OSMITROL Injection (Mannitol Injection, USP) in VIAFLEX Plastic Container

For Therapeutic Use Only

**Description**

OSMITROL Injection (Mannitol Injection, USP) is a sterile, nonelectrolyte, obligatory, nonpyrogenic solution of Mannitol, USP in a single dose container for intravenous administration. It contains no preservatives. Mannitol is a semi-sweet sugar alcohol obtained by the chemical reduction of xylitol. It is found naturally in fruits and vegetables. Mannitol is an obligate cosmotropic solute. The solution is made isotonic with sodium hydroxide or hydrochloric acid. Composition, osmolarity, and pH are shown in Table 1.

**Clinical Pharmacology**

OSMITROL Injection (Mannitol Injection, USP) is one of the nonelectrolyte, obligatory, nonelectrolyte, nonpyrogenic solutions. It is freely filterable through a 0.2 micrometer filter and is not secreted by the tubule, and is pharmacologically inert. Mannitol, when administered intravenously, exerts its osmotic effect as a result of relatively small osmotic pressure being largely confined to the extracellular space. Only relatively small amounts of the dose administered is metabolized. Mannitol is readily filtered through the glomerulus of the kidney even at a wide range of normal and impaired renal function.

**Indications and Usage**

OSMITROL Injection (Mannitol Injection, USP) is indicated for:

- The reduction of intracranial pressure and treatment of cerebral edema by reducing the degree of appropriate patient monitoring.
- Promoting the urinary excretion of toxic substances.

**Contraindications**

OSMITROL Injection (Mannitol Injection, USP) is contraindicated in patients with:

- Well established anuria due to severe renal disease.
- Severe pulmonary congestion or frank pulmonary edema.
- Active intracranial bleeding except during craniotomy.
- Severe dehydration.
- Progressive heart failure or dysrhythmia after institution of mannitol therapy, including inducing diuresis and diaphoresis.
- Progressive heart failure or pulmonary congestion after institution of mannitol therapy.

**Warnings**

In patients with severe impairment of renal function, a test dose should be utilized (see Dosage and Administration). A second test dose may be tried if there is an inadequate response, but no more than two test doses should be attempted. The obligatory diuretic response following rapid infusion of 15% or 20% mannitol injection may further aggravate preexisting hemococoncentration. Excessive loss of water and sodium in renal failure may lead to severe dehydration. Serum sodium and potassium should be carefully monitored during mannitol administration. If urine output continues to decline during mannitol infusion, the patient's clinical status should be closely monitored. Accumulated mannitol in the extracellular fluid which may already exist, may modify existing or latent congestive heart failure.

Excessive loss of water and electrolytes may lead to serious irregularities. With continued administration of mannitol, loss of water in excess of electrolytes can cause hypernatremia. Electrolyte measurements, including sodium and potassium, are therefore, of vital importance in monitoring the infusion of mannitol.

**Precautions**

The cardiovascular status of the patient should be carefully evaluated before rapidly administering mannitol since sudden expansion of the extracellular fluid may lead to hemodynamic congestive heart failure.

Shift of sodium free intracellular fluid into the extracellular compartment following mannitol infusion may lower serum sodium concentration and aggravate preexisting renal insufficiency.

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

Electrolyte free mannitol injections should not be given conjointly with blood. If it is essential that both be given simultaneously, at least 20 mEq of sodium chloride should be administered, at least 20 mEq of sodium chloride should be added to each filter of mannitol solution to avoid pseudopagglutination.

When exposed to low temperatures, solutions of mannitol may crystallize. Concentrations greater than 15% have a greater tendency to crystallize. Heat crystals prior to use. No more than 15% mannitol injection should be added to 0.9% sodium chloride solution up to 70°C with agitation. Above the solution to cool to room temperature before reinspection for crystals.

**Dosage and Administration**

Administer intravenously using sterile, filter-type plastic containers as well as by infusion tubing for plastic containers as well as by infusion tubing for plastic containers. By sustaining diuresis, mannitol administration may obscure and intensify inadequate hydration or hypotension. Add 20 mEq sodium chloride to 1 liter of 15% mannitol solution to avoid postdeglutination. With continued administration of mannitol, loss of water in excess of electrolytes can cause hypernatremia. Electrolyte measurements, including sodium and potassium, are therefore, of vital importance in monitoring the infusion of mannitol.

**Laboratory Tests**

Although blood levels of mannitol can be measured, there is no reliable clinical benefit in doing so. The appropriate monitoring of blood levels of sodium and potassium, degree of hemococoncentration or hemodilution, if any, and the degree of renal, cardiac, and pulmonary function are paramount in avoiding excessive fluid and electrolyte shifts. The routine features of physical examination and clinical chemistry suffice in obtaining an adequate degree of appropriate patient monitoring.

**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 administered to a nursing woman.

**Table 1**

<table>
<thead>
<tr>
<th>Component</th>
<th>Composition</th>
<th>Osmolarity (mOsmol/L)</th>
<th>pH</th>
</tr>
</thead>
<tbody>
<tr>
<td>10% OSMITROL Injection (5% Mannitol Injection, USP)</td>
<td>1000</td>
<td>50</td>
<td>274</td>
</tr>
<tr>
<td>20% OSMITROL Injection (15% Mannitol Injection, USP)</td>
<td>500</td>
<td>100</td>
<td>549</td>
</tr>
<tr>
<td>30% OSMITROL Injection (20% Mannitol Injection, USP)</td>
<td>250</td>
<td>200</td>
<td>823</td>
</tr>
<tr>
<td>50% OSMITROL Injection (20% Mannitol Injection, USP)</td>
<td>500</td>
<td>100</td>
<td>1000</td>
</tr>
</tbody>
</table>

*Normal physiologic osmolarity range is approximately 280 to 310 mOsmol/L. Administration of substantially hypertonic solutions (> 15% mannitol injection) may cause vein damage.

**Proofreading Approval ________________________ ________________________ ________

07-19-47-259
Pediatric Use

Safety and effectiveness in children below the age of 12 have not been established.

Usage in Elderly

Dosage requirements for patients 70 years of age and under have not been established.

Geriatric Use

Clinical studies of OSMITROL Injection (Mannitol Injection, USP) did not include sufficient numbers of subjects aged 65 years 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 based on a knowledge of the drug's pharmacology and on the clinical condition of the patient. This drug is known to be substantially excreted by the kidney, and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it may be useful to monitor renal function.

Adverse Reactions

Eosinophilia of unknown etiology has rarely been reported in patients receiving mannitol. Patients with a history of allergies or hypersensitivity to this drug should be observed for manifestations of allergy. The urine may be dark brown due to the production of amino acids and amino sugars. The most frequent side reactions are hypotension, headache, blurred vision, convulsions and congestive cardiac failure. In addition to the reactions described above, other reports have included vomiting, rhinitis, local pain, skin necrosis and thrombophlebitis at the site of injection, chills, diarhoea, urticaria, hypotension, hypokalemia, hyperglycemia, fever and angina-like chest pain.

Of greater clinical significance is a variety of events that are related to inappropriate, recognition and monitoring of fluid shifts. There are no extrinsic adverse reactions to the drug but the consequences of mismanagement normally by any agency in a therapeutically inappropriate manner. Failure to recognize severe impairment of renal function with the high likelihood of nonrenal response can lead to unneeded administration of tissues and increased vascular fluid load. Induced diuresis in the presence of preexisting heart congestion and preexisting deficiency of water and electrolytes can lead to serious instability. Expansion of the extracellular space can aggravate cardiac decompensation or cause the formation of isolated heart failure. Perioperative diuretic in isolation can be antithetical. The clearance of water and electrolytes should be adequate. Specific use in the presence of preexisting heart failure is not recommended. Expansion of the extracellular space can aggravate cardiac decompensation or cause the formation of isolated heart failure. Perioperative diuretic in isolation can be antithetical. The clearance of water and electrolytes should be adequate. Specific use in the presence of preexisting heart failure is not recommended.

Reduction of Intracranial Pressure

A dose of 1.5 to 2.0 g/kg as a 20% solution (7.5 to 10 mL/kg) or as a 15% solution (10 to 15 mL/kg) may be given over a period as short as 30 minutes in order to obtain a prompt and maximal effect. When used prophylactically the dose should be given once to one and one-half hours before surgery to achieve maximal reduction of intracranial pressure before operation.

Reduction of Intravascular Pressure

Usually a maximum reduction in intravascular pressure in adults can be achieved with a dose of 0.5 to 2 g/kg given not more than every six to eight hours. An exponential gradient between the blood and cerebrospinal fluid of approximately 10% difference will yield the satisfactory reduction in intracranial pressure. Adequate therapy for Intoxication: As an agent to produce diuresis in intoxications, 5%, 10%, 15%, or 20% mannitol is indicated. The concentration will depend upon the final requirement and urinary output of the patient.

Measurement of glomerular filtration rate by radiolabeled clearance may be useful for determination of dosage. All injections in VIAFLEX containers are intended for intravenous administration using sterile equipment. The use of supplemental additives medication is not recommended.

How Supplied

OSMITROL Injection (Mannitol Injection, USP) in VIAFLEX plastic containers is available in solutions of:

<table>
<thead>
<tr>
<th>Code</th>
<th>Size (mL)</th>
<th>NDC</th>
<th>Product Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>250564</td>
<td>1000</td>
<td>0338-0351-04</td>
<td>5% OSMITROL Injection</td>
</tr>
<tr>
<td>250561</td>
<td>500</td>
<td>0338-0352-03</td>
<td>10% OSMITROL Injection</td>
</tr>
<tr>
<td>250562</td>
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<td>15% OSMITROL Injection</td>
</tr>
<tr>
<td>250563</td>
<td>500</td>
<td>0338-0354-03</td>
<td>20% OSMITROL Injection</td>
</tr>
<tr>
<td>250565</td>
<td>250</td>
<td>0338-0355-03</td>
<td>20% OSMITROL Injection</td>
</tr>
<tr>
<td>250566</td>
<td>250</td>
<td>0338-0356-03</td>
<td>20% OSMITROL Injection</td>
</tr>
</tbody>
</table>

Exposure of pharmaceutical products to heat should be minimized. Avoid excessive heat. It is recommended the product be stored at room temperature (25°C). Seed exposure up to 40°C does not adversely affect the product.

Directions for Use of VIAFLEX Plastic Container

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

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

Preparation for Administration

1. Inspect container from market support.
2. Remove protective cap from outlet port at bottom of container.
3. Achieve administration set. Refer to complete directions accompanying set.