LACTATED RINGERS- sodium chloride, sodium lactate, potassium chloride, calcium chloride injection, solution
Becton Dickinson and Company

Lactated Ringer's Injection, USP

in **free**-*flex*® Bag

freeflex®

DESCRIPTION:

Lactated Ringer's Injection, USP is a sterile, nonpyrogenic solution for fluid and electrolyte replenishment in single dose containers for intravenous administration. It contains no antimicrobial agents. Composition, osmolarity, pH, ionic concentration and caloric content are shown in Table 1.

Table 1

		Composition (g/L)						Ionic Composition (mEq/L)					
	Size (mL)	Sodium Chloride, USP (NaCl)	Sodium Lactate, USP ($C_3H_5NaO_3$)	Potassium Chloride, USP (KCl)	Calcium Chloride, USP ($CaCl_2 \cdot 2H_2O$)	Osmolarity (mOsmol/L) (calc)	pH	Sodium	Potassium	Calcium	Chloride	Lactate	Caloric Content (kcal/L)
Lactated Ringer's Injection, USP	250 500 1,000	6	3.1	0.3	0.2	273	6.5 (6.0 to 7.5)	130	4	2.7	109	28	9

The flexible container is fabricated from a specially formulated non-plasticized, film containing polypropylene and thermoplastic elastomers (**free***flex*® bag). The amount of water that can permeate from inside the container into the overwrap is insufficient to affect the solution significantly. Solutions in contact with the flexible container can leach out certain of the container's chemical components in very small amounts within the expiration period. The suitability of the container material has been confirmed by tests in animals according to USP biological tests for plastic containers.

CLINICAL PHARMACOLOGY:

Lactated Ringer's Injection has value as a source of water and electrolytes. It is capable of inducing diuresis depending on the clinical condition of the patient.

Lactated Ringer's Injection produces a metabolic alkalinizing effect. Lactate ions are metabolized ultimately to carbon dioxide and water, which requires the consumption of hydrogen cations.

INDICATIONS AND USAGE:

Lactated Ringer's Injection is indicated as a source of water and electrolytes or as an alkalinizing agent.

CONTRAINDICATIONS:

As for other calcium-containing infusion solutions, concomitant administration of ceftriaxone and Lactated Ringer's Injection is contraindicated in newborns (≤ 28 days of age), even if separate infusion lines are used (risk of fatal ceftriaxone-calcium salt precipitation in the neonate's bloodstream).

In patients older than 28 days (including adults), ceftriaxone must not be administered simultaneously with intravenous calcium-containing solutions, including Lactated Ringer's Injection, through the same infusion line (e.g., via Y-connector). If the same infusion line is used for sequential administration, the line must be thoroughly flushed between infusions with a compatible fluid.

Lactated Ringer's Injection is contraindicated in patients with a known hypersensitivity to sodium lactate.

WARNINGS:

Although Lactated Ringer's Injection has a potassium concentration similar to the concentration in plasma, it is insufficient to produce a useful effect in case of severe potassium deficiency; therefore, it should not be used for this purpose.

Lactated Ringer's Injection is not for use for the treatment of lactic acidosis or severe metabolic acidosis.

Lactated Ringer's Injection should not be administered simultaneously with citrate anticoagulated/preserved blood through the same administration set because of the likelihood of coagulation.

The infusion must be stopped immediately if any signs or symptoms of a suspected hypersensitivity reaction develop. Appropriate therapeutic countermeasures must be instituted as clinically indicated. Hypersensitivity reactions are reported more frequently during pregnancy.

Depending on the volume and the rate of infusion, the intravenous administration of Lactated Ringer's Injection can cause fluid and/or solute overloading resulting in dilution of serum electrolyte concentrations, overhydration, congested states, pulmonary edema or acid-base imbalance. The risk of dilutional states is inversely proportional to the electrolyte concentrations of the injections. The risk of solute overload causing congested states with peripheral and pulmonary edema is directly proportional to the electrolyte concentrations of the injections.

Clinical evaluation and periodic laboratory determinations may be necessary to monitor changes in fluid balance, electrolyte concentrations, and acid base balance during prolonged parenteral therapy or whenever the condition of the patient or the rate of administration warrants such evaluation.

Lactated Ringer's Injection should be administered with particular caution, if at all, to patients with hyperkalemia or conditions predisposing to hyperkalemia (such as severe renal impairment or adrenocortical insufficiency, acute dehydration, or extensive tissue injury or burns) and in patients with cardiac disease.

Lactated Ringer's Injection should be administered with particular caution, if at all, to patients with alkalosis or at risk for alkalosis. Because lactate is metabolized to bicarbonate, administration may result in, or worsen, metabolic alkalosis.

Lactated Ringer's Injection should be administered with particular caution, if at all, to patients with severe renal impairment, hypervolemia, overhydration, or conditions that may cause sodium and/or potassium retention, fluid overload, or edema.

PRECAUTIONS:

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

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.

Lactated Ringer's Injection should be administered with particular caution, if at all, to patients with conditions associated with increased lactate levels or impaired lactate utilization, such as severe hepatic insufficiency.

Hyperlactatemia can develop in patients with severe hepatic insufficiency, since lactate metabolism may be impaired. In addition, Lactated Ringer's Injection may not produce its alkalinizing action in patients with severe hepatic insufficiency, since lactate metabolism may be impaired.

Solutions containing calcium salts should be used with caution in patients with hypercalcemia or conditions predisposing to hypercalcemia, such as patients with severe renal impairment and granulomatous diseases associated with increased calcitriol synthesis such as sarcoidosis, calcium renal calculi or history of such calculi.

Lactate is a substrate for gluconeogenesis. This should be taken into account when Lactated Ringer's Injection is used in patients with type 2 diabetes.

Pediatric Use

Safety and effectiveness of Lactated Ringer's Injection in pediatric patients have not been established by adequate and well controlled trials, however, the use of electrolyte solutions in the pediatric population is referenced in the medical literature. The warnings, precautions and adverse reactions identified in the label copy should be observed in the pediatric population.

Lactate-containing solutions should be administered with particular caution to neonates and infants less than 6 months of age.

Geriatric Use

Clinical studies of Lactated Ringer's Injection 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.

Drug Interactions

Ceftriaxone (see **CONTRAINDICATIONS**).

Caution is advised when administering Lactated Ringer's Injection to patients treated with drugs that may increase the risk of sodium and fluid retention, such as corticosteroids.

Caution is advised when administering Lactated Ringer's Injection to patients treated with drugs for which renal elimination is pH dependent. Due to the alkalinizing action of lactate (formation of bicarbonate), Lactated Ringer's Injection may interfere with the elimination of such drugs.

- Renal clearance of acidic drugs such as salicylates and barbiturates may be increased.
- Renal clearance of alkaline drugs, such as sympathomimetics (e.g., ephedrine, pseudoephedrine) and dextroamphetamine (dexamphetamine) sulfate, may be decreased.

Renal clearance of lithium may also be increased. Caution is advised when administering Lactated Ringer's Injection to patients treated with lithium.

Because of its potassium content, Lactated Ringer's Injection should be administered with caution in patients treated with agents or products that can cause hyperkalemia or increase risk of hyperkalemia, such as potassium sparing diuretics (amiloride, spironolactone, triamterene), with ACE inhibitors, angiotensin II receptor antagonists, or the immunosuppressants tacrolimus and cyclosporine.

Caution is advised when administering Lactated Ringer's Injection to patients treated with thiazide diuretics or vitamin D, as these can increase the risk of hypercalcemia.

Pregnancy

Teratogenic Effects

Pregnancy Category C.

Animal reproduction studies have not been conducted with Lactated Ringer's Injection. It is also not known whether Lactated Ringer's Injection can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Lactated Ringer's Injection should be given to a pregnant woman only if clearly needed.

For Hypersensitivity Reactions During Pregnancy (see **WARNINGS**).

Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term studies in animals to evaluate carcinogenic potential or studies to evaluate mutagenic potential have not been performed with Lactated Ringer's Injection. Studies to evaluate the possible impairment of fertility have not been performed.

Labor and Delivery

Studies have not been conducted to evaluate the effects of Lactated Ringer's Injection on labor and delivery. Caution should be exercised when administering this drug during labor and delivery.

Nursing Mothers

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Lactated Ringer's Injection is administered to a nursing mother.

ADVERSE REACTIONS:

Post-Marketing Adverse Reactions

The following adverse reactions have been reported in the post-marketing experience, listed by MedDRA System Organ Class (SOC).

Immune System Disorders

Hypersensitivity/infusion reactions, including anaphylactic/anaphylactoid reactions, and the following manifestations: angioedema, chest pain, chest discomfort, decreased heart rate, tachycardia, blood pressure decreased, respiratory distress, bronchospasm, dyspnea, cough, urticaria, rash, pruritus,

erythema, flushing, throat irritation, paresthesia, hypoesthesia oral, dysgeusia, nausea, anxiety, pyrexia, headache.

Metabolism and Nutrition Disorders

Hyperkalemia.

General Disorders and Administration Site Conditions

Infusion site reactions, including phlebitis, infusion site inflammation, infusion site swelling, infusion site rash, infusion site pruritus, infusion site erythema, infusion site pain, infusion site burning.

Class Reactions

Hypersensitivity reactions, including, laryngeal edema and sneezing

Hypervolemia

Infusion site reactions, including infection at the site of injection, extravasation, and infusion site anesthesia (numbness)

Overdose

An excessive volume or too high a rate of administration of Lactated Ringer's Injection may lead to fluid and sodium overload with a risk of edema (peripheral and/or pulmonary), particularly when renal sodium excretion is impaired.

Excessive administration of lactate may lead to metabolic alkalosis. Metabolic alkalosis may be accompanied by hypokalemia.

Excessive administration of potassium may lead to the development of hyperkalemia, especially in patients with severe renal impairment.

Excessive administration of calcium salts may lead to hypercalcemia.

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:

As directed by a physician. Dosage, rate and duration of administration are to be individualized and dependent upon the indication for use, the patient's age, weight, concomitant treatment and clinical condition of the patient as well as laboratory determinations.

All injections in flexible plastic containers are intended for intravenous administration using sterile and nonpyrogenic equipment.

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.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit. Do not administer unless the solution is clear and seal is intact.

When making additions to Lactated Ringer's Injection, aseptic technique must be used. Mix the solution thoroughly when additives have been introduced. Do not store solutions containing additives.

Additives may be incompatible with Lactated Ringer's Injection. As with all parenteral solutions, compatibility of the additives with the solution must be assessed before addition, by checking for a possible color change and/or the appearance of precipitates, insoluble complexes, or crystals. Before adding a substance or medication, verify that it is soluble and/or stable in water and that the pH range of Lactated Ringer's Injection is appropriate.

The instructions for use of the medication to be added and other relevant literature must be consulted. Additives known or determined to be incompatible should not be used.

HOW SUPPLIED:

Lactated Ringer's Injection, USP in a single dose flexible plastic container, is available as follows:

Product	Each	Unit of Sale
1727171005	NDC 17271-710-05 One 250 mL freeflex® Bag	NDC 17271-710-05 Sold in units of 30
1727171006	NDC 17271-710-06	NDC 17271-710-06

	One 500 mL freeflex® Bag	Sold in units of 20
1727171007	NDC 17271-710-07 One 1,000 mL freeflex® Bag	NDC 17271-710-07 Sold in units of 10

Exposure of pharmaceutical products to heat should be minimized. Avoid excessive heat.

STORE AT: 20° to **25°**C (**68°** to **77°**F) [see USP Controlled Room Temperature]; brief exposure up to 40°C does not adversely affect the product.

The container closure is not made with natural rubber latex. Non-PVC, Non-DEHP, Sterile.

INSTRUCTIONS FOR USE:

Check flexible container solution composition, lot number, and expiry date.

Do not remove solution container from its overwrap until immediately before use.

Use sterile equipment and aseptic technique.

To Open

1. Turn solution container over so that the text is face down. Using the pre-cut corner tabs, peel open the overwrap and remove solution container.
2. Check the solution container for leaks by squeezing firmly. If leaks are found, or if the seal is not intact, discard the solution.
3. Do not use if the solution is cloudy or a precipitate is present.

Preparation for Administration

1. Immediately before inserting the infusion set, break off BLUE Infusion Port Cap with the arrow pointing away from container.
2. Use a non-vented infusion set or close the air-inlet on a vented set.
3. Close the roller clamp of the infusion set.
4. Hold the base of BLUE Infusion Port.
5. Insert spike through BLUE Infusion Port by rotating wrist slightly until the spike is inserted. **NOTE:** See full directions accompanying administration set.

To Add Medication Prior to Solution Administration

1. Identify WHITE Additive Port with arrow pointing toward container.
2. Immediately before injecting additives, break off WHITE Additive Port Cap with the arrow pointing toward container.
3. Hold base of WHITE Additive Port horizontally.
4. Prepare medication site.
5. Insert an 18 to 23 gauge needle horizontally through the center of WHITE Additive Port's septum and inject additives.
6. Mix container contents thoroughly. For high density medication such as potassium chloride, squeeze ports while ports are upright and mix thoroughly.

To Add Medication During Solution Administration

1. Close the clamp on the set.
2. Identify WHITE Additive Port with arrow pointing toward container.
3. Immediately before injecting additives, if the Cap has not been broken off, break off WHITE Additive Port Cap with the arrow pointing toward container.
4. Hold base of WHITE Additive Port horizontally.
5. Prepare medication site.
6. Using a syringe with an 18 to 23 gauge needle, horizontally insert through the center of WHITE Additive Port's septum and inject additives.
7. Remove container from IV pole and/or turn to an upright position.
8. Mix container contents thoroughly.
9. Using aseptic technique, repeat steps 4-7 as necessary.
10. Return container to in use position and continue administration.

WARNING: Do not use flexible container in series connections.

Manufactured for:

BD

Becton, Dickinson and Company
1 Becton Drive
Franklin Lakes, NJ 07417 USA
For product inquiry: 1-800-523-0502
Distributed by BD
Manufactured by Fresenius Kabi.
Made in Norway
451620

Issued: February 2019

PACKAGE LABEL - PRINCIPAL DISPLAY – Lactated Ringer's Injection, USP 250 mL Bag

NDC 17271-710-05

250 mL Lactated Ringer's Injection, USP

For intravenous use. Rx only

mEq/L:

Each 100 mL contains: Na^+ 130

Sodium Chloride, USP 600 mg K^+ 4

Sodium Lactate, USP 310 mg Ca^{2+} 2.7

Potassium Chloride, USP 30 mg Cl^- 109

Calcium Chloride, USP 20 mg Lactate 28

273 mOsmol/L (calc.) pH 6.5 (6.0 to 7.5)

Single Dose Only. Discard Unused Portion.

Not for use in the treatment of lactic acidosis.

Additives may be incompatible. Consult with pharmacist. When introducing additives, use aseptic technique, mix thoroughly and do not store. Use only if solution is clear and container is undamaged. Must not be used in series connections. Do not administer simultaneously with blood.

Usual dosage: See package insert.

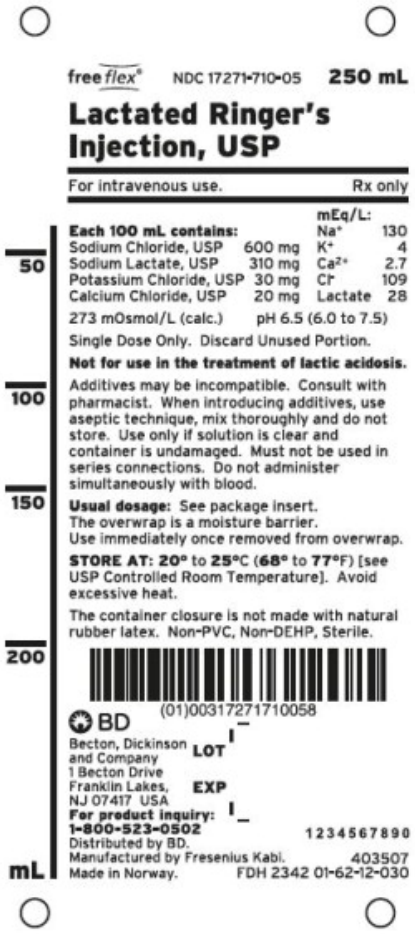
The overwrap is a moisture barrier.

Use immediately once removed from overwrap.

STORE AT: 20° to **25°**C (**68°** to **77°**F) [see USP Controlled Room Temperature].
Avoid excessive heat.

The container closure is not made with natural rubber latex.
Non-PVC, Non-DEHP, Sterile.

Becton, Dickinson and Company 1 Becton Drive Franklin Lakes, NJ 07417 USA	**LOT** **EXP**
For product inquiry: **1-800-523-0502** Distributed by BD Manufactured by Fresenius Kabi. Made in Norway	1234567890 403507 FDH 2342 01-62-12-030



PACKAGE LABEL - PRINCIPAL DISPLAY – Lactated Ringer's Injection, USP 500 mL Bag

NDC 17271-710-06

500 mL

Lactated Ringer's Injection, USP

For intravenous use. Rx only

mEq/L:

Each 100 mL contains: Na^+ 130

Sodium Chloride, USP 600 mg K^+ 4

Sodium Lactate, USP 310 mg Ca^{2+} 2.7

Potassium Chloride, USP 30 mg Cl^- 109

Calcium Chloride, USP 20 mg Lactate 28

273 mOsmol/L (calc.) pH 6.5 (6.0 to 7.5)

Single Dose Only. Discard Unused Portion.

Not for use in the treatment of lactic acidosis.

Additives may be incompatible. Consult with pharmacist. When introducing additives, use aseptic technique, mix thoroughly and do not store. Use only if solution is clear and container is undamaged. Must not be used in series connections. Do not administer simultaneously with blood.

Usual dosage: See package insert.

The overwrap is a moisture barrier.

Use immediately once removed from overwrap.

STORE AT: 20° to **25°**C (**68°** to **77°**F) [see USP Controlled Room Temperature]. Avoid excessive heat.

The container closure is not made with natural rubber latex.
Non-PVC, Non-DEHP, Sterile.

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Franklin Lakes,
NJ 07417 USA

For product inquiry:
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1234567890
403508
FDH 2343 01-62-12-031

PACKAGE LABEL - PRINCIPAL DISPLAY – Lactated Ringer's Injection, USP 1,000 mL Bag

NDC 17271-710-07

1,000 mL

Lactated Ringer's Injection, USP

For intravenous use. Rx only

mEq/L:

Each 100 mL contains: Na^+ 130

Sodium Chloride, USP 600 mg K^+ 4

Sodium Lactate, USP 310 mg Ca^{2+} 2.7

Potassium Chloride, USP 30 mg Cl^- 109

Calcium Chloride, USP 20 mg Lactate 28

273 mOsmol/L (calc.) pH 6.5 (6.0 to 7.5)

Single Dose Only. Discard Unused Portion.

Not for use in the treatment of lactic acidosis.

Additives may be incompatible. Consult with pharmacist. When introducing additives, use aseptic technique, mix thoroughly and do not store. Use only if solution is clear and container is undamaged. Must not be used in series connections. Do not administer simultaneously with blood.

Usual dosage: See package insert.

The overwrap is a moisture barrier.

Use immediately once removed from overwrap.

STORE AT: 20° to **25°**C (**68°** to **77°**F) [see USP Controlled Room Temperature].
Avoid excessive heat.

The container closure is not made with natural rubber latex.
Non-PVC, Non-DEHP, Sterile.

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403509
FDH 2344 01-62-12-032
1234567890

LACTATED RINGERS

sodium chloride, sodium lactate, potassium chloride, calcium chloride injection, solution

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:17271-710
Route of Administration	INTRAVENOUS		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
SODIUM CHLORIDE (UNII: 451W47IQ8X) (SODIUM CATION - UNII:LYR4M0NH37, CHLORIDE ION - UNII:Q32ZN48698)	SODIUM CHLORIDE	600 mg in 100 mL
SODIUM LACTATE (UNII: TU7HW0W0QT) (SODIUM CATION - UNII:LYR4M0NH37, LACTIC ACID - UNII:33X04XA5AT)	SODIUM LACTATE	310 mg in 100 mL
POTASSIUM CHLORIDE (UNII: 660YQ98I10) (POTASSIUM CATION - UNII:295O53K152, CHLORIDE ION - UNII:Q32ZN48698)	POTASSIUM CHLORIDE	30 mg in 100 mL
CALCIUM CHLORIDE (UNII: M4I0D6VV5M) (CALCIUM CATION - UNII:2M83C4R6ZB, CHLORIDE ION - UNII:Q32ZN48698)	CALCIUM CHLORIDE	20 mg in 100 mL

Inactive Ingredients	
Ingredient Name	**Strength**
WATER (UNII: 059QF0KO0R)	

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:17271-710-05	30 in 1 CARTON	01/28/2019	

1		250 mL in 1 BAG; Type 0: Not a Combination Product		
2	NDC:17271-710-06	20 in 1 CARTON	01/28/2019	
2		500 mL in 1 BAG; Type 0: Not a Combination Product		
3	NDC:17271-710-07	10 in 1 CARTON	01/28/2019	
3		1000 mL in 1 BAG; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA209338	01/28/2019	

Labeler - Becton Dickinson and Company (124987988)

Establishment

Name	Address	ID/FEI	Business Operations
Fresenius Kabi Norge As		731170932	MANUFACTURE(17271-710)

Establishment

Name	Address	ID/FEI	Business Operations
Fresenius Kabi Deutschland GmbH		506719546	ANALYSIS(17271-710) , MANUFACTURE(17271-710)

Revised: 3/2019 Becton Dickinson and Company