Claims

1. A pharmaceutical composition comprising crizanlizumab that has light chain and heavy chain amino acid sequences in SEQ ID NO: 10 and SEQ ID NO: 9 respectively, and a variant of crizanlizumab (iso-crizanlizumab), in which amino acid aspartic acid at position 32 of SEQ ID NO: 10 is changed to iso-aspartic acid.

2. The pharmaceutical composition of claim 1 further comprising succinimide of crizanlizumab at position 32 of SEQ ID NO: 10.

3. The pharmaceutical composition of claim 1 or 2, wherein the iso-crizanlizumab consists of homo-iso-crizanlizumab and hetero-iso-crizanlizumab.

4. The pharmaceutical composition of any one of the claims 1 to 3 comprising from about 20% to about 50% crizanlizumab of the total charge variants in the pharmaceutical composition.

5. The pharmaceutical composition of any one of the preceding claims further comprising a buffer system, wherein the composition has a pH from about 5.5 to about 7.5.

6. The pharmaceutical composition of claim 5, wherein the pH is about 5.5 to about 7, preferably about 5.5 to about 6.5, preferably about 5.7 to about 6.3, preferably the pH is about 5.9 to about 6.1.

7. The pharmaceutical composition of claim 7 or claim 6, wherein the buffer system is citrate buffer phosphate buffer.

8. The pharmaceutical composition of any one of the preceding claims further comprising a stabilizer, preferably the stabilizer is sucrose, preferably sucrose is in a concentration of 50 mM to 350 mM, preferably 100 mM to 300 mM.

9. The pharmaceutical composition of any one of the preceding claims further comprising an isotonizing agent, preferably the isotonizing agent is sodium chloride, preferably sodium chloride is in a concentration of 50 mM to 300 mM.

10. The pharmaceutical composition of any one of the preceding claims further comprising a surfactant, preferably the surfactant is a non-ionic surfactant, preferably the surfactant is polysorbate, preferably polysorbate 80, preferably the surfactant, preferably polysorbate, is in a concentration of 0.01% w/v (0.1 mg/mL) to 0.1% w/v (1 mg/mL).

11. The pharmaceutical composition of any one of the preceding claims, comprising antibody in a concentration from 5 mg/ml to 50 mg/ml.

12. A pharmaceutical composition comprising antibody in a concentration from about 5 to about 50 mg/ml, and a buffer system, wherein the composition has a pH from about 5.5 to about 7.5, preferably the pH is about 5.7 to about 6.3.

13. The pharmaceutical composition according to claim 12, wherein the buffer system is citrate (e.g. sodium citrate) and/or phosphate (e.g. potassium phosphate).

14. The pharmaceutical composition according to claim 12 or claim 13 further comprising a stabilizer, preferably the stabilizer is sucrose, preferably the stabilizer is present in a concentration of about 50 mM to about 300 mM.

15. The pharmaceutical composition according to any one of the claims 12 to 14 further comprising a non-ionic surfactant, preferably the surfactant is polysorbate 80, preferably the surfactant, preferably polysorbate 80, is present in a concentration of about 0.01% w/v (0.1 mg/ml) to 0.1% w/v (1 mg/ml).

16. The pharmaceutical composition according to any one of the claims 12 to 15 further comprising an isotonizing agent, preferably the isotonizing agent is NaCl, preferably the isotonizing agent, preferably NaCl is present in a concentration of about 50 mM to 300 mM.

17. A pharmaceutical composition comprising antibody (crizanlizumab and any variants thereof) in a concentration from about 5 to about 50 mg/ml, sucrose in a concentration of about 50 mM to about 350mM, and a buffer system, wherein the composition has a pH from about 5.5 to about 7.5, preferably about 5.7 to about 6.3, e.g. about 6.0, and wherein the buffer system is citrate buffer and/or phosphate buffer.

18. The pharmaceutical composition according to any one of the preceding claims in a lyophilized form.

19. The pharmaceutical composition according to any one of the preceding claims, wherein the IC50 determined by using the pharmaceutical composition is in the range of about 4.6-6.2 µg/ml, the IC50 is determined in vitro.

20. The pharmaceutical composition according to any one of claims 1-19 for use in a method of treating sickle cell disease, especially preventing Vascular Occlusion Crises (VOC) in a subject in need thereof, wherein a therapeutically effective dose of antibody (crizanlizumab and any variants thereof) is to be administered to subject, wherein the therapeutically effective dose is 5mg or 7.5mg per kilogram of the body weight of subject, wherein preferably the first 2 doses are to be administered 2 weeks apart, followed by administration of the same dose every four weeks, preferably the pharmaceutical composition is to be administered to a subject by intravenous route.