SUMMARY

[0008] Provided herein are stable aqueous pharmaceutical formulations comprising an antibody. The formulation comprises an antibody (e.g., an anti-PDL1 antibody), a buffer, sucrose, and a surfactant, wherein the formulation has a pH of about 5.0 to about 7.0.

[0009] In one aspect, provided herein is a stable aqueous pharmaceutical formulation, the formulation comprising an anti-PDL1 monoclonal antibody in a concentration of 40 mg/ml to 125 mg/ml, histidine acetate or sodium acetate in a concentration of 15 mM to 25 mM, sucrose in a concentration of 60 mM to 240 mM, polysorbate in a concentration of 0.005% (w/v) to 0.06% (w/v), and pH 5.0 to 6.3; wherein said monoclonal antibody comprises

(a) a light chain variable region comprising:

(1) HVR-L1 comprising the amino acid sequence RASQDVSTAVA (SEQ ID NO:1);

(2) HVR-L2 comprising the amino acid sequence SASFLYS (SEQ ID NO:2);

(3) HVR-L3 comprising the amino acid sequence QQYLYHPAT (SEQ ID NO:3); and

(b) a heavy chain variable region comprising:

(1) HVR-H1 comprising the amino acid sequence GFTFSDSWIH (SEQ ID NO:4);

(2) HVR-H2 comprising the amino acid sequence AWISPYGGSTYYADSVKG (SEQ ID NO:5);

(3) HVR-H3 comprising the amino acid sequence RHWPGGFDY (SEQ ID NO:6).

[0010] In some embodiments, the monoclonal antibody in the formulation is about 40 mg/ml to about 80 mg/ml. In some embodiments, the monoclonal antibody in the formulation is about 54 mg/ml to about 66 mg/ml. In some embodiments, the monoclonal antibody in the formulation is about 60 mg/ml. In some embodiments, the monoclonal antibody in the formulation is about 60 mg/ml to about 125 mg/ml. In some embodiments, the monoclonal antibody in the formulation is about 125 mg/ml.

[0011] In some embodiments, said histidine acetate or sodium acetate in the formulation is in a concentration of about 17 mM to about 22 mM. In some embodiments, said histidine acetate or sodium acetate in the formulation is in a concentration of about 20 mM.

[0012] In some embodiments, said sucrose in the formulation is about 60 mM to about 180 mM. In some embodiments, said sucrose in the formulation is about 120 mM. In some embodiments, said sucrose in the formulation is about 240 mM.

[0013] In some embodiments, the formulation has a pH of about 5.5 to about 6.1. In some embodiments, the formulation has a pH of about 5.5 or about 5.8.

[0014] In some embodiments, said polysorbate in the formulation is polysorbate 20. In some embodiments, said polysorbate (e.g., polysorbate 20) in the formulation is about 0.02% to about 0.04%.

[0015] In some embodiments, said monoclonal antibody in the formulation is about 60 mg/ml, sucrose in the formulation is about 120 mM, and pH is about 5.8. In some embodiments, said monoclonal antibody in the formulation is about 125 mg/ml, sucrose in the formulation is about 240 mM, and pH is about 5.5.

[0016] In some embodiments, the formulation comprises a monoclonal antibody (e.g., an anti-PDL1 antibody described herein) in an amount of about 60 mg/mL, histidine acetate in a concentration of about 20 mM, sucrose in a concentration of about 120 mM, and polysorbate

CLAIMS

WHAT IS CLAIMED IS:

1. A stable aqueous pharmaceutical formulation, the formulation comprising an anti-PDL1 monoclonal antibody in a concentration of 40 mg/ml to 125 mg/ml, histidine acetate or sodium acetate in a concentration of 15 mM to 25 mM, sucrose in a concentration of 60 mM to 240 mM, polysorbate in a concentration of 0.005% (w/v) to 0.06% (w/v), and pH 5.0 to 6.3; wherein said monoclonal antibody comprises
   (a) a light chain variable region comprising:
      (1) HVR-L1 comprising the amino acid sequence RASQDVSTAVA (SEQ ID NO:1);
      (2) HVR-L2 comprising the amino acid sequence SASFLYS (SEQ ID NO:2);
      (3) HVR-L3 comprising the amino acid sequence QQYLYHPAT (SEQ ID NO:3); and
   (b) a heavy chain variable region comprising:
      (1) HVR-H1 comprising the amino acid sequence GFTFSDSWIH (SEQ ID NO:4);
      (2) HVR-H2 comprising the amino acid sequence AWISPYGGSTYYADSVKG (SEQ ID NO:5);
      (3) HVR-H3 comprising the amino acid sequence RHWPGGFDY (SEQ ID NO:6).
2. The formulation of claim 1, wherein said monoclonal antibody in the formulation is 40 mg/ml to 80 mg/ml.
3. The formulation of claim 1, wherein said monoclonal antibody in the formulation is 54 mg/ml to 66 mg/ml.
4. The formulation of claim 1, wherein said monoclonal antibody in the formulation is 60 mg/ml.
5. The formulation of claim 1, wherein said monoclonal antibody in the formulation is 60 mg/ml to 125 mg/ml.
6. The formulation of claim 1, wherein said monoclonal antibody in the formulation is 125 mg/ml.
7. The formulation of any one of claims 1-6, wherein said histidine acetate or sodium acetate is in a concentration of 17 mM to 22 mM.
8. The formulation of any one of claims 1-6, wherein said histidine acetate or sodium acetate is in a concentration of 20 mM.
9. The formulation of any one of claims 1-8, wherein said sucrose in the formulation is 60 mM to 180 mM.
10. The formulation of any one of claims 1-8, wherein said sucrose in the formulation is 120 mM.
11. The formulation of any one of claims 1-10, wherein the formulation has a pH of 5.5 to 6.1.
12. The formulation of any one of claims 1-10, wherein the formulation has a pH of 5.5 or 5.8.

13. The formulation of any one of claims 1-12, wherein said polysorbate in the formulation is polysorbate 20.
14. The formulation of any one of claims 1-13, wherein said polysorbate in the formulation is 0.02% (w/v) to 0.04% (w/v).
15. The formulation of any one of claims 1-5 and 7-14, wherein said monoclonal antibody in the formulation is 60 mg/ml, sucrose in the formulation is 120 mM, and pH is 5.8.
16. The formulation of claim 1 or 6, wherein said monoclonal antibody in the formulation is 125 mg/ml, sucrose in the formulation is 240 mM, and pH is 5.5.
17. The formulation of any one of claims 1-16, wherein said monoclonal antibody is not subject to prior lyophilization.
18. The formulation of any one of claims 1-17, wherein said monoclonal antibody is a full length antibody.
19. The formulation of any one of claims 1-18, wherein said monoclonal antibody is an IgG1, an IgG2, an IgG3 or an IgG4 antibody.
20. The formulation of any one of claims 1-19, wherein said monoclonal antibody is a humanized antibody.
21. The formulation of any one of claims 1-20, wherein said monoclonal antibody is an antibody fragment comprising an antigen-binding region.
22. The formulation of claim 21, wherein the antibody fragment is a Fab or $F(ab')_2$ fragment.

23. The formulation of any one of claims 1-22, wherein said monoclonal antibody comprises a light chain variable region comprising the amino acid sequence of SEQ ID NO:7, and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:8.
24. The formulation of any one of claims 1-22, wherein said monoclonal antibody comprises a light chain variable region comprising the amino acid sequence of SEQ ID NO:7, and a heavy chain variable region comprising the amino acid sequence of SEQ ID NO:32.
25. The formulation of claim 23 or 24, wherein said monoclonal antibody comprises a light chain comprising the amino acid sequence of SEQ ID NO:9, and a heavy chain comprising the amino acid sequence of SEQ ID NO:10.
26. The formulation of any one of claims 1-25, wherein said monoclonal antibody is stored in a glass vial or a metal alloy container.
27. The formulation of any one of claims 1-26, wherein the formulation is stable at 2-8°C for at least 6 months, at least 12 months, at least 18 months or at least 24 months.
28. The formulation of claim 27, wherein the antibody in the formulation retains at least 80% of its biological activity after storage.
29. The formulation of claim 28, wherein the biological activity is measured by antibody binding to PD-L1.
30. The formulation of any one of claim 1-29 which is sterile.
31. The formulation of any one of claim 1-30 which is suitable to be administered to a subject.
32. The formulation of any one of claim 1-31 which is for intravenous (IV) administration.
33. The formulation of claim 1, wherein said monoclonal antibody is in an amount of 60 mg/mL, said histidine acetate is in a concentration of 20 mM, said sucrose is in a concentration of 120 mM, and said polysorbate is polysorbate 20 in a concentration of 0.04% (w/v), and said formulation has a pH of 5.8.

34. The formulation of claim 1, wherein said monoclonal antibody is in an amount of 125 mg/mL, said histidine acetate is in a concentration of 20 mM, said sucrose is in a concentration of 240 mM, and said polysorbate is polysorbate 20 in a concentration of 0.02% (w/v), and said formulation has a pH of 5.5.

35. An article of manufacture comprising a container holding the stable aqueous pharmaceutical formulation of any one of claims 1-34.

36. The article of claim 35, wherein the container is a glass vial or a metal alloy container.

37. Use of the formulation of any one of claims 1-34 in the manufacture of a medicament for treating a disease or disorder in a subject, wherein the disease or disorder is selected from the group consisting of infection, cancer, and inflammatory disease.

38. The formulation of any one of claims 1-34, wherein the monoclonal antibody comprises a N297A or D265A/N297A substitution in the constant region, numbering of the residue is that of the EU index as in Kabat.