

PRESCRIBING INFORMATION

**5% DEXTROSE INJECTION USP**

**10% DEXTROSE INJECTION USP**

**In Excel Plastic Containers**

Solution for Infusion, Intravenous

Intravenous Fluid and Nutrient Replenisher

**B|BRAUN**

**B. Braun Medical Inc.**  
824 Twelfth Avenue  
Bethlehem, PA 18018-3524 USA

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**B. Braun of Canada, Ltd.**  
2000 Ellesmere Road, Unit 16  
Scarborough, Ontario M1H 2W4

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**5% Dextrose Injection USP  
10% Dextrose Injection USP  
In Excel Plastic Containers**

**SUMMARY PRODUCT INFORMATION**

5% Dextrose Injection USP and 10% Dextrose Injection USP are sterile, nonpyrogenic solutions for fluid replenishment and caloric supply in single dose containers for intravenous administration. They contain no bacteriostatic or antimicrobial agents or added buffers.

The composition, osmolarity, approximate pH, and caloric content of 5% Dextrose Injection USP and 10% Dextrose Injection USP are shown in **Table 1**.

**Table 1: Product Information**

Product Name	DIN	Package Size (mL)	Composition (g/100 mL)*	Osmolarity (mOsmol/L)	pH (range)	Caloric Content (cal/L)
			Hydrous Dextrose USP**			
5% Dextrose Injection USP	01924281	250	5	250	4.4 (3.5 - 6.5)	170
		500				
		1000				
10% Dextrose Injection USP	01924427	250	10	505	4.4 (3.5 - 6.5)	340
		500				
		1000				

\* Non-medicinal ingredient = Water for Injection (qs)

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

Excel Plastic Container not made with natural rubber latex, PVC or DEHP.

The plastic container is made from a multilayered film specifically developed for parenteral drugs. It contains no plasticizers and exhibits virtually no leachables. The solution contact layer is a rubberized copolymer of ethylene and propylene. The container is nontoxic and biologically inert. The container-solution unit is a closed system and is not dependent upon entry of external air during administration.

The container is overwrapped to provide protection from the physical environment and to provide an additional moisture barrier when necessary.

The closure system has two ports; the one for the administration set has a tamper evident plastic protector and the other is a medication addition site. Refer to the **Directions for Use of Excel Container**.

**ACTIONS**

5% Dextrose Injection USP and 10% Dextrose Injection USP have 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 and 10% Dextrose Injection USP are indicated as a source of water and calories.

## CONTRAINDICATIONS

5% Dextrose Injection USP and 10% Dextrose Injection USP are 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.
- Clinically significant hyperglycemia
- Known allergy to corn or corn products since dextrose in the products 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 may cause hemolysis due to its relatively low osmolarity (see **Table 1**).

Administration of 10% Dextrose Injection USP may cause vein irritation and phlebitis due to its high osmolarity (**Table 1**).

5% Dextrose Injection USP and 10% Dextrose Injection USP (electrolyte-free dextrose aqueous solutions) should not be administered simultaneously with blood through the same administration set because of the possibility of pseudoagglutination or hemolysis.

Excessive administration of these potassium-free products may result in significant hypokalemia.

5% Dextrose Injection USP and 10% 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.

These products may contain fructose as an impurity in the dextrose material. Exercise caution when they are used in patients with hereditary fructose intolerance due to aldolase deficiency. 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:** These products contain 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.

These products contain no more than 25 mcg/L of aluminum.

## **Risk of Air Embolism**

Do not connect flexible plastic containers in series connections. Such use could result in air embolism due to possible 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 and 10% 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, intravenous administration of dextrose can cause:

- Hyperosmolality, osmotic diuresis and dehydration
- Hypo- or hyperosmotic hypoosmolality (see below),
- Electrolyte disturbances such as
  - Hyponatremia,
  - Hypokalemia,
  - Hypophosphatemia,
  - Hypomagnesemia,
  - Overhydration/Hypervolemia and, for example, congested states, including pulmonary congestion and edema.

The above effects do not only result from the administration of electrolyte-free fluid but also from dextrose administration. In addition:

- An increase in serum glucose concentration is associated with an increase in serum osmolarity. Osmotic diuresis associated with hyperglycemia can result in or contribute to the development of dehydration and in electrolyte losses.
- Hyperglycemia also causes a transcellular shift of water, leading to a decrease in extracellular sodium concentrations and hyponatremia.

- Since the dextrose in Dextrose 5% Injection USP and Dextrose 10% Injection USP is metabolized, infusion of Dextrose 5% Injection USP and Dextrose 10% Injection USP corresponds to increasing the body's load of free water, possibly leading to hypoosmotic hyponatremia.

Monitoring of serum sodium is particularly important. High volume infusion must be used under specific monitoring in patients with cardiac or pulmonary failure, and in patients with non-osmotic vasopressin release (including syndrome of inappropriate antidiuretic hormone secretion (SIADH)), due to the risk of hospital-acquired hyponatremia.

### **Hypoosmotic Hyponatremia**

Acute hyponatremia can lead to acute hyponatremic encephalopathy (brain edema) characterized by headache, nausea, seizures, lethargy and vomiting. Patients with brain edema are at particular risk of severe, irreversible and life-threatening brain injury.

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

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.

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 and 10% 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 and 10% 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 and 10% Dextrose Injection USP in pregnant or lactating women.

It is not known whether 5% Dextrose Injection USP and 10% Dextrose Injection USP can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. 5% Dextrose Injection USP and 10% 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 and 10% 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 and 10% 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 5% Dextrose Injection USP and 10% Dextrose Injection USP.

### **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.

HYPORGlycemia 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.

Acute hyponatremia can lead to acute hyponatremic encephalopathy (brain edema) characterized by headache, nausea, seizures, lethargy and vomiting. Patients with brain edema are at particular risk of severe, irreversible and life-threatening brain injury.

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 and 10% 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 other similar products include:

- Hyponatremia, which may be symptomatic (see “Hypoosmotic hyponatremia” in WARNINGS AND PRECAUTIONS).
- Hyponatremic encephalopathy
- Infusion site thrombophlebitis (associated with Hyperosmolar solutions) [for 10% Dextrose Injection USP only]
- Adverse reactions reported with parenteral nutrition to which the dextrose component may play a causal or contributory role include [for 10% Dextrose Injection USP only]:
  - Hepatic failure, Hepatic cirrhosis, Hepatic fibrosis, Cholestasis, Hepatic steatosis, Blood bilirubin increased, Hepatic enzyme increased, Cholecystitis, Cholelithiasis
  - Pulmonary vascular precipitates

## DRUG INTERACTIONS

Studies have not been conducted to evaluate additional drug/drug or drug/food interactions with 5% Dextrose Injection USP and 10% Dextrose Injection USP.

Both the glycemic effects of 5% Dextrose Injection USP and 10% Dextrose Injection USP and its effects on water and electrolyte balance should be taken into account when using 5% Dextrose Injection USP and 10% Dextrose Injection USP in patients treated with other substances that affect glycemic control, or fluid and/or electrolyte balance.

Caution is advised when administering 5% Dextrose Injection USP and 10% Dextrose Injection USP to patients treated with drugs leading to an increased vasopressin effect. The below listed drugs increase the vasopressin effect, leading to reduced renal electrolyte free water excretion and may increase the risk of hyponatremia following treatment with intravenous fluids (See Warnings and Precautions and Adverse Reactions)

**Drugs stimulating vasopressin release** such as chlorpropamide, clofibrate, carbamazepine, vincristine, selective serotonin reuptake inhibitors (SSRIs), 3,4-methylenedioxy-N-methamphetamine, ifosfamide, antipsychotics, opioids.

**Drugs potentiating vasopressin action** such as chlorpropamide, non steroidal anti inflammatories (NSAIDS), cyclophosphamide.

**Vasopressin analogues** such as desmopressin, oxytocin, vasopressin, terlipressin.

Caution is advised when administering 5% Dextrose Injection USP and 10% Dextrose Injection USP to patients treated with drugs that may increase the risk of hyponatremia, such as diuretics and antiepileptics (e.g., oxcarbazepine).

## 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.

5% Dextrose Injection USP has an osmolarity of 250 mOsmol/L. 10% Dextrose Injection USP has an osmolarity of 505 mOsmol/L. Administration of hyperosmolar solutions may cause venous

irritation and phlebitis. For 10% Dextrose Injection USP, the osmolarity of a final admixed infusion 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.

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 the container and seal is intact.

5% Dextrose Injection USP and 10% Dextrose Injection USP in Excel plastic container are 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 and 10% 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 and 10% 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. After opening the Excel plastic container, the contents should be used immediately and should not be stored for a subsequent infusion. Do not reconnect any partially used Excel plastic containers. Discard any unused portion.

## **OVERDOSAGE**

Excess administration of 5% Dextrose Injection USP and 10% Dextrose Injection USP can cause hyperglycemia, adverse effects on water and electrolyte balance, 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 5% Dextrose Injection USP and 10% Dextrose Injection USP administration, dose reduction, administration of insulin and other measures as indicated for the specific clinical constellation.

Clinically significant overdose of 5% Dextrose Injection USP and 10% Dextrose Injection USP may, therefore, constitute a medical emergency.

## DOSAGE FORM, COMPOSITION AND PACKAGING

### How supplied

**Table 1** shows the composition, osmolarity, approximate pH, calories/litre and available sizes of 5% Dextrose Injection USP and 10% Dextrose Injection USP.

5% Dextrose Injection USP and 10% Dextrose Injection USP are supplied in sterile and nonpyrogenic EXCEL<sup>®</sup> Containers. The 1000 mL containers are packaged 12 per case, the 500 mL and 250 mL containers are packaged 24 per case.

### Directions for use of Excel Container

**Caution:** Do not use plastic containers in series connection.

### To Open

Tear overwrap down at notch and remove solution container. Check for minute leaks by squeezing solution container firmly. If leaks are found, discard solution as sterility may be impaired. If supplemental medication is desired, follow directions below before preparing for administration.

**NOTE:** Before use, perform the following checks:

- Inspect each container. Read the label. Ensure solution is the one ordered and is within the expiration date.
- Invert container and carefully inspect the solution in good light for cloudiness, haze, or particulate matter. Any container, which is suspect, should not be used.
- Use only if solution is clear and container and seals are intact.

### Preparation for Administration

1. Remove plastic protector from sterile set port at bottom of container.
2. Attach administration set. Refer to complete directions accompanying set.

### To Add Medication

**Warning:** Some additives may be incompatible.

Addition of medication should be accomplished using complete aseptic technique.

### To Add Medication before Solution Administration

1. Prepare medication site.
2. Using syringe with 18–22 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 18–22 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.

## **STORAGE**

Exposure of pharmaceutical products to heat should be minimized. Avoid excessive heat. Protect from freezing. It is recommended that the product be stored at room temperature (25°C); however, brief exposure up to 40°C does not adversely affect the product.

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