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# Methohexital Sodium for Injection

$C_{14}H_{17}N_2NaO_3$ 284.29

2,4,6(1*H*,3*H*,5*H*)-Pyrimidinetrione, 1-methyl-5-(1-methyl-2-pentynyl)-5-(2-propenyl)-, (±)-, monosodium salt.

Sodium 5-allyl-1-methyl-5-(1-methyl-2-pentynyl)barbiturate CAS RN®: 309-36-4; 22151-68-4; UNII: 60200PNZ7Q.

» Methohexital Sodium for Injection is a freeze-dried, sterile mixture of methohexital sodium and anhydrous Sodium Carbonate as a buffer, prepared from an aqueous solution of Methohexital, Sodium Hydroxide, and Sodium Carbonate. It contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of methohexital sodium ($C_{14}H_{17}N_2NaO_3$).

**Packaging and storage**—Preserve as described in *Packaging and Storage Requirements ⟨659⟩, Injection Packaging*. Store at controlled room temperature. Injection may be packaged in 50-mL multiple-dose containers.

**USP Reference standards ⟨11⟩**—
USP Methohexital RS

**Completeness of solution**—Mix 1 g with 20 mL of carbon dioxide–free water: after 1 minute, the solution is clear and free from undissolved solid.

**Constituted solution**—At the time of use, it meets the requirements for *Injections and Implanted Drug Products (Parenterals)—Product Quality Tests ⟨1⟩, Specific Tests, Completeness and clarity of solutions*.

**Identification**—

**A:** Dissolve about 500 mg in 10 mL of water in a separator, add 10 mL of 3 N hydrochloric acid, and extract the liberated methohexital with two 25-mL portions of chloroform. Evaporate the combined chloroform extracts to dryness, add 10 mL of ether, evaporate again, and dry the residue in vacuum at 80° for 4 hours. Dissolve 50 mg of the residue so obtained in 5 mL of chloroform: the solution exhibits IR absorption maxima at the same wavelengths as that of a similar preparation of USP Methohexital RS.

**B:** The methohexital obtained and dried as directed for *Identification* test *A* melts between 92° and 96°.

**Bacterial Endotoxins Test ⟨85⟩**—It contains not more than 0.5 USP Endotoxin Unit per mg of methohexital sodium.

**Uniformity of dosage units ⟨905⟩**: meets the requirements.

*Procedure for content uniformity*—

*Standard solution*—Transfer about 23 mg of USP Methohexital RS, accurately weighed, to a 250-mL volumetric flask, add 50 mL of water, 0.5 mL of sodium hydroxide solution (1 in 10), and 1.5 mL of sodium carbonate solution (1 in 1000), and mix. Dilute with water to volume, and mix. Transfer 20.0 mL of this solution to a 100-mL volumetric flask, dilute with water to volume, and mix.

*Test solution*—Transfer the contents of 1 vial of Methohexital Sodium for Injection with the aid of water to a 1000-mL volumetric flask, dilute with water to volume, and mix. Transfer an accurately measured volume of this solution, equivalent to about 100 mg of methohexital sodium, to a 1000-mL volumetric flask, add about 200 mL of water and 2.0 mL of sodium hydroxide solution (1 in 10), mix, dilute with water to volume, and again mix. Transfer 20.0 mL of the resulting solution to a 100-mL volumetric flask, dilute with water to volume, and mix.

*Procedure*—Concomitantly determine the absorbances of the *Standard solution* and the *Test solution* in 1-cm cells at the wavelength of maximum absorbance at about 247 nm, with a suitable spectrophotometer, using water as the blank. Calculate the quantity, in mg, of $C_{14}H_{17}N_2NaO_3$ in the Methohexital Sodium for Injection taken by the formula:

$$(284.29/262.30)(TC/D)(A_U/A_S)$$

in which 284.29 and 262.30 are the molecular weights of methohexital sodium and methohexital, respectively; $T$ is the labeled quantity, in mg, of methohexital sodium in the Methohexital Sodium for Injection; $C$ is the concentration, in µg per mL, of USP Methohexital RS in the *Standard solution*; $D$ is the concentration, in µg per mL, of methohexital sodium in the *Test solution* based on the labeled quantity per container and the extent of dilution; and $A_U$ and $A_S$ are the absorbances of the *Test solution* and the *Standard solution*, respectively.

**pH ⟨791⟩**: between 10.6 and 11.6 in the solution prepared in the test for *Completeness of solution*.

**Loss on drying ⟨731⟩**—Dry it at 105° for 4 hours: it loses not more than 2.0% of its weight.

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

**Assay**—

*Internal standard solution*—Dissolve aprobarbital in chloroform to obtain a solution having a concentration of about 1.35 mg per mL.

*Standard preparation*—Dissolve an accurately weighed quantity of USP Methohexital RS in chloroform to obtain a solution having a known concentration of about 0.46 mg per mL. Transfer 5.0 mL of the resulting solution to a 10-mL volumetric flask, add 2.0 mL of *Internal standard solution*, dilute with chloroform to volume, and mix to obtain a *Standard preparation* having a known concentration of about 230 µg per mL.

*Assay preparation*—Combine and mix the constituted solutions prepared from the contents of 5 vials of Methohexital Sodium for Injection. Transfer an accurately measured volume of the resulting solution, equivalent to about 50 mg of methohexital sodium, to a 125-mL separator containing 25 mL of water, and mix. Add 0.2 mL of dilute hydrochloric acid (1 in 2), and mix. Extract with three 25-mL portions of chloroform, shaking each extraction for 2 minutes and filtering the extracts through about 15 g of anhydrous sodium sulfate, that previously has been washed with about 5 mL of chloroform, into a 100-mL volumetric flask. Wash the sodium sulfate with several small portions of chloroform, collecting the washings in the 100-mL volumetric flask. Dilute with chloroform to volume, and mix. Transfer 5.0 mL of this solution to a 10-mL volumetric flask, add 2.0 mL of *Internal standard solution*, dilute with chloroform to volume, and mix.

*Chromatographic system* (see *Chromatography* ⟨621⟩)—The gas chromatograph is equipped with a flame-ionization detector and contains a 1.2-m × 4-mm column packed with 3% phase G10 on support S1AB. The column is maintained at about 230°, the injection port at about 265°, and the detector block at about 265°. Dry helium is used as the carrier gas at a flow rate of about 60 mL per minute. Chromatograph replicate injections of the *Standard preparation,* and record the peak responses as directed for *Procedure:* the resolution, *R,* between methohexital and aprobarbital is not less than 4.0, and the relative standard deviation is not more than 2.0%.

*Procedure*—Separately inject equal volumes (about 2 µL) of the *Assay preparation* and the *Standard preparation* into the gas chromatograph, and measure the peak responses for the major peak. The relative retention times are about 0.6 for methohexital and 1.0 for aprobarbital. Calculate the quantity, in mg, of methohexital sodium ($C_{14}H_{17}N_2NaO_3$) in the portion of Methohexital Sodium for Injection taken by the formula:

$$(284.29/262.30)(0.2C)(R_U/R_S)$$

in which 284.29 and 262.30 are the molecular weights of methohexital sodium and methohexital, respectively; $C$ is the concentration, in µg per mL, of USP Methohexital RS in the *Standard preparation;* and $R_U$ and $R_S$ are the peak response ratios obtained from the *Assay preparation* and the *Standard preparation,* respectively.

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

| Topic/Question | Contact | Expert Committee |
|---|---|---|
| METHOHEXITAL SODIUM FOR INJECTION | Documentary Standards Support | SM52020 Small Molecules 5 |
| REFERENCE STANDARD SUPPORT | RS Technical Services<br>RSTECH@usp.org | SM52020 Small Molecules 5 |

**Chromatographic Database Information:** Chromatographic Database

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