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Mannitol Injection

» Mannitol Injection is a sterile solution, which may be supersaturated, of Mannitol in Water for Injection. It may require warming or autoclaving before use if crystallization has occurred. It contains not less than 95.0 percent and not more than 105.0 percent of the labeled amount of mannitol ($C_6H_{14}O_6$). It contains no antimicrobial agents.

Packaging and storage—Preserve in single-dose glass or plastic containers. Glass containers are preferably of Type I or Type II glass.

Labeling—The label states the total osmolar concentration in mOsmol per L. Where the contents are less than 100 mL, or where the label states that the Injection is not for direct injection but is to be diluted before use, the label alternatively may state the total osmolar concentration in mOsmol per mL. The label also states that it should be warmed before use to dissolve any crystals that may have formed.

USP Reference standards ⟨11⟩—

USP Mannitol RS

Identification—

A: Evaporate a portion of Injection on a steam bath to dryness, and dry the residue at 105° for 4 hours. To 3 mL of freshly prepared solution of catechol in water (1 in 10) add 6 mL of sulfuric acid with cooling. Place 3 mL of this solution in each of two separate test tubes. To one tube add 0.3 mL of water (reagent blank) and to the other add 0.3 mL of a solution of it in water (1 in 10). Heat the tubes over an open flame for about 30 seconds: the solution in the tube containing mannitol is dark pink or wine red, and the solution in the tube containing the reagent blank is light pink.

B: The retention time for the major peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation,* as obtained in the *Assay*.

Specific rotation ⟨781⟩— +137° to +145°. Transfer an accurately measured volume of Injection, equivalent to about 1 g of mannitol as determined by the *Assay*, to a 100-mL volumetric flask. Add 40 mL of a 1-in-10 ammonium molybdate solution, previously filtered if necessary. Add 20 mL of 1 N sulfuric acid, and dilute with water to volume.

Bacterial Endotoxins Test ⟨85⟩—It contains not more than 0.04 USP Endotoxin Unit per mg of mannitol where the labeled amount of mannitol in the Injection is 10% or less, and not more than 2.5 USP Endotoxin Units per g of mannitol where the labeled amount of mannitol in the Injection is greater than 10%.

pH ⟨791⟩: between 4.5 and 7.0, determined potentiometrically, on a portion to which 0.30 mL of saturated potassium chloride solution has been added for each 100 mL, and which previously has been diluted with water, if necessary, to a concentration of not more than 5% of mannitol.

Particulate Matter in Injections ⟨788⟩: meets the requirements for small-volume injections.

Other requirements—It meets the requirements under *Injections and Implanted Drug Products ⟨1⟩*.

Assay—

Mobile phase—Use degassed water.

Resolution solution—Dissolve sorbitol and USP Mannitol RS in water to obtain a solution having concentrations of about 4.8 mg per mL of each.

Chromatographic system (see Chromatography ⟨621⟩)—The liquid chromatograph is equipped with a refractive index detector that is maintained at a constant temperature and a 4-mm × 25-cm column that contains packing L19. The column temperature is maintained at a temperature between 30° and 85° controlled within ±2° of the selected temperature, and the flow rate is about 0.5 mL per minute. Chromatograph the *Standard preparation*, and record the peak responses as directed for *Procedure*: the relative standard deviation for replicate injections is not more than 2.0%. In a similar manner, chromatograph the *Resolution solution*: the resolution, *R*, between the sorbitol and mannitol peaks is not less than 2.0.

Standard preparation—Dissolve an accurately weighed quantity of USP Mannitol RS in water, and dilute quantitatively with water to obtain a solution having a known concentration of about 5 mg per mL.

Assay preparation—Transfer an accurately measured volume of Injection, equivalent to about 500 mg of mannitol, to a 100-mL volumetric flask, dilute with water to volume, and mix.

Procedure—Separately inject equal volumes (about 20 µL) of the *Assay preparation* and the *Standard preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in mg, of mannitol ($C_6H_{14}O_6$) in each mL of the Injection taken by the formula:

$$100(C/V)(r_U/r_S)$$

in which V is the volume, in mL, of Injection taken; and the other terms are as defined therein.

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
MANNITOL INJECTION	Documentary Standards Support	SM22020 Small Molecules 2
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM22020 Small Molecules 2

Chromatographic Database Information: Chromatographic Database

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