

Patent Claims

1. An aqueous pharmaceutical antibody formulation, comprising

(i) Avelumab in a concentration of 1 mg/mL to about 20 mg/mL as the antibody;

5 (ii) glycine in a concentration of 5 mM to 15 mM as the buffering agent, and not comprising any other buffering agent;

(iii) lysine monohydrochloride, dextrose, sucrose or sorbitol in a concentration of 100 mM to 320 mM as the stabiliser, and not comprising any other stabiliser;

10 (iv) polyvinylpyrrolidone of CAS number 9003-39-8 (molecular weight: 2000-3000 g/mol), polyoxyl 35 castor oil or Polysorbate 80 in a concentration of 0.25 mg/mL to 0.75 mg/mL, as the surfactant, and not comprising any other surfactant; wherein the formulation has a pH of 3.8 to 4.6.

2. An aqueous pharmaceutical antibody formulation, comprising

15 (i) Avelumab in a concentration of 1 mg/mL to about 20 mg/mL as the antibody;

(ii) succinate in a concentration of 5 mM to 15 mM as the buffering agent, and not comprising any other buffering agent;

(iii) lysine monohydrochloride, dextrose, sucrose or sorbitol in a concentration of 100 mM to 320 mM as the stabiliser, and not comprising any other stabiliser;

20 (iv) polyvinylpyrrolidone of CAS number 9003-39-8 (molecular weight: 2000-3000 g/mol) or polyoxyl 35 castor oil in a concentration of 0.25 mg/mL to 0.75 mg/mL, as the surfactant, and not comprising any other surfactant; wherein the formulation has a pH of 4.9 to 5.2.

25 3. An aqueous pharmaceutical antibody formulation, comprising

(i) Avelumab in a concentration of 1 mg/mL to about 20 mg/mL as the antibody;

(ii) histidine in a concentration of 5 mM to 15 mM as the buffering agent, and not comprising any other buffering agent;

30 (iii) lysine monohydrochloride, dextrose, sucrose, inositol or sorbitol in a concentration of 100 mM to 320 mM as the stabiliser, and not comprising any other stabiliser;

(iv) polyvinylpyrrolidone of CAS number 9003-39-8 (molecular weight: 2000-3000 g/mol) or polyoxyl 35 castor oil in a concentration of 0.25 mg/mL to 0.75 mg/mL, as the surfactant, and not comprising any other surfactant;

wherein the formulation has a pH of 4.8 to 5.2.

41. An aqueous pharmaceutical antibody formulation~~The formulation of claim 1,~~
comprising

- (i) Avelumab in a concentration of 1 mg/mL to about 20 mg/mL as the antibody;
 - 5 (ii) glycine in a concentration of about 10 mM as the buffering agent, and not comprising any other buffering agent;
 - (iii) lysine monohydrochloride in a concentration of about 140 mM as the stabiliser, and not comprising any other stabiliser;
 - (iv) polyoxyl 35 castor oil in a concentration of about 0.5 mg/mL as the surfactant, and
 - 10 not comprising any other surfactant;
- wherein the formulation has a pH of 4.2 to 4.6.

52. An aqueous pharmaceutical antibody formulation~~The formulation of claim 1,~~
comprising

- 15 (i) Avelumab in a concentration of 1 mg/mL to about 20 mg/mL as the antibody;
 - (ii) glycine in a concentration of about 10 mM as the buffering agent, and not comprising any other buffering agent;
 - (iii) lysine acetate in a concentration of about 140 mM as the stabiliser, and not comprising any other stabiliser;
 - 20 (iv) polyoxyl 35 castor oil in a concentration of about 0.5 mg/mL as the surfactant, and not comprising any other surfactant;
- wherein the formulation has a pH of 4.2 to 4.6.

63. An aqueous pharmaceutical antibody formulation~~The formulation of claim 3,~~
25 comprising

- (i) Avelumab in a concentration of 1 mg/mL to about 20 mg/mL as the antibody;
 - (ii) histidine in a concentration of about 10 mM as the buffering agent, and not comprising any other buffering agent;
 - (iii) sucrose in a concentration of about 280 mM as the stabiliser, and not comprising
 - 30 any other stabiliser;
 - (iv) polyoxyl 35 castor oil ~~Kolliphor ELP~~ in a concentration of about 0.5 mg/mL as the surfactant, and not comprising any other surfactant;
- wherein the formulation has a pH of 4.8 to 5.2.

74. An aqueous pharmaceutical antibody formulation~~The formulation of claim 2,~~
comprising

- (i) Avelumab in a concentration of 1 mg/mL to about 20 mg/mL as the antibody;
- (ii) succinate in a concentration of about 10 mM as the buffering agent, and not
- 5 comprising any other buffering agent;
- (iii) lysine monohydrochloride in a concentration of about 140 mM as the stabiliser, and not comprising any other stabiliser;
- (iv) polyoxyl 35 castor oil in a concentration of about 0.5 mg/mL as the surfactant, and not comprising any other surfactant;

10 wherein the formulation has a pH of 4.8 to 5.2.

85. The formulation of claim 41, consisting of:

- (i) Avelumab in a concentration of 20 mg/mL;
 - (ii) glycine in a concentration of 10 mM;
 - 15 (iii) lysine monohydrochloride in a concentration of 140 mM;
 - (iv) polyoxyl 35 castor oil in a concentration of 0.5 mg/mL;
 - (v) HCl or NaOH to adjust the pH;
 - (vi) water (for injection) as the solvent;
- wherein the formulation has a pH of 4.4 (± 0.1).

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96. The formulation of claim 52, consisting of:

- (i) Avelumab in a concentration of 20 mg/mL;
 - (ii) glycine in a concentration of 10 mM;
 - (iii) lysine acetate in a concentration of 140 mM;
 - 25 (iv) polyoxyl 35 castor oil in a concentration of 0.5 mg/mL;
 - (v) HCl or NaOH to adjust the pH;
 - (vi) water (for injection) as the solvent;
- wherein the formulation has a pH of 4.4 (± 0.1).

30 107. The formulation of claim 63, consisting of:

- (i) Avelumab in a concentration of 20 mg/mL;
- (ii) histidine in a concentration of 10 mM;
- (iii) sucrose in a concentration of 280 mM;
- (iv) polyoxyl 35 castor oil Kolliphor ELP in a concentration of 0.5 mg/mL;

(v) HCl or NaOH to adjust the pH;
(vi) water (for injection) as the solvent;
wherein the formulation has a pH of 5.0 ($\pm$ 0.1).

5 ~~118.~~ The formulation of claim ~~74~~, consisting of:

- (i) Avelumab in a concentration of 20 mg/mL;
- (ii) succinate in a concentration of 10 mM;
- (iii) lysine monohydrochloride in a concentration of 140 mM;
- (iv) polyoxyl 35 castor oil in a concentration of 0.5 mg/mL;

10 (v) HCl or NaOH to adjust the pH;
(vi) water (for injection) as the solvent;
wherein the formulation has a pH of 5.0 ($\pm$ 0.1).

15 ~~12. The formulation of any of claims 1-11, wherein said Avelumab has the heavy chain sequence of either (SEQ ID NO:1) or (SEQ ID NO:2), the light chain sequence of (SEQ ID NO:3), and carries a glycosylation on Asn300 comprising FA2 and FA2G1 as the main glycan species, having a joint share of $> 70\%$ of all glycan species.~~

20 ~~13. The formulation of claim 12, wherein in the Avelumab glycosylation said FA2 has a share of $44\% - 54\%$ and said FA2G1 has a share of $25\% - 41\%$ of all glycan species.~~

~~14. The formulation of claim 3, wherein in the Avelumab glycosylation said FA2 has a share of $47\% - 52\%$ and said FA2G1 has a share of $29\% - 37\%$ of all glycan species.~~

25 ~~15. The formulation of claim 14, wherein in the Avelumab glycosylation said FA2 has a share of about 49% and said FA2G1 has a share of $30\% - 35\%$ of all glycan species.~~

30 ~~16. The formulation of any one of claims 12-15, wherein the Avelumab glycosylation further comprises as minor glycan species A2 with a share of $< 5\%$, A2G1 with a share of $< 5\%$, A2G2 with a share of $< 5\%$ and FA2G2 with a share of $< 7\%$ of all glycan species.~~

~~17. The formulation of claim 16, wherein in the Avelumab glycosylation said A2 has a share of 3%-5%, said A2G1 has a share of < 4%, said A2G2 has a share of < 3% and said FA2G2 has a share of 5%-6% of all glycan species.~~

5 ~~18. The formulation of claim 17, wherein in the Avelumab glycosylation said A2 has a share of 3.5% - 4.5%, said A2G1 has a share of 0.5% - 3.5%, said A2G2 has a share of < 2.5% and said FA2G2 has a share of about 5.5% of all glycan species.~~

10 ~~19. The formulation of any one of claims 12-18, wherein said Avelumab has the heavy chain sequence of (SEQ ID NO:2).~~

~~20. The formulation of any one of claims 1-19 which is for intravenous (IV) administration.~~

15 ~~21. A vial containing the formulation of claim 20.~~

~~22. The vial of claim 21 which contains 200 mg avelumab in 10 mL of solution for a concentration of 20 mg/mL.~~

20 ~~23. The vial of claims 21 or 22 which is a glass vial.~~

~~24. The formulation of any one of claims 1-20 for use in treating cancer.~~

25 ~~25. The formulation for use according to claim 24 wherein the cancer is selected from non-small cell lung cancer, urothelial carcinoma, bladder cancer, mesothelioma, Merkel cell carcinoma, gastric or gastroesophageal junction cancer, ovarian cancer, breast cancer, thymoma, adenocarcinoma of the stomach, adrenocortical carcinoma, head and neck squamous cell carcinoma, renal cell carcinoma, melanoma, and/or classical Hodgkin's lymphoma.~~

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