Accordingly, the present disclosure, relates to a freeze-dried powder for preparing a thermogel comprising:

- from 1% to 35% of 2-[(3-aminopropyl)amino]ethanethiol or one of its pharmaceutically acceptable salt;
- from 40% to 85% of one or more poloxamer; and
- from 0,1% to 20% of one or more carbohydrate compound.

The present disclosure, in one aspect, relates to a freeze-dried powder for preparing a thermogel comprising:

- from 1% to 35% of 2-[(3-aminopropyl)amino]ethanethiol or one of its pharmaceutically acceptable salt;
- from 40% to 85% of one or more poloxamer; and
- from 0,1% to 20% of one or more carbohydrate compound chosen among mannitol, lactose, sucrose, trehalose, sorbitol, glucose or raffinose.

The present disclosure, in another aspect, relates to a process for preparing a freeze-dried powder as defined herein, said process comprising the following steps:

- hydrolysing amifostine into amifostine thiol under acidic conditions;
- preparing a solution containing the excipients by:
    - dissolving and mixing firstly all excipients presented in the formulation, except the poloxamer(s);
    - cooling the temperature before adding gradually the polaxamer(s) to get a homogenous excipient solution;
- mixing the obtained amifostine thiol solution with the obtained excipient solution;
- freeze-drying the obtained solution; and
- nitrogen inerting before sealing.

The present disclosure, in another aspect, relates to a process for preparing a thermogel comprising the reconstitution of the freeze-dried powder as defined herein with an aqueous solution.

The present disclosure, in another aspect, relates to a thermogel obtainable by a process as defined herein.

The present disclosure, in another aspect, relates to a thermogel as defined herein for use in treating or protecting mucosal or cutaneous tissue from damage

associated with anticancer therapy, in particular with radiation and/or chemotherapeutic treatment of cancers.

The present disclosure, in another aspect, relates to use of the thermogel as defined herein in the manufacture of a medicament for treating or protecting mucosal or cutaneous tissue from damage associated with anticancer therapy, in particular with radiation and/or chemotherapeutic treatment of cancers.

Freeze-dried powder according to the present disclosure can be stored for months at ambient temperature without observing significant degradation of 2-[(3-aminopropyl)amino]ethanethiol into disulfide impurity. In addition, it can be easily reconstituted for obtaining a thermogel that can be used for treating or protecting mucosal or cutaneous tissue from damage associated with anticancer therapy, in particular with radiation and/or chemotherapeutic treatment of cancers, by topical application.

In the context of the present invention:

- “freeze-dried powder” (or “lyophilised powder”) designates any powder containing less than 8% of water, preferably less than 5% of water, still preferably less than 2% of water;
- “2-[(3-aminopropyl)amino]ethanethiol” designates the active cytoprotective thiol metabolite of amifostine, also designated by “amifostine thiol” or “WR-1065”;
- “poloxamer” designates non-ionic block copolymers of ethylene oxide (EO) and propylene oxide (PO) synthesized by sequential addition of propylene oxide first and then ethylene oxide to a low molecular weight water-soluble propylene glycol (ref. G. Bonacucina et al., “Thermosensitive Self-Assembling Block Copolymers as Drug Delivery Systems”, *Polymers 2011*, 3, 779-811). Poloxamer are commercialised under various names among which Pluronics®, Lutrol®, Kolliphor®;
- “carbohydrate compound” designates any biomolecule having the following formula: $C_m(H_2O)_n$ (where m may be different from n). Carbohydrate compounds are also known as “saccharides”. Preferably, “carbohydrate compound” designates monosaccharide or disaccharide, i.e. sugars;
- “thermogel” (or “thermosensitive gel”) designates any polymer solution exhibiting the property of transitioning between a liquid and a firm gel during temperature transition. Preferably, “thermogel” designates an hydrogel which is liquid at room temperature, and gels at body temperature and capable of adhering to the mucous membrane and skin by its gelled state;

CLAIMS

1. A freeze-dried powder for preparing a thermogel comprising:
- from 1% to 35% of 2-[(3-aminopropyl)amino]ethanethiol or one of its pharmaceutically acceptable salt;
- from 40% to 85% of one or more poloxamer; and
- from 0,1% to 20% of one or more carbohydrate compound chosen among mannitol, lactose, sucrose, trehalose, sorbitol, glucose or raffinose.

2. A freeze-dried powder according to claim 1, characterised in that it contains from 5% to 30% of 2-[(3-aminopropyl)amino]ethanethiol.

3. A freeze-dried powder according to claim 1 or 2, characterised in that it contains from 45% to 80% of poloxamer.

4. A freeze-dried powder according to claim 3, characterised in that it contains from 60% to 75% of poloxamer.

5. A freeze-dried powder according to any of claims 1 to 4, characterised in that poloxamer is chosen as being Poloxamer 407 or Poloxamer 188.

6. A freeze-dried powder according to any of claims 1 to 5, characterised in that it contains a mixture of Poloxamer 407 and Poloxamer 188.

7. A freeze-dried powder according to any of claims 1 to 6, characterised in that it contains from 0,5% to 15% of a carbohydrate compound.

8. A freeze-dried powder according to claim 7, characterised in that it contains from 1% to 10% of carbohydrate compound.

9. Freeze-dried powder according to any one of claims 1-8, characterised in that carbohydrate compound is chosen as being sorbitol or mannitol.

10. A freeze-dried powder according to any of claims 1 to 9, characterised in that it further contains one or more of the following ingredients:

- flavouring agent such as apple, banana, cherry, coconut, lemon, menthol, orange, raspberry, strawberry, coconut, tutti frutti or vanilla; and/or
- high-intensity sweetener such as saccharin, aspartame, acesulfame potassium, sucralose or neotame.

11. A process for preparing a freeze-dried powder according to any of claims 1 to 10, said process comprising the following steps:

- hydrolysing amifostine into amifostine thiol under acidic conditions;
- preparing a solution containing the excipients by:
    - dissolving and mixing firstly all excipients presented in the formulation, except the poloxamer(s);
    - cooling the temperature before adding gradually the polaxamer(s) to get a homogenous excipient solution;
- mixing the obtained amifostine thiol solution with the obtained excipient solution;
- freeze-drying the obtained solution; and
- nitrogen inerting before sealing.

12. A process for preparing a thermogel comprising the reconstitution of the freeze-dried powder according to any of claims 1 to 10 with an aqueous solution.

13. A thermogel obtainable by a process according to claim 12.

14. A thermogel according to claim 13 for use in treating or protecting mucosal or cutaneous tissue from damage associated with anticancer therapy, in particular with radiation and/or chemotherapeutic treatment of cancers.

15. Use of the thermogel according to claim 13 in the manufacture of a medicament for treating or protecting mucosal or cutaneous tissue from damage associated with anticancer therapy, in particular with radiation and/or chemotherapeutic treatment of cancers.