CLAIMS

1. A process for the preparation of an injectable sustained release pharmaceutical composition of lanreotide, comprising the steps of:

   - combining a lanreotide salt and an aqueous acetic acid solution;
   - lyophilizing the resulting mixture only once; and
   - hydrating the lyophilizate;

wherein the final pH of the composition ranges between pH 5 to 7, and during the lyophilization step, the temperature of the mixture is

. initially reduced from room temperature to a temperature between 1 and 5°C and then retained constant,

. further reduced from 1 to 5°C to a temperature less than -30°C and then retained constant.

2. The process of claim 1 wherein the final pH of the composition ranges between 5.8 to 6.4.

3. The process of claim 1 wherein water is used to hydrate the lyophilizate.

4. The process of claim 3 wherein water used to hydrate the lyophilizate preferably contains acid at a suitable concentration to provide the requisite final pH.

5. The process of claim 3 wherein water used to hydrate the lyophilizate contains acetic acid at a suitable concentration to provide an anhydrous acetate content of 9 ± 2 % by weight of the composition.

6. The process of claim 3 wherein water used to hydrate the lyophilizate contains acetic acid at a suitable concentration to provide an anhydrous acetate content of 9.7 ± 0.3 % by weight of the composition.

7. The process of claim 1 wherein 25 ± 2 g/l lanreotide and 15 ± 2 % by weight acetic acid are combined in the first step.

8. The process of claim 1 wherein, during the lyophilization step, the temperature of the mixture is:

   - initially reduced from room temperature to 2 °C ± 1 °C and then retained constant;
   - further reduced from 2 ± 1 °C to -40 ± 5 °C and then retained constant;

- initially increased from -40 ± 5 °C to 25 ± 5 °C and then retained constant; and
- further increased to 35 ± 5 °C and then retained constant.

9. The process of claim 8 wherein the duration of the lyophilization step is at least 40 hours, more preferably at least 60 hours

10. The process of claim 8 wherein, during the lyophilization step, the temperature of the mixture is:

- initially reduced over up to 30 minutes, preferably up to 10 minutes, and then retained constant for 3 ± 1 hours;
- further reduced over up to 15 minutes, preferably up to 10 minutes, and then retained constant for 3.5 ± 1 hours;
- initially increased over 20 ± 5 hours and then retained constant for at least 40 hours; and
- further increased over 1 ± 0.5 hours and then retained constant for at least 16 hours.

11. The process of claim 7 wherein, after the temperature of the mixture is decreased, the atmospheric pressure is reduced to 20 ± 5 µbar and the atmospheric pressure remains constant as the temperature of the mixture increases.

12. The process according to any of claims 1 to 10 wherein the amount of water in which the lyophilizate is dissolved is less than 50 %, preferably less than 30 %, more preferably less than 10 %, of the amount needed to completely dissolve the lanreotide salt and adapted to give the composition a semi-solid consistency.

13. A sustained release pharmaceutical composition prepared according to the process of any of claims 1-12.

14. The composition of claim 13 capable of releasing the lanreotide over a period of at least 15 days, preferably 1 month, and more preferably 2 months.

15. The composition of any of claims 13 or 14 comprising between 15 and 35 % by weight, preferably 25 ± 5 % by weight, and more preferably approximately 24.6 ± 2.5 % by weight, of lanreotide base.

16. The composition of any claims 13 to 15 suitable for use after storage at between 2 and 8 °C for more than 12 months, preferably for more than 24 months.

CLAIMS

1. A process for the preparation of an injectable sustained release pharmaceutical composition of lanreotide, comprising the steps of:

   - combining a lanreotide salt and an aqueous acetic acid solution;
   - lyophilizing the resulting mixture only once; and
   - hydrating the lyophilizate;

   wherein the final pH of the composition ranges between pH 5 to 7, and during the lyophilization step, the temperature of the mixture is

   . initially reduced from room temperature to a temperature between 1 and 5°C and then retained constant for at least one hour,

   . further reduced from 1 to 5°C to a temperature between -40 ± 5 °C and then retained constant for at least 2 hours,

   . initially increased for at least 10 hours from -40 ± 5 °C to 20-30 °C and then retained constant for at least 20 hours; and

   . further increased to 30-40 °C over 1 ± 0.5 hours and then retained constant for at least 16 hours.

2. The process of claim 1 wherein the final pH of the composition ranges between 5.8 to 6.4.

3. The process of claim 1 wherein water is used to hydrate the lyophilizate.

4. The process of claim 4 wherein water used to hydrate the lyophilizate preferably contains acid at a suitable concentration to provide the requisite final pH.

5. The process of claim 4 wherein water used to hydrate the lyophilizate contains acetic acid at a suitable concentration to provide an anhydrous acetate content of 9 ± 2 % by weight of the composition.

6. The process of claim 4 wherein water used to hydrate the lyophilizate contains acetic acid at a suitable concentration to provide an anhydrous acetate content of 9.7 ± 0.3 % by weight of the composition.

7. The process of claim 1 wherein 25 ± 2 g/l lanreotide and 15 ± 2 % by weight acetic acid are combined in the first step.

8. The process of claim 1 wherein, during the lyophilization step, the temperature of the mixture is:

- initially reduced from room temperature to 2 °C ± 1 °C and then retained constant;
- further reduced from 2 ± 1 °C to -40 ± 5 °C and then retained constant;
- initially increased from -40 ± 5 °C to 25 ± 5 °C and then retained constant; and
- further increased to 35 ± 5 °C and then retained constant.

9. The process of claim 8 wherein the duration of the lyophilization step is at least 40 hours, more preferably at least 60 hours

10. The process of claim 8 wherein, during the lyophilization step, the temperature of the mixture is:

- initially reduced over up to 30 minutes, preferably up to 10 minutes, and then retained constant for 3 ± 1 hours;
- further reduced over up to 15 minutes, preferably up to 10 minutes, and then retained constant for 3.5 ± 1 hours;
- initially increased over 20 ± 5 hours and then retained constant for at least 40 hours; and
- further increased over 1 ± 0.5 hours and then retained constant for at least 16 hours.

11. The process of claim 7 wherein, after the temperature of the mixture is decreased, the atmospheric pressure is reduced to 20 ± 5 μbar and the atmospheric pressure remains constant as the temperature of the mixture increases.

12. The process according to any of claims 1 to 10 wherein the amount of water in which the lyophilizate is dissolved is less than 50 %, preferably less than 30 %, more preferably less than 10 %, of the amount needed to completely dissolve the lanreotide salt and adapted to give the composition a semi-solid consistency.

13. The process according to any of claims 1 to 12 wherein the sustained release composition is capable of releasing the lanreotide over a period of at least 15 days, preferably 1 month, and more preferably 2 months.

14. The process according to any of claims 1 to 12 wherein the sustained release composition comprises between 15 and 35 % by weight, preferably 25 ± 5 % by weight, and more preferably approximately 24.6 ± 2.5 % by weight, of lanreotide base.

15. The process according to any of claims 1 to 12 wherein the sustained release composition is suitable for use after storage at between 2 and 8 °C for more than 12 months, preferably for more than 24 months.