HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use RINGER'S INJECTION safely and effectively. See full prescribing information for RINGER'S INJECTION.

RINGER'S injection, for intravenous use
Initial U.S. Approval: 1971

---------- RECENT MAJOR CHANGES ----------

Dosage and Administration (2.1, 2.2, 2.3, 2.4)	03/2026
Contraindications (4)	03/2026
Warnings and Precautions (5.1,5.2, 5.3, 5.4, 5.5, 5.6, 5.7)	03/2026

---------- INDICATIONS AND USAGE ----------
Ringer's Injection is indicated for use as a source of water and electrolytes in adults and pediatric patients. (1)

---------- DOSAGE AND ADMINISTRATION ----------
- The recommended dosage and duration are based on the patient's age, weight, clinical condition, and concomitant therapy. (2.1)
- To reduce the risk of air embolism, adhere to the preparation instructions. (2.2, 5.2)
- Ringer's Injection is for intravenous use (2.3)
- Do not administer Ringer's Injection simultaneously with ceftriaxone in neonates (28 days of age or younger) due to serious risks. (2.4)
- See full prescribing information for information dosage considerations, preparation, administration, and drug incompatibilities. (2)

---------- DOSAGE FORMS AND STRENGTHS ----------
Injection: Ringer's Injection USP packaged in single-dose flexible plastic container: 1,000 mL (3)

---------- CONTRAINDICATIONS ----------
- Concomitant treatment with ceftriaxone in neonates (28 days of age or younger). (4)
- Patients with known hypersensitivity to Ringer's Injection. (4)

---------- WARNINGS AND PRECAUTIONS ----------
- Serious Risks with Inappropriate Use with Ceftriaxone: Deaths have occurred in neonates (28 days of age or younger) who received concomitant intravenous calcium-containing solutions with ceftriaxone. In patients older than 28 days, ceftriaxone and Ringer's Injection may be administered sequentially if the infusion lines are thoroughly flushed between infusions. (4, 5.1, 8.4)
- Air Embolism: Use a non-vented infusion set or close the vent on a vented set and use a dedicated line without any connections. Pressure infusion is not recommended to increase flow rates, but if necessary, remove all air from the bag prior to initiating infusion. (5.2)
- Hypersensitivity Reactions: Stop the Ringer's Injection infusion immediately if signs or symptoms of a hypersensitivity reaction develop. (5.3)
- Potassium Imbalances, Hyponatremia, Hypercalcemia, Fluid Overload: See Full Prescribing Information for risk management recommendations. (5.4, 5.5, 5.6, 5.7)

---------- ADVERSE REACTIONS ----------
Common adverse reactions include infusion site reactions and symptoms of hypersensitivity reactions (e.g., pruritus, dyspnea, urticaria, rash, cough). (6)

To report SUSPECTED ADVERSE REACTIONS, contact ICU Medical, Inc. at 1-800-4410-4100 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

---------- DRUG INTERACTIONS ----------
- Drugs that Affect Electrolyte and/or Fluid Balance: Avoid concomitant use. If concomitant use cannot be avoided, closely monitor electrolyte concentrations and fluid balance. (7.1)
- Lithium: Avoid concomitant use. If concomitant use is unavoidable monitor serum lithium concentrations more frequently. (7.2)
- Digoxin: Consider reducing the volume or rate of Ringer's Injection due to the increased risk of digoxin toxicity with calcium-containing solutions. (7.3)

---------- USE IN SPECIFIC POPULATIONS ----------
- Closely monitor plasma electrolyte concentrations in young pediatric patients with immature kidney function. (8.4)
- Geriatric patients are more likely to have decreased renal function. Consider monitoring renal function and starting the infusion at the low end of the dosing range. (8.5)
- Avoid in patients with severe renal impairment. (8.6)

Revised: 03/2026

FULL PRESCRIBING INFORMATION: CONTENTS*

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

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Ringer's Injection is indicated for use as a source of water and electrolytes in adults and pediatric patients.

2 DOSAGE AND ADMINISTRATION

2.1 Dosage Considerations

The recommended dosage and duration of Ringer's Injection is based on the patient's age, weight, clinical condition, and concomitant therapy. Evaluate the patient's clinical status and monitor changes in electrolyte concentrations especially during prolonged use of Ringer's Injection to optimize clinical status.
Fluid administration should be based on calculated maintenance or replacement fluid requirements for each patient.

2.2 Important Preparation Instructions

Visually inspect the Ringer's Injection solution for particulate matter and discoloration. Do not administer Ringer's Injection unless the solution is clear and the container is undamaged and the container seals are intact.

If additives are determined to be compatible with Ringer's Injection, then using aseptic technique, mix thoroughly; do not store solutions containing additives. After mixing, do not use if there is discoloration or formation of precipitates.

To reduce the risk of air embolism, adhere to the following Ringer's Injection preparation instructions *[see Warnings and Precautions (5.2)]*:

- Use a non-vented infusion set or close the vent on a vented set.
- Use a dedicated line without any connections (do not connect flexible containers in series).
- The use of pressure infusion is not recommended as a method to increase flow rates. However, if pressure infusion is required, ensure that any air within the bag is fully evacuated prior to initiation of infusion. If using a pumping device to administer Ringer's Injection, turn off the pump before the container is empty.

<u>To Open:</u>

Tear outer wrap at notch and remove solution container. If supplemental medication is desired, follow directions below before preparing for administration. 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.

<u>Preparation for Administration</u>

(Use aseptic technique)

1. Close flow control clamp of administration set.
2. Remove cover from outlet port at bottom of container.
3. Insert piercing pin of administration set into port with a twisting motion until the set is firmly seated.
   NOTE: See administration set carton for complete directions.
4. Suspend container from hanger.

5. Squeeze and release drip chamber to establish proper fluid level in chamber.
6. Open flow control clamp and clear air from set. Close clamp.
7. Attach set to venipuncture device. If device is not indwelling, prime and make venipuncture.
8. Regulate rate of administration with flow control clamp.

2.3 Important Administration Instructions

Ringer's Injection is for intravenous use.

Use immediately after opening the container. Discard the unused portion.

Some additives may be incompatible *[see Dosage and Administration (2.4)]*.

To Add Medication Before Solution Administration

1. Prepare medication site.
2. Using syringe with the recommended gauge needle, puncture medication port and inner diaphragm and inject.
3. Squeeze and tap ports while ports are upright and 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 the recommended gauge needle of appropriate length (at least 5/8 inch), puncture resealable medication port and inner diaphragm and inject.
4. Remove container from IV pole and/or turn to an upright position.
5. Evacuate both ports by tapping and squeezing them while container is in the upright position.
6. Mix solution and medication thoroughly.
7. Return container to in use position and continue administration.

2.4 Drug Incompatibilities

Do not administer Ringer's Injection simultaneously with ceftriaxone in neonates (28 days of age or younger) due to serious risks *[see Contraindications (4) and Warnings and Precautions (5.1)]*. However, in patients older than 28 days, ceftriaxone and Ringer's Injection may be administered sequentially if the infusion lines are thoroughly flushed between infusions with a compatible fluid *[see Warnings and Precautions (5.1)]*.

Do not administer Ringer's Injection simultaneously with citrate anticoagulated/preserved blood through the same administration set because of the likelihood of coagulation precipitated by the calcium content of Ringer's Injection.

3 DOSAGE FORMS AND STRENGTHS

Injection: Ringer's Injection USP as a clear, sterile, and nonpyrogenic solution packaged in a single-dose flexible plastic container: 1,000 mL.

4 CONTRAINDICATIONS

Ringer's Injection is contraindicated in:

- Neonates (28 days of age or younger) who are receiving concomitant treatment with ceftriaxone, even if

separate infusion lines are used, due to the risk of fatal ceftriaxone-calcium salt precipitation in the neonate's bloodstream *[see Warnings and Precautions (5.1)* and *Specific Populations (8.4)]*.
- Patients with known hypersensitivity to any components of Ringer's Injection *[see Warnings and Precautions (5.3)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Serious Risk with Concomitant Use with Ceftriaxone

Precipitation of ceftriaxone-calcium can occur when ceftriaxone is mixed with calcium-containing solutions, such as Ringer's Injection in the same intravenous administration line. Deaths have occurred in neonates (28 days of age or younger) who received concomitant intravenous calcium-containing solutions with ceftriaxone resulting from calcium-ceftriaxone precipitates in the lungs and kidneys, even when separate infusion lines were used.

Ringer's Injection is contraindicated in neonates who receive ceftriaxone *[see Contraindications (4), Use in Specific Populations (8.4)]*. However, in patients older than 28 days, ceftriaxone and Ringer's Injection may be administered sequentially if the infusion lines are thoroughly flushed between infusions with a compatible fluid.

5.2 Air Embolism

Cases of air embolism have been reported with pressurized administration of intravenous fluids. Air embolism may result in stroke, organ ischemia and/or infarction, and death.

Use a non- vented infusion set or close the vent on a vented set and use a dedicated line without any connections. If administration is controlled by a pumping device, care must be taken to discontinue the pumping action before the container is empty. Pressure infusion is not recommended to increase flow rates, but if necessary, ensure all air is removed from the bag before infusion. Refrain from applying excessive pressure (>300mmHg) causing distortion to the container such as wringing or twisting. Such handling could result in breakage of the container *[see Dosage and Administration (2.2)]*.

5.3 Hypersensitivity Reactions

Hypersensitivity reactions, including anaphylaxis and angioedema, have been reported with Ringer's Injection. Stop the Ringer's Injection infusion immediately and treat patient accordingly if signs or symptoms of a hypersensitivity reaction develop. Initiate appropriate treatment as clinically indicated.

5.4 Potassium Imbalances

Hyperkalemia

Potassium-containing solutions, including Ringer's Injection, may increase the risk of hyperkalemia. This risk is increased in patients predisposed to hyperkalemia including those with severe renal impairment, acute dehydration, extensive tissue injury or burns, heart failure, or in those using concomitant drugs that are associated with hyperkalemia.

Avoid use of Ringer's Injection in patients with, or at increased risk for, hyperkalemia. If use cannot be avoided in these patients, closely monitor serum potassium concentrations.

Hypokalemia

The potassium concentration in Ringer's Injection is similar to the concentration in plasma. It is insufficient to normalize the serum potassium in patients with severe hypokalemia.

5.5 Hyponatremia

Ringer's Injection may cause hyponatremia. Hyponatremia can lead to acute hyponatremic encephalopathy characterized by headache, nausea, seizures, lethargy and vomiting. The risk of hospital-acquired hyponatremia is increased in younger pediatric patients, geriatric patients, patients treated with diuretics, and patients with cardiac or pulmonary failure or with the syndrome of inappropriate antidiuretic hormone (SIADH) (e.g., postoperative patients, patients concomitantly treated with arginine vasopressin analogs or certain antiepileptic, psychotropic, or cytotoxic drugs) *[see Drug Interactions (7.1), Use in Specific Populations (8.4)]*.

Avoid Ringer's Injection in patients with or at risk for hyponatremia. If use cannot be avoided in these patients, closely monitor serum sodium concentrations.

Rapid correction of hyponatremia may result in serious neurologic complications such as osmotic demyelination syndrome (ODS). To avoid complications, monitor serum sodium and chloride concentrations, fluid status, acid-base balance, and neurologic status.

5.6 Hypercalcemia

Ringer's Injection contains calcium salts and may cause hypercalcemia. Avoid administration of Ringer's Injection in patients with hypercalcemia, those with calcium-containing renal calculi or history of such calculi, those with conditions predisposing to hypercalcemia, or those treated with concomitant thiazide diuretics or vitamin D.

5.7 Fluid Overload

Depending on the administered volume and the infusion rate, administration of Ringer's Injection can cause fluid overload, including pulmonary edema.

Avoid Ringer's Injection in patients at risk for fluid and/or solute overload. If use cannot be avoided in these patients, monitor fluid balance, electrolyte concentrations and acid base balance, especially during prolonged use.

6 ADVERSE REACTIONS

The following serious adverse reactions are discussed in greater detail in other sections of the labeling:

- Serious Risk with Concomitant Use with Ceftriaxone *[see Warnings and Precautions (5.1)]*
- Air Embolism *[see Warnings and Precautions (5.2)]*
- Hypersensitivity Reactions *[see Warnings and Precautions (5.3)]*
- Potassium Imbalances *[see Warnings and Precautions (5.4)]*
- Hyponatremia *[see Warnings and Precautions (5.5)]*
- Hypercalcemia *[see Warnings and Precautions (5.6)]*
- Fluid Overload *[see Warnings and Precautions (5.7)]*

The following adverse reactions have been identified during post approval use of Ringer's Products. 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:

General Disorders and Administration Site Conditions:
Phlebitis, extravasation, infusion site inflammation, infusion site swelling, infusion site rash, infusion site pruritus, infusion site erythema, infusion site pain, infusion site burning, and infusion site hypoesthesia.

Hypersensitivity Reactions and Infusion Reactions:
Angioedema, chest pain/discomfort, bradycardia or tachycardia, hypotension, respiratory distress, bronchospasm, dyspnea, cough, urticaria, rash, pruritus, erythema, flushing, throat irritation, paresthesia, oral hypoesthesia, dysgeusia, nausea, anxiety, pyrexia, headache, laryngeal edema, sneezing, and injection site infection.

Metabolism and Nutrition Disorders:
Hyperkalemia, hyponatremia, and hypervolemia.

Nervous System Disorders:
Hyponatremic encephalopathy.

7 DRUG INTERACTIONS

7.1 Drugs that Affect Electrolyte and/or Fluid Balance

Hyperkalemia
Administration of Ringer's Injection to patients concomitantly treated or recently treated with drugs that are associated with hyperkalemia increases the risk of severe and potentially fatal hyperkalemia, especially in the presence of other hyperkalemia risk factors. Avoid use of Ringer's Injection in patients receiving drugs that are associated with hyperkalemia (e.g., potassium-sparing diuretics, ACE inhibitors, angiotensin II receptor antagonists, or calcineurin inhibitors). If concomitant use cannot be avoided, closely monitor serum potassium concentrations during concomitant use *[see Warnings and Precautions (5.4)]*.

Hyponatremia
Administration of Ringer's Injection to patients treated concomitantly with drugs associated with hyponatremia may increase the risk of developing hyponatremia. These drugs include diuretics and those that cause SIADH (e.g., arginine vasopressin analogs, certain antiepileptic, psychotropic, or cytotoxic drugs. Avoid use of Ringer's Injection in patients receiving such drugs. If use cannot be avoided, closely monitor serum sodium concentrations during concomitant use *[see Warnings and Precautions (5.5)]*.

Hypercalcemia
Avoid the use of Ringer's Injection in patients treated with thiazide diuretics or vitamin D because these drugs can increase the risk of hypercalcemia. If use cannot be avoided, closely monitor serum calcium concentrations during concomitant use *[see Warnings and Precautions (5.6)]*.

Hypernatremia and Fluid Retention
Administration of Ringer's Injection to patients treated concomitantly with drugs associated with sodium and fluid retention (e.g., corticosteroids or corticotropin) may increase the risk of hypernatremia and volume overload. Avoid use of Ringer's Injection in patients receiving such drugs. If use cannot be avoided, closely monitor serum electrolytes, fluid balance, and acid-base balance during concomitant use.

7.2 Lithium

Renal sodium and lithium clearance may be increased during concomitant use of Ringer's Injection and lithium and may result in decreased lithium concentrations. Avoid use of Ringer's Injection in patients receiving lithium. If use cannot be avoided, increase the frequency of monitoring of serum lithium concentrations during concomitant use.

7.3 Digoxin

Administration of calcium via use of Ringer's Injection may increase digoxin's effects and lead to digoxin toxicity including serious or fatal cardiac arrhythmias. In digoxin-treated patients, consider reducing the volume and/or rate of Ringer's Injection administration.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Exposure to Ringer's Injection during pregnancy is not expected to cause major birth defects, miscarriage, or adverse maternal or fetal outcomes. Animal reproduction studies have not been conducted with this drug.

The background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively.

8.2 Lactation

Risk Summary

The use of Ringer's Injection is not expected to cause harm to a breastfed infant. There are no data on the presence of Ringer's Injection in human milk, the effects on the breastfed infant, or the effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Ringer's Injection and any potential adverse effects on the breastfed infant from Ringer's Injection or from the underlying maternal condition.

8.4 Pediatric Use

Ringer's Injection is contraindicated in neonates (28 days of age or younger) who are receiving ceftriaxone due to reported deaths that occurred when neonates received ceftriaxone and intravenous calcium- containing solutions concomitantly *[see Warnings and Precautions (5.1)]*.

The safety and effectiveness of Ringer's Injection for use as a source of water and electrolytes have been established in pediatric patients of all ages, including neonates.

Closely monitor plasma electrolyte concentrations in young pediatric patients with immature kidney function who may have decreased ability to maintain fluid and electrolyte balance *[see Warnings and Precautions (5.4, 5.5, 5.6, 5.7)]*.

8.5 Geriatric Use

Geriatric patients treated with Ringer's Injection are at increased risk of developing electrolyte imbalances. Ringer's Injection is substantially excreted by the kidney, and the risk of adverse reactions to Ringer's Injection may be greater in patients with renal impairment than in patients with normal renal function. Because geriatric patients are more likely to have decreased renal function, consider monitoring renal function in geriatric patients and consider starting the infusion at the low end of the dosing range.

8.6 Renal Impairment

Administration of Ringer's Injection to patients with or at risk of severe renal impairment, may result in

hyperkalemia and/or fluid overload *[see Warnings and Precautions (5.4, 5.7)]*. Avoid Ringer's Injection in patients with severe renal impairment. If use cannot be avoided in such patients, monitor for development of these adverse reactions.

10 OVERDOSAGE

Excessive administration of Ringer's Injection can cause:

- Hyperkalemia and hypernatremia, especially in patients with severe renal impairment.
- Fluid overload (which can lead to pulmonary and/or peripheral edema).
- Hypercalcemia

Overdose interventions include Ringer's Injection discontinuation, treatment of electrolyte imbalances, and close monitoring of fluid balance and electrolyte concentrations *[see Warnings and Precautions (5.4, 5.5, 5.6, 5.7)]*.

11 DESCRIPTION

Ringer's Injection, USP is a sterile, nonpyrogenic solution for fluid and electrolyte replenishment in a single-dose flexible container for intravenous administration.

Composition, osmolarity, pH, ionic concentration and caloric content are shown in Table 1.

Table 1

	Size (mL)	Composition (g/L)[a]			Osmolarity (mOsmol/L) (calc)[b]*	pH	Ionic Concentration (mEq/L)				Caloric Content (kcal/L)
		Sodium Chloride, USP	Calcium Chloride, USP, Dihydrate	Potassium Chloride, USP			Sodium	Potassium	Calcium	Chloride	
Ringer's Injection, USP	1000	8.6	0.33	0.3	309	5.4 (5.0 to 7.5)	147	4	4	155	0

[a] May contain hydrochloric acid or sodium hydroxide for pH adjustment.

[b] Normal physiologic osmolarity range is approximately 280 to 310 mOsmol/L.

The chemical name, structural formula, and molecular weight of the active ingredients are shown in Table 2.

Table 2

Ingredients	Structural Formula	Molecular Weight (g/mol)

Sodium Chloride USP	$Na^{+}Cl^{-}$	58.44
Potassium Chloride USP	$K^{+}Cl^{-}$	74.55
Calcium Chloride Dihydrate USP	$2H_2O{\bullet}Cl^{-}Ca^{+2}Cl^{-}$	147.02

The flexible plastic container is fabricated from polyvinylchloride. The container is overwrapped to provide protection from the physical environment and to provide an additional moisture barrier when necessary. Solution inside the plastic container also can leach out certain chemical components in small amounts before the expiration period is attained. The safety of the plastic has been confirmed by tests in animals according to USP biological standards for plastic containers.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Ringer's Injection is a source of water, and electrolytes.

- Sodium, the major cation of the extracellular fluid, functions primarily in the control of water distribution, fluid balance, and osmotic pressure of body fluids. Sodium is also associated with chloride and bicarbonate in the regulation of the acid-base equilibrium of body fluid.
- Potassium, the principal cation of intracellular fluid, participates in carbohydrate utilization and protein synthesis and is critical in the regulation of nerve conduction and muscle contraction, particularly in the heart.
- Chloride, the major extracellular anion, closely follows the metabolism of sodium, and changes in the acid-base balance of the body are reflected by changes in the chloride concentration..
- Calcium, an important cation, provides the framework of bones and teeth in the form of calcium phosphate and calcium carbonate. In the ionized form, calcium is essential for the functional mechanism of the clotting of blood, normal cardiac function, and regulation of neuromuscular irritability.

12.2 Pharmacodynamics

The exposure-response relationship and time course of pharmacodynamic response for the safety and effectiveness of Ringer's Injection have not been fully characterized.

12.3 Pharmacokinetics

Elimination
Metabolism/Excretion

Potassium: Normally about 80 to 90% of the potassium intake is excreted in the urine; the remainder is excreted in feces and to a smaller extent, in perspiration.

Sodium and Chloride: The distribution and excretion of sodium (Na^{+}) and chloride (Cl-) are largely under the control of the kidney which maintains a balance between intake and output.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenicity, genetic toxicology, and animal fertility studies have not been conducted with Ringer's Injection.

16 HOW SUPPLIED/STORAGE AND HANDLING

How Supplied

Ringer's Injection, USP is a clear solution supplied as:

1000 mL in a single-dose flexible plastic container: NDC 0990-7982-09

Storage and Handling

Store at 20°C to 25°C (68°F to 77°F); excursions permitted between 15°C to 30°C (59°F to 86°F). [See USP Controlled Room Temperature.]

Protect from freezing.

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