PRESCRIBING INFORMATION

PLASMA-LYTE 148 and 5% Dextrose Injection

Multiple Electrolyte Solution with Dextrose

IV Fluid, Nutrient and Electrolyte Replenisher

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SUMMARY PRODUCT INFORMATION

PLASMA-LYTE 148 (An Electrolyte Solution) and 5% Dextrose Injection is a sterile, nonpyrogenic intravenous solution which contains no bacteriostatic or antimicrobial agents or added buffers. The composition, osmolarity and approx. pH of the individual solutions are shown in Table 1.

Table 1

	DIN	Size (mL)	Composition (g/L)								Osmolarity (mOsmol/L)	pH	Ionic Concentration (mmol/L)									Caloric Content (kcal/L)
			Dextrose*	Sodium Chloride, USP	Potassium Chloride, USP	Sodium Gluconate, USP	Sodium Acetate, USP	Magnesium Chloride,USP	Potassium Acetate, USP	Magnesium Acetate,USP			Sodium	Potassium	Chloride	Magnesium	Calcium	Acetate	Gluconate	Lactate	Dextrose	
PLASMA-LYTE 148 and 5% Dextrose Injection	00260592	1000	50	5.26	0.37	5.02	3.68	0.30	0	0	546	5.0 (4.0 – 6.5)	140	5	98	1.5	0	27	23	0	50	165

*The dextrose is purified from corn and may contain fructose.

ACTIONS

PLASMA-LYTE 148 and 5% Dextrose Injection is a source of water for hydration and provides electrolytes and calories. It is capable of inducing diuresis depending on the clinical conditions of the patient. See Table 1 for calories per litre and ionic concentration of PLASMA-LYTE 148 and 5% Dextrose Injection.

PLASMA-LYTE 148 and 5% Dextrose Injection contains acetate and gluconate anions which produce a metabolic alkalinizing effect. These anions are metabolized in the liver to glycogen, and ultimately to carbon dioxide and water, which requires the consumption of hydrogen cations.

INDICATIONS AND CLINICAL USE

PLASMA-LYTE 148 and 5% Dextrose Injection is indicated for volume replacement, as a source of water, electrolytes and calories, and as an alkalinizing agent.

CONTRAINDICATIONS

PLASMA-LYTE 148 and 5% Dextrose Injection, is contraindicated in the following conditions:

- Patients who are hypersensitive to this drug or to any ingredient in the formulation or component of the container. For a complete listing, see the SUMMARY PRODUCT INFORMATION section of the Prescribing Information.
- Known allergy to corn or corn products since dextrose in the products is purified from corn.
- Clinically significant hyperglycemia

WARNINGS AND PRECAUTIONS

General

PLASMA-LYTE 148 and 5% Dextrose Injection is not indicated for the treatment of hypochloremic hypokalemic alkalosis and should be used with caution, if at all, in patients with hypochloremic hypokalemic alkalosis (e.g., due to prolonged vomiting, pyloric stenosis, prolonged nasogastric suctioning).

PLASMA-LYTE 148 and 5% Dextrose Injection should be used with great care, if at all, in patients with congestive heart failure, severe renal insufficiency, and in clinical states in which there exists edema with sodium retention.

PLASMA-LYTE 148 and 5% Dextrose Injection is not indicated for the primary treatment of severe metabolic acidosis.

Although PLASMA-LYTE 148 and 5% Dextrose 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 correction of severe potassium deficiency.

PLASMA-LYTE 148 and 5% Dextrose Injection is not indicated for the treatment of hypomagnesemia.

Caution must be exercised in the administration of parenteral fluids, especially those containing sodium ion, to patients receiving corticosteroids or corticotropin.

Blood

PLASMA-LYTE 148 and 5% Dextrose Injection should not be administered with blood through the same administration set because of the possibility of pseudoagglutination or hemolysis.

Hypersensitivity Reactions

Hypersensitivity/infusion reactions, including anaphylaxis, have been reported with PLASMA-LYTE 148 and 5% Dextrose Injection (see Adverse Reactions).

The infusion must be stopped immediately if any signs or symptoms of a suspected hypersensitivity/infusion reaction develop. Appropriate therapeutic countermeasures must be instituted as clinically indicated.

Since the dextrose in PLASMA-LYTE 148 and 5% Dextrose Injection is derived from corn, the product should not be used in patients with known allergy to corn or corn products (see CONTRAINDICATIONS section).

Risk of Fluid and/or Solute Overload and Electrolyte Disturbances

Depending on the volume and rate of infusion, the intravenous administration of PLASMA-LYTE 148 and 5% Dextrose Injection can cause

− fluid and/or solute overload resulting in dilution of serum electrolyte concentrations, overhydration/hypervolemia, congested states, pulmonary edema or acid-base imbalance.

The risk of dilutional states is inversely proportional to the electrolyte concentrations of PLASMA-LYTE 148 and 5% Dextrose Injection. The risk of solute overload causing congested states with peripheral and pulmonary edema is proportional to the volume of PLASMA-LYTE 148 and 5% Dextrose Injection administered.

Clinical evaluation and periodic laboratory determinations are 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.

Use in Patients with or at Risk for Hypermagnesemia

Solutions containing magnesium should be used with caution, if at all, in patients with

− hypermagnesemia or conditions predisposing to hypermagnesemia, including but not limited to severe renal impairment or magnesium therapy such as for eclampsia.
− myasthenia gravis.

Use in Patients with or at Risk for Alkalosis

PLASMA-LYTE 148 and 5% Dextrose Injection should be administered with particular caution, if at all, to patients with alkalosis or at risk for alkalosis.

Excess administration of PLASMA-LYTE 148 and 5% Dextrose Injection can result in metabolic alkalosis

Use in Patients with Hypervolemia or Overhydration, or Conditions that Cause Sodium Retention and Edema

PLASMA-LYTE 148 and 5% Dextrose Injection should be used with particular caution, in patients with or at risk for:

- Hypervolemia or overhydrated patients
- Conditions that may cause sodium retention, fluid overload and edema (central and peripheral), such as patients with primary hyperaldosteronism, secondary hyperaldosteronism (associated with, for example., hypertension, congestive heart failure, renal artery stenosis, or nephrosclerosis), or preeclampsia

- Medications that may increase the risk of sodium and fluid retention, such as corticosteroids.

Use in Patients with Hypocalcemia

PLASMA-LYTE 148 and 5% Dextrose Injection contains no calcium, and an increase in plasma pH due to its alkalinizing effect may lower the concentration of ionized (not protein-bound) calcium. PLASMA-LYTE 148 and 5% Dextrose Injection should be administered with particular caution, if at all, to patients with hypocalcemia.

Use in Patients with or at Risk for Hyperkalemia

PLASMA-LYTE 148 and 5% Dextrose 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.

Use in Patients with Severe Renal Impairment

PLASMA-LYTE 148 and 5% Dextrose Injection should be administered with particular caution, if at all, to patients with or at risk of (severe) renal impairment. In such patients administration of PLASMA-LYTE 148 and 5% Dextrose Injection may result in sodium and/or potassium or magnesium retention.

Osmolarity

Normal physiologic osmolarity range is approximately 280-310 mOsmol/litre. PLASMA-LYTE 148 and 5% Dextrose Injection is a hyper-osmotic solution, having an osmolarity of 546 mOsmol/L.

Administration of hypertonic solutions may cause venous irritation or vein damage, including phlebitis.

Hyperosmolar solutions should be administered with caution, if at all, to patients with hyperosmolar states.

Risk of Air Embolism

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.

Use in Patients with or at Risk for Hyperglycemia

Solutions containing dextrose should be used with caution in patients with impaired glucose tolerance or overt diabetes mellitus.

Because PLASMA-LYTE 148 and 5% Dextrose Injection contains dextrose as well as gluconate (a portion of which may be metabolized to glucose), administration of PLASMA-LYTE 148 and 5% Dextrose Injection that exceeds the metabolic capacity for glucose may lead to hyperglycemia.

Rapid administration of dextrose solutions may produce substantial hyperglycemia and hyperosmolar syndrome.

In order to avoid hyperglycemia the infusion rate should not exceed the patient's ability to utilize glucose.

To reduce the risk of hyperglycemia-associated complications, the infusion rate must be adjusted and/or insulin administered if blood glucose levels exceed levels considered acceptable for the individual patient.

Intravenous dextrose should be administered with caution in patients with, for example:

- Impaired glucose tolerance (such as in diabetes mellitus, renal impairment, or in the presence of sepsis, trauma, or shock),
- Severe malnutrition (risk of precipitating a refeeding syndrome),
- Thiamine deficiency, e.g., in patients with chronic alcoholism (risk of severe lactic acidosis due to impaired oxidative metabolism of pyruvate),
- Water and electrolyte disturbances that could be aggravated by increased glucose and/or free water load

Other groups of patients in whom PLASMA-LYTE 148 and 5% Dextrose Injection should be used with caution include:

- Patients with ischemic stroke. Hyperglycemia has been implicated in increasing cerebral ischemic brain damage and impairing recovery after acute ischemic strokes.
- Patients with severe traumatic brain injury (in particular during the first 24 hours following the trauma). Early hyperglycemia has been associated with poor outcomes in patients with severe traumatic brain injury.
- In newborns, the risk of hyperglycemia due to infusion of dextrose containing solutions appears to be greater with lower birth weight. In these patients, hyperglycemia and increased serum osmolarity has been associated with an increased risk of intraventricular cerebral hemorrhage. For risk of hypo- or hyperglycemia in newborns see SPECIAL POPULATIONS - USE IN PEDIATRIC PATIENTS and PEDIATRIC GLYCEMIA-

RELATED ISSUES.

Prolonged intravenous administration of dextrose and associated hyperglycemia may result in decreased rates of glucose-stimulated insulin secretion.

Refeeding Syndrome

Refeeding severely undernourished patients may result in the refeeding syndrome that is characterized by the shift of potassium, phosphorus, and magnesium intracellularly as the patient becomes anabolic. Thiamine deficiency and fluid retention may also develop. Careful monitoring and slowly increasing nutrient intakes while avoiding overfeeding can prevent these complications.

Special Populations
Pregnancy and Lactation

There are no adequate data from the use of PLASMA-LYTE 148 and 5% Dextrose Injection in pregnant or lactating women.

Intrapartum maternal intravenous infusion of glucose-containing solutions may result in fetal hyperglycemia, metabolic acidosis as well as increased fetal insulin production, which may result in rebound hypoglycemia in the neonate.
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 PLASMA-LYTE 148 and 5% Dextrose Injection is administered to a nursing mother.

Physicians should carefully consider the potential risks and benefits for each specific patient before administering PLASMA-LYTE 148 and 5% Dextrose Injection.

Use in Pediatric Patients

Safety and effectiveness of PLASMA-LYTE 148 and 5% Dextrose Injection in children have not been established by adequate and well controlled trials.

The infusion rate and volume depends on the age, weight, clinical and metabolic conditions of the patient, concomitant therapy and should be determined by the consulting physician experienced in pediatric intravenous fluid therapy. Plasma electrolyte concentrations should be closely monitored in the pediatric population as this population may have impaired ability to regulate fluids and electrolytes.

Pediatric Glycemia-related Issues

Newborns – especially those born premature and with low birth weight – are at increased risk of developing hypo- or hyperglycemia and therefore need close monitoring during treatment with intravenous glucose solutions to ensure adequate glycemic control in order to avoid potential

long term adverse effects. [See USE IN PATIENTS WITH OR AT RISK FOR HYPERGLYCEMIA].

Hypoglycemia in the newborn can cause, e.g.,
- prolonged seizures,
- coma and
- cerebral injury, including brain damage.

Hyperglycemia has been associated with
- cerebral injury, including intraventricular hemorrhage,
- late onset bacterial and fungal infection,
- retinopathy of prematurity,
- necrotizing enterocolitis,
- increased oxygen requirements including bronchopulmonary dysplasia,
- prolonged length of hospital stay, and
- death.

Use in Geriatric Patients

When selecting the type of infusion solution and the volume/rate of infusion for a geriatric patient, consider that geriatric patients are generally more likely to have cardiac, renal, hepatic, and other diseases or concomitant drug therapy. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range.

Monitoring and Laboratory Tests

There have been reports of false-positive test results using the Bio-Rad Laboratories Platelia Aspergillus EIA test in association with the use of Baxter gluconate-containing PLASMA-LYTE solutions. Therefore, positive test results for this test in patients receiving Baxter gluconate-containing PLASMA-LYTE solutions should be interpreted cautiously and confirmed by other diagnostic methods.

ADVERSE REACTIONS

Febrile response may occur because of the solution or the technique of administration.

If any adverse reaction does occur, discontinue the infusion, evaluate the patient, institute appropriate therapeutic countermeasures, and save the remainder of the fluid and administration set for examination if deemed necessary.

Post-marketing Adverse Reactions

The following adverse reactions have been reported in the postmarketing experience, with unspecified PLASMA-LYTE products and PLASMA-LYTE products with Dextrose**,** listed by MedDRA System Organ Class (SOC), then by Preferred Term in order of severity, where feasible.

IMMUNE SYSTEM DISORDERS: Hypersensitivity/infusion reactions, including Anaphylactoid reaction, and the following manifestations: Hypotension, Chest discomfort, Dyspnea, Wheezing, Flushing, Hyperemia, Asthenia, Urticaria, Cold sweat, Pyrexia, Chills

METABOLISM AND NUTRITION DISORDERS:
Hyperkalemia, Hyperglycemia

GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS: Infusion site reactions (e.g., Burning sensation)

Class Reactions

Other adverse reactions, reported with PLASMA-LYTE products without Dextrose, are:

- Other manifestations of hypersensitivity/infusion reactions: Tachycardia, Palpitations, Chest pain, Respiratory rate increased, Feeling abnormal, Piloerection, Edema peripheral
- Infusion site pain

DRUG INTERACTIONS

Caution is advised when administering PLASMA-LYTE 148 and 5% Dextrose Injection to patients treated with drugs that may increase the risk of sodium and fluid retention, such as corticosteroids or corticotropin [See also WARNINGS AND PRECAUTIONS].

Caution is advised when administering PLASMA-LYTE 148 and 5% Dextrose Injection to patients treated with drugs for which renal elimination is pH dependent. Due to its alkalinizing effect (formation of bicarbonate), PLASMA-LYTE 148 and 5% Dextrose Injection may interfere with the elimination of such drugs.

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

Because of its potassium content, PLASMA-LYTE 148 and 5% Dextrose Injection should be administered with caution in patients treated with agents or products that can cause hyperkalemia or increase the risk of hyperkalemia, such as potassium sparing diuretics (amiloride, spironolactone, triamterene), with ACE inhibitors, angiotensin II receptor antagonists, or the immunosuppressants tacrolimus and cyclosporine.

DOSAGE AND ADMINISTRATION

Dosing Considerations

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, and concomitant treatment, and on the patient's clinical and laboratory response to treatment.

For patients with electrolyte and glucose abnormalities and for pediatric patients, consult a physician experienced in intravenous fluid therapy.

PLASMA-LYTE 148 and 5% Dextrose Injection in VIAFLEX plastic container is intended for intravenous infusion using sterile equipment. It is recommended that intravenous administration apparatus be replaced at least once every 24 hours.

The infusion rate and volume of intravenous solutions containing dextrose should be selected with caution in children [See USE IN PEDIATRIC PATIENTS].

Use of an in-line filter is recommended during administration of all parenteral solutions where possible.

Hyperosmolar solutions may cause venous irritation and phlebitis. Thus, any hyperosmolar solutions are recommended to be administered through a large central vein, for rapid dilution of the hypertonic solution. See Table 1 for information on the product's osmolarity.

The osmolarity of a final admixed solution must be taken into account when peripheral administration is considered.

A gradual increase of flow rate should be considered when starting administration of dextrose-containing products.

Electrolyte supplementation may be indicated according to the clinical needs of the patient.

Additives may be incompatible. Compatibility of additives must be checked before adding medication. Those additives known to be incompatible should not be used. When introducing additives to PLASMA-LYTE 148 and 5% Dextrose Injection, the instructions for use of the medication to be added and other relevant literature must be consulted.

If in the informed judgment of the physician it is deemed advisable to introduce additives, use aseptic technique.

Before adding a substance or medication, verify that it is soluble in and/or stable in PLASMA-LYTE 148 and 5% Dextrose Injection and that the pH range of PLASMA-LYTE 148 and 5% Dextrose Injection is appropriate.

After addition, check for a possible color change and/or the appearance of precipitates, insoluble complexes or crystals.

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 the seal is intact.

Thorough and careful mixing of any additive is mandatory. Do not store solutions containing additives. For single use only.

Discard any unused portion.

Administration

Directions for use of VIAFLEX Plastic Container

WARNING: Do not use plastic containers in series connections. Such use could result in air embolism due to residual air (approximately 15 mL) being drawn from the primary container before administration of the fluid from the secondary container is completed [See WARNINGS AND PRECAUTIONS].

The VIAFLEX plastic container is fabricated from a specially formulated polyvinyl chloride (PL 146 Plastic). 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 plastic container can leach out certain of its chemical components in very small amounts within the expiration period, e.g. di-2-ethylhexyl phthalate (DEHP), up to 5 parts per million. However, the safety of the plastic has been confirmed in tests in animals according to USP biological tests for plastic containers as well as by tissue culture toxicity studies.

Do not remove unit from overwrap until ready to use.

To Open:

Tear overwrap down side at slit and remove solution container. If supplemental medication is desired, follow directions below before preparing administration. Some opacity of the plastic due to moisture absorption during sterilization process may be observed. This is normal and does not affect the solution quality and safety. The opacity will diminish gradually. Check for leaks by squeezing inner bag firmly. If leaks are found discard solution as sterility may be impaired.

Preparation for Administration:

1. Suspend container from eyelet support.
2. Remove plastic protector from outlet port at bottom of container.
3. Attach administration set. Refer to complete directions accompanying set.

To Add Medication:

1. Prepare medication site.
2. Using a syringe and a 20 – 22 gauge needle, puncture resealable rubber plug at target area and inject. Multiple additions may be made in this manner.
3. Mix solution and medication thoroughly. For high density medications such as potassium chloride, squeeze ports while ports are upright and mix thoroughly.

OVERDOSAGE

For management of a suspected drug overdose, contact your regional Poison Control Centre.

Excessive administration of PLASMA-LYTE 148 and 5% Dextrose Injection can cause:

- Hyperglycemia, hyperosmolarity, osmotic diuresis, and dehydration.
- Metabolic alkalosis may be accompanied by hypokalemia as well as a decrease in ionized serum calcium and magnesium.
- Fluid and sodium overload with a risk of edema (peripheral and/or pulmonary), particularly when renal sodium excretion is impaired.
- Excessive administration of potassium may lead to the development of hyperkalemia, especially in patients with severe renal impairment.
- Excessive administration of magnesium may lead to hypermagnesemia.
- See also **WARNINGS AND PRECAUTIONS** and **ADVERSE REACTIONS** sections

When assessing an overdose, any additives in the solution must also be considered.

Clinically significant overdose of PLASMA-LYTE 148 and 5% Dextrose Injection may, therefore, constitute a medical emergency.

Interventions include discontinuation of PLASMA-LYTE 148 and 5% Dextrose Injection administration, dose reduction, administration of insulin and other measures as indicated for the specific clinical constellation.

SPECIAL HANDLING INSTRUCTIONS

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.

DOSAGE FORM, COMPOSITION AND PACKAGING

How Supplied

Table 1 shows the composition, osmolarity, approx pH, calories/litre and ionic concentration of PLASMA-LYTE 148 and 5% Dextrose Injection.

PLASMA-LYTE 148 and 5% Dextrose Injection is packaged in a 1000 mL Viaflex plastic container which is fabricated from a specially formulated polyvinyl chloride (PL 146 Plastic).

Storage

Store at 15ºC to 25ºC.

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