**Fresenius Kabi USA, LLC**

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# 0.9% SODIUM CHLORIDE INJECTION SOLUTION AVAILABILITY

**Subject: Importation of European Drug Product**

October 16, 2014

Dear Healthcare Professional,

Due to the current critical shortage of 0.9% Sodium Chloride Injection in the U.S. market, Fresenius Kabi USA, LLC (Fresenius Kabi USA) is coordinating with the U.S. Food and Drug Administration (FDA) to increase the availability of the drug. Fresenius Kabi USA has initiated temporary importation of a European Sodium Chloride 0.9% Freeflex Injection Solution for Intravenous Infusion into the U.S. market. The European product contains the same active ingredient in the same concentration as the 0.9% Sodium Chloride Injection products approved in the United States. The Sodium Chloride 0.9% Freeflex Injection Solution product is manufactured near Halden, Norway, at Fresenius Kabi Norge AS, an FDA inspected facility. At its most recent FDA inspection, this facility was found to be in compliance with current good manufacturing practices.

At this time, FDA is not objecting to the importation and distribution of Sodium Chloride 0.9% Freeflex Injection Solution for Intravenous Infusion, by Fresenius Kabi USA, to address the critical shortage of 0.9% Sodium Chloride Injection. Importation or distribution of Fresenius Kabi's Sodium Chloride 0.9% Freeflex Injection Solution for Intravenous Infusion by any entity other than Fresenius Kabi USA, or its Authorized Distributors, is not within the scope of this decision and may be subject to enforcement action by the FDA. FDA has not approved Fresenius Kabi's Sodium Chloride 0.9% Freeflex Injection Solution products in the United States.

Effective immediately, and during this temporary period, Fresenius Kabi USA will offer the following presentations of Sodium Chloride 0.9% Freeflex Injection Solution for Intravenous Infusion:

| **Fresenius Kabi's Sodium Chloride 0.9% Freeflex Injection Solution for Intravenous Infusion** | | |
|---|---|---|
| **Product Name** | **Volume** | **Ingredients** |
| Sodium Chloride 0.9% Freeflex Injection Solution for Intravenous Infusion | 50 mL | Each 50 mL contains:<br>Sodium Chloride 450 mg, Water for Injections to 50 mL<br><br>Total Electrolytes per 50 mL approx:<br>Sodium 7.7 mmol*, Chloride 7.7 mmol* |
| Sodium Chloride 0.9% Freeflex Injection Solution for Intravenous Infusion | 100 mL | Each 100 mL contains:<br>Sodium Chloride 900 mg, Water for Injections to 100 mL<br><br>Total Electrolytes per 100 mL approx:<br>Sodium 15.4 mmol*, Chloride 15.4 mmol* |
| Sodium Chloride 0.9% w/v for Intravenous Infusion | 500 mL | Each 500 mL contains:<br>Sodium Chloride 4.5 g, Water for Injections to 500 mL<br><br>Total Electrolytes per 500 mL approx:<br>Sodium 77 mmol*, Chloride 77 mmol* |
| Sodium Chloride 0.9% w/v for Intravenous Infusion | 1000 mL | Each 1000 mL contains:<br>Sodium Chloride 9 g, Water for Injections to 1000 mL<br><br>Total Electrolytes per 1000 mL approx:<br>Sodium 154 mmol*, Chloride 154 mmol* |

* For monovalent ions, such as sodium and chloride, the numeric value of the millimole and milliequivalent are identical.

Fresenius Kabi's Sodium Chloride 0.9% Injection Solution for Intravenous Infusion is packaged in **free***flex*®, a flexible bag with self-sealing ports and made of multilayer Polyolefin film that is PVC-free, plasticizer-free, latex-free and non-DEHP.

**Freeflex Bag**

**Additive Port and Infusion Port of Freeflex Bag**

It is important to note that there are differences in the formatting and content of the labeling between the U.S. marketed 0.9% Sodium Chloride solutions, and Fresenius Kabi's Sodium Chloride 0.9% Freeflex Injection Solution for Intravenous Infusion. Refer to comparison table attached.

| **Differences Between U.S. Prescribing Information and Fresenius Kabi's Prescribing Information** | | |
|---|---|---|
| **Property** | **0.9% Sodium Chloride U.S. Products** | **Sodium Chloride 0.9% Freeflex Injection Solution for Intravenous Infusion** |
| **Active Ingredients** | Sodium 154 mEq/L* | Sodium 154 mmol/L* |
| | Chloride 154 mEq/L* | Chloride 154 mmol/L* |
| | Osmolarity 308 mOsmol/L (calc.) | Osmolality 308 mOsmol/kg water** (calc.) |
| **Indications for Use** | See manufacturer's package insert | Normal saline can be used as the vehicle for many parenteral drugs and as a sterile irrigation medium. |
| **Contraindications** | See manufacturer's package insert | Sodium Chloride 0.9% is contraindicated in patients with congestive heart failure, severe renal impairment, conditions of sodium retention, edema, liver cirrhosis and irrigation during electrosurgical procedures. |
| **Warnings** | Caution must be exercised in the administration of parenteral fluids, especially those containing sodium ions to patients receiving corticosteroids or corticotropin. | Refer to Fresenius Kabi's package insert or visit www.fresenius-kabi.us |

| | | |
|---|---|---|
| **Adverse Reactions** | See manufacturer's package insert | Excessive amounts of sodium chloride may cause hypernatremia, hypokalemia and acidosis. Proper use of normal saline as a vehicle for parenteral drugs or as an electrolyte replacement therapy is unlikely to result in adverse effects.<br><br>Hypernatremia rarely occurs with therapeutic doses of sodium chloride, but may occur in excessive administration. A serious complication of this is dehydration of the brain causing somnolence and confusion, which may progress to convulsions, coma and ultimately respiratory failure and death. Pulmonary embolism or pneumonia may also result. Other symptoms include thirst, reduced salivation and lacrimation, fever, tachycardia, hypertension, headache, dizziness, restlessness, weakness and irritability.<br><br>Displaced catheters or drainage tubes can lead to irrigation or infiltration of unintended structures or cavities. Excessive volume or pressure during irrigation of closed cavities may result in distension or disruption of tissues. Inadvertent contamination from careless technique may transmit infection. Adverse effects resulting from irrigation of body cavities, tissues or indwelling catheters and tubes are usually avoidable when appropriate procedures are followed. |
| **Drug Interactions** | See manufacturer's package insert | Co-medication of drugs inducing sodium retention may exacerbate any systemic effects. |
| **Overdose and Treatment** | See manufacturer's package insert | **Overdose**<br>Infusion of excess intravenous fluid may cause hypervolemia and electrolyte imbalances. Excess sodium chloride in the body produces general gastrointestinal effects of nausea, vomiting, diarrhea and cramps. Salivation and lacrimation are reduced, while thirst and sweating are increased. Hypotension, tachycardia, renal failure, peripheral and pulmonary edema and respiratory arrest may occur. CNS symptoms include headache, dizziness, restlessness, irritability, weakness, muscular twitching and rigidity, convulsions, coma and death. If any adverse effects are observed during administration, discontinue infusion, evaluate the patient and institute appropriate supportive treatment.<br><br>**Treatment**<br>Normal plasma sodium concentrations should be carefully restored at a rate not greater than 10-15 mmol/day using I.V. hypotonic saline. Dialysis may be necessary if there is significant renal impairment, the patient is moribund or plasma sodium levels are greater than 200 mmol/L. Convulsions may require diazepam or other appropriate treatment. |
| **Container Type** | See manufacturer's package insert | Packaged in **free***flex*® bag. Made of multilayer polyolefin film. Non-DEHP, non-PVC, and latex-free. |
| **Barcode** | Readable U.S. barcodes | Any barcodes on Fresenius Kabi's Sodium Chloride 0.9% **free***flex*® solution will not be appropriately recognized by scanning systems used in the United States and should not be used.<br><br>Institutions should manually input the product into their systems and confirm that barcode systems do not provide incorrect information when the product is scanned. |

* For monovalent ions, such as sodium and chloride, the numeric value of the millimole and milliequivalent are identical

** 1 kilogram of water is equal to 1 liter of water

**Refer to the package insert for Sodium Chloride 0.9% Freeflex Injection Solution for Intravenous Infusion for full prescribing information**

This communication and product information is available on the Fresenius Kabi USA web site www.fresenius-kabi.us as well as on the FDA Drug Shortage web site. http://www.fda.gov/Drugs/DrugSafety/DrugShortages/default.htm.

**REPORTING ADVERSE EVENTS:**

To report adverse events or quality problems experienced with the use of this product, call Fresenius Kabi USA Vigilance and Medical Affairs at 1-800-551-7176, Monday – Friday, between the hours of 8 a.m. and 5 p.m. (CST), or e-mail appmedicalinfo@APPpharma.com.

**Fresenius Kabi USA CONTACT NUMBERS:** Please use the following contact numbers as appropriate:

| Reason To Call | Department | Number |
|---|---|---|
| ADE Reporting/Clinical/Technical Info. | Vigilance and Medical Affairs Dept. | 1-800-551-7176 |
| Product Availability & Ordering | Customer Service Department | 1-888-386-1300 |

Adverse events may also be reported to the FDA's MedWatch Adverse Event Reporting program either online, by regular mail or by fax.

- **Online**: www.fda.gov/medwatch/report.htm
- **Regular Mail**: use postage-paid FDA form 3500 available at: www.fda.gov/MedWatch/getforms.htm. Mail to: MedWatch 5600 Fishers Lane, Rockville, MD 20852-9787
- **Fax**: 1-800-FDA-0178

Sincerely,

Melanie Power-Burns
Senior Director, U.S. Quality & Compliance

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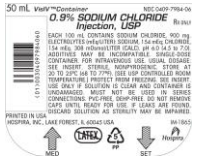
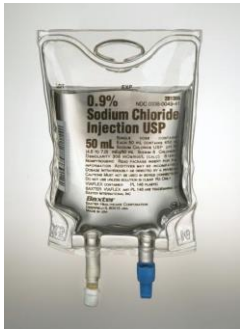
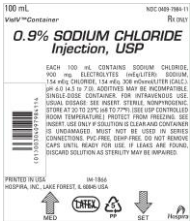
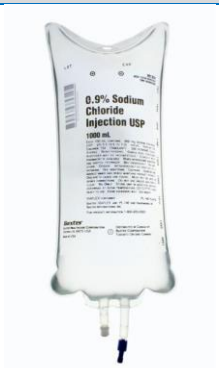
**Comparison Table of U.S. 0.9% Sodium Chloride Injection to Fresenius Kabi's Sodium Chloride 0.9% Freeflex Injection Solution for Intravenous Infusion**

| | Fresenius Kabi | Hospira | Hospira | Hospira | Baxter | Baxter | Baxter |
|---|---|---|---|---|---|---|---|
| |  |  |  |  |  | Product Image Not Available |  |
| **Product** | Sodium Chloride 0.9% Freeflex Injection Solution for Intravenous Infusion | 0.9% Sodium Chloride Injection, USP | 0.9% Sodium Chloride Injection, USP | 0.9% Sodium Chloride Injection, USP | 0.9% Sodium Chloride Injection, USP | 0.9% Sodium Chloride Injection, USP | 0.9% Sodium Chloride Injection, USP |
| **NDC#** | 63323-623-50 | 0409-7984-06 | 0409-7984-13 | 0409-7984-36 | 0338-0049-11 | 0338-0049-31 | 0338-0049-41 |
| **Volume** | 50 mL | 50 mL | 50 mL | 50 mL | 50 mL | 50 mL | 50 mL |
| **Container Type** | **free***flex*® | VisIV™ Flexible plastic container | Flexible plastic container | Flexible plastic container | VIAFLEX plastic container | VIAFLEX plastic container | VIAFLEX plastic container |
| **Container Description** | Made of multilayer polyolefin film. Non-DEHP, non-PVC, and latex free. | Fabricated from a clear mutilayer polyolefin plastic film. PVC, DEHP, and latex free. | PVC container. Contains DEHP, latex free. | PVC container. Contains DEHP, latex free. | PVC container. Contains DEHP, non-latex. | PVC container. Contains DEHP, non-latex. | PVC container. Contains DEHP, non-latex. |
| **Preservative Free** | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| **Case Size** | 60 | 60 | 48 | 80 (Quad Pack) | 96 (Quad Pack) | 96 (Multi Pack) | 96 |

| | Fresenius Kabi | Hospira | Hospira | Hospira | Baxter | Baxter | Baxter |
|---|---|---|---|---|---|---|---|
| |  |  |  |  |  |  |  |
| **Product** | Sodium Chloride 0.9% Freeflex Injection Solution for Intravenous Infusion | 0.9% Sodium Chloride Injection, USP | 0.9% Sodium Chloride Injection, USP | 0.9% Sodium Chloride Injection, USP | 0.9% Sodium Chloride Injection, USP | 0.9% Sodium Chloride Injection, USP | 0.9% Sodium Chloride Injection, USP |
| **NDC#** | 63323-623-00 | 0409-7984-11 | 0409-7984-23 | 0409-7984-37 | 0338-0049-18 | 0338-0049-38 | 0338-0049-48 |
| **Volume** | 100 mL | 100 mL | 100 mL | 100 mL | 100 mL | 100 mL | 100 mL |
| **Container Type** | ***freeflex***® | VisIV™Flexible plastic container | Flexible plastic container | Flexible plastic container | VIAFLEX plastic container | VIAFLEX plastic container | VIAFLEX plastic container |
| **Preservative Free** | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| **Container Description** | Made of multilayer polyolefin film. Non-DEHP, non-PVC, and latex free. | Fabricated from a clear mutilayer polyolefin plastic film. PVC, DEHP, and latex free. | PVC container. Contains DEHP, latex free. | PVC container. Contains DEHP, latex free. | PVC container. Contains DEHP, non-latex. | PVC container. Contains DEHP, non-latex. | PVC container. Contains DEHP, non-latex. |
| **Case Size** | 50 | 60 | 48 | 80 (Quad Pack) | 96 (Quad Pack) | 96 (Multi Pack) | 96 |

| | Fresenius Kabi | Hospira | Hospira | Baxter |
|---|---|---|---|---|
| |  |  |  |  |
| **Product** | Sodium Chloride 0.9% w/v for Intravenous Infusion | 0.9% Sodium Chloride Injection, USP | 0.9% Sodium Chloride Injection, USP | 0.9% Sodium Chloride Injection, USP |
| **NDC#** | 63323-623-59 | 0409-7983-03 | 0409-7983-55 | 0338-0049-03 |
| **Volume** | 500 mL | 500 mL | 500 mL | 500 mL |
| **Container Type** | **free***flex*® | Flexible plastic container | Flexible plastic container | VIAFLEX plastic container |
| **Preservative Free** | Yes | Yes | Yes | Yes |
| **Container Description** | Made of multilayer polyolefin film. Non-DEHP, non PVC, and latex free. | PVC container. Contains DEHP, latex free. | PVC container. Contains DEHP, latex free. | PVC container. Contains DEHP, non-latex. |
| **Case Size** | 20 | 24 | 18 | 24 |

| | Fresenius Kabi | Hospira | Baxter |
|---|---|---|---|
| |  |  |  |
| **Product** | Sodium Chloride 0.9% w/v for Intravenous Infusion | 0.9% Sodium Chloride Injection, USP | 0.9% Sodium Chloride Injection, USP |
| **NDC#** | 63323-623-10 | 0409-7983-09 | 0338-0049-04 |
| **Volume** | 1000 mL | 1000 mL | 1000 mL |
| **Container Type** | **free***flex*® | Flexible plastic container | VIAFLEX plastic container |
| **Preservative Free** | Yes | Yes | Yes |
| **Container Description** | Made of multilayer polyolefin film. Non-DEHP, non-PVC, and latex free. | Fabricated from a clear mutilayer polyolefin plastic film. PVC, DEHP, and latex free. | PVC container. Contains DEHP, latex free. |
| **Case Size** | 10 | 12 | 14 |

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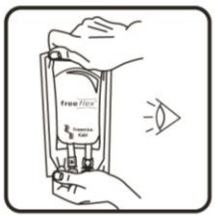
freeflex®

# Instructions for Use

1



Check the freeflex® IV container solution composition, lot number, and expiry date.

Inspect the container for damage or solution leakage. If damaged, do not use.

Check the freeflex® solution for visible particles or cloudiness. Do not use unless the solution is clear.

2

Turn the freeflex® IV container over so that the text is face down. Using the pre-cut corner tabs peel open the overwrap to remove the primary bag. The overwrap adheres slightly to the primary bag to improve handling even when wearing disposable gloves.

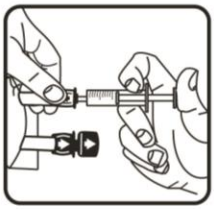
3

If additives are required, identify the white additive port. If no additives are required, go to figure 6.

4

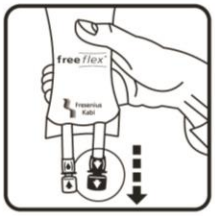
Flip off the white tamper-evident cover from the freeflex® IV container addition port.

5



Insert the needle horizontally through the center of the septum of the additive port and inject the additives (with known compatibility). Use syringes with a 21-23 gauge needle. The additive port can be pierced up to 20 times.

6

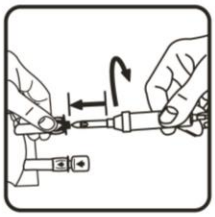


Identify the blue infusion port.

7

Flip off the blue tamper-evident cover from the freeflex® IV container infusion port.

8



Use a non-vented infusion set or on a vented set, close the air inlet. Follow the instructions for use for the infusion set. Hold the base of the infusion port. Insert the spike through the infusion port, by rotating your wrist slightly until the spike is inserted.

## WARNINGS

1. Do not remove the freeflex® IV container from its overwrap until immediately before use.
2. Do not administer unless the solution is clear, free from particles and the freeflex® IV container is undamaged.
3. Discontinue the infusion if adverse reaction occurs.
4. Do not vent.
5. It is recommended that administration sets are changed at least once every 24 hours.
6. Partially used freeflex® IV container must be discarded.
7. Additives may be incompatible and expert advice should be sought before adding medication to a freeflex® IV container. If the physician decides to add medication, aseptic technique must be employed. - Additions must be made by an authorized person.