

CLAIMS

1. A pharmaceutical composition, comprising:
 - (1) a histidine buffer with a concentration of 10 mM to 30 mM and a pH of 5.0-6.5; and
 - (2) an anti-BTLA antibody or an antigen-binding fragment thereof, wherein the anti-BTLA antibody or the antigen-binding fragment thereof has an HCDR1, an HCDR2 and an HCDR3 having amino acid sequences set forth in SEQ ID NO: 1, SEQ ID NO: 2 and SEQ ID NO: 3, respectively, and an LCDR1, an LCDR2 and an LCDR3 having amino acid sequences set forth in SEQ ID NO: 4, SEQ ID NO: 5 and SEQ ID NO: 6, respectively;
 - (3) a stabilizer, which is sodium chloride, mannitol, sorbitol, sucrose, maltose, xylitol or trehalose, or is a combination of sodium chloride with mannitol, sorbitol, sucrose or trehalose; and
 - (4) a surfactant selected from polysorbate 80 and polysorbate 20.
2. The pharmaceutical composition according to claim 1, wherein the histidine buffer is a histidine-hydrochloride buffer.
3. The pharmaceutical composition according to claim 2, wherein the histidine buffer is a histidine-histidine hydrochloride buffer.
4. The pharmaceutical composition according to claim 2, wherein the histidine buffer has a pH of 5.0-6.0.
5. The pharmaceutical composition according to claim 1, wherein the stabilizer is a combination of trehalose and sodium chloride.
6. The pharmaceutical composition according to claim 1, wherein the stabilizer is sodium chloride at a concentration of 50-200 mM; or the stabilizer is mannitol at a concentration of 100-300 mM; or the stabilizer is sorbitol at a concentration of 100-300 mM; or the stabilizer is sucrose at a concentration of 100-300 mM; or the stabilizer is trehalose at a concentration of 100-300 mM; or the stabilizer is a combination of 30-100 mM sodium chloride and 50-200 mM mannitol; or the stabilizer is a combination of 30-100 mM sodium chloride and 50-200 mM sorbitol; or the stabilizer is a combination of 30-100 mM sodium chloride and 50-200 mM sucrose; or the stabilizer is a combination of 30-100 mM sodium chloride and 50-200 mM trehalose.
7. The pharmaceutical composition according to claim 6, wherein the stabilizer is the combination of 30-100 mM sodium chloride and 50-200 mM trehalose.
8. The pharmaceutical composition according to claim 1, wherein the surfactant is polysorbate 80.
9. The pharmaceutical composition according to claim 8, wherein the surfactant has a concentration of 0.01%-0.1% (w/v).

10. The pharmaceutical composition according to claim 9, wherein, the surfactant has a concentration of 0.01%-0.05% (w/v).

11. The pharmaceutical composition according to claim 1, wherein the anti-BTLA antibody has a heavy chain variable region having an amino acid sequence set forth in SEQ ID NO: 7 and a light chain variable region having an amino acid sequence set forth in SEQ ID NO: 8; or has a heavy chain variable region having an amino acid sequence set forth in SEQ ID NO: 7 and a light chain variable region having an amino acid sequence set forth in SEQ ID NO: 9; or has a heavy chain variable region having an amino acid sequence set forth in SEQ ID NO: 7 and a light chain variable region having an amino acid sequence set forth in SEQ ID NO: 10.

12. The pharmaceutical composition according to claim 1, wherein the anti-BTLA antibody has a heavy chain amino acid sequence set forth in SEQ ID NO: 11 and a light chain amino acid sequence set forth in SEQ ID NO: 12.

13. The pharmaceutical composition according to any one of claims 1-12, wherein the anti-BTLA antibody or the antigen-binding fragment thereof has a concentration of 5-100 mg/mL.

14. The pharmaceutical composition according to claim 13, wherein the anti-BTLA antibody or the antigen-binding fragment thereof has a concentration of 10-50 mg/mL.

15. The pharmaceutical composition according to claim 14, wherein the anti-BTLA antibody or the antigen-binding fragment thereof has a concentration of 15-25 mg/mL.

16. The pharmaceutical composition according to any one of claims 1-12, comprising or consisting of components as shown in any one of (1) to (10) below:

(1) (a) 10 mg/mL to 50 mg/mL of the anti-BTLA antibody or the antigen-binding fragment thereof; (b) 10-30 mM histidine buffer at a pH of 5.0-6.0; (c) a combination of 30 mM to 100 mM sodium chloride and 50-200 mM trehalose; and (d) 0.01%-0.05% (w/v) of polysorbate 80;

(2) (a) 10 mg/mL to 50 mg/mL of the anti-BTLA antibody or the antigen-binding fragment thereof; (b) 10-30 mM histidine buffer at a pH of 5.0-6.0; (c) a combination of 30 mM to 100 mM sodium chloride and 50-200 mM mannitol; and (d) 0.01%-0.05% (w/v) of polysorbate 80;

(3) (a) 10 mg/mL to 50 mg/mL of the anti-BTLA antibody or the antigen-binding fragment thereof; (b) 10-30 mM histidine buffer at a pH of 5.0-6.0; (c) a combination of 30 mM to 100 mM sodium chloride and 50-200 mM sucrose; and (d) 0.01%-0.05% (w/v) of polysorbate 80;

(4) (a) 10 mg/mL to 50 mg/mL of the anti-BTLA antibody or the antigen-binding fragment thereof; (b) 10-30 mM histidine buffer at a pH of 5.0-6.0; (c) a combination of 30 mM to 100 mM sodium chloride and 50-200 mM sorbitol; and (d) 0.01%-0.05% (w/v) of polysorbate 80;

(5) (a) 10 mg/mL to 50 mg/mL of the anti-BTLA antibody or the antigen-binding fragment thereof; (b) 10-30 mM histidine buffer at a pH of 5.0-6.0; (c) 100 mM to 300 mM trehalose; and (d) 0.01%-0.05% (w/v) of polysorbate 80;

(6) (a) 20 mg/mL of the anti-BTLA antibody or the antigen-binding fragment thereof; (b) 20 mM histidine buffer at a pH of 6.0; (c) a combination of 54 mM sodium chloride and 132 mM trehalose; and (d) 0.02% (w/v) of polysorbate 80;

(7) (a) 20 mg/mL of the anti-BTLA antibody or the antigen-binding fragment thereof; (b) 20 mM histidine buffer at a pH of 5.5; (c) 220 mM trehalose; and (d) 0.02% (w/v) of polysorbate 80;

(8) (a) 20 mg/mL of the anti-BTLA antibody or the antigen-binding fragment thereof; (b) 20 mM histidine buffer at a pH of 5.5; (c) a combination of 50 mM sodium chloride and 140 mM mannitol; and (d) 0.02% (w/v) of polysorbate 80;

(9) (a) 20 mg/mL of the anti-BTLA antibody or the antigen-binding fragment thereof; (b) 20 mM histidine buffer at a pH of 5.5; (c) a combination of 50 mM sodium chloride and 140 mM trehalose; and (d) 0.02% (w/v) of polysorbate 80; and

(10) (a) 20 mg/mL of the anti-BTLA antibody or the antigen-binding fragment thereof; (b) 20 mM histidine buffer at a pH of 5.0-6.0; (c) a combination of 50 mM sodium chloride and 140 mM trehalose; and (d) 0.02% (w/v) of polysorbate 80.

17. The pharmaceutical composition according to claim 1, wherein the pharmaceutical composition comprises or consists of: a histidine-histidine hydrochloride buffer at a pH of 5.5 ± 0.3 and with a concentration of 20 ± 5 mM, 40-80 mM sodium chloride, 120-150 mM trehalose, 0.02-0.04% (w/v) of polysorbate 80, and 15-25 mg/mL of the anti-BTLA antibody or the antigen-binding fragment thereof; wherein the anti-BTLA antibody has a heavy chain amino acid sequence set forth in SEQ ID NO: 11 and a light chain amino acid sequence set forth in SEQ ID NO: 12.

18. Use of the pharmaceutical composition according to any one of claims 1-12 in the preparation of a medicament for treating BTLA-mediated diseases, wherein the diseases are tumors.

19. The use according to claim 18, wherein the tumors include melanoma, breast cancer, renal cancer, prostate cancer, colon cancer, lung cancer, pancreatic cancer, bone cancer, skin cancer, head or neck cancer, uterine cancer, ovarian cancer, rectal cancer, anal cancer, stomach cancer, testicular cancer, small intestine cancer, cervical cancer, vaginal cancer, Hodgkin's disease, non-Hodgkin's lymphoma, esophageal cancer, cancer of the endocrine system, thyroid cancer, carcinoma of adrenal gland, soft tissue cancer, urethral cancer, chronic or acute leukemia, chronic myeloid leukemia, acute lymphoblastic leukemia, chronic lymphocytic leukemia, childhood solid tumor, lymphocytic lymphoma, bladder cancer, kidney or ureteral cancer, renal pelvis cancer, neoplasms of the central nervous system, primary central nervous system lymphoma, tumor angiogenesis, spinal axis tumor, brain stem glioma, pituitary adenoma,

Kaposi's sarcoma, epidermoid carcinoma, squamous cell carcinoma, T-cell lymphoma and environmentally induced cancers.