

PRESCRIBING INFORMATION

5% Dextrose Injection, USP
In AVIVA Plastic Container

IV Fluid and Nutrient Replenisher

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5% Dextrose Injection, USP

In AVIVA Plastic Container

SUMMARY PRODUCT INFORMATION

5% Dextrose Injection, USP is a sterile, nonpyrogenic solution for fluid replenishment and caloric supply in single dose containers for intravenous administration. It contains no bacteriostatic or antimicrobial agents or added buffers.

The composition, osmolarity and approx. pH of 5% Dextrose Injection, USP are shown in Table 1.

Table 1. Product information

	DIN	Package Size	Composition (g/L)	Osmolarity (mOsmol/L)	pH	Caloric Content (cal/L)
			Dextrose Hydrous*, USP			
5% Dextrose Injection, USP	00060348	250mL	50	252	3.2 – 6.5	170

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

The flexible AVIVA plastic container is made with non-latex plastic materials specially designed for a wide range of parenteral drugs including those requiring delivery in containers made of polyolefins or polypropylene. For example, the AVIVA container system is compatible with the admixture and administration of paclitaxel. In addition, the AVIVA container system is compatible with the admixture and administration of all drugs deemed compatible with existing polyvinyl chloride container systems. The solution contact materials do not contain PVC, DEHP or other plasticizers.

No safety issues of the plastic material were identified in Class VI U.S.Pharmacopeia (USP) testing for plastic containers.

The flexible container is a closed system and air is pre-filled in the container to facilitate drainage. The container does not require entry of external air during administration.

The container has two ports: one is the administration outlet port for attachment of an intravenous administration set and the other port has a medication site for addition of supplemental medication (See Directions for Use). The primary function of the overwrap is to protect the container from the physical environment.

ACTIONS

5% Dextrose Injection, USP has value as a source of water and calories. It is capable of inducing diuresis depending on the clinical condition of the patient.

INDICATIONS

5% Dextrose Injection, USP is indicated as a source of water and calories.

CONTRAINDICATIONS

5% Dextrose Injection, USP, is contraindicated in the following conditions:

- Hypersensitive to any ingredient in the formulation or component of the container. For a complete listing, see the Dosage Forms, Composition and Packaging section of the Prescribing Information.
- Hyperglycemia

- Known allergy to corn or corn products since dextrose in the product is purified from corn.

WARNINGS AND PRECAUTIONS

General

Normal physiologic isotonicity range is approximately 280-310 mOsmol/liter. Rapid administration of a large volume of 5% Dextrose Injection, USP may cause hemolysis due to its relatively low osmolarity (see Table 1).

5% Dextrose Injection, USP (an electrolyte-free dextrose aqueous solution) should not be administered simultaneously with blood through the same administration set because of the possibility of pseudoagglutination or hemolysis.

Excessive administration of this potassium-free product may result in significant hypokalemia.

5% Dextrose Injection, USP should be used with caution in patients with overt or subclinical diabetes mellitus.

Caution must be exercised in the administration of parenteral fluids to patients receiving corticosteroids or corticotropin.

This product may contain fructose as an impurity in the dextrose material. Exercise caution when the product is used in patients with hereditary fructose intolerance. In these patients, fructose may result in hypoglycemia, metabolic acidosis, liver toxicity which manifests as vomiting, nausea, sweating, jaundice, hemorrhage, seizures or coma or even death. The severity of the reactions is dependent on the amount and duration of fructose intake.

WARNING: This product contains aluminum which may be toxic. Aluminum may reach toxic levels with prolonged parenteral administration if kidney function is impaired. Premature neonates are particularly at risk because their kidneys are immature, and they require large amounts of calcium and phosphate solutions, which contain aluminum.

Research indicates that patients with impaired kidney function, including premature neonates, who receive parenteral levels of aluminum at greater than 4 to 5 mcg/kg/day accumulate aluminum at levels associated with central nervous system and bone toxicity. Tissue loading may occur at even lower rates of administration.

This product contains no more than 25 mcg/L of aluminum.

Risk of Air Embolism

Do not use plastic containers in series connections. Such use could result in air embolism due to residual air being drawn from the primary container before the administration of the fluid from the secondary container is completed.

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.

Hypersensitivity Reactions

Hypersensitivity/infusion reactions, including anaphylactic/anaphylactoid reactions, have been reported with 5% Dextrose Injection, USP (see Adverse Reactions).

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.

Dilution and other effects on serum electrolytes

Depending on the volume and rate of infusion and depending on a patient's underlying clinical condition and capability to metabolize dextrose, administration of this product can cause:

- Hyperosmolality, osmotic diuresis and dehydration
- Hypoosmolality
- Electrolyte disturbances such as
 - Hyponatremia,
 - Hypokalemia,

- Hypophosphatemia,
- Hypomagnesemia,
- overhydration/Hypervolemia and, for example, congested states, including pulmonary congestion and edema

Hypoosmotic Hyponatremia

Hypoosmotic hyponatremia can lead to headache, nausea, seizures, lethargy, coma, cerebral edema, and death. Acute symptomatic hyponatremic encephalopathy is considered a medical emergency.

The risk for developing hypoosmotic hyponatremia is increased, for example,

- in children
- in elderly patients
- in women
- postoperatively
- in persons with psychogenic polydipsia

The risk for developing encephalopathy as a complication of hypoosmotic hyponatremia is increased, for example,

- in pediatric patients (≤ 16 years of age)
- in women (in particular, premenopausal women)
- in patients with hypoxemia
- in patients with underlying central nervous system disease

Particular caution is advised in patients at increased risk of and from water and electrolyte disturbances that could be aggravated by increased free water load, hyperglycemia or possibly required insulin administration (see below).

Preventive and corrective measures must be instituted as clinically indicated.

Hyperglycemia

Rapid administration of dextrose solutions may produce substantial hyperglycemia which may result in or contribute to electrolyte losses, dehydration and hypovolemia due to osmotic diuresis and a hyperosmolar syndrome. At certain clinical conditions it also may increase the risk of hypoosmotic hyponatremia by shifting of intracellular water to extracellular space.

Use with caution in critically ill patients in whom hyperglycemia commonly occurs due to diabetes, impaired glucose tolerance, impaired fasting glucose, or is stress-induced.

Hyperglycemia may increase the risk of cardiac complications, infection, systemic sepsis, acute renal failure and even death in certain clinical conditions, especially in acute stress conditions.

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 to the level suitable to the patient's ability to utilize glucose and/or insulin administered if blood glucose levels exceed levels considered acceptable for the individual patient.

5% Dextrose Injection, USP 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 (see above)
- 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.
- Newborns (see Special Populations/Pediatrics)

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.

MONITORING AND LABORATORY TESTS

Clinical evaluation and periodic laboratory determination 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.

Carcinogenesis and Mutagenesis

Studies with 5% Dextrose Injection, USP have not been performed to evaluate carcinogenic potential, mutagenic potential, or effects on fertility.

SPECIAL POPULATIONS

Pregnancy and Lactation

There are no adequate data from the use of 5% Dextrose Injection, USP in pregnant or lactating women.

It is not known whether 5% Dextrose Injection, USP can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. 5% Dextrose Injection, USP should be given to a pregnant woman only if clearly needed.

Studies have not been conducted to evaluate the effects of 5% Dextrose Injection, USP on labour and delivery. Caution should be exercised when administering this drug during labour and delivery.

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 5% Dextrose Injection, USP is administered to a nursing woman.

Intrapartum maternal intravenous dextrose infusion may result in fetal insulin production, with an associated risk of fetal hyperglycemia and metabolic acidosis as well as rebound hypoglycemia in the neonate.

Healthcare practitioners should carefully consider the potential risks and benefits for each specific patient before administering.

Pediatrics

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.

Pediatric Glycemia-related Issues

Newborns – especially those born premature and with low birth weight, are at increased risk of developing hypo- or hyperglycemia. Close monitoring during treatment with intravenous dextrose solutions is needed to ensure adequate glycemic control, in order to avoid potential long term adverse effects.

HYPOglycemia in the newborn can cause:

- prolonged seizures,
- coma, and
- cerebral injury.

HYPERglycemia has been associated with

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

Pediatric Hyponatremia-related Issues

Children (including neonates and older children) are at increased risk of developing hypoosmotic hyponatremia as well as for developing hyponatremic encephalopathy.

Hypoosmotic hyponatremia can lead to headache, nausea, seizures, lethargy, coma, cerebral edema and death; therefore, acute symptomatic hyponatremic encephalopathy is considered a medical emergency.

Plasma electrolyte concentrations should be closely monitored in the pediatric population.

Rapid correction of hypoosmotic hyponatremia is potentially dangerous (risk of serious neurologic complications). Dosage, rate, and duration of administration should be determined by a physician experienced in pediatric intravenous fluid therapy.

Geriatrics

Clinical studies of 5% Dextrose Injection, USP 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 drug therapy.

ADVERSE REACTIONS

Reactions which may occur because of the solution or the technique of administration include infection at the site of injection, venous thrombosis or phlebitis extending from the site of injection, extravasation and hypervolemia.

The list of adverse reactions in this Prescribing Information is based on post-marketing reports (see below).

If an 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 post-marketing experience, listed by MedDRA System Organ Class (SOC), then, where feasible, by Preferred Term in order of severity.

IMMUNE SYSTEM DISORDERS: Hypersensitivity/infusion reactions, including anaphylactic/anaphylactoid reactions, including reactions with mild manifestations, e.g., Pruritus, and reactions with severe manifestations, e.g., Bronchospasm, Cyanosis, Angioedema and Hypotension; Pyrexia, Chills

METABOLISM AND NUTRITION DISORDERS: Hyperglycemia

SKIN AND SUBCUTANEOUS TISSUE DISORDERS: Rash

GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS: Infusion site reactions including, Infusion site phlebitis, Infusion site erythema

Other adverse reactions reported with dextrose injection/infusions include:

Hyponatremia, which may be symptomatic (see "Hypoosmotic hyponatremia" in WARNINGS AND PRECAUTIONS).

DRUG INTERACTIONS

Studies have not been conducted to evaluate additional drug/drug or drug/food interactions with 5% Dextrose Injection, USP.

Both the glycemic effects of 5% Dextrose Injection, USP and its effects on water and electrolyte balance should be taken into account when using 5% Dextrose Injection, USP in patients treated with other substances that affect glycemic control, or fluid and/or electrolyte balance.

DOSAGE AND ADMINISTRATION

As directed by a physician. Dosage is dependent upon the age, weight and clinical condition of the patient as well as laboratory determinations.

The infusion rate and volume depends on the age, weight, clinical and metabolic conditions of the patient, as well as concomitant therapy. For pediatric patients, consult a physician experienced in pediatric intravenous fluid therapy.

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

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

Do not administer unless solution is clear and seal is intact.

5% Dextrose Injection, USP in AVIVA plastic container is intended for intravenous administration using sterile equipment. It is recommended that intravenous administration apparatus be replaced at least once every 24 hours.

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

Additives may be incompatible. When introducing additives to 5% Dextrose Injection, USP, the instructions for use of the medication to be added and other relevant literature must be consulted.

Those additives known to be incompatible with dextrose should not be used. Consult with pharmacist if available. If in the informed judgment of the physician it is deemed advisable to introduce additives, aseptic technique must be used.

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

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

Mix thoroughly when additives have been introduced. Do not store solutions containing additives.

For single use only.

Discard any unused portion.

OVERDOSAGE

Excess administration of the product can cause significant disturbance in water and electrolyte balance, hyperglycemia and corresponding complications (see Warnings and Precautions and Adverse Reactions). For example, severe hyperglycemia and severe dilutional hyponatremia, and their complications, can be fatal.

Interventions include discontinuation of infusion of the product dose reduction, administration of insulin and/or other measures as indicated for the specific clinical constellation.

Clinically significant overdose of the product may, therefore, constitute a medical emergency.

DOSAGE FORM, COMPOSITION AND PACKAGING

How Supplied

Table 1 shows the composition, osmolarity, approx pH, calories/litre, ionic concentration and available sizes of 5% Dextrose Injection, USP in AVIVA Plastic Container.

Per 100 mL: Dextrose Hydrous 5 g, Water for Injection

Directions for use of AVIVA 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.

Do not remove unit from overwrap until ready to use.

To Open

Tear overwrap down side at slit and remove solution container. Moisture and 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 and safety. The opacity will diminish gradually. Check for minute leaks by squeezing inner bag firmly. If leaks are found discard solution as sterility may be impaired. If supplemental medication is desired, follow "To Add Medication" directions below.

Preparation for Administration

Caution: Do not use plastic containers in series connections

Caution: Use only with a non-vented set or a vented set with the vent closed.

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

Additives may be incompatible.

To add medication before solution administration:

1. Prepare medication site.
2. Using syringe with 19 to 22 gauge needle, puncture resealable medication port and inject.
3. Mix solution and medication thoroughly. For high density medications such as potassium chloride, squeeze ports while ports are upright and mix thoroughly.

To add medication during solution administration:

1. Close clamp on the set.
2. Prepare medication site.
3. Using syringe with 19 to 22 gauge needle, puncture resealable medication port and inject.
4. Remove container from IV pole and/or turn to an upright position.
5. Evacuate both ports by 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.

Storage

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

Store at 15°C to 25°C

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