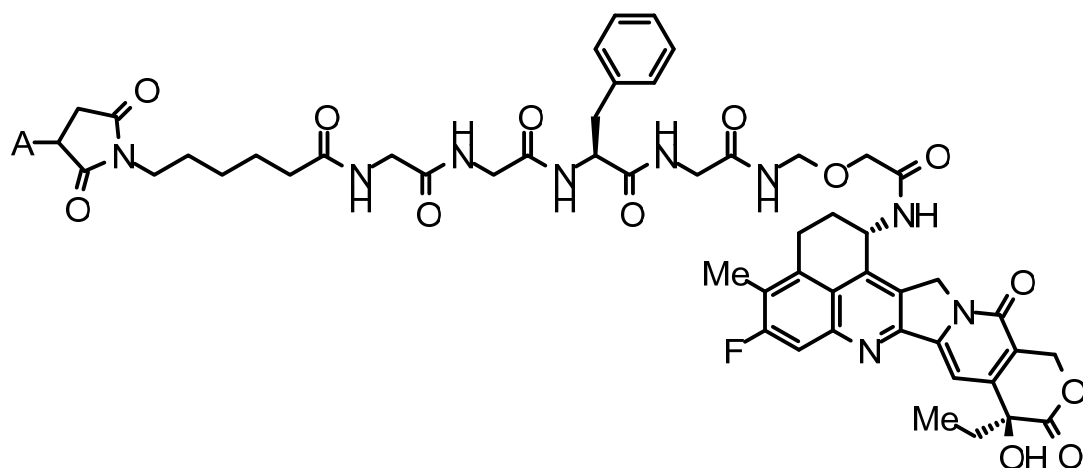


Claims

1. A pharmaceutical composition comprising

- (i) an antibody-drug conjugate,
- (ii) a histidine buffer,
- (iii) sucrose, and
- (iv) polysorbate 80 or polysorbate 20,

wherein the antibody-drug conjugate is an antibody-drug conjugate in which a drug-linker represented by the following formula:



wherein A represents a connecting position to an antibody,

is conjugated to the antibody via a thioether bond, and wherein the amount of polysorbate 80 or polysorbate 20 is, per 20mg of the antibody-drug conjugate, 0.2 to 0.4 mg.

2. The pharmaceutical composition according to claim 1, wherein the amount of polysorbate 80 or polysorbate 20

is, per 20 mg of the antibody-drug conjugate, 0.2 to 0.3 mg.

3. The pharmaceutical composition according to claim 2, wherein the amount of polysorbate 80 or polysorbate 20 is, per 20 mg of the antibody-drug conjugate, 0.2 or 0.3 mg.

4. The pharmaceutical composition according to any one of claims 1 to 3, wherein the amount of sucrose is 24 to 320 mg per 20 mg of the antibody-drug conjugate.

5. The pharmaceutical composition according to claim 4, wherein the amount of sucrose is 90 mg per 20 mg of the antibody-drug conjugate.

6. The pharmaceutical composition according to any one of claims 1 to 5, wherein the histidine buffer is a mixture of L-histidine and L-histidine hydrochloride.

7. The pharmaceutical composition according to claim 6, wherein the histidine buffer is a mixture of L-histidine and L-histidine hydrochloride hydrate.

8. The pharmaceutical composition according to any one of claims 1 to 7, wherein the pH of the composition when

the antibody-drug conjugate is dissolved in water at a concentration of 20 mg/mL is 4.0 to 7.0.

9. The pharmaceutical composition according to any one of claims 1 to 8, wherein the antibody in the antibody-drug conjugate is an anti-HER2 antibody, an anti-HER3 antibody, an anti-TROP2 antibody, an anti-B7-H3 antibody, or an anti-GPR20 antibody.

10. The pharmaceutical composition according to claim 9, wherein the antibody in the antibody-drug conjugate is an anti-HER2 antibody.

11. The pharmaceutical composition according to claim 10, wherein the anti-HER2 antibody is an antibody comprising a heavy chain consisting of an amino acid sequence consisting of amino acid residues 1 to 449 of SEQ ID NO: 1 and a light chain consisting of an amino acid sequence consisting of amino acid residues 1 to 214 of SEQ ID NO: 2, or an antibody comprising a heavy chain consisting of an amino acid sequence represented by SEQ ID NO: 1 and a light chain consisting of an amino acid sequence represented by SEQ ID NO: 2.

12. The pharmaceutical composition according to claim 10 or 11, wherein the average number of units of the drug-

linker conjugated per antibody molecule in the antibody-drug conjugate is in the range of from 7 to 8.

13. The pharmaceutical composition according to any one of claims 10 to 12 comprising,

- (i) per 20 mg of the antibody-drug conjugate,
- (ii) 0.89 mg of L-histidine and 4.04 mg of L-histidine hydrochloride hydrate,
- (iii) 90 mg of sucrose, and
- (iv) 0.3 mg of polysorbate 80.

14. The pharmaceutical composition according to any one of claims 10 to 12 comprising

- (i) 100 mg of the antibody-drug conjugate,
- (ii) 4.45 mg of L-histidine and 20.2 mg of L-histidine hydrochloride hydrate,
- (iii) 450 mg of sucrose, and
- (iv) 1.5 mg of polysorbate 80.

15. The pharmaceutical composition according to claim 9, wherein the antibody in the antibody-drug conjugate is an anti-HER3 antibody.

16. The pharmaceutical composition according to claim 15, wherein the anti-HER3 antibody is an antibody comprising a heavy chain consisting of an amino acid sequence represented by SEQ ID NO: 3 and a light chain

consisting of an amino acid sequence represented by SEQ ID NO: 4, or a variant of the antibody in which a lysine residue at the carboxyl terminus of the heavy chain is deleted.

17. The pharmaceutical composition according to claim 15 or 16, wherein the average number of units of the drug-linker conjugated per antibody molecule in the antibody-drug conjugate is in the range of from 7 to 8.

18. The pharmaceutical composition according to any one of claims 15 to 17 comprising,

- (i) per 20 mg of the antibody-drug conjugate,
- (ii) 0.81 mg of L-histidine and 4.14 mg of L-histidine hydrochloride hydrate,
- (iii) 90 mg of sucrose, and
- (iv) 0.3 mg of polysorbate 20.

19. The pharmaceutical composition according to any one of claims 15 to 17 comprising

- (i) 100 mg of the antibody-drug conjugate,
- (ii) 4.06 mg of L-histidine and 20.7 mg of L-histidine hydrochloride hydrate,
- (iii) 450 mg of sucrose, and
- (iv) 1.5 mg of polysorbate 20.

20. The pharmaceutical composition according to claim 9, wherein the antibody in the antibody-drug conjugate is an anti-TROP2 antibody.

21. The pharmaceutical composition according to claim 20, wherein the anti-TROP2 antibody is an antibody comprising a heavy chain consisting of an amino acid sequence consisting of amino acid residues 20 to 470 of SEQ ID NO: 5 and a light chain consisting of an amino acid sequence consisting of amino acid residues 21 to 234 of SEQ ID NO: 6, or a variant of the antibody in which a lysine residue at the carboxyl terminus of the heavy chain is deleted.

22. The pharmaceutical composition according to claim 20 or 21, wherein the average number of units of the drug-linker conjugated per antibody molecule in the antibody-drug conjugate is in the range of from 3 to 5.

23. The pharmaceutical composition according to any one of claims 20 to 22 comprising,

- (i) per 20 mg of the antibody-drug conjugate,
- (ii) 0.78 mg of L-histidine and 1.05 mg of L-histidine hydrochloride hydrate,
- (iii) 90 mg of sucrose, and
- (iv) 0.2 or 0.3 mg of polysorbate 80.

24. The pharmaceutical composition according to any one of claims 20 to 22 comprising

- (i) 100 mg of the antibody-drug conjugate,
- (ii) 3.88 mg of L-histidine and 5.26 mg of L-histidine hydrochloride hydrate,
- (iii) 450 mg of sucrose, and
- (iv) 1.0 or 1.5 mg of polysorbate 80.

25. The pharmaceutical composition according to claim 9, wherein the antibody in the antibody-drug conjugate is an anti-B7-H3 antibody.

26. The pharmaceutical composition according to claim 25, wherein the anti-B7-H3 antibody is an antibody comprising a heavy chain consisting of an amino acid sequence consisting of amino acid residues 20 to 471 of SEQ ID NO: 7 and a light chain consisting of an amino acid sequence consisting of amino acid residues 21 to 233 of SEQ ID NO: 8, or a variant of the antibody in which a lysine residue at the carboxyl terminus of the heavy chain is deleted.

27. The pharmaceutical composition according to claim 25 or 26, wherein the average number of units of the drug-linker conjugated per antibody molecule in the antibody-drug conjugate is in the range of from 3 to 5.

28. The pharmaceutical composition according to any one of claims 25 to 27 comprising,

- (i) per 20 mg of the antibody-drug conjugate,
- (ii) 0.65 mg of L-histidine and 1.22 mg of L-histidine hydrochloride hydrate,
- (iii) 90 mg of sucrose, and
- (iv) 0.2 or 0.3 mg of polysorbate 20.

29. The pharmaceutical composition according to any one of claims 25 to 27 comprising

- (i) 100 mg of the antibody-drug conjugate,
- (ii) 3.23 mg of L-histidine and 6.12 mg of L-histidine hydrochloride hydrate,
- (iii) 450 mg of sucrose, and
- (iv) 1.0 or 1.5 mg of polysorbate 20.

30. The pharmaceutical composition according to claim 9, wherein the antibody in the antibody-drug conjugate is an anti-GPR20 antibody.

31. The pharmaceutical composition according to claim 30, wherein the anti-GPR20 antibody is an antibody comprising a heavy chain consisting of an amino acid sequence consisting of amino acid residues 20 to 472 of SEQ ID NO: 9 and a light chain consisting of an amino acid sequence consisting of amino acid residues 21 to 234 of SEQ ID NO: 10, or a variant of the antibody in which a

lysine residue at the carboxyl terminus of the heavy chain is deleted.

32. The pharmaceutical composition according to claim 30 or 31, wherein the average number of units of the drug-linker conjugated per antibody molecule in the antibody-drug conjugate is in the range of from 7 to 8.

33. The pharmaceutical composition according to any one of claims 30 to 32 comprising,

- (i) per 20 mg of the antibody-drug conjugate,
- (ii) 0.32 mg of L-histidine and 1.66 mg of L-histidine hydrochloride hydrate,
- (iii) 90 mg of sucrose, and
- (iv) 0.3 mg of polysorbate 80.

34. The pharmaceutical composition according to any one of claims 30 to 32 comprising

- (i) 100 mg of the antibody-drug conjugate,
- (ii) 1.62 mg of L-histidine and 8.29 mg of L-histidine hydrochloride hydrate,
- (iii) 450 mg of sucrose, and
- (iv) 1.5 mg of polysorbate 80.

35. The pharmaceutical composition according to any one of claims 1 to 34, wherein the composition is in the form of an injection.

36. The pharmaceutical composition according to claim 35, wherein the composition is in the form of an aqueous injection.

37. The pharmaceutical composition according to claim 36, wherein the concentration of the antibody-drug conjugate is 20 mg/mL.

38. The pharmaceutical composition according to claim 36 or 37, wherein the composition is frozen.

39. The pharmaceutical composition according to claim 35, wherein the composition is in the form of a lyophilized injection.

40. The pharmaceutical composition according to claim 39, wherein the composition is stored in a brown vial.

41. The pharmaceutical composition according to any one of claims 1 to 40, for use in therapy.

42 Use of the pharmaceutical composition according to any one of claims 1 to 40, for the preparation of a medicament for treating cancer.

43. A method for producing a pharmaceutical composition according to claim 39, comprising the steps of:

- (1) preparing an aqueous solution comprising predetermined amounts of
 - (i) an antibody-drug conjugate,
 - (ii) a histidine buffer,
 - (iii) sucrose, and
 - (iv) polysorbate 80 or polysorbate 20,
- (2) if necessary, adjusting the pH of the aqueous solution to a predetermined value, and then
- (3) lyophilizing the aqueous solution.

44. The production method according to claim 43, wherein the step of lyophilizing the aqueous solution comprises a process of annealing at a shelf temperature which is near the eutectic point of the aqueous solution, wherein near the eutectic point indicates the range of from a temperature which is 1.5°C lower than the eutectic point to a temperature which is 1.5°C higher than the eutectic point.

45. The production method according to claim 44, characterized in that the time for a process of primary drying is shortened compared with that when annealing at a shelf temperature which is 5°C lower than the eutectic point is performed.

46. The production method according to claim 44 or 45, characterized in that a lyophilized cake having less

shrinkage is obtained compared with that when annealing at a shelf temperature which is 5°C lower than the eutectic point is performed.

47. The production method according to claim 43, wherein the step of lyophilizing the aqueous solution comprises a process of performing annealing at a shelf temperature of -4 to -1°C.

48. The production method according to claim 47, wherein the step of lyophilizing the aqueous solution further comprises a process of primary drying at a shelf temperature of -5 to 5°C under a vacuum of 5 to 15 Pa.

49. The production method according to claim 48, wherein the step of lyophilizing the aqueous solution further comprises a process of secondary drying at a shelf temperature of 40 to 50°C under a vacuum of 5 to 15 Pa.