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12. CLINICAL PHARMACOLOGY

Peritoneal dialysis uses the peritoneal membrane of the abdominal cavity as a semi-permeable membrane to remove excess water and toxins from the bloodstream. Osmotic and diffusion gradients between the bloodstream and the dialysate cause excess fluid and toxins to move from the bloodstream into the dialysate. The glucose in the dialysate creates the osmotic gradient that drives ultrafiltration. The other components in the dialysate function to correct electrolyte and acid-base imbalances.

The solution does not contain potassium. After careful evaluation of serum and total body potassium, potassium may be added to the dialysate (up to a concentration of 4 mEq/L) as indicated upon direction of the prescriber.

Clinical studies have demonstrated that the use of low magnesium solutions resulted in significant increases in serum CO_2 and decreases in serum magnesium levels. The decrease in magnesium levels did not cause clinically significant hypomagnesemia.

13. NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Long term animal studies with DELFLEX peritoneal dialysis solutions have not been performed to evaluate the carcinogenic potential, mutagenic potential or effect on fertility.

16. HOW SUPPLIED/STORAGE AND HANDLING

DELFLEX peritoneal dialysis solutions are available in the sizes and formulations shown in Table 1 [Dosage Forms and Strengths]. (3)

Table 3. DELFLEX peritoneal dialysis NDC designations

	DELFLEX - NDC 49230-188-50
	DELFLEX - NDC 49230-188-60
	DELFLEX - NDC 49230-191-50
	DELFLEX - NDC 49230-191-60
	DELFLEX - NDC 49230-206-20
	DELFLEX - NDC 49230-206-30
	DELFLEX - NDC 49230-206-50
	DELFLEX - NDC 49230-206-60
DELFLEX in Biofine - NDC 49230-188-62	DELFLEX - NDC 49230-209-23
DELFLEX in Biofine - NDC 49230-191-62	DELFLEX - NDC 49230-209-30
DELFLEX in Biofine - NDC 49230-206-32	DELFLEX - NDC 49230-209-50
DELFLEX in Biofine - NDC 49230-206-62	DELFLEX - NDC 49230-209-60
DELFLEX in Biofine - NDC 49230-209-32	DELFLEX - NDC 49230-212-23
DELFLEX in Biofine - NDC 49230-209-62	DELFLEX - NDC 49230-212-30
DELFLEX in Biofine - NDC 49230-212-32	DELFLEX - NDC 49230-212-50
DELFLEX in Biofine - NDC 49230-212-62	DELFLEX - NDC 49230-212-60

Storage Conditions

Store at 20°C to 25°C (68°F to 77°F); excursions permitted between 15°C and 30°C (between 59°F and 86°F). See USP Controlled Room Temperature. Brief exposure to temperatures up to 40°C (104°F) may be tolerated provided the mean kinetic temperature does not exceed 25°C (77°F); however, such exposure should be minimized.

Keep DELFLEX and all medicines out of the reach of children.

17. PATIENT COUNSELING INFORMATION

Aseptic technique must be used throughout the procedure and at its termination in order to reduce the possibility of infection.

The outerwrap should remain intact until time of use.

Administer only if the solution is clear, all seals are intact, and there is no evidence of leaking.

DELFLEX peritoneal dialysis solution should NOT be heated in a microwave oven. Using a microwave oven may increase the risk of uneven temperatures within the solution bag and the potential for hot spots of solution which may burn the peritoneum.

Care should be taken to ensure that there is not any leakage around the catheter, since if not controlled, the leakage can create edema from subcutaneous infiltration of the dialysis solution. The leakage will also create an inaccurate fluid balance measurement. If any leakage is identified, do not proceed with infusion and notify your physician.

Not for intravenous injection. Do not microwave.

Warm solution as directed by your health care provider.

FRESENIUS MEDICAL CARE

Fresenius Medical Care North America
920 Winter Street
Waltham, MA 02451
1-800-323-5188

89 - 905 - 69

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DELFLEX®

Dextrose Peritoneal Dialysis Solution
for Intraperitoneal Administration Only

Prescribing Information

No Latex

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use DELFLEX peritoneal dialysis solution safely and effectively. See full prescribing information for DELFLEX peritoneal dialysis solution.

DELFLEX (dextrose) peritoneal dialysis solution for intraperitoneal administration only.

Initial U.S. Approval: 1984

---------- INDICATIONS AND USAGE ----------

For treatment of chronic renal failure. (1)

------- DOSAGE AND ADMINISTRATION -------

For intraperitoneal administration only. (2)

------- DOSAGE FORMS AND STRENGTHS -------

DELFLEX solutions are available in multiple compositions, calculated osmolarity, pH, and ionic concentrations. See full prescribing information for detailed descriptions of each formulation. (3, 11)

---------- CONTRAINDICATIONS ----------

None.

------- WARNINGS AND PRECAUTIONS -------

- Aseptic technique must be used during connection and disconnection.
- Lactate buffered solutions should be used with great care in patients with metabolic or respiratory alkalosis.
- Monitor patient for fluid and electrolyte imbalances.
- Routine evaluation of electrolyte blood chemistries and hematologic factors should be performed on all patients.

---------- ADVERSE REACTIONS ----------

Adverse reactions may include: peritonitis, catheter site infection, electrolyte and fluid imbalances, hypovolemia, hypervolemia, hypertension, disequilibrium syndrome, muscle cramping, abdominal pain, abdominal distension, and abdominal discomfort.

To report SUSPECTED ADVERSE REACTIONS, contact Fresenius Medical Care North America at 1-800-323-5188 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

---------- DRUG INTERACTIONS ----------

Additives may be incompatible. When introducing additives, use aseptic technique, mix thoroughly, and do not store.

------- USE IN SPECIFIC POPULATIONS -------

See 17 for PATIENT COUNSELING INFORMATION

Revised: MM/YYYY

FULL PRESCRIBING INFORMATION: CONTENTS*

***Sections or subsections omitted from the full prescribing information are not listed.**

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FULL PRESCRIBING INFORMATION

1. INDICATIONS AND USAGE

DELFLEX peritoneal dialysis solutions are indicated in the treatment of chronic renal failure patients being maintained on peritoneal dialysis when nondialytic medical therapy is judged to be inadequate.

2. DOSAGE AND ADMINISTRATION

2.1 Basic Dosing Information

DELFLEX peritoneal dialysis solutions are provided for intraperitoneal administration only. The mode of therapy, frequency of treatment, formulation, exchange volume, duration of dwell, and length of dialysis should be selected by the physician responsible for the treatment of the individual patient.

To avoid the risk of severe dehydration or hypovolemia and to minimize the loss of protein, it is advisable to select the peritoneal dialysis solution with lowest level of osmolarity consistent with the fluid removal requirements for that exchange.

Parenteral drug products, such as DELFLEX, should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit.

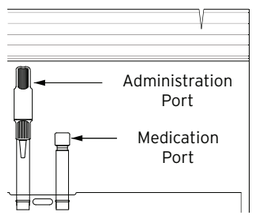
Additives may be incompatible. Please refer to manufacturer's product insert. Do not store solutions containing additives.

2.2 Directions for Use (aseptic technique is required)

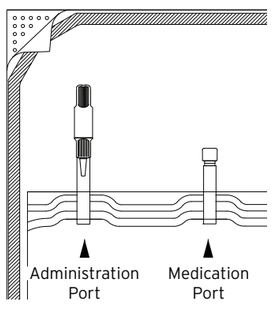
Get Ready

1. Clean work surface.
2. Gather supplies:
   - DELFLEX peritoneal dialysis bag(s).
   - Prescribed medication(s), if ordered by your healthcare provider.
   - Mask.
3.

DELFLEX	DELFLEX in Biofine®
Tear the outerwrap from the slit edge down the length of the inner bag to open.	Locate pull tabs on overwrap. Grasping one tab in each hand, pull outward, down the length of the inner bag to open.



Wipe away any moisture from the solution bags. Some opacity may be observed in the plastic of the bag and/or tubing and is 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.



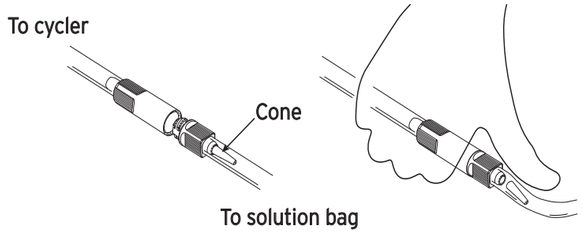
Wipe away any moisture from the solution bags.

Inspect DELFLEX Solution Bag:

4. After removing the overwrap, check your DELFLEX solution bag(s) for S.C.A.L.E. (strength, clarity, amount, leaks, and expiration date). Do not use DELFLEX solution if leaks are found, the solution bag is damaged, and/or the solution is cloudy or discolored, or the product is expired. Color may vary from clear to slightly yellow but does not affect efficacy and may be used.
5. Visually check that the solution bag tubing is free from kinks. If kinks are present, straighten tubing to allow the solution to flow freely.

   Note: Retain DELFLEX peritoneal dialysis bag sample for manufacturer evaluation and notify your healthcare provider if any of the above defects are found.

   Note: DELFLEX peritoneal dialysis solutions utilize the Safe-Lock® Connection System. This unique system consists of two Safe-Lock connectors, one located on the administration port of the bag, and the mating connector is located on the cycler set. The Safe-Lock connectors were designed to reduce the potential risk of touch contamination of the internal connection components.
6. Put on mask. Wash your hands.
7. If you will be adding medication(s):
   - Clean hands (as per facility's protocol).
   - Clean the medication port as instructed by your healthcare provider.
   - Add the medicine(s).
   - Turn the bag upside down several times to mix the medicine(s).
8. To connect the bag(s) to the cycler set, unscrew the protective caps of the administration port and the stay safe PIN connector. Secure these two connectors with a twisting motion to lock in place, so that the cycler set connector is seated over the administration port O-ring to assure a firm and tight fit.
9. After completing Step 8, wait for the cycler prompt to break the administration port cone and initiate solution flow. Do this by placing the thumb firmly on the tube over the cone and pressing towards the outer wall of the tube and away from the bag.



10. Perform your treatment as prescribed.
11. At the end of your treatment, throw away the fluid and used set as instructed by your healthcare provider. In case of cloudiness, save the fluid and the used set and immediately contact your healthcare provider. Dispose of your empty solution bag according to your local recycling program.

3. DOSAGE FORMS AND STRENGTHS

DELFLEX peritoneal dialysis solutions are delivered in single-dose flexible bags comprised of either polyvinyl chloride (PVC), or a proprietary blend of polyolefins called Biofine®. All DELFLEX peritoneal dialysis solutions have overfills declared on the bag label.

DELFLEX peritoneal dialysis solutions are available in the sizes and formulations shown in Table 1.

Table 1. DELFLEX peritoneal dialysis solution sizes and formulations

	2L	3L	5L	6L	3L	6L
DELFLEX Standard with 1.5% Dextrose			X	X		X
DELFLEX Standard with 2.5% Dextrose			X	X		X
DELFLEX Low Magnesium, Low Calcium with 1.5% Dextrose	X	X	X	X	X	X
DELFLEX Low Magnesium, Low Calcium with 2.5% Dextrose	X	X	X	X	X	X
DELFLEX Low Magnesium, Low Calcium with 4.25% Dextrose	X	X	X	X	X	X

4. CONTRAINDICATIONS

None known.

5. WARNINGS AND PRECAUTIONS

Not for intravenous injection.

Use aseptic technique.

After removing the outerwrap, check for leaks by squeezing the solution bag firmly. If leaks are found, DO NOT use the product because the sterility may be compromised. A small amount of moisture may be present inside the outerwrap, this is condensation from the sterilization process.

Table 2. Composition, calculated osmolarity, pH and ionic concentration

	Composition/100mL					Total Osmolarity (mOsmoL/L) (calc)	pH (5.0 - 6.0)	Ionic Concentration (mEq/L)				
	Dextrose Hydrous, USP ($C_6H_{12}O_6 \cdot H_2O$)	Sodium Chloride, USP (NaCl)	Sodium Lactate ($C_3H_5NaO_3$)	Calcium Chloride, USP ($CaCl_2 \cdot 2H_2O$)	Magnesium Chloride, USP ($MgCl_2 \cdot 6H_2O$)			Sodium	Calcium	Magnesium	Chloride	Lactate
DELFLEX Standard with 1.5% Dextrose	1.5 g	567 mg	392 mg	25.7 mg	15.2 mg	347	5.5	132	3.5	1.5	102	35
DELFLEX Standard with 2.5% Dextrose	2.5 g	567 mg	392 mg	25.7 mg	15.2 mg	398	5.5	132	3.5	1.5	102	35
DELFLEX Low Magnesium, Low Calcium with 1.5% Dextrose	1.5 g	538 mg	448 mg	18.4 mg	5.08 mg	344	5.5	132	2.5	0.5	95	40
DELFLEX Low Magnesium, Low Calcium with 2.5% Dextrose	2.5 g	538 mg	448 mg	18.4 mg	5.08 mg	394	5.5	132	2.5	0.5	95	40
DELFLEX Low Magnesium, Low Calcium with 4.25% Dextrose	4.25g	538 mg	448 mg	18.4 mg	5.08 mg	483	5.5	132	2.5	0.5	95	40

Peritoneal dialysis should be done with great care in patients with a number of conditions, including disruption of the peritoneal membrane or diaphragm by surgery or trauma, extensive adhesions, bowel distention, undiagnosed abdominal disease, abdominal wall infection, hernias or burns, fecal fistula or colostomy, tense ascites, obesity, large polycystic kidneys, recent aortic graft replacement, lactic acidosis, and severe pulmonary disease. When assessing peritoneal dialysis as the mode of therapy in such extreme situations, the benefits to the patient must be weighed against the possible complications.

Encapsulating peritoneal sclerosis is considered a known, rare complication of peritoneal dialysis therapy which can infrequently lead to a fatal outcome.

Solutions containing the lactate ion should be used with great care in patients with metabolic or respiratory alkalosis. Lactate should be administered with great care in those conditions in which there is an increased level or an impaired utilization of this ion, such as severe hepatic insufficiency.

An accurate fluid balance record must be kept and the weight of the patient carefully monitored to avoid over or under hydration. Severe consequences of over or under hydration include congestive heart failure, volume deletion, and/or shock.

Excessive use of DELFLEX peritoneal dialysis solutions with 4.25% dextrose during a peritoneal dialysis treatment can result in significant removal of water from the patient.

Monitor serum calcium levels and consider adjustment of the PD solution accordingly.

Chronic patients that have been stabilized on peritoneal dialysis therapy should have routine evaluation of electrolyte blood chemistries and hematologic factors measured in order to determine the patient's ongoing condition.

DELFLEX peritoneal dialysis solution do not include potassium. Potassium chloride should only be added under the direction of a physician after careful evaluation of both serum and total body potassium.

Significant loss of protein, amino acids, and water soluble vitamins may occur during peritoneal dialysis. Replacement therapy should be provided as necessary.

DELFLEX peritoneal dialysis solution should NOT be heated in a microwave oven. Using a microwave oven may increase the risk of uneven temperatures within the solution bag and the potential for hot spots of solution which may burn the peritoneum.

6. ADVERSE REACTIONS

Solution related adverse reactions may include peritonitis, catheter site infection, electrolyte and fluid imbalances, hypovolemia, hypervolemia, hypertension, hypotension, disequilibrium syndrome, muscle cramping abdominal pain, abdominal distension, and abdominal discomfort.

If an adverse reaction does occur, institute appropriate therapeutic procedures according to the patient's needs and conditions, and save the remainder of the fluid in the bag for evaluation if deemed necessary.

7. DRUG INTERACTIONS

Additives may be incompatible. When introducing additives, use aseptic technique, mix thoroughly, and do not store.

Studies of the following medications have demonstrated stability in DELFLEX peritoneal dialysis solutions: cefazolin, ceftazidime, gentamicin, and vancomycin.

8. USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Animal reproduction studies have not been conducted with DELFLEX peritoneal dialysis solutions. It is also not known if DELFLEX peritoneal dialysis solutions can cause fetal harm when administered to pregnant women or affect reproduction capacity. DELFLEX peritoneal dialysis solutions should be given to pregnant women only if clearly needed.

8.2 Lactation

Caution should be exercised when DELFLEX peritoneal dialysis solutions are administered to nursing women.

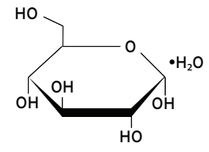
8.4 Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

11. DESCRIPTION

The DELFLEX peritoneal dialysis solutions (standard and low magnesium/low calcium) are sterile, non-pyrogenic formulations of dextrose and electrolytes in water for injection, USP, for use in peritoneal dialysis. These solutions do not contain antimicrobial agents or additional buffers. Composition, calculated osmolarity, pH, and ionic concentrations are shown in Table 2.

Dextrose, USP, is chemically designated D-glucose monohydrate ($C_6H_{12}O_6 \cdot H_2O$) a hexose sugar freely soluble in water. The structural formula is shown here:



Calcium chloride, USP, is chemically designated calcium chloride dihydrate ($CaCl_2 \cdot 2H_2O$) white fragments or granules freely soluble in water.

Magnesium chloride, USP, is chemically designated magnesium chloride hexahydrate ($MgCl_2 \cdot 6H_2O$) colorless flakes or crystals very soluble in water.

Sodium lactate solution, USP, is chemically designated ($CH_3CH(OH)COONa$), a 60% aqueous solution miscible in water.

Sodium chloride, USP, is chemically designated (NaCl), a white, crystalline compound freely soluble in water.

Water for injection, USP, is chemically designated (H_2O).

Hydrochloric Acid or Sodium Hydroxide may be added for pH adjustment. pH is 5.5 ± 0.5.

Exposure to temperatures above 25°C (77°F) during transport and storage will lead to minor losses in moisture content. Higher temperatures lead to greater losses. It is unlikely that these minor losses will lead to clinically significant changes within the expiration period. Since the inner bag is compounded from flexible plastic, water may permeate from the inner bag into the outerwrap in quantities insufficient to affect the solution significantly. Solutions in contact with the plastic inner bag can cause certain chemical components of the bag to leach out in very small amounts; however, the safety of the plastic formulation is supported by biological tests for plastic containers.