MANNITOL- mannitol injection, solution
Fresenius Kabi USA, LLC

Mannitol Injection, USP

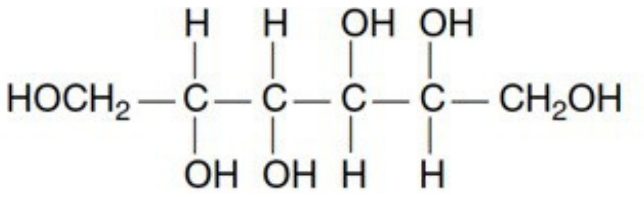
Rx only

25%

For Intravenous Use and Urologic Irrigation

DESCRIPTION

Mannitol is a 6-carbon sugar alcohol and has the following structure:



$C_6H_{14}O_6$ **182.17**

Mannitol occurs naturally in fruits and vegetables, and is metabolically inert in humans.

Mannitol Injection, USP, 25%, an osmotic diuretic, is a sterile, nonpyrogenic solution of mannitol in Water for Injection. It is a supersaturated solution at room temperature.

Each mL contains: Mannitol 250 mg; Water for Injection q.s. The osmolar concentration is 1372 mOsmol/L (calc.). It contains no antimicrobial agents. The pH of a 5% solution is between 4.5 and 7.0.

CLINICAL PHARMACOLOGY

Mannitol is an osmotic diuretic. After intravenous injection it is confined to the extracellular space, metabolized only slightly and excreted rapidly by the kidneys. Approximately 80% of a 100 g dose appears in the urine in three hours. Mannitol is freely filtered by the glomeruli with less than 10% tubular reabsorption. It is not secreted by tubular cells. It induces diuresis by elevating the osmolarity of the glomerular filtrate and thereby hinders tubular reabsorption of water. Urinary output of water and excretion of sodium and chloride are enhanced. Mannitol is poorly absorbed from the gastrointestinal tract.

Mannitol injection is free of electrolytes and is used in urology as a nonhemolytic irrigant. The amount of mannitol absorbed intravascularly during transurethral prostatic surgery is variable and depends primarily on the extent of the surgery. Such mannitol is excreted by the kidneys and produces osmotic diuresis.

INDICATIONS AND USAGE

For Intravenous Injection

Mannitol Injection, USP is indicated for the following therapeutic uses:

• The promotion of diuresis, in the prevention and/or treatment of the oliguric phase of acute renal failure before irreversible renal failure becomes established.

• The reduction of intracranial pressure and treatment of cerebral edema by reducing brain mass.

• The reduction of elevated intraocular pressure when it cannot be lowered by other means.

• The promotion of urinary excretion of toxic substances.

For Urologic Irrigation

Mannitol solution, 2.5% is indicated as an irrigation solution in transurethral prostatic resection or other transurethral surgical procedures.

CONTRAINDICATIONS

• Well established anuria due to severe renal disease.

• Severe pulmonary congestion or frank pulmonary edema.

• Active intracranial bleeding except during craniotomy.

• Severe dehydration.

• Progressive renal damage or dysfunction after institution of mannitol therapy, including increasing oliguria and azotemia.

• Progressive heart failure or pulmonary congestion after mannitol therapy is started.

WARNINGS

In severe impairment of renal function a test dose should be given (see **DOSAGE AND ADMINISTRATION**). A second test dose may be given if there is an inadequate response. No more than two test doses should be attempted.

Excessive loss of water and electrolytes may lead to serious imbalances. Serum sodium and potassium should be carefully monitored during mannitol therapy.

The diuresis after rapid infusion of mannitol may increase preexisting hemoconcentration. With continued use of mannitol a loss of water in excess of electrolytes can cause hypernatremia.

Shift of sodium-free intracellular fluid into the extracellular compartment after mannitol infusion may lower serum sodium concentration and aggravate preexisting hyponatremia.

Closely monitor the urine output and discontinue mannitol infusion promptly if output is low. Inadequate urine output results in accumulation of mannitol, expansion of

extracellular fluid volume and could result in water intoxication or congestive heart failure. Renal function must be closely monitored during mannitol infusion.

Mannitol solution must be used with caution in patients with significant cardiopulmonary or renal dysfunction.

Irrigating solutions used in transurethral prostatectomy have been shown to enter the systemic circulation in relatively large volumes, exert a systemic effect and may significantly alter cardiopulmonary and renal dynamics.

PRECAUTIONS

General

Crystals, if present in mannitol injection, 25%, may be dissolved by placing the vial in a hot water bath maintained at 60° to 80°C with occasional shaking. The resulting solution should be allowed to cool to body temperature before injection.

An administration set with a filter should be used for intravenous infusions of solutions containing 20% or more of mannitol.

NOTE: Use of any other method to heat the vial may result in its explosion.

The cardiovascular status should be carefully evaluated before mannitol is administered by rapid intravenous injection or before and during transurethral resection since expansion of extracellular fluid may lead to fulminating congestive heart failure.

By sustaining diuresis, mannitol may obscure and intensify inadequate hydration or hypovolemia.

Unless it is essential, electrolyte-free mannitol solutions should not be combined with blood. When it is essential to give the combination, at least 20 mEq of sodium chloride should be added to each liter of mannitol solution to avoid pseudoagglutination. The contents of opened containers should be used promptly and unused contents should be discarded.

A white flocculant mannitol precipitate may result from contact with PVC surfaces which act as nuclei for rapid rate crystallization of small crystals. This condition has also been reported to occur when mannitol has come in contact with other plastic and rough glass surfaces. Attempting to resolubilize the white flocculant precipitate with the aid of heat is not useful because crystallization may recur in a short period of time.

Carcinogenesis, Mutagenesis, Impairment of Fertility

In an early study of 1, 5 or 10% mannitol, given for 94 weeks in the diet of Wistar rats, a low incidence of benign thymomas occurred in females which was apparently treatment related. A subsequent life-time study at similar dose levels in Spraque-Dawley, Fischer and Wistar rats revealed no carcinogenic effect in the thymus.

Mannitol had no mutagenic activity in a series of *in vitro* and *in vivo* test systems.

Adequate studies measuring the effects of mannitol on fertility have not been done.

Pregnancy

Pregnancy Category B–Teratogenic studies in the mouse, rat and rabbit at oral doses up to 1600 mg/kg did not reveal harm to the fetus or adverse effects on reproduction due to mannitol. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nursing Mothers

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when mannitol is given to a nursing mother.

Pediatric Use

Dosage requirements in children below the age of 12 years have not been established.

ADVERSE REACTIONS

Reactions are infrequent and may include:

To report SUSPECTED ADVERSE REACTIONS, contact Fresenius Kabi USA, LLC at 1-800-551-7176 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Metabolic: fluid and electrolyte imbalance, acidosis, dehydration.

Gastrointestinal: dryness of mouth, nausea, vomiting, diarrhea.

Genitourinary: osmotic nephrosis, urinary retention.

Central Nervous System: headache, convulsions, dizziness.

Special Senses: Blurred vision, rhinitis.

Cardiovascular: pulmonary edema, edema, hypotension, hypertension, tachycardia, angina-like chest pains.

Dermatologic: skin necrosis, thrombophlebitis.

Hypersensitivity: urticaria.

Miscellaneous: thirst, arm pain, chills, fever.

DOSAGE AND ADMINISTRATION

For Intravenous Injection

General Recommendations–Give mannitol injection only intravenously. The total dosage, concentration and rate of administration should be governed by the nature and severity of the condition being treated, fluid requirement and urinary output. Usual adult dosage ranges from 50 to 200 g in 24 hours but in most instances an adequate response will be achieved at a dosage of approximately 100 g in 24 hours. The rate is usually adjusted to maintain an adequate urine flow (at least 30 to 50 mL/hr).

Test Dose–In marked oliguria or inadequate renal function a test dose of mannitol should be given. The test dose may be approximately 0.2 g/kg (about 50 mL of a 25% solution)

infused in three to five minutes to produce an adequate urine flow (at least 30 to 50 mL/hr). If urine flow does not increase within two or three hours a second test dose may be given. If there is an inadequate response the patient should be reevaluated.

Prevention of Acute Renal Failure (Oliguria)–When used during surgery, immediately postoperatively or following trauma, 50 to100 g of mannitol as a 5 to 25% solution maybe given. The concentration and amount will depend upon the fluid requirements of the patient. Following suspected or actual hemolytic transfusion reactions 20 g of mannitol may be given intravenously over a five minute period to provoke diuresis. If diuresis does not occur the 20 g dose may be repeated. If there is an adequate urine flow (30 to 50 mL/hr) then intravenous fluids containing not more than 50 to 75 mEq of sodium per liter should be given in sufficient volume to match the desired urine flow (100 mL/hr) until fluids can be taken orally.

Treatment of Oliguria–The usual dose for treatment of oliguria is 50 to 100 g as a 15 to 25% solution.

Reduction of Intracranial Pressure, Cerebral Edema or Intraocular Pressure–A 25% solution of mannitol is recommended since its effectiveness depends on establishing intravascular hyperosmolarity. When used before or after surgery, a total dose of 1.5 to 2 g/kg can be given over a period of 30 to 60 minutes. Careful evaluation must be made of the circulatory and renal reserve prior to and during use of mannitol at this relatively high dose and rapid infusion rate. Careful attention must be paid to fluid and electrolyte balance, body weight, and total input and output before and after infusion of mannitol. Evidence of reduced cerebral spinal fluid pressure may be observed within 15 minutes after starting infusion.

Maximal reduction of intraocular pressure occurs 30 to 60 minutes after injection.

Urinary Excretion of Toxic Substances–Mannitol in 5 to 25% solutions is used as an infusion as long as indicated if the level of urinary output remains high. The concentration will depend upon the fluid requirement and urinary output. Intravenous water and electrolytes must be given to replace the loss of these substances in the urine, sweat and expired air. If benefits are not observed after 200 g of mannitol are given, discontinue it.

PREPARATION OF DILUTIONS FOR INTRAVENOUS INJECTION

Concentration	How Prepared	
Test dose	Use as supplied (25%)	
5% –	50 mL of mannitol plus 200 mL	of 5% Dextrose Injection or in a clinically appropriate electrolyte solution
10% –	50 mL of mannitol plus 75 mL	
15% –	50 mL of mannitol plus 33.3 mL	
20% –	50 mL of mannitol plus 12.5 mL	
25% –	Use as supplied	

For Urologic Irrigation

A 2.5% solution is used. The use of 2.5% mannitol solution minimizes the hemolytic effect of water alone, the entrance of hemolyzed blood into the circulation, and the

resulting hemoglobinemia which is considered a major factor in producing serious renal complications.

PREPARATION OF DILUTIONS FOR UROLOGIC IRRIGATION	
Concentration	**How Prepared**
2.5%	Add contents of two 50 mL vials (25% mannitol) to 900 mL Sterile Water for Injection.

HOW SUPPLIED:

Mannitol Injection, USP, 25%

Product Code	Unit of Sale	Strength	Each
1550	NDC 63323-024-25 Unit of 25	250 mg per mL	NDC 63323-024-01 50 mL Single Dose Flip-off Top Vial

Use only if solution is clear and seal intact and undamaged.

Store at 20° to 25°C (68° to 77°F) [see USP Controlled Room Temperature].

Preservative Free. Discard unused portion.

www.fresenius-kabi.com/us

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Revised: November 2022

PACKAGE LABEL - PRINCIPAL DISPLAY - Mannitol 50 mL Single Dose Vial Label

NDC63323-024-01 1550

MANNITOL

INJECTION, USP

25%

12.5 g per 50 mL

(250 mg per mL)

For Intravenous Use

and Urologic Irrigation

50 mL
Single Dose Vial

Rx only

PACKAGE LABEL - PRINCIPAL DISPLAY - Mannitol 50 mL Single Dose Vial Tray Label

NDC 63323-024-25 1550

MANNITOL

INJECTION, USP

25%

12.5 g per 50 mL

(250 mg per mL)

For Intravenous Use and

Urologic Irrigation

25 x 50 mL

Single Dose Vials Rx only

MANNITOL

mannitol injection, solution

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:63323-024
Route of Administration	INTRAVENOUS		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
MANNITOL (UNII: 3OWL53L36A) (MANNITOL - UNII:3OWL53L36A)	MANNITOL	250 mg in 1 mL

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:63323-024-25	25 in 1 TRAY	03/19/2000	
1	NDC:63323-024-01	50 mL in 1 VIAL, SINGLE-DOSE; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA080677	03/19/2000	

Labeler - Fresenius Kabi USA, LLC (608775388)

Establishment

Name	Address	ID/FEI	Business Operations
Fresenius Kabi USA, LLC		840771732	manufacture(63323-024) , analysis(63323-024)