carton)	79672-0613-03
500 (20 units in one carton)	79672-0613-04
1000 (10 units in one carton)	79672-0613-05

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 PLASTIC CONTAINER

For Information on Risk of Air Embolism – see **PRECAUTIONS**

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. Remove protector from outlet port at bottom of container.
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. Using syringe with 19 to 22 gauge needle, puncture resealable 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. Using syringe with 19 to 22 gauge needle, puncture resealable 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.

Laboratorios Grifols, S.A.
Murcia - SPAIN
Printed in SPAIN
Rev. 05/2018
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GRIFOLS
Laboratorios Grifols, S.A. Calle Marte nº4 – Polígono Industrial Los Llanos
30565 Las Torres de Cotillas- Murcia SPAIN

FAQ

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 in order 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.

IV Solutions

NEXTGEN PHARMACEUTICALS

Manufactured by:
Laboratorios Grifols S.A.
Calle Marte nº4
Polígono Industrial Los Llanos
30565 Las Torres de Cotillas- Murcia
SPAIN
www.grifols.com

Distributed by:

Nextgen Pharmaceuticals
1613 Broadway
Brooklyn, NY 11207
www.nextgenpharmaceuticals.com