Edition: BP 2025 (Ph. Eur. 11.6 update)

# Thiopental Injection

General Notices

**Action and use**

Intravenous barbiturate; general anaesthetic.

## DEFINITION

Thiopental Injection is a sterile solution of Thiopental Sodium in Water for Injections. It is prepared by dissolving Thiopental Sodium for Injection in the requisite amount of Water for Injections.

*The injection complies with the requirements stated under Parenteral Preparations.*

## STORAGE

Thiopental Injection should be used immediately after preparation but, in any case, within the period recommended by the manufacturer when prepared and stored strictly in accordance with the manufacturer's instructions.

## THIOPENTAL SODIUM FOR INJECTION

## DEFINITION

Thiopental Sodium for Injection is a sterile material consisting of Thiopental Sodium with or without excipients. It is supplied in a sealed container.

*The contents of the sealed container comply with the requirements for Powders for Injections or Infusions stated under Parenteral Preparations and with the following requirements.*

**Content of $C_{11}H_{18}N_2O_2S$**

77.0 to 92.0% of the stated amount of Thiopental Sodium.

**Content of Na**

9.4 to 11.8% of the stated amount of Thiopental Sodium.

## IDENTIFICATION

A. In the test for Related substances, the principal peak in the chromatogram obtained with solution (1) corresponds to the peak due to thiopental in the chromatogram obtained with solution (4).
B. Yield the reaction characteristic of *non-nitrogen substituted barbiturates*, Appendix VI.

C. Yield reaction A characteristic of *sodium salts*, Appendix VI.

## TESTS

### Clarity and colour of solution

A 10.0% w/v solution in *carbon dioxide-free water* is *clear*, Appendix IV A, and not more intensely coloured than *reference solution* $GY_3$, Appendix IV B, Method II.

### Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions prepared immediately before use.

(1) Dissolve a quantity of the contents of a sealed container containing 0.1 g of Thiopental Sodium in 80 mL of the mobile phase, add sufficient mobile phase to produce 100 mL and filter.
(2) Dilute 1 volume of solution (1) to 200 volumes with mobile phase.
(3) Dilute 1 volume of solution (2) to 5 volumes with mobile phase.
(4) 0.03% w/v of *thiopental for system suitability EPCRS* in mobile phase.
(5) Dilute 1 volume of solution (3) to 2 volumes with the mobile phase.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (5 µm) (Inertsil ODS 3 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 225 nm.
(f) Inject 10 µL of each solution.
(g) Allow the chromatography to proceed for twice the retention time of thiopental.

MOBILE PHASE

35 volumes of *acetonitrile* and 65 volumes of 0.02M *orthophosphoric acid*.

When the chromatograms are recorded under the prescribed conditions the retention times relative to thiopental (retention time = about 19 minutes) are: impurity A = about 0.3; impurity B = about 0.4; impurity C = about 0.9; impurity D = about 1.3.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (4):

the *resolution factor* between the peaks due to thiopental impurity A and thiopental impurity B is at least 4.0;

the *resolution factor* between the peaks due to thiopental impurity C and thiopental is at least 1.5.

LIMITS

Identify any peak in the chromatogram obtained with solution (1) corresponding to thiopental impurity B using solution (4) and multiply the area of the peak by 1.6.

In the chromatogram obtained with solution (1):

the area of any peak corresponding to thiopental impurity A is not greater than the area of the principal peak in the chromatogram obtained with solution (3) (0.1%);

the area of any peak corresponding to thiopental impurity B is not greater than twice the area of the principal peak in the chromatogram obtained with solution (2) (1%);

the area of any peak corresponding to thiopental impurity C is not greater than 6 times the area of the principal peak in the chromatogram obtained with solution (2) (3%);

the area of any peak corresponding to thiopental impurity D is not greater than 3 times the area of the principal peak in the chromatogram obtained with solution (3) (0.3%);

the area of any other *secondary peak* is not greater than the area of the principal peak in the chromatogram obtained with solution (3) (0.1%);

the sum of the areas of any *secondary peaks* is not greater than 10 times the area of the principal peak in the chromatogram obtained with solution (2) (5%).

Disregard any peak with an area less than the area of the principal peak in the chromatogram obtained with solution (5) (0.05%).

### Loss on drying

When dried at 100° at a pressure not exceeding 2.7 kPa for 4 hours, lose not more than 2.5% of their weight. Use 0.5 g.

## ASSAY

Determine the weight of the contents of 10 containers as described in the test for *uniformity of weight*, Appendix XII C1, Powders for Parenteral Administration. Carry out the following procedures using the mixed contents of the 10 containers.

***For sodium***

Dissolve a quantity of the powder for injection containing 0.6 g of Thiopental Sodium in 20 mL of *water* and titrate with *0.1M hydrochloric acid VS*, using *methyl red solution* as indicator, until the yellow colour changes to pink; boil gently for 1 or 2 minutes, cool and if necessary continue the titration with *0.1M hydrochloric acid VS* until the pink colour is restored.
Each mL of *0.1M hydrochloric acid VS* is equivalent to 2.299 mg of Na.

***For thiopental***

To the liquid from the completed Assay for Na add a further 5 mL of 0.1M *hydrochloric acid* and extract with successive quantities of 25, 25, 20, 15, 15 and 10 mL of *chloroform*, washing each extract with the same 5 mL of *water*. Evaporate the chloroform from the mixed extracts and dry the residue of $C_{11}H_{18}N_2O_2S$ to constant weight at 105°. Calculate the content of $C_{11}H_{18}N_2O_2S$ in a container of average content weight.