

Status: Effectivity information can only be shown for content published to the website.

Update information can only be shown for content published to the website.

Thiopental Injection

General Notices

Details for the public consultation of this monograph are as follows:

EAG/Panel/Working Party	Medicinal Chemicals 3
Contact Details	Michael.Whaley@mhra.gov.uk Maryna.Dmitriieva@mhra.gov.uk Sophie.Cherrington@mhra.gov.uk bpcom@mhra.gov.uk
Deadline for Comment	31 st December 2026
Target Publication Date (subject to change)	BP 2028
Notes	Revised monograph If limits are too restrictive, please provide batch/stability data to demonstrate that an increase is required. Content Limits tightened for Thiopental and Sodium. Related substances Quantitative limits introduced, correction factors introduced, system suitability, limits and retention times revised. Assay Thiopental gravimetric assay replaced with LC procedure. Impurities Section added.

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 intended to be prepared by dissolving the dry ingredients in the specified volume just before issue for use.

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 $C_{11}H_{18}N_2O_2S$

84.0 to 87.0% of the stated amount of Thiopental.

Content of Na

10.2 to 11.2% of the stated amount of 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 (3).
- 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 GY₃*, [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 mixed contents of the 10 containers containing the equivalent of 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. Dilute 1 volume of solution (2) to 5 volumes with mobile phase
- (3) 0.03% w/v of [*thiopental impurity mixture EPCRS*](#) (containing impurities A, B, C, and D) in mobile phase.
- (4) Dilute 1 volume of solution (2) to 5 volumes with the mobile phase.

CHROMATOGRAPHIC CONDITIONS

- (a) Use a stainless steel column (15 cm × 4.6 mm) packed with [*base-deactivated end-capped 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 two times the retention time of thiopental.

MOBILE PHASE

35 volumes of [*acetonitrile*](#) and 65 volumes of 0.1% w/v [*orthophosphoric acid*](#).

SYSTEM SUITABILITY

In the chromatogram obtained with solution (4) the [*signal-to-noise ratio*](#) of the peak due to thiopental is at least 20.

The test is not valid unless, in the chromatogram obtained with solution (3):

the [*resolution*](#) between the peaks due to impurity A and impurity B is at least 1.5;

the [*resolution*](#) between the peaks due to impurity C and thiopental is at least 1.5.

CALCULATION OF IMPURITIES

For each impurity, use the concentration of thiopental in solution (2).

For the reporting threshold, use the concentration of thiopental in solution (4).

For peak identification, use solution (3).

Thiopental retention time: about 19 minutes.

Relative retentions: impurity A, about 0.4; impurity B, about 0.45; impurity C, about 0.9; impurity D, about 1.3.

Correction factors: impurity B, multiply by 1.6; impurity D, multiply by 1.9.

LIMITS

— impurity B: not more than 1.0%;

- impurity D: not more than 0.5%;
- unspecified impurities: for each impurity, not more than 0.2%;
- total impurities: not more than 2.0%;
- reporting threshold: 0.1%.

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

Carry out the method for [liquid chromatography](#), [Appendix III D](#), using the following solutions.

- (1) Dissolve a quantity of the mixed contents of the 10 containers containing the equivalent of 0.1 g of Thiopental Sodium in 80 mL of the mobile phase. Add sufficient mobile phase to produce 100 mL and filter.
- (2) 0.085% w/v of [thiopental for ID and assay EPCRS](#) in mobile phase.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related substances should be used.

DETERMINATION OF CONTENT

Calculate the content of thiopental, $C_{11}H_{18}N_2O_2S$, in the injection from the chromatograms obtained and using the declared content of $C_{11}H_{18}N_2O_2S$ in [thiopental for ID and assay EPCRS](#).

IMPURITIES

The impurities limited by the requirements of this monograph include those listed under [Thiopental Sodium](#).

DRAFT MONOGRAPH
SUBJECT TO CHANGE