CLAIMS

1. A liquid aqueous formulation comprising:

(1) an isolated human anti-TNFα antibody comprising a light chain variable region (LCVR) having a CDR3 domain comprising the amino acid sequence of SEQ ID NO: 3, a CDR2 domain comprising the amino acid sequence of SEQ ID NO: 5, and a CDR1 domain comprising the amino acid sequence of SEQ ID NO: 7; and comprises a heavy chain variable region (HCVR) having a CDR3 domain comprising the amino acid sequence of SEQ ID NO: 4, a CDR2 domain comprising the amino acid sequence of SEQ ID NO: 6, and a CDR1 domain comprising the amino acid sequence of SEQ ID NO: 8;

(2) a polysorbate; and,

(3) less than 50 mg/ml of mannitol or sorbitol;

wherein the formulation has a pH of 4.7 to 5.7 and does not contain a buffer or a salt, and wherein injection of the formulation into a human subject results in a Pain Visual Analog Scale (VAS) score of less than 1.0.

2. A liquid aqueous formulation comprising:

(1) an isolated human anti-TNFα antibody comprising a light chain variable region (LCVR) having a CDR3 domain comprising the amino acid sequence of SEQ ID NO: 3, a CDR2 domain comprising the amino acid sequence of SEQ ID NO: 5, and a CDR1 domain comprising the amino acid sequence of SEQ ID NO: 7; and comprises a heavy chain variable region (HCVR) having a CDR3 domain comprising the amino acid sequence of SEQ ID NO: 4, a CDR2 domain comprising the amino acid sequence of SEQ ID NO: 6, and a CDR1 domain comprising the amino acid sequence of SEQ ID NO: 8;

(2) a polysorbate; and,

(3) less than 50 mg/ml of mannitol or sorbitol;

wherein the formulation has a pH of 4.7 to 5.7 and does not contain a buffer or a salt, and

wherein injection of the formulation reduces pain associated with the injection in a human subject by at least about 50% when compared to injection of an otherwise identical formulation that comprises a salt and/or a buffer.

3. A liquid aqueous formulation consisting essentially of:

(1) more than 50 mg/ml of an isolated human anti-TNFα antibody-comprising a light chain variable region (LCVR) having a CDR3 domain comprising the amino acid

sequence of SEQ ID NO: 3, a CDR2 domain comprising the amino acid sequence of SEQ ID NO: 5, and a CDR1 domain comprising the amino acid sequence of SEQ ID NO: 7; and comprises a heavy chain variable region (HCVR) having a CDR3 domain comprising the amino acid sequence of SEQ ID NO: 4, a CDR2 domain comprising the amino acid sequence of SEQ ID NO: 6;

(2) a polysorbate; and,

(3) less than 50 mg/ml of mannitiol or sorbitol,

wherein the formulation has a pH of 4.7 to 5.7, and wherein injection of the formulation into a human subject results in a Pain Visual Analog Scale (VAS) score of less than 1.0.

4. The formulation of claim 2, wherein the pain associated with the injection is assessed using a Pain Visual Analog Scale (VAS).

5. The formulation of claim 2, wherein the otherwise identical formulation comprises a citrate phosphate buffer and sodium chloride.

6. A liquid aqueous formulation comprising:

(1) an isolated human anti-TNFα antibody comprising a light chain variable region (LCVR) having a CDR3 domain comprising the amino acid sequence of SEQ ID NO: 3, a CDR2 domain comprising the amino acid sequence of SEQ ID NO: 5, and a CDR1 domain comprising the amino acid sequence of SEQ ID NO: 7; and comprises a heavy chain variable region (HCVR) having a CDR3 domain comprising the amino acid sequence of SEQ ID NO: 4, a CDR2 domain comprising the amino acid sequence of SEQ ID NO: 6;

(2) a polysorbate; and,

(3) less than 50 mg/ml of mannitol or sorbitol,

wherein the formulation has a pH of 4.7 to 5.7 and does not contain a buffer or a salt, and wherein the formulation is stable up to about 30°C for at least 6 days.

7. The formulation of claim 6, wherein the formulation is stable up to about 30°C for 10 days.

8. The formulation of claim 6, wherein the formulation is stable up to about 30°C for 14 days.

9. The formulation of any one of claims 1-8, comprising about 38-46 mg/ml of mannitol.

10. The formulation of any one of claims 1-9, wherein the polysorbate is polysorbate 80.

11. The formulation of any one of claims 1-9, wherein the concentration of polysorbate is about 0.1 to 1.5.

12. The formulation of any one of claims 1-11, wherein the concentration of the anti-TNFα antibody is 95-105 mg/ml.

13. The formulation of any one of claims 1-12, wherein the antibody has a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO: 1 and a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO: 2.

14. The formulation of any one of claims 1-12, wherein the antibody is adalimumab or golimumab, or a biosimilar thereof.

15. A liquid aqueous formulation consisting essentially of

(1) a concentration of 90-110 mg/ml of an isolated human anti-TNFα antibody, having a light chain variable region (LCVR) having a CDR3 domain comprising the amino acid sequence of SEQ ID NO: 3, a CDR2 domain comprising the amino acid sequence of SEQ ID NO: 5, and a CDR1 domain comprising the amino acid sequence of SEQ ID NO: 7; and having a heavy chain variable region (HCVR) having a CDR3 domain comprising the amino acid sequence of SEQ ID NO: 4, a CDR2 domain comprising the amino acid sequence of SEQ ID NO: 6, and a CDR1 domain comprising the amino acid sequence of SEQ ID NO: 8;

(2) a polysorbate; and,

(3) about 38-46 mg/ml of mannitol,

wherein the formulation has a pH of 4.7 to 5.7.

16. The formulation of any one of claims 1-15 comprising about 30-90 mg of the antibody.

17. A liquid aqueous formulation comprising:

(1) an isolated human anti-TNFα antibody comprising a light chain variable region (LCVR) having a CDR3 domain comprising the amino acid sequence of SEQ ID NO: 3, a CDR2 domain comprising the amino acid sequence of SEQ ID NO: 5, and a CDR1 domain comprising the amino acid sequence of SEQ ID NO: 7; and comprises a heavy chain variable region (HCVR) having a CDR3 domain comprising the amino acid sequence of SEQ ID NO: 4, a CDR2 domain comprising the amino acid sequence of SEQ ID NO: 6;

(2) polysorbate-80; and,

(3) less than 50 mg/ml of mannitiol,

wherein the formulation has a pH of 4.7 to 5.7 and does not contain a buffer or a salt, and wherein the formulation has a characteristic selected from the group consisting of:

a) a conductivity of less than about 2 mS/cm;

b) a hydrodynamic diameter (D_h) which is at least about 50% less than the D_h of the protein in a buffered solution at a given concentration; and

c) a hydrodynamic diameter (D_h) of less than about 4 nm.

18. Use of the formulation of any one of claims 1-17 in the manufacture of a medicament for the treatment of a disorder associated with detrimental TNFα activity in a patient, wherein said medicament is to be administered to the patient.

19. The use of claim 18, wherein the disorder is selected from the group consisting of rheumatoid arthritis, Crohn's disease, psoriatic arthritis, psoriasis, juvenile idiopathic arthritis, ankylosing spondylitis, ulcerative colitis, and hidradenitis suppurativa.

20. The use of claim 18, wherein the formulation is administered to the patient according to a periodicity selected from the group consisting of weekly, biweekly, every three weeks, and monthly.

21. The use of claim 20 wherein the administration is self-administration.

22. Use of a formulation comprising an isolated human anti-TNFα antibody in the manufacture of a medicament to be subcutaneously administered to a patient, such that injection pain is reduced upon administration,

wherein the formulation comprises more than 50 mg/ml of adalimumab; polysorbate-80; and less than 50 mg/ml of mannitol,

wherein the formulation has a pH of 4.7 to 5.7 and does not contain a buffer or a salt.

23. The use of claim 22, wherein the injection pain is determined to be less than 1.0 according to a Pain Visual Analog Scale (VAS).

24. The use of claim 22 or 23, wherein the concentration of polysorbate is about 0.1 to 1.5.

25. The use of any one of claims 22-24, wherein the formulation comprises more than 75 mg/ml of the antibody.

26. The use of any one of claims 22-25, wherein the formulation comprises 38-46 mg/ml of mannitol.

CLAIMS

1. A liquid aqueous formulation comprising:

(1) an isolated human anti-TNFα antibody comprising a light chain variable region (LCVR) having a CDR3 domain comprising the amino acid sequence of SEQ ID NO: 3, a CDR2 domain comprising the amino acid sequence of SEQ ID NO: 5, and a CDR1 domain comprising the amino acid sequence of SEQ ID NO: 7; and comprises a heavy chain variable region (HCVR) having a CDR3 domain comprising the amino acid sequence of SEQ ID NO: 4, a CDR2 domain comprising the amino acid sequence of SEQ ID NO: 6, and a CDR1 domain comprising the amino acid sequence of SEQ ID NO: 8;

(2) a polysorbate; and,

(3) less than 50 mg/ml of mannitol or sorbitol;

wherein the formulation has a pH of 4.7 to 5.7 and does not contain a buffer or a salt, and wherein injection of the formulation into a human subject results in a Pain Visual Analog Scale (VAS) score of less than 1.0.

2. A liquid aqueous formulation comprising:

(1) an isolated human anti-TNFα antibody comprising a light chain variable region (LCVR) having a CDR3 domain comprising the amino acid sequence of SEQ ID NO: 3, a CDR2 domain comprising the amino acid sequence of SEQ ID NO: 5, and a CDR1 domain comprising the amino acid sequence of SEQ ID NO: 7; and comprises a heavy chain variable region (HCVR) having a CDR3 domain comprising the amino acid sequence of SEQ ID NO: 4, a CDR2 domain comprising the amino acid sequence of SEQ ID NO: 6, and a CDR1 domain comprising the amino acid sequence of SEQ ID NO: 8 ;

(2) a polysorbate; and,

(3) less than 50 mg/ml of mannitol or sorbitol;

wherein the formulation has a pH of 4.7 to 5.7 and does not contain a buffer or a salt, and

wherein injection of the formulation reduces pain associated with the injection in a human subject by at least about 50% when compared to injection of an otherwise identical formulation that comprises a salt and/or a buffer.

3. A liquid aqueous formulation consisting essentially of:

(1) more than 50 mg/ml of an isolated human anti-TNFα antibody comprising a light chain variable region (LCVR) having a CDR3 domain comprising the amino acid sequence of SEQ ID NO: 3, a CDR2 domain comprising the amino acid sequence of SEQ ID NO: 5, and a CDR1 domain comprising the amino acid sequence of SEQ ID NO: 7; and comprises a heavy chain variable region (HCVR) having a CDR3 domain comprising the amino acid sequence of SEQ ID NO: 4, a CDR2 domain comprising the amino acid sequence of SEQ ID NO: 6;

(2) a olysorbate; and

(3) less than 50 mg/ml of mannitiol or sorbitol,

wherein the formulation has a pH of 4.7 to 5.7, and wherein injection of the formulation into a human subject results in a

Pain Visual Analog Scale (VAS) score of less than 1.0.

4. The formulation of claim 2, wherein the pain associated with the injection is assessed using a Pain Visual Analog Scale (VAS).

5. The formulation of claim 2, wherein the otherwise identical formulation comprises a citrate phosphate buffer and sodium chloride.

6. A liquid aqueous formulation comprising:

(1) an isolated human anti-TNFα antibody comprising a light chain variable region (LCVR) having a CDR3 domain comprising the amino acid sequence of SEQ ID NO: 3, a CDR2 domain comprising the amino acid sequence of SEQ ID NO: 5, and a CDR1 domain comprising the amino acid sequence of SEQ ID NO: 7; and comprises a heavy chain variable region (HCVR) having a CDR3 domain comprising the amino acid sequence of SEQ ID NO: 4, a CDR2 domain comprising the amino acid sequence of SEQ ID NO:;

(2) a polysorbate; and,

(3) less than 50 mg/ml of mannitol or sorbitol ;

wherein the formulation has a pH of 4.7 to 5.7 and does not contain a buffer or a salt, and wherein the formulation is stable up to about 30°C for at least 6 days.

7. The formulation of claim 6, wherein the formulation is stable up to about 30°C for 10 days.

8. The formulation of claim 6, wherein the formulation is stable up to about 30°C for 14 days.

9. The formulation of any one of claims 1-8, comprising about 38-46 mg/ml of mannitol.

10. The formulation of any one of claims 1-8 and 9~~claim~~, wherein the polysorbate is polysorbate 80.

11. The formulation of any one of claims 1-8 and 9, wherein the concentration of polysorbate is about 0.1 to 1.5.

12. The formulation of any one of claims 1-8, 9, and 11, wherein the concentration of the anti-TNFα antibody, is 95-105 mg/ml.

13. The formulation of any one of claims 1-12, wherein the antibody, has a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO: 1 and a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO: 2.

14. The formulation of any one of claims 1-12, wherein the antibody is adalimumab or golimumab, or a biosimilar thereof.

15. A liquid aqueous formulation consisting essentially of

(1) a concentration of 90-110 mg/ml of an isolated human anti-TNFα antibodyhaving a light chain variable region (LCVR) having a CDR3 domain comprising the amino acid sequence of SEQ ID NO: 3, a CDR2 domain comprising the amino acid sequence of SEQ ID NO: 5, and a CDR1

domain comprising the amino acid sequence of SEQ ID NO: 7; and having a heavy chain variable region (HCVR) having a CDR3 domain comprising the amino acid sequence of SEQ ID NO: 4, a CDR2 domain comprising the amino acid sequence of SEQ ID NO: 6, and a CDR1 domain comprising the amino acid sequence of SEQ ID NO: 8;

(2) a polysorbate; and,

(3) about 38-46 mg/ml of mannitol, wherein the formulation has a pH of 4.7 to 5.7.

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16. The formulation of any one of claims 1-8, 9, 10-12, 13, 14, and 15, comprising about 30-90 mg of the antibody.

17. A liquid aqueous formulation comprising:

(1) an isolated human anti-TNFα antibody comprising a light chain variable region (LCVR) having a CDR3 domain comprising the amino acid sequence of SEQ ID NO: 3, a CDR2 domain comprising the amino acid sequence of SEQ ID NO: 5, and a CDR1 domain comprising the amino acid sequence of SEQ ID NO: 7; and comprises a heavy chain variable region (HCVR) having a CDR3 domain comprising the amino acid sequence of SEQ ID NO: 4, a CDR2 domain comprising the amino acid sequence of SEQ ID NO: 6;

(2) polysorbate-80; and,

(3) less than 50 mg/ml of a mannitiol;

wherein the formulation has a pH of 4.7 to 5.7 and does not contain a buffer or a salt, and wherein the formulation has a characteristic selected from the group consisting of:

a) a conductivity of less than about 2 mS/cm;

b) a hydrodynamic diameter (D_h) which is at least about 50% less than the D_h of the protein in a buffered solution at a given concentration; and

c) a hydrodynamic diameter (D_h) of less than about 4 nm.

18. Use of the formulation of any one of claims 1-17in the manufacture of a medicament for the treatment of a disorder associated with detrimental TNFα activity in a patient, wherein said medicament is to be administered to the patient.

19. The use of claim 18, wherein the disorder is selected from the group consisting of rheumatoid arthritis, Crohn's disease, psoriatic arthritis, psoriasis, juvenile

idiopathic arthritis, ankylosing spondylitis, ulcerative colitis, and hidradenitis suppurativa.

20. The use of claim 18, wherein the formulation is administered to the patient according to a periodicity selected from the group consisting of weekly, biweekly, every three weeks, and monthly.

21. The use of claim 20wherein the administration is self-administration.

22. Use of a formulation comprising an isolated human anti-TNFα antibody in the manufacture of a medicament to be subcutaneously administered to a patient, such that injection pain is reduced upon administration,

wherein the formulation comprises more than 50 mg/ml of adalimumab; polysorbate -80; and less than 50 mg/ml of mannito,

wherein the formulation has a pH of 4.7 to 5.7 and does not contain a butter or a salt.

23. The use of claim 22, wherein the injection pain is determined to be less than 1.0 according to a Pain Visual Analog Scale (VAS).

24. The use of claim 22 or 23, wherein the concentration of polysorbate is about 0.1 to 1.5.

25. The use of any one of claims 22-24, wherein the formulation comprises more than 75 mg/ml of the antibody.

26. The use of any one of claims 22-25, wherein the formulation comprises 38-46 mg/ml of mannitol.









