

Patent Claims

1. An aqueous pharmaceutical antibody formulation, comprising:

(i) Avelumab in a concentration of 1 mg/mL to 30 mg/mL as the antibody;

5 (ii) glycine, succinate, citrate phosphate or histidine in a concentration of 5 mM to 35 mM as the buffering agent;

(iii) lysine monohydrochloride, lysine monohydrate, lysine acetate, dextrose, sucrose, sorbitol or inositol in a concentration of 100 mM to 320 mM as the stabiliser;

10 (iv) povidone, polyoxyl castor oil or polysorbate in a concentration of 0.25 mg/mL to 0.75 mg/mL, as the surfactant;

wherein the formulation does not comprise methionine, and
further wherein the formulation has a pH of 3.8 to 5.2.

2. The formulation of claim 1, wherein the formulation does not comprise an antioxidant.

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3. The formulation of claim 1, wherein the concentration of Avelumab is about 10 mg/mL to about 20 mg/mL.

4. The formulation of claim 1-3, wherein the concentration of said glycine, succinate,
20 citrate phosphate or histidine is about 10 mM to about 20 mM.

5. The formulation of claim 1-3, wherein the concentration of said lysine monochloride is about 140 mM to about 280 mM, or the concentration of said lysine monohydrate is about 280 mM, or the concentration of the said lysine acetate is about 140 mM.

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6. The formulation of claim 1-3, wherein the concentration of said dextrose, sucrose, sorbitol or inositol is about 280 mM.

7. The formulation of claim 1-3, wherein the concentration of said povidone, polyoxyl
30 castor oil or polysorbate is about 0.5 mg/mL.

8. The formulation of claim 1-3, wherein the said povidone is the low molecular weight povidone Kollidon 12PF or 17PF, or wherein the said polyoxyl castor oil is Polyoxyl 35 Castor Oil, or wherein the said polysorbate is Polysorbate 80.

9. The formulation of any one of claims 1-8, wherein the concentration of Avelumab is about 20 mg/ml.

- 5 10. The formulation of claim 2, comprising
- (i) Avelumab in a concentration of 1 mg/mL to about 20 mg/mL as the antibody;
 - (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
- 10 mM to 320 mM as the stabiliser, and not comprising any other stabiliser;
- (iv) Kollidon 12PF, 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.
- 15 11. 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 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
- 20 mM to 320 mM as the stabiliser, and not comprising any other stabiliser;
- (iv) Kollidon 12PF 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 12. The formulation of claim 2, comprising
- (i) Avelumab in a concentration of 1 mg/mL to about 20 mg/mL as the antibody;
 - (ii) citrate phosphate in a concentration of 10 mM to 20 mM as the buffering agent, and not comprising any other buffering agent;
 - (iii) lysine monohydrochloride, dextrose, sucrose or sorbitol in a concentration of 100
- 30 mM to 320 mM as the stabiliser, and not comprising any other stabiliser;
- (iv) Kollidon 12PF 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 3.8 to 4.7.

13. The formulation of claim 2, 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

5 comprising any other buffering agent;

(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) Kollidon 12PF 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;

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

14. The formulation of claim 10, comprising

(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

15 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;

20 wherein the formulation has a pH of 4.2 to 4.6.

15. The formulation of claim 10, comprising

(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

25 any other buffering agent;

(iii) lysine acetate 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;

30 wherein the formulation has a pH of 4.2 to 4.6.

16. The formulation of claim 13, 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 any other stabiliser;
5 (iv) Kollidon 12PF 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.

17. The formulation of claim 11, comprising

- 10 (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 comprising any other buffering agent;
(iii) lysine monohydrochloride in a concentration of about 140 mM as the stabiliser, and not comprising any other stabiliser;
15 (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 4.8 to 5.2.

18. The formulation of claim 14, consisting of:

- 20 (i) Avelumab in a concentration of 20 mg/mL;
(ii) glycine 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;
(v) HCl or NaOH to adjust the pH;
25 (vi) water (for injection) as the solvent;
wherein the formulation has a pH of 4.4 (± 0.1).

19. The formulation of claim 15, consisting of:

- (i) Avelumab in a concentration of 20 mg/mL;
30 (ii) glycine in a concentration of 10 mM;
(iii) lysine acetate 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).

20. The formulation of claim 16, consisting of:

- (i) Avelumab in a concentration of 20 mg/mL;
- 5 (ii) histidine in a concentration of 10 mM;
- (iii) sucrose in a concentration of 280 mM;
- (iv) Kollidon 12PF in a concentration of 0.5 mg/mL;
- (v) HCl or NaOH to adjust the pH;
- (vi) water (for injection) as the solvent;

10 wherein the formulation has a pH of 5.0 (± 0.1).

21. The formulation of claim 17, consisting of:

- (i) Avelumab in a concentration of 20 mg/mL;
- (ii) succinate 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 5.0 (± 0.1).

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22. The formulation of any of claims 1-21, 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.

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23. The formulation of claim 22, 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.

24. The formulation of claim 23, 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.

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25. The formulation of claim 24, wherein in the Avelumab glycosylation said FA2 has a share of about 49% and said FA2G1 has a share of about 30% - about 35% of all glycan species.

26. The formulation of any one of claims 22-25, 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.

27. The formulation of claim 26, 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.

28. The formulation of claim 27, wherein in the Avelumab glycosylation said A2 has a share of about 3.5% - about 4.5%, said A2G1 has a share of about 0.5% - about 3.5%, said A2G2 has a share of < 2.5% and said FA2G2 has a share of about 5.5% of all glycan species.

29. The formulation of any one of claims 22-28, wherein said Avelumab has the heavy chain sequence of (SEQ ID NO:2) .

30. The formulation of any one of claims 1-29 which is for intravenous (IV) administration.

31. A vial containing the formulation of claim 30.

32. The vial of claim 31 which contains 200 mg avelumab in 10 mL of solution for a concentration of 20 mg/mL.

33. The vial of claims 31 or 32 which is a glass vial.

34. The formulation of any one of claims 1-30 for use in treating cancer.

35. The formulation for use according to claim 34 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.