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(54) **Title:** STABLE INJECTABLE PHARMACEUTICAL COMPOSITION OF THIOPENTAL; METHOD FOR STABILIZING AQUEOUS SOLUTIONS OF THIOPENTAL AND, USE OF THIOPENTAL FOR PRODUCING A MEDICAMENT

(57) **Abstract:** The present invention describes an injectable and stable pharmaceutical composition of thiopental ready-to-use, whose can be packed in glass ampoules for single doses or multidose vials for multiple doses. A method for stabilizing an aqueous solution of thiopental and, the use of thiopental to make a medicament are also described.

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STABLE INJECTABLE PHARMACEUTICAL COMPOSITION OF THIOPENTAL; METHOD FOR STABILIZING AQUEOUS SOLUTIONS OF THIOPENTAL AND, USE OF THIOPENTAL FOR PRODUCING A MEDICAMENT.

The present invention describes an injectable and stable pharmaceutical composition of thiopental ready-to-use that can be placed in glass ampoules for unitary dose or in multidose vials for multiple administrations. It is also described a method for the stabilization of aqueous solutions of thiopental as well the use of thiopental for producing a medicament.

Thiopental is an anesthetic drug used by intravenous route for inducing general anesthesia for producing complete anesthesia of short duration. Other uses for this drug include the supplementation of regional anesthesia or low potency agents like nitric oxide, the control of convulsive states and the use as hypnotic agent [M. J. McLeish, in: K. Florey (Ed.) Analytical Profiles of Drugs Substances and Excipients, Vol. 21, Academic Press, New York, 1992, pp.535-572].

After its intravenous administration, the beginning of action of thiopental happens within 30 to 60 seconds due its elevated lipidic solubility. Thiopental rapidly crosses the blood-brain barrier distributing itself into the brain and other body tissues, being its anesthetic activity duration of about a period of 10 to 30 minutes (DRUGDEX DRUG EVALUATIONS - Thiopental - Specific Monograph).

Because of the low solubility of its free acid form in water, thiopental is usually employed as its sodium salt, which solubility is relatively higher in water.

Sodium thiopental is known by the chemical name as (±)-5-ethyl-5-(1-methylbutyl)-2-thiobarbituric acid sodium salt or (±)- 5- ethyldihydro- 5- (1-methylbutyl)-2-thioxo-4,6(1H,5H)-pyrimidinedione monosodium salt.

Commercially available pharmaceutical compositions of thiopental are formulated in vials as a sterile lyophilized powder with sodium carbonate, being the health professional responsible for the reconstitution of the solution by adding sterile diluents free from carbon dioxide, like distilled water, 0.9% saline solution or glucose solution immediately before its administration. Also available are kits constituted of thiopental and vials with appropriate diluents. In both cases thiopental solution must be completely consumed within 24 to 48 hours after the reconstitution because after this period it precipitates from the solution and can not be administered.

The reconstitution of thiopental is laborious due to the lengthy time needed to the preparation of the final composition. In the case of the product furnished without the sterile diluent kit it is necessary to treat the diluent agents for the sterilization and carbon dioxide elimination, the least one a critical step that has to be well done and monitored to avoid the turbidity of the final solution which makes inviable its use or administration. In the case of thiopental furnished with its diluent's kit, it is yet necessary to employ a period of time for transferring the diluent to the thiopental vial, besides the time expended for promoting its dissolution.

As the reconstitution of thiopental solution consumes a precious time, very often its medicine utilization is avoided in relation to other products that behaves therapeutically similar and are easier available to health professionals as a ready-to-use composition.

Thiopental stability in solution depends from lots of features including diluents types, storage temperature and carbon dioxide amount absorbed by the diluent. Generally any factor or condition that changes the ideal solution pH to a

lower pH will considerably increase the possibility of precipitation of its acid form making inviable the therapeutic use of the product.

It is possible to notice that available nowadays pharmaceutical compositions presents some inconveniences associated to their preparation method when compared to ready-to-use compositions. So, the development of a stable liquid pharmaceutical composition comprising thiopental is of great interest to promote its easy access to health professionals.

The literature describes some propositions on obtaining stable pharmaceutical compositions of thiopental. For example, patent GB 699,555 (1950), where the authors describe the preparation of several stable aqueous solutions comprising thiobarbiturics in a mixture of water and polyethylene glycols with molecular weight ranging from 200 and 600 used in a concentration ranging from 30% to 75% of the final composition. Although the authors claim the stabilization of thiobarbiturics within this condition, it is known that elevated concentration of low molecular weight polyethylene glycols causes hemolysis, and besides, there are several reports about allergic reactions associated to the use of this excipient.

Patents GB 747,635, GB 761,189, US 3,133,858 describe a stable non-aqueous pharmaceutical composition comprising a thiobarbituric and also a method to prepare such composition. This composition comprises a thiobarbituric acid dissolved in a mixture or combination of two or more organic solvents and an alkalinizing agent. Solvents used are polyethylene glycol and ethanol and the alkalinizing agent is generated *"in situ"* by using metallic sodium. The resulting solution presents high concentration of the thiobarbituric agent, being equal or superior to 25%, and

has a long stability when kept under room temperature. Besides the delicate preparation method, by using metallic sodium during its production, the resulting composition needs to be diluted with water before its final administration and doesn't eliminate the work to be done by the health professional before its use. The authors do not relate about the stability of the aqueous solution, a strong indication of its lack of stability.

Patent application WO 0072848 claims an injectable pharmaceutical composition ready-to-use, which is composed by acid thiopental and the solvent employed for its dissolution is the 2,5- di- O- methyl- 1,4:3,6- dianhydro- D-glucytol (dimethyl isosorbide) combined or not with a low water percentage (maximum of 5%). Like some previous references, the selected organic solvent also promotes hemolysis, being its hemolytic power a little bit lower than of ethanol. The use of this solvent can not be compared to water usage preference, mainly when considering the toxicity issue.

It is possible to observe that ready-to-use pharmaceutical compositions until now disclosed are based in the use of organic solvents. Although these organic solvents had been described as toxicological acceptable, the preference for aqueous compositions, which are safer for intravenous administration, is out of question.

The present invention describes an injectable pharmaceutical composition of thiopental, as a stable aqueous solution ready-to-use, that enables the direct usage of this medicament without any previous preparation. It is also described a stabilization method for thiopental aqueous solutions.

As disclosed earlier, thiopental nowadays is marked as a sterile powder of its sodium salt with sodium carbonate,

being reconstituted with water, sodium chloride solution or glucose just before its usage. The solution preparation is laborious and lengthy due to the care with the diluents to guarantee the sterility of the solution and also to avoid the precipitation of the acid form of thiopental. Commonly, health professionals employ a commercial available 0.9% saline solution or 5% glucose solution to prepare this composition. Due to variable pH of these commercial solutions frequently occurs the incomplete dissolution of composition, which stoops the clinical use of reconstituted thiopental.

The precipitation of thiopental is significantly influenced by variations on the solution pH. Despite the commercial product has a carbonate buffer, if the diluent presents a considerable amount of absorbed carbon dioxide, the final pH of the composition will be lower than the indicate, interfering in the product solubility.

The pharmaceutical composition of thiopental of the present invention is prepared in aqueous media and sterilized by conventional methods. This composition is in the form of an aqueous solution and employs an adequate organic buffer to stabilize the thiopental, avoiding its precipitation even when stored for long periods of time in ampoules or multidose vials for a single and multiple doses, respectively.

The injectable pharmaceutical composition of the present invention consists of an aqueous solution characterized to comprise thiopental in its free acid or appropriated pharmaceutical salt form as the therapeutic agent, an inorganic base to adjust the final pH between 9 and 12, an appropriated organic buffer to stabilize the composition pH in the range between 9 and 12, water as the solvent, and optionally, conservative or preservative agents

and inorganic acids to correct the pH in the range of 9 to 12.

According to the present invention, the injectable pharmaceutical composition of thiopental comprises:

a) thiopental or an appropriate pharmaceutical salt of thiopental employed in a concentration from 0.10% to 20% in weight of the final composition;

b) an appropriate inorganic base to adjust the pH of the medium in the range from 9 to 12;

c) an organic buffer to stabilize the pH in the range from 9 to 12 employed in a concentration ranging from 0.001% to 30% in weight of the final composition;

d) water, employed as solvent in a quantity sufficient to promote the thiopental dissolution to the appropriate therapeutic concentration;

e) optionally, may contain conservative or preservative agents, employed in a concentration ranging from 0.0% to 5.0% in weight of the final composition;

f) optionally, may have inorganic acids employed to adjust the pH of the final composition in the range from 9 to 12.

In the present invention, thiopental is employed in its acid or in an appropriate pharmaceutical salt form selected from the group constituted of sodium thiopental, calcium thiopental or potassium thiopental. Preferably the pharmaceutical salt of thiopental is the sodium one. The ideal concentration of thiopental in the pharmaceutical composition is in the range from 0.10% to 20% in weight of the final composition. More preferably the concentration of thiopental is in the range from 0.10% to 10% in weight of the final composition.

The pharmaceutical composition of the present invention employs 2- amine- 2- hydroximethyl- 1,3- propanediol, known as tromethamine (CAS 77-86-1), as an organic buffer agent, usually used to control the blood metabolic acidosis. The function of tromethamine is to stabilize the medium preventing the precipitation of thiopental due to the natural absorption of carbon dioxide by aqueous solutions. In the present invention Tromethamine was employed in a concentration from 0.001% to 30% in weight of the final composition. Preferably, concentration is in the range from 0.01% to 20% in weight of the final composition.

The carbon dioxide when absorbed from the environment by the aqueous solutions reduces the pH due of the formation of carbonic acid. As the equilibrium of thiopental in aqueous solution is extremely feeble and dependent of the pH, the use of tromethamine as a buffer prevents the pH variation due to the carbon dioxide absorbed avoiding the precipitation of thiopental.

The pharmaceutical composition of the present invention also employs an alkaline agent like an inorganic base to adjust the pH in the range between 9 and 12. Among the inorganic bases preferably employed are carbonates, bicarbonates and hydroxides of sodium, potassium, calcium or ammonium. Especially sodium carbonate and/or sodium hydroxide are used to adjust the pH in compositions comprising sodium thiopental.

Water is the solvent employed in the pharmaceutical composition described in the present invention, which are employed in a quantity sufficient to (q.s.t.) promote the dissolution of the constituents and lead to the therapeutic desired concentration of thiopental.

A particular interest of the present invention is to prepare a pharmaceutical composition employing thiopental in

its acid form. The sodium thiopental is hygroscopic and its industrial precipitation by usual methods is difficult. Industrially, thiopental is produced through lyophilization whose technique increases it cost. The preparation of the pharmaceutical composition of the present invention, in one of their embodiments, can employs thiopental in its acid form which are easily converted in the sodium form adding an inorganic base.

When the acid form of thiopental is employed in the preparation of the pharmaceutical composition of the present invention, the dissolution of thiopental in water is preferably made with addition of sodium hydroxide and the final pH of the composition is adjusted with this alkalinizing agent or with carbonates or bicarbonates and when necessary with inorganic acids to diminish the final pH.

Optionally, the pharmaceutical composition of the present invention may comprise some appropriated pharmaceutical conservative agents, whose yields microbiologic stability. Among the appropriated conservative agents for thiopental pharmaceutical composition of the present invention, are benzyl alcohol, parabens like methylparaben and propylparaben, chlorobutanol, m-cresol, benzethonium chloride and/or mixture among them are detached, being employed in a concentration from 0.0% to 5.0% in weight of the final composition.

In adjusting the pharmaceutical composition pH of the present invention, occasionally can be necessary the use of an inorganic acid, in the case of pH achieves values superior than 12. In this case, preferably is employed hydrochloric acid in gas or solution forms to adjust the pH in the range from 9 to 12.

The method for stabilizing aqueous solution of thiopental consists in the use of tromethamine as an organic buffer to stabilize the solution pH in the range from 9 to 12, which is used in a concentration from 0.001% to 30% in weight of the final composition. This buffer inhibits the conversion of the adsorbed carbon dioxide in carbonic acid with concomitant pH reduction and consequent precipitation of thiopental.

The pharmaceutical composition of the present invention can be sterilized by conventional techniques, being more interesting the use of sterile membranes.

The pharmaceutical composition of the present invention is stable when stored at room temperature or under refrigeration. The solutions formulated according to the present invention and stored at room temperature and under refrigeration, presented satisfactory analysis results without any evidence of degradation or significant alteration in the assay or precipitation after nine months.

The injectable pharmaceutical composition of thiopental described in the present invention gives a stable and a ready-to-use medicament for health professionals, excluding the undesirable previous preparation. This composition of thiopental is adequate to the same actual drug applications which are induction of anesthesia, complete anesthesia, and supplemental regional anesthesia, to control convulsive states and as hypnotic in human or veterinary medicine.

The experimental part described below is made up for illustrative examples, but not exhaustive ones, about obtainment of an injectable and stable pharmaceutical composition of thiopental.

EXAMPLE 1

In a reactor with agitation were added sodium thiopental (50.00 g), sodium carbonate (3.00 g), tromethamine (12.50 g) and water for injectable (900 mL, CO_2 free). The mixture was stirred under nitrogen atmosphere until complete dissolution of the solids. The pH was adjusted and the solution was diluted to the final volume (1000 mL) with water. The solution was filtered through a sterile membrane (0.22 μ) and filled in ampoules of 20 mL, presenting a final concentration of 5% of sodium thiopental.

EXAMPLE 2

In a reactor with agitation were added thiopental (45.84 g), sodium carbonate (3.00 g), tromethamine (12.50 g) and water for injectable (900 mL, CO_2 free). The mixture was stirred under nitrogen atmosphere and simultaneously, an aqueous solution of 10% sodium hydroxide was added dropwise. The entire solubilization of thiopental was observed, furnishing a clear and colorless solution. The pH of the mixture was checked and didn't need adjust. The mixture was diluted with water to the final volume (1000 mL), was filtrate through a sterile membrane (0.22 μ) and filled in ampoules of 20 mL, presenting a final concentration of 5% of sodium thiopental.

EXAMPLE 3

An injectable pharmaceutical composition of thiopental (5.0 %) in aqueous solutions form was prepared as described in example 1, employing the constituents in the proportion listed below:

Sodium thiopental - 50.0 g
Tromethamine - 25.0 g
Sodium carbonate - 3.0 g
Water - q.s.t. 1 L

EXAMPLE 4

An injectable pharmaceutical composition of thiopental (5.0 %) in aqueous solution form was prepared as described in example 1, employing the constituents in the proportion listed below:

Sodium thiopental - 50.0 g
Tromethamine - 50.0 g
Sodium carbonate - 3.0 g
Water - q.s.t. 1 L

EXAMPLE 5

An injectable pharmaceutical composition of thiopental (5.0 %) in aqueous solutions form was prepared as described in example 1, employing the constituents in the proportion listed below:

Sodium thiopental - 50.0 g
Tromethamine - 100.0 g
Sodium carbonate - 3.0 g
Water - q.s.t. 1 L

EXAMPLE 6

An injectable pharmaceutical composition of thiopental (2.5 %) in aqueous solutions form was prepared as described in example 1, employing the constituents in the proportion listed below:

Sodium thiopental - 25.0 g
Tromethamine - 6.25 g
Sodium carbonate - 1.5 g
Water - q.s.t. 1 L

EXAMPLE 7

An injectable pharmaceutical composition of thiopental (2.5 %) in aqueous solutions form was prepared as described

in example 1, employing the constituents in the proportion listed below:

Sodium thiopental - 25.0 g
Tromethamine - 12.5 g
Sodium carbonate - 1.5 g
Water - q.s.t. 1 L

EXAMPLE 8

An injectable pharmaceutical composition of thiopental (2.5 %) in aqueous solutions form was prepared as described in example 1, employing the constituents in the proportion listed below:

Sodium thiopental - 25.0 g
Tromethamine - 25.0 g
Sodium carbonate - 1.5 g
Water - q.s.t. 1 L

EXAMPLE 9

An injectable pharmaceutical composition of thiopental (5.0 %) in aqueous solutions form was prepared as described in example 1, employing the constituents in the proportion listed below:

Sodium thiopental - 50.0 g
Tromethamine - 12.5 g
Sodium carbonate - 3.0 g
Methylparaben - 0.25 g
Propylparaben - 0.25 g
Water - q.s.t. 1 L

EXAMPLE 10

An injectable pharmaceutical composition of thiopental (5.0 %) in aqueous solutions form was prepared as described in example 1, employing the constituents in the proportion listed below:

Sodium thiopental - 50.0 g
Tromethamine - 12.5 g
Sodium carbonate - 3.0 g
Methylparaben - 2.5 g
Propylparaben - 0.25 g
Water - q.s.t. 1 L

EXAMPLE 11

An injectable pharmaceutical composition of thiopental (5.0 %) in aqueous solutions form was prepared as described in example 1, employing the constituents in the proportion listed below:

Sodium thiopental - 50.0 g
Tromethamine - 25.0 g
Sodium carbonate - 3.0 g
Methylparaben - 2.5 g
Propylparaben - 0.5 g
Water - q.s.t. 1 L

EXAMPLE 12

An injectable pharmaceutical composition of thiopental (5.0 %) in aqueous solutions form was prepared as described in example 1, employing the constituents in the proportion listed below:

Sodium thiopental - 50.0 g
Tromethamine - 50.0 g
Sodium carbonate - 3.0 g
Methylparaben - 0.25 g
Propylparaben - 0.25 g
Water - q.s.t. 1 L

EXAMPLE 13

An injectable pharmaceutical composition of thiopental (5.0 %) in aqueous solutions form was prepared as described

in example 2, employing the constituents in the proportion listed below:

Acid thiopental - 45.84 g
Tromethamine - 25.0 g
Sodium carbonate - 3.0 g
Water - q.s.t. 1 L

EXAMPLE 14

An injectable pharmaceutical composition of thiopental (5.0 %) in aqueous solutions form was prepared as described in example 2, employing the constituents in the proportion listed below:

Acid thiopental - 45.84 g
Tromethamine - 50.0 g
Sodium carbonate - 3.0 g
Water - q.s.t. 1 L

EXAMPLE 15

An injectable pharmaceutical composition of thiopental (5.0 %) in aqueous solutions form was prepared as described in example 2, employing the constituents in the proportion listed below:

Acid thiopental - 45.84 g
Tromethamine - 100.0 g
Sodium carbonate - 3.0 g
Water - q.s.t. 1 L

EXAMPLE 16

An injectable pharmaceutical composition of thiopental (2.5 %) in aqueous solutions form was prepared as described in example 2, employing the constituents in the proportion listed below:

Acid thiopental - 22.92 g
Tromethamine - 6.25 g

Sodium carbonate - 1.5 g
Water - q.s.t. 1 L

EXAMPLE 17

An injectable pharmaceutical composition of thiopental (2.5 %) in aqueous solutions form was prepared as described in example 2, employing the constituents in the proportion listed below:

Acid thiopental - 22.92 g
Tromethamine - 12.5 g
Sodium carbonate - 1.5 g
Water - q.s.t. 1 L

EXAMPLE 18

An injectable pharmaceutical composition of thiopental (2.5 %) in aqueous solutions form was prepared as described in example 2, employing the constituents in the proportion listed below:

Acid thiopental - 22.92 g
Tromethamine - 25.0 g
Sodium carbonate - 1.5 g
Water - q.s.t. 1 L

EXAMPLE 19

An injectable pharmaceutical composition of thiopental (5.0 %) in aqueous solutions form was prepared as described in example 2, employing the constituents in the proportion listed below:

Acid thiopental - 45.84 g
Tromethamine - 12.5 g
Sodium carbonate - 3.0 g
Methylparaben - 0.25 g
propylparaben - 0.25 g
Water - q.s.t. 1 L

EXAMPLE 20

An injectable pharmaceutical composition of thiopental (5.0 %) in aqueous solutions form was prepared as described in example 2, employing the constituents in the proportion listed below:

Acid thiopental	- 45.84 g
Tromethamine	- 12.5 g
Sodium carbonate	- 3.0 g
Methylparaben	- 2.5 g
Water	- q.s.t. 1 L

EXAMPLE 21

An injectable pharmaceutical composition of thiopental (5.0 %) in aqueous solutions form was prepared as described in example 2, employing the constituents in the proportion listed below:

Acid thiopental	- 45.84 g
Tromethamine	- 25.0 g
Sodium carbonate	- 3.0 g
Methylparaben	- 2.5 g
Propylparaben	- 0.5 g
Water	- q.s.t. 1 L

EXAMPLE 22

An injectable pharmaceutical composition of thiopental (5.0 %) in aqueous solutions form was prepared as described in example 2, employing the constituents in the proportion listed below:

Acid thiopental	- 45.84 g
Tromethamine	- 100.0 g
Sodium carbonate	- 3.0 g
Methylparaben	- 0.5 g
Water	- q.s.t. 1 L

EXAMPLE 23

An injectable pharmaceutical composition of thiopental (5.0 %) in aqueous solutions form was prepared as described in example 2, employing the constituents in the proportion listed below:

Acid thiopental - 45.84 g
Tromethamine - 12.5 g
Sodium carbonate - 3.0 g
Propylparaben - 0.5 g
Water - q.s.t. 1 L

EXPERIMENT 1

A stress test was elaborated for the evaluation of the capacity of tromethamine to retard the precipitation of thiopental in aqueous solution. Two solutions were prepared and called Test 1 and Test 2 and have the composition listed below:

Test 1:

Sodium thiopental - 1.0 g
Sodium carbonate - 0.06 g
Water - q.s.t. 20 mL

Test 2:

Sodium thiopental - 1.0 g
Sodium carbonate - 0.06 g
Tromethamine - 0.400 g
Water - q.s.t. 20 mL

The water employed in these compositions was sterile and CO_2 free. In each test were added solid carbon dioxide (1 g) and the velocity of precipitation was monitored.

The Test 1 solution showed immediately precipitation in contact with carbon dioxide while test 2 solution with

tromethamine showed slowly precipitation only after ten minutes.

EXPERIMENT 2

For the evaluation of the stability, the aqueous solution prepared above was stored at room temperature and under refrigeration. The analytical parameters evaluated were appearance and assay for each solution.

The results are listed below and match the partial analysis up to now:

Composition	Initial analysis		Analysis after 9 month Room temperature	
	Appearance	Assay (%)	Appearance	Assay (%)
Example 1	Clear, colorless solution	99.23	Clear, colorless solution	99.17
Example 2	Clear, colorless solution	99.86	Clear, colorless solution	99.75
Example 7	Clear, colorless solution	98.51	Clear, colorless solution	98.23
Example 9	Clear, colorless solution	101.60	Clear, colorless solution	101.44
Example 12	Clear, colorless solution	99.98	Clear, colorless solution	99.93
Example 14	Clear, colorless solution	100.41	Clear, colorless solution	100.36
Example 19	Clear, colorless solution	100.02	Clear, colorless solution	99.76
Example 22	Clear, colorless solution	99.77	Clear, colorless solution	99.32

Composition	Initial analysis		Analysis after 9 month Temperature=4-8°C	
	Appearance	Assay (%)	Appearance	Assay (%)
Example 1	Clear, colorless solution	99.23	Clear, colorless solution	99.19
Example 2	Clear, colorless solution	99.86	Clear, colorless solution	99.81
Example 7	Clear, colorless solution	98.51	Clear, colorless solution	98.48
Example 9	Clear, colorless solution	101.60	Clear, colorless solution	101.55
Example 12	Clear, colorless solution	99.98	Clear, colorless solution	99.92
Example 14	Clear, colorless solution	100.41	Clear, colorless solution	100.45
Example 19	Clear, colorless solution	100.02	Clear, colorless solution	100.00
Example 22	Clear, colorless solution	99.77	Clear, colorless solution	99.49

We claims

1. A stable and injectable pharmaceutical composition of thiopental characterized by comprising thiopental in the acid or a pharmaceutical acceptable salt form, an inorganic base to adjust the final pH between 9 and 12, an appropriate organic buffer to stabilize this final pH in the range from 9 to 12, water as a solvent and, optionally a conservative or preservative agents and an inorganic acid to correct the final pH.

2. Pharmaceutical composition in accordance with claim 1 characterized by comprising thiopental in its acid form in a concentration ranging from 0.10 % to 20% in weight of the final composition.

3. Pharmaceutical composition in accordance with claim 1 characterized by comprising sodium, calcium or potassium thiopental in a concentration from 0.10% to 20% in weight of the final composition.

4. Pharmaceutical composition in accordance with claim 3 characterized by comprising preferably sodium thiopental in a concentration from 0.10% to 10% in weight of the final composition.

5. Pharmaceutical composition in accordance with claim 1 characterized by comprising an inorganic base selected from the group of carbonates, bicarbonates or hydroxides of preferably sodium, potassium, calcium or ammonium ones, employed to adjust the pH in the range from 9 to 12.

6. Pharmaceutical composition in accordance with claim 5 characterized by comprising preferably sodium carbonate and/or sodium hydroxide, employed to adjust the pH in the range from 9 to 12.

7. Pharmaceutical composition in accordance with claim 1 characterized by comprising tromethamine as an organic buffer in a concentration ranging from 0.001% to 30% in weight of the final composition.

8. Pharmaceutical composition in accordance with claim 7 characterized by comprising tromethamine preferably in a concentration ranging from 0.01% to 20% in weight of the final composition.

9. Pharmaceutical composition in accordance with claim 1 characterized by comprising water as a solvent in a quantity sufficient to dilute the composition to the appropriate therapeutic concentration.

10. Pharmaceutical composition in accordance with claim 1 characterized by optionally comprising a preservative selected from the group of benzyl alcohol, parabens like methylparaben and propylparaben, chlorobutanol, m-cresol, benzethonium chloride or mixture between them and, preferably in a concentration ranging from 0.0% to 5.0% in weight of the final composition.

11. Pharmaceutical composition in accordance with claim 1 characterized by optionally comprising an inorganic acid employed to adjust the pH of the final composition in the range between 9 and 12.

12. Pharmaceutical composition in accordance with claim 11 characterized by optionally comprising hydrochloric acid in gas or solution form to adjust the final pH.

13. Pharmaceutical composition in accordance with claims 1 to 12 characterized by being a stable aqueous solution ready-to-use.

14. Method for stabilizing an aqueous solution of thiopental characterized by consisting in the use of tromethamine as an organic buffer to stabilize the solution pH in the range from 9 to 12.

15. Method in accordance with claim 14 characterized by using tromethamine in a concentration ranging from 0.001% to 30% in weight of the final solution.

16. Use of thiopental to produce a medicament in accordance with claim 1 characterized by providing induction of anesthesia, complete anesthesia, supplemental regional anesthesia, control of convulsive states or as hypnotic in human or veterinary medicine.