CLAIMS

1. An aqueous, buffered pharmaceutical composition comprising adalimumab and a buffer, wherein (i) the composition is free or substantially free of a buffer combination that comprises both a citrate buffer and a phosphate buffer; and (ii) the composition exhibits long term stability.

2. The composition of claim 1 wherein a histidine buffer, or the combination of a histidine buffer and succinate buffer, constitute essentially the sole buffers in the composition; and the composition comprises: 50 to 150 mg of adalimumab, and at least one of the following: (i) up to 300 mM of at least one stabilizer selected from glycine and arginine; (ii) up to 300 mM of at least one polyol selected from the group consisting of mannitol, sorbitol and trehalose.

3. The composition of claim 2 further comprising at least one of (a) 0.01 to 0.1 wt% of a polysorbate or poloxamer surfactant; and (b) up to 150 mM sodium chloride.

4. The composition of claim 3 wherein the buffer consists of, or consists essentially of, histidine buffer, and the composition comprises said surfactant and either (a) both stabilizer and polyol; or (b) polyol or stabilizer, but not both.

5. The composition of claim 4 further comprising up to 100 mM sodium chloride.

6. An aqueous, buffered pharmaceutical composition, free or substantially free of citrate buffer, exhibiting long term stability, said composition comprising: (i) adalimumab; (ii) a histidine buffer; (iii) a polysorbate or poloxamer surfactant; and (iv) one or both of the following:

   (a) a stabilizer selected from glycine and arginine, and combinations thereof; and

   (b) a polyol selected from sorbitol, mannitol, and trehalose, and combinations thereof.

7. The composition of claim 6 comprising up to 100 mM sodium chloride.

8. The composition of claim 6 wherein the amount of adalimumab is 50 to 150 mg/ml; the buffer is present in an amount up to 50 mM; the amount of

stabilizer (if present) is up to 300 mM; the amount of polyol (if present) is up to 300 mM; and the amount of surfactant is 0.01 to 0.1 wt.%

9. The composition of claim 7 in which either the polyol is present; or the stabilizer is present; but not both.

10. The composition of claim 9 in which the polyol is present, but the stabilizer is absent.

11. The composition of claim 9 in which the stabilizer is present, but the polyol is absent.

12. An aqueous, buffered pharmaceutical composition comprising (a) adalimumab and (b) histidine as a sole buffer, wherein the composition further comprises at least one of the following: (i) a polyol selected from mannitol, sorbitol and trehalose or combinations thereof; (ii) a stabilizer selected from glycine and arginine or combinations thereof; and (iii) a surfactant selected from polysorbate and poloxamer surfactants or combination thereof.

13. The composition of claim 12 wherein the stabilizer is present; and the composition is free or substantially free of polyol.

14. The composition of claim 12 wherein the polyol is present and comprises mannitol; and the composition is free or substantially free of the stabilizer.

15. The composition of claim 12 wherein the polyol is present and comprises sorbitol; and the composition is free or substantially free of the stabilizer.

16. The composition of claim 12 wherein the stabilizer comprises glycine or arginine, but not both.

17. The composition of claim 12 wherein the stabilizer comprises up to 100 mM sodium choride.

18. The composition of claim 12 wherein the composition does not comprise both the stabilizer and the polyol.

19. A method for enhancing long term stability in an aqueous, buffered adalimumab formulation, comprising one or more of the steps of:

(a) incorporating histidine buffer, succinate buffer, or a combination thereof, in the formulation based on empirical data indicating that such buffers contribute to the stability of the formulation to a greater extent than other buffers or buffer combinations; or

(b) incorporating glycine, arginine or a combination thereof as stabilizers in the formulation, based upon empirical data indicating that such stabilizers contribute to the stability of the formulation to a greater extent than other stabilizers; or

(c) substantially excluding the presence of buffer or buffer combinations comprising citrate buffer, based upon empirical data indicating that such buffer or buffer combinations perform poorly in terms of stabilizing the formulation in comparison to other buffers.

20. A single dosage composition of adalimumab exhibiting long term stability consisting of, or consisting essentially of: (i) about 40 mg/ml adalimumab; (ii) buffer consisting solely of histidine; (iii) glycine; (iv) sodium chloride; and (v) polysorbate 80.

Claims

1. A buffered aqueous pharmaceutical composition comprising:

   (i) adalimumab;

   (ii) buffer; and

   (iii) stabilizer;

   wherein the composition is free of both polyol and surfactant, has a pH of about 5 to about 6, and is stable for one week at 40° C or two weeks at 25° C.

2. The composition of claim 1 wherein the stabilizer is selected from the group consisting of an amino acid, a salt, EDTA and a metal ion.

3. The composition of claim 2 wherein the amino acid is selected from the group consisting of glycine, arginine and combinations thereof.

4. The composition of claim 2 wherein the salt is selected from the group consisting of sodium chloride and sodium sulfate.

5. The composition of claim 4 wherein the salt is, or includes, sodium sulfate.

6. The composition of claim 1 wherein the buffer contains no citrate and consists of histidine, succinate, or a combination thereof; and wherein the composition may further optionally include phosphate acting as a stabilizer and not as a buffer.

7. The composition of claim 6 wherein histidine is the sole buffer in the composition; the composition has osmolality of about 180 to 420 mOsM; the composition is suitable for administration to a subject as a single dosage; the composition has a concentration of adalimumab in the range of 30 to about 50 mg/ml; and the dosage contains about 10 to 80 mg of adalimumab.

8. The composition of claim 7 wherein the dosage is about 40 mg and results in less pain upon administration to a subject in comparison to an adalimumab composition having a buffer that comprises citrate.

9. A buffered aqueous pharmaceutical composition having pH of about 5 to about 6, comprising:

(i) adalimumab;

(i) buffer consisting essentially of histidine, succinate, or both;

(ii) stabilizer consisting essentially of:

(a) glycine, arginine, or both; or

(a) and (b); where (b) is sodium chloride, sodium sulfate or both;

wherein the composition is free of both polyol and surfactant, and is stable for one week at 40° C or two weeks at 25° C.

10. The composition of claim 9 comprising histidine as the sole buffer, and glycine.

11. The composition of claim 9 comprising histidine as the sole buffer, and arginine.

12. The composition of claim 9 wherein (b) is, or includes, sodium sulfate.

13. The composition of claim 9 further comprising phosphate acting as a stabilizer and not as a buffer such that the composition has pH from about 5 to about 6 without phosphate.

14. The composition of claim 9 having osmolality of about 180 to 420 mOsM; wherein the composition is suitable for administration to a subject as a single dosage; the composition has a

concentration of adalimumab in the range of 30 to about 50 mg/ml; and the dosage contains about 10 to 80 mg of adalimumab.

15. The composition of claim 14 wherein the dosage is about 40 mg and results in less pain upon administration to a subject in comparison to an adalimumab composition having a buffer comprising citrate.

16. An aqueous buffered pharmaceutical composition comprising adalimumab and a citrate-free buffer, wherein the composition is free or substantially free of both polyol and surfactant, has a pH of about 5 to about 6, and is stable for one week at 40° C or two weeks at 25° C.

17. The composition of claim 16 comprising: (i) adalimumab; (ii) buffer consisting solely of histidine, succinate, or combination thereof; and (iii) glycine, arginine or both.

18. The composition of claim 17 further comprising phosphate acting as a stabilizer and not as a buffer.

19. The composition of claim 17 further comprising a salt selected from sodium chloride and sodium sulfate.

20. The composition of claim 17 having osmolality of about 180 to 420 mOsM; wherein the composition is suitable for administration to a subject as a single dosage; said composition having a concentration of adalimumab in the range of 30 to about 50 mg/ml; said dosage containing about 40 mg of adalimumab and resulting in less pain upon administration to a subject in comparison to an adalimumab composition having a buffer that comprises citrate.