SUMMARY

In an aspect of the present disclosure, there is provided a pharmaceutical composition comprising about 400 U/mL to about 600 U/mL of C1 esterase inhibitor, a citrate buffer or a phosphate buffer, and a pH range from about 6.5 to about 8.0, and wherein said composition is to be subcutaneously administered to a subject in need thereof.

In another aspect of the present disclosure, there is provided a pharmaceutical composition comprising about 400 U/mL to about 600 U/mL of C1 esterase inhibitor, a citrate buffer, and a pH range from about 6.5 to about 8.0, and wherein said composition is to be subcutaneously administered to a subject in need thereof.

In a further aspect of the present disclosure, there is provided a pharmaceutical composition comprising about 400 U/mL to about 600 U/mL of C1 esterase inhibitor, a phosphate buffer, and a pH range from about 6.5 to about 8.0, and wherein said composition is to be subcutaneously administered to a subject in need thereof.

In another aspect of the present disclosure, there is provided a pharmaceutical composition comprising C1 esterase inhibitor and a citrate buffer or a phosphate buffer, wherein said composition is to be subcutaneously administered to a subject in need thereof in liquid form of said C1 esterase inhibitor at a concentration of about 400 U/mL to about 600 U/mL and at a pH from about 6.5 to about 8.0.

In a further aspect of the present disclosure, there is provided a pharmaceutical composition comprising C1 esterase inhibitor and a citrate buffer, wherein said composition is to be subcutaneously administered to a subject in need thereof in liquid form of said C1 esterase inhibitor at a concentration of about 400 U/mL to about 600 U/mL and at a pH from about 6.5 to about 8.0.

In another aspect of the present disclosure, there is provided a pharmaceutical composition comprising C1 esterase inhibitor and a phosphate buffer, wherein said composition is to be subcutaneously administered to a subject in need thereof in liquid form of said C1 esterase inhibitor at a concentration of about 400 U/mL to about 600 U/mL and at a pH from about 6.5 to about 8.0.

In a further aspect of the present disclosure, there is provided a pharmaceutical composition for use to treat, inhibit, and/or prevent hereditary angioedema (HAE) in a subject in need thereof, said composition comprising about 400 U/mL to about 600 U/mL of Cl esterase inhibitor, a citrate buffer or a phosphate buffer, and a pH range from about 6.5 to about 8.0, and wherein the composition is to be subcutaneously administered to a subject in need thereof.

In another aspect of the present disclosure, there is provided a pharmaceutical composition for use to treat, inhibit, and/or prevent hereditary angioedema (HAE) in a subject in need thereof, said composition comprising about 400 U/mL to about 600 U/mL of Cl esterase inhibitor, a citrate buffer, and a pH range from about 6.5 to about 8.0, and wherein the composition is to be subcutaneously administered to a subject in need thereof.

In a further aspect of the disclosure, there is provided a pharmaceutical composition for use to treat, inhibit, and/or prevent hereditary angioedema (HAE) in a subject in need thereof, said composition comprising about 400 U/mL to about 600 U/mL of Cl esterase inhibitor, a phosphate buffer, and a pH range from about 6.5 to about 8.0, and wherein the composition is to be subcutaneously administered to a subject in need thereof.

In another aspect of the present disclosure, there is provided a pharmaceutical composition comprising about 400 U/mL to about 600 U/mL of an isolated protein comprising an amino acid sequence at least 90% identical to residues 23 to 500 of SEQ ID NO: 1 as a C1 esterase inhibitor, a citrate buffer or a phosphate buffer, and a pH range from about 6.5 to about 8.0, and wherein said composition is to be subcutaneously administered to a subject in need thereof.

In a further aspect of the present disclosure, there is provided a pharmaceutical composition comprising about 400 U/mL to about 600 U/mL of a glycoprotein comprising an amino acid sequence at least 90% identical to residues 23 to 500 of SEQ ID NO: 1 as a C1 esterase inhibitor, a citrate buffer or a phosphate buffer, and a pH range from about 6.5 to about 8.0, and wherein said composition is to be subcutaneously administered to a subject in need thereof.

In another aspect of the present disclosure, there is provided a pharmaceutical composition comprising a C1 esterase inhibitor, sodium citrate, and having a pH ranging from about 6.5 to about 8.0, wherein the C1 esterase inhibitor is present at a concentration of about 400 to about 600 U/mL, and wherein the C1 esterase inhibitor comprises the amino acid sequence of residues 23 to 500 of SEQ ID NO: 1, wherein said composition is to be subcutaneously administered to a subject in need thereof.

In a further aspect of the present disclosure, there is provided a lyophilized composition to be subcutaneously administered to a subject in need thereof following reconstitution, wherein reconstitution produces the pharmaceutical composition as disclosed herein.

In another aspect of the present disclosure, there is provided a solid composition to be subcutaneously administered to a subject in need thereof following reconstitution, wherein reconstitution produces the composition as disclosed herein.

In a further aspect of the present disclosure, there is provided a composition in powder form to be subcutaneously administered to a subject in need thereof following reconstitution, wherein reconstitution produces the composition as disclosed herein.

In another aspect of the present disclosure, there is provided a lyophilized preparation of a C1 esterase inhibitor to be subcutaneously administered to a subject in need thereof following reconstitution, wherein reconstitution produces the pharmaceutical composition as disclosed herein.

In a further aspect of the present disclosure, there is provided a lyophilized pharmaceutical composition comprising sodium citrate, and at least 2000 U of C1 esterase inhibitor and less than 5000 U of C1 esterase inhibitor, wherein following reconstitution, said lyophilized composition achieves a solution comprising: (i) a concentration of about 400 to about 600 U/mL of C1 esterase inhibitor, (ii) citrate at a concentration of about 5mM to about 15mM, and (iii) a pH ranging from about 6.5 to about 8.0, wherein the solution is to be subcutaneously administered to a subject in need thereof to treat HAE and wherein the C1 esterase inhibitor comprises the amino acid sequence of residues 23 to 500 of SEQ ID NO: 1.

In another aspect of the present disclosure, there is provided a lyophilized pharmaceutical composition comprising sodium citrate, and at least 2000 U of C1 esterase inhibitor and less than 5000 U of C1 esterase inhibitor, wherein following reconstitution said lyophilized composition achieves a solution comprising: (i) a concentration of 500 U/mL of C1 esterase inhibitor, (ii) citrate at a concentration of about 5mM to about 15mM, and (iii) a pH ranging from about 6.5 to about 8.0, wherein the solution is to be subcutaneously administered to a subject in need thereof to treat HAE and wherein the C1 esterase inhibitor consists of the amino acid sequence of residues 23 to 500 of SEQ ID NO: 1

In a further aspect of the present disclosure, there is provided a kit comprising the composition as disclosed herein and at least one syringe and/or a reconstitution buffer.

In another aspect of the present disclosure, there is provided a kit comprising at least one syringe pre-loaded with the composition as disclosed herein, and instructions for using said kit.

In a further aspect of the present disclosure, there is provided a use of a composition as disclosed herein in the manufacture of a medicament for increasing the level of Cl esterase inhibitor in the blood of a subject in need thereof

In another aspect of the present disclosure, there is provided a use of a composition as disclosed herein in the manufacture of a medicament for the treatment, inhibition and/or prevention of hereditary angioedema (HAE) in a subject in need thereof, wherein the composition is to be subcutaneously administered to the subject in need thereof.

In a further aspect of the present disclosure, there is provided a use of a composition in the manufacture of a medicament for the treatment, inhibition, and/or prevention of hereditary angioedema (HAE) in a subject in need thereof, wherein said composition comprises about 400 U/mL to about 600 U/mL of C1 esterase inhibitor, a citrate buffer or a phosphate buffer, and a pH range from about 6.5 to about 8.0, and wherein said medicament is to be subcutaneously administered to a subject in need thereof.

In another aspect of the present disclosure, there is provided a of a pharmaceutical composition in the manufacture of a medicament for the treatment, inhibition and/or prevention of hereditary angioedema (HAE) in a subject in need thereof, said pharmaceutical composition, comprising:

about 400 U/mL to about 600 U/mL of C1 esterase inhibitor and a dose of at least 2000 U of a C1 esterase inhibitor;

a citrate buffer or a phosphate buffer;

a pH ranging from about 6.5 to about 8.0;

wherein the C1 esterase inhibitor comprises an amino acid sequence at least 95% identical to residues 23 to 500 of SEQ ID NO:1; and

wherein the pharmaceutical composition is to be subcutaneously administered to the subject in need thereof which increases the level of C1 esterase inhibitor in the blood of the subject to at least 0.4 U/mL.

In a further aspect of the present disclosure, there is provided a use of a pharmaceutical composition in the manufacture of a medicament for the treatment, inhibition and/or prevention of hereditary angioedema (HAE) in a subject in need thereof, said pharmaceutical composition, comprising:

about 400 U/mL to about 600 U/mL of C1 esterase inhibitor and a dose of at least 2000 U of a C1 esterase inhibitor;

a citrate buffer,

a pH ranging from about 6.5 to about 8.0;

wherein the C1 esterase inhibitor comprises an amino acid sequence at least 95% identical to residues 23 to 500 of SEQ ID NO:1; and

wherein the pharmaceutical composition is to be subcutaneously administered to the subject in need thereof which increases the level of C1 esterase inhibitor in the blood of the subject to at least 0.4 U/mL.

In another aspect of the present disclosure, there is provided a use of a pharmaceutical composition in the manufacture of a medicament for the treatment, inhibition and/or prevention of hereditary angioedema (HAE) in a subject in need thereof, said pharmaceutical composition, comprising:

about 400 U/mL to about 600 U/mL of C1 esterase inhibitor and a dose of at least 2000 U of a C1 esterase inhibitor;

a phosphate buffer,

a pH ranging from about 6.5 to about 8.0;

wherein the C1 esterase inhibitor comprises an amino acid sequence at least 95% identical to residues 23 to 500 of SEQ ID NO:1; and

wherein the pharmaceutical composition is to be subcutaneously administered to the subject in need thereof which increases the level of C1 esterase inhibitor in the blood of the subject to at least 0.4 U/mL.

In a further aspect of the present disclosure, there is provided a medicament of C1 esterase inhibitor to be subcutaneously administered to a subject in need thereof, said medicament comprising C1 esterase inhibitor and a citrate buffer or a phosphate buffer, wherein said medicament is formulated in a powder form for reconstitution with sterile water in order to provide a liquid solution to be subcutaneously administered to the subject in need thereof, said liquid solution comprising a pH of about 6.5 to about 8.0 and comprising about 400 U/mL to about 600 U/mL of C1 esterase inhibitor.

In another aspect of the present disclosure, there is provided a use of the medicament as disclosed herein in the manufacture of a medicament for the treatment, inhibition and/or prevention of hereditary angioedema (HAE) in a subject in need thereof.

In a further aspect of the present disclosure, there is provided a use of C1 esterase inhibitor in the manufacture of a medicament to be subcutaneously administered to a subject in need thereof, wherein said medicament comprises C1 esterase inhibitor and a citrate buffer or a phosphate buffer, wherein said medicament is formulated in powder form for reconstitution with sterile water in order to provide a liquid solution to be subcutaneously administered to the subject in need thereof, wherein said liquid solution comprises a pH of about 6.5 to about 8.0 and comprises about 400 U/mL to about 600 U/mL of C1 esterase inhibitor.

In another aspect of the present disclosure, there is provided a use of a pharmaceutical composition in the manufacture of a medicament for prophylactic treatment of hereditary angioedema (HAE) in a subject in need thereof, comprising C1 esterase inhibitor, sodium citrate, and having a pH ranging from about 6.5 to about 8.0, wherein the C1 esterase inhibitor has a concentration of about 500 U/mL, and wherein the C1 esterase inhibitor comprises the amino acid sequence of residues 23 to 500 of SEQ ID NO: 1, wherein the pharmaceutical composition is to be subcutaneously administered

to the subject in need thereof, and wherein the pharmaceutical composition is for administration to the subject to increase the level of the C1 esterase inhibitor in the blood of the subject to at least 0.4 U/mL.

In a further aspect of the present disclosure, there is provided a composition comprising at least one C1 esterase inhibitor wherein the at least one C1 esterase inhibitor is present at 400 U/ml to 500 U/ml for use in treating, inhibiting, or preventing hereditary angioedema (HAE) in a subject in need thereof and wherein

(i) said composition is to be subcutaneously administered to a subject in need thereof,

(ii) the hereditary angioedema is Type I or Type II HAE,

(iii) the composition comprises at least one amino acid or salt thereof,

(iv) the composition has a pH of between 6.5 and 8.0, and

(v) the composition comprises a buffer which comprises about 10 to about 30 mM sodium citrate.

In accordance with the instant disclosure, methods for inhibiting, treating, and/or preventing a disorder associated with a deficiency in C1 esterase inhibitor in a subject are provided. In a particular example, the method comprises administering a composition comprising at least one C1 esterase inhibitor.

In accordance with the instant disclosure, therapeutic compositions are also provided. In a particular example, the composition comprises at least one C1 esterase inhibitor and, optionally, at least one pharmaceutically acceptable carrier for delivery (e.g. intravenous or subcutaneous delivery). Kits comprising a composition comprising at least one C1 esterase inhibitor are also provided herein.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 provides an amino acid sequence of human C1 esterase inhibitor.

Figure 2 provides a graph of the effect of protein concentration on viscosity for initial spin concentration samples.

DETAILED DESCRIPTION OF THE INVENTION

The restoration of active C1 esterase inhibitor levels in patients having a disorder associated with deficient or reduced levels of active C1 esterase inhibitor (e.g., HAE) is an effective measure for treating such disorders. Currently, C1 esterase inhibitor (such as Cinryze® (ViroPharma, Inc.; Exton, PA)) is administered to a patient intravenously by a medical professional. Herein, formulations of a C1 esterase inhibitor (such as Cinryze®) are provided which are also effective for subcutaneous (SC) administration. Surprisingly, the subcutaneous administration of the C1 esterase inhibitor is sufficient to maintain the blood levels of the C1 esterase inhibitor. The SC administration of a C1 esterase

inhibitor fulfills an unmet medical need due to the limitations of intravenous administration in HAE patients.

In accordance with the instant invention, compositions and methods for inhibiting (e.g., reducing or slowing), treating, and/or preventing a disorder associated with C1 esterase inhibitor deficiency in a subject are provided. In a particular embodiment, the methods comprise administering (e.g., subcutaneously or intravenously) to a subject in need thereof at least one C1 esterase inhibitor. In a particular embodiment, the C1 esterase inhibitor is administered subcutaneously after an initial administration of the C1 esterase inhibitor intravenously.

What is claimed is:

1. A pharmaceutical composition comprising about 400 U/mL to about 600 U/mL of C1 esterase inhibitor, a citrate buffer or a phosphate buffer, and a pH range from about 6.5 to about 8.0, and wherein said composition is to be subcutaneously administered to a subject in need thereof.

2. A pharmaceutical composition comprising about 400 U/mL to about 600 U/mL of C1 esterase inhibitor, a citrate buffer, and a pH range from about 6.5 to about 8.0, and wherein said composition is to be subcutaneously administered to a subject in need thereof.

3. A pharmaceutical composition comprising about 400 U/mL to about 600 U/mL of C1 esterase inhibitor, a phosphate buffer, and a pH range from about 6.5 to about 8.0, and wherein said composition is to be subcutaneously administered to a subject in need thereof.

4. A pharmaceutical composition comprising C1 esterase inhibitor and a citrate buffer or a phosphate buffer, wherein said composition is to be subcutaneously administered to a subject in need thereof in liquid form of said C1 esterase inhibitor at a concentration of about 400 U/mL to about 600 U/mL and at a pH from about 6.5 to about 8.0.

5. A pharmaceutical composition comprising C1 esterase inhibitor and a citrate buffer, wherein said composition is to be subcutaneously administered to a subject in need thereof in liquid form of said C1 esterase inhibitor at a concentration of about 400 U/mL to about 600 U/mL and at a pH from about 6.5 to about 8.0.

6. A pharmaceutical composition comprising C1 esterase inhibitor and a phosphate buffer, wherein said composition is to be subcutaneously administered to a subject in need thereof in liquid form of said C1 esterase inhibitor at a concentration of about 400 U/mL to about 600 U/mL and at a pH from about 6.5 to about 8.0.

7. A pharmaceutical composition for use to treat, inhibit, and/or prevent hereditary angioedema (HAE) in a subject in need thereof, said composition comprising about 400 U/mL to about 600 U/mL of Cl esterase inhibitor, a citrate buffer or a phosphate

buffer, and a pH range from about 6.5 to about 8.0, and wherein the composition is to be subcutaneously administered to a subject in need thereof .

8. A pharmaceutical composition for use to treat, inhibit, and/or prevent hereditary angioedema (HAE) in a subject in need thereof, said composition comprising about 400 U/mL to about 600 U/mL of Cl esterase inhibitor, a citrate buffer, and a pH range from about 6.5 to about 8.0, and wherein the composition is to be subcutaneously administered to a subject in need thereof.

9. A pharmaceutical composition for use to treat, inhibit, and/or prevent hereditary angioedema (HAE) in a subject in need thereof, said composition comprising about 400 U/mL to about 600 U/mL of Cl esterase inhibitor, a phosphate buffer, and a pH range from about 6.5 to about 8.0, and wherein the composition is to be subcutaneously administered to a subject in need thereof.

10. A pharmaceutical composition comprising about 400 U/mL to about 600 U/mL of an isolated protein comprising an amino acid sequence at least 90% identical to residues 23 to 500 of SEQ ID NO: 1 as a C1 esterase inhibitor, a citrate buffer or a phosphate buffer, and a pH range from about 6.5 to about 8.0, and wherein said composition is to be subcutaneously administered to a subject in need thereof.

11. A pharmaceutical composition comprising about 400 U/mL to about 600 U/mL of a glycoprotein comprising an amino acid sequence at least 90% identical to residues 23 to 500 of SEQ ID NO: 1 as a C1 esterase inhibitor, a citrate buffer or a phosphate buffer, and a pH range from about 6.5 to about 8.0, and wherein said composition is to be subcutaneously administered to a subject in need thereof.

12. The composition of any one of claims 10 to 11 wherein the buffer is the citrate buffer.

13. The composition of any one of claims 10 to 11 wherein the buffer is the phosphate buffer.

14. The composition of any one of claims 1, 2, 4, 5, 7, 8, 10, 11, 12, or 13, wherein the buffer comprises sodium citrate.

15. The composition of any one of claims 1, 2, 4, 5, 7, 8, 10, 11, 12, 13, or 14, wherein citrate is present at about 5 mM to about 50 mM.

16. The composition of any one of claims 1 to 15, wherein the Cl esterase inhibitor, isolated protein or glycoprotein comprises an amino acid sequence more than 90% identical to residues 23 to 500 of SEQ ID NO: 1.

17. The composition of any one of claims 1 to 16, wherein the Cl esterase inhibitor, isolated protein or glycoprotein is present at about 500 U/mL.

18. The composition of any one of claims 1 to 17, wherein the composition comprises about 100 U to about 5,000 U of the C1 esterase inhibitor, isolated protein or glycoprotein.

19. The composition of any one of claims 1 to 18, wherein the C1 esterase inhibitor, isolated protein, or glycoprotein has less than a 10% loss in monomer content when stored for two years at 4° C.

20. The composition of any one of claims 1 to 18, wherein the C1 esterase inhibitor, isolated protein, or glycoprotein has less than about 10% loss in monomer content loss when stored for two weeks at 25° C.

21. The composition of any one of claims 1 to 18, wherein the C1 esterase inhibitor, isolated protein, or glycoprotein has less than about 1% loss in purity when stored for two weeks at 25° C.

22. A pharmaceutical composition comprising a C1 esterase inhibitor, sodium citrate, and having a pH ranging from about 6.5 to about 8.0, wherein the C1 esterase inhibitor is present at a concentration of about 400 to about 600 U/mL, and wherein the C1 esterase inhibitor comprises the amino acid sequence of residues 23 to 500 of SEQ ID NO: 1, wherein said composition is to be subcutaneously administered to a subject in need thereof.

23. The pharmaceutical composition of claim 22, wherein the C1 esterase inhibitor is present at a concentration of about 500 U/mL.

24. The composition of any one of claims 1 to 23, wherein the composition has a viscosity of less than about 35 mPa-s.

25. The composition of any one of claims 1 to 24, for increasing the level of Cl esterase inhibitor in the blood of a subject in need thereof.

26. The composition of any one of claims 1 to 25, wherein the pH ranges from about 6.5 to about 7.5.

27. The composition of any one of claims 1 to 26, wherein the composition is reconstituted from a lyophilized powder.

28. A lyophilized composition to be subcutaneously administered to a subject in need thereof following reconstitution, wherein reconstitution produces the pharmaceutical composition as defined in any one of claims 1 to 27.

29. A solid composition to be subcutaneously administered to a subject in need thereof following reconstitution, wherein reconstitution produces the composition as defined in any one of claims 1 to 26.

30. A composition in powder form to be subcutaneously administered to a subject in need thereof following reconstitution, wherein reconstitution produces the composition of claim 26.

31. A lyophilized preparation of a C1 esterase inhibitor to be subcutaneously administered to a subject in need thereof following reconstitution, wherein reconstitution produces the pharmaceutical composition as defined in any one of claims 1 to 27.

32. A lyophilized pharmaceutical composition comprising sodium citrate, and at least 2000 U of C1 esterase inhibitor and less than 5000 U of C1 esterase inhibitor, wherein following reconstitution, said lyophilized composition achieves a solution comprising: (i) a concentration of about 400 to about 600 U/mL of C1 esterase inhibitor, (ii) citrate at a concentration of about 5mM to about 15mM, and (iii) a pH ranging from about 6.5 to about 8.0, wherein the solution is to be subcutaneously administered to a subject in need thereof to treat HAE and wherein the C1 esterase

inhibitor comprises the amino acid sequence of residues 23 to 500 of SEQ ID NO: 1.

33. A lyophilized pharmaceutical composition comprising sodium citrate, and at least 2000 U of C1 esterase inhibitor and less than 5000 U of C1 esterase inhibitor, wherein following reconstitution said lyophilized composition achieves a solution comprising: (i) a concentration of 500 U/mL of C1 esterase inhibitor, (ii) citrate at a concentration of about 5mM to about 15mM, and (iii) a pH ranging from about 6.5 to about 8.0, wherein the solution is to be subcutaneously administered to a subject in need thereof to treat HAE and wherein the C1 esterase inhibitor consists of the amino acid sequence of residues 23 to 500 of SEQ ID NO: 1.

34. The composition of claim 32 or claim 33, wherein the pH of the solution ranges from about 6.5 to about 7.5.

35. The lyophilized pharmaceutical composition of claim 32 or claim 33, wherein the concentration of citrate in the solution is about 10 mM.

36. The composition of any one of claims 32 to 35, wherein the composition is for HAE prophylactic treatment.

37. A kit comprising the composition as defined in any one of claims 1 to 36 and at least one syringe and/or a reconstitution buffer.

38. A kit comprising at least one syringe pre-loaded with the composition of any one of claims 1 to 36, and instructions for using said kit.

39. Use of a composition as defined in any one of claims 1 to 36 in the manufacture of a medicament for increasing the level of Cl esterase inhibitor in the blood of a subject in need thereof.

40. The use according to claim 39, wherein the composition is for increasing the level of C1 esterase inhibitor in the blood of the subject to at least 0.3 U/mL.

41. The use of claim 40, wherein the composition is for maintaining increased blood levels of Cl esterase inhibitor at least 50% of the time between uses of the composition.

42. Use of a composition as defined in any one of claims 1 to 36 in the manufacture of a medicament for the treatment, inhibition and/or prevention of hereditary angioedema (HAE) in a subject in need thereof, wherein the composition is to be subcutaneously administered to the subject in need thereof.

43. The use of any one of claims 39 to 42, wherein the composition is to be administered to the subject in a high initial dose of Cl esterase inhibitor, followed by at least one subsequent lower maintenance dose.

44. The use according to claim 43, wherein the high initial dose comprises about 500 U to about 10,000 U of C1 esterase.

45. The use of claim 43 to claim 44, wherein:

(i) the hereditary angioedema is Type I or Type II HAE,

(ii) the administration of the Cl esterase inhibitor results in HAE prophylactic treatment,

(iii) the treatment of HAE results in at least a reduction in the severity and/or number of HAE attacks, or

(iv) the administration of the at least one C1 esterase inhibitor results in treatment of an HAE attack.

46. Use of a composition in the manufacture of a medicament for the treatment, inhibition, and/or prevention of hereditary angioedema (HAE) in a subject in need thereof, wherein said composition comprises about 400 U/mL to about 600 U/mL of C1 esterase inhibitor, a citrate buffer or a phosphate buffer, and a pH range from about 6.5 to about 8.0, and wherein said medicament is to be subcutaneously administered to a subject in need thereof .

47. Use of a pharmaceutical composition in the manufacture of a medicament for the treatment, inhibition and/or prevention of hereditary angioedema (HAE) in a subject in need thereof, said pharmaceutical composition, comprising:

about 400 U/mL to about 600 U/mL of C1 esterase inhibitor and a dose of at least 2000 U of a C1 esterase inhibitor;

a citrate buffer or a phosphate buffer;

a pH ranging from about 6.5 to about 8.0;

wherein the C1 esterase inhibitor comprises an amino acid sequence at least 95% identical to residues 23 to 500 of SEQ ID NO:1; and

wherein the pharmaceutical composition is to be subcutaneously administered to the subject in need thereof which increases the level of C1 esterase inhibitor in the blood of the subject to at least 0.4 U/mL.

48. Use of a pharmaceutical composition in the manufacture of a medicament for the treatment, inhibition and/or prevention of hereditary angioedema (HAE) in a subject in need thereof, said pharmaceutical composition, comprising:

about 400 U/mL to about 600 U/mL of C1 esterase inhibitor and a dose of at least 2000 U of a C1 esterase inhibitor;

a citrate buffer,

a pH ranging from about 6.5 to about 8.0;

wherein the C1 esterase inhibitor comprises an amino acid sequence at least 95% identical to residues 23 to 500 of SEQ ID NO:1; and

wherein the pharmaceutical composition is to be subcutaneously administered to the subject in need thereof which increases the level of C1 esterase inhibitor in the blood of the subject to at least 0.4 U/mL.

49. Use of a pharmaceutical composition in the manufacture of a medicament for the treatment, inhibition and/or prevention of hereditary angioedema (HAE) in a subject in need thereof, said pharmaceutical composition, comprising:

about 400 U/mL to about 600 U/mL of C1 esterase inhibitor and a dose of at least 2000 U of a C1 esterase inhibitor;

a phosphate buffer,

a pH ranging from about 6.5 to about 8.0;

wherein the C1 esterase inhibitor comprises an amino acid sequence at least 95% identical to residues 23 to 500 of SEQ ID NO:1; and

wherein the pharmaceutical composition is to be subcutaneously administered to the subject in need thereof which increases the level of C1 esterase inhibitor in the blood of the subject to at least 0.4 U/mL.

50. The use of any one of claims 47 to 49, wherein the composition comprises about 2000 U of the C1 esterase inhibitor.

51. The use of any one of claims 47 to 49, wherein the composition comprises about 5000 U of the C1 esterase inhibitor.

52. The use of any one of claims 39 to 51, wherein the pH ranges from about 6.5 to about 7.5.

53. The use of any one of claims 46 to 48, wherein the buffer comprises sodium citrate.

54. The use of claim 53, wherein the citrate is present at about 5 mM to about 50 mM.

55. A medicament of C1 esterase inhibitor to be subcutaneously administered to a subject in need thereof, said medicament comprising C1 esterase inhibitor and a citrate buffer or a phosphate buffer, wherein said medicament is formulated in a powder form for reconstitution with sterile water in order to provide a liquid solution to be subcutaneously administered to the subject in need thereof, said liquid solution comprising a pH of about 6.5 to about 8.0 and comprising about 400 U/mL to about 600 U/mL of C1 esterase inhibitor.

56. Use of the medicament as defined in claim 55 in the manufacture of a medicament for the treatment, inhibition and/or prevention of hereditary angioedema (HAE) in a subject in need thereof.

57. Use of C1 esterase inhibitor in the manufacture of a medicament to be subcutaneously administered to a subject in need thereof, wherein said medicament comprises C1 esterase inhibitor and a citrate buffer or a phosphate buffer, wherein said medicament is formulated in powder form for reconstitution with sterile water in order to provide a liquid solution to be subcutaneously administered to the subject in need thereof, wherein said liquid solution comprises a pH of about 6.5 to about 8.0 and comprises about 400 U/mL to about 600 U/mL of C1 esterase inhibitor.

58. Use of a pharmaceutical composition in the manufacture of a medicament for prophylactic treatment of hereditary angioedema (HAE) in a subject in need thereof, comprising C1 esterase inhibitor, sodium citrate, and having a pH ranging from about 6.5 to about 8.0, wherein the C1 esterase inhibitor has a concentration of

about 500 U/mL, and wherein the C1 esterase inhibitor comprises the amino acid sequence of residues 23 to 500 of SEQ ID NO: 1, wherein the pharmaceutical composition is to be subcutaneously administered to the subject in need thereof, and wherein the pharmaceutical composition is for administration to the subject to increase the level of the C1 esterase inhibitor in the blood of the subject to at least 0.4 U/mL.

59. The use of claim 58, wherein the pharmaceutical composition is to be subcutaneously administered to a subject in need thereof.

60. The use of claim 58 or claim 59, wherein the pharmaceutical composition is to be administered to the subject to result in at least a reduction in the severity and/or number of HAE attacks.

61. The use of any one of claims 58 to 60, wherein the pharmaceutical composition is reconstituted from a lyophilized powder prior to use.

62. A composition comprising at least one C1 esterase inhibitor wherein the at least one C1 esterase inhibitor is present at 400 U/ml to 500 U/ml for use in treating, inhibiting, or preventing hereditary angioedema (HAE) in a subject in need thereof and wherein

(i) said composition is to be subcutaneously administered to a subject in need thereof,
(ii) the hereditary angioedema is Type I or Type II HAE,
(iii) the composition comprises at least one amino acid or salt thereof,
(iv) the composition has a pH of between 6.5 and 8.0, and
(v) the composition comprises a buffer which comprises about 10 to about 30 mM sodium citrate.

63. The composition for use according to claim 62, wherein the at least one C1 esterase inhibitor is present at 500 U/ml.

64. The composition for use according to claim 62 or claim 63, wherein the at least one C1 esterase inhibitor is to be administered to the subject at a dose ranging from 500 Units to 5,000 Units.

65. The composition for use according to any one of claims 62 to 64, wherein the composition is to be administered to the subject, wherein the at least one C1 esterase inhibitor leads to increased levels of the C1 esterase inhibitor in the blood of the subject, wherein the blood levels of the C1 esterase inhibitor are increased to at least 0.3 U/mL.

66. The composition for use according to any one of claims 62 to 65, wherein the composition is for maintaining blood levels of the C1 esterase inhibitor at or above 0.4 U/mL for at least 50% of the time between uses of the composition.

67. The composition for use according to any one of claims 62 to 66, wherein:

(i) the composition is for HAE prophylactic treatment,
(ii) the composition is for treatment of HAE resulting in at least a reduction in the severity and/or number of HAE attacks, or
(iii) the composition is for treatment of an HAE attack.

68. The composition for use according to any one of claims 62 to 67, wherein the composition comprises a buffer which comprises about 20 mM sodium citrate.

69. The composition for use according to any one of claims 62 to 67, wherein the composition has a pH of between 6.5 and 7.5.

70. The composition for use according to any one of claims 62 to 69, wherein the composition is formed from a lyophilized form by reconstitution in a buffer prior to use.

71. The use of any one of claims 46 to 54, wherein the composition comprises 400 U/mL to 500 U/mL of C1 esterase inhibitor.