manufacturability and/or tolerability of a formulated therapeutic antibody in an aqueous pharmaceutical formulation. Thus, while a specific formulation adjustment may provide a beneficial impact to a given aspect of the formulation, the same adjustment may also negatively impact other aspects of the formulation. Even further adding to the complexity, a nearly limitless number of different formulation components (e.g., buffers and excipients), as well as concentrations and ratios thereof, have been reported. However, there remains little-to-no correlation for predicting the impact of a specific formulation on the various properties and characteristics of a given therapeutic antibody.

Accordingly, there is a need for an aqueous pharmaceutical formulation of therapeutic antibodies suitable for SQ, IM and/or IP administration and which is well tolerated by patients, exhibiting a therapeutically beneficial level of injection-associated pain. More particularly, there is a need for such aqueous pharmaceutical formulation for highly concentrated therapeutic antibodies possessing an isoelectric point not compatible with neutral pH in solution, requiring aqueous formulation at an acidic pH. Even more particularly, there is a need for an aqueous pharmaceutical formulation of ixekizumab suitable for SQ, IM and/or IP administration and which is well tolerated by patients, exhibiting an improved level of injection-associated pain over the commercial pharmaceutical formulation of ixekizumab (as described in U.S. Patent Number 9,376,491). Such aqueous pharmaceutical formulation must also provide stability for the therapeutic antibody and preserve the properties of the therapeutic antibody essential for therapeutic efficacy. Such aqueous pharmaceutical formulations must also be amendable to manufacturing, preferably having an extended shelf life.

Summary

In one aspect of the present disclosure, there is provided a~~n~~ bufferless aqueous pharmaceutical formulation comprising:

(i) an anti-IL-17A antibody at a concentration of 80 mg/mL +/- 10%;

(ii) sucrose in a concentration of 234mM +/- 10%; and

(iii) a surfactant in a concentration of between 0.005% w/v +/- 10% to 0.05% w/v +/- 10%,

wherein, the pharmaceutical formulation is an aqueous solution at a pH between 5.2 to 6.5, the pharmaceutical formulation is substantially free of an ionic tonicity excipient and

the anti-IL17A antibody comprises a light chain variable region (LCVR) and a heavy chain variable region (HCVR), wherein the LCVR comprises complementarity determining regions (CDRs) LCDR1, LCDR2, and LCDR3 and the HCVR comprises CDRs HCDR1, HCDR2, and HCDR3, wherein:

LCDR1 comprises the amino acid sequence of SEQ ID NO. 1,
LCDR2 comprises the amino acid sequence of SEQ ID NO. 2,
LCDR3 comprises the amino acid sequence of SEQ ID NO. 3,
HCDR1 comprises the amino acid sequence of SEQ ID NO. 4,
HCDR2 comprises the amino acid sequence of SEQ ID NO. 5, and
HCDR3 comprises the amino acid sequence of SEQ ID NO. 6.

In another aspect of the present disclosure, there is provided a use of a bufferless pharmaceutical formulation disclosed herein, in the manufacture of a medicament for treating RA, Ps, GenPs, Pruritus, AS, PA, PPP, HS or MM.

In a further aspect of the present disclosure, there is provided a use of a~~n~~ bufferless aqueous pharmaceutical formulation disclosed herein, in the manufacture of a medicament for reducing injection-associated pain experienced by a patient ~~at the time of, or shortly after~~, wherein the formulation is to be SQ, IP and/or IM ~~administration of an aqueous pharmaceutical formulation comprising an anti-IL17A antibody, wherein the pharmaceutical formulation is to be~~ administered to the patient~~,~~ and the reduction in injection-associated pain experienced by a patient is upon administration of the formulation,
wherein the administration provides a therapeutically favorable level of injection-associated pain comprising a VAS score of less than 30 mm or less than 20mm.

In another aspect of the present disclosure, there is provided a pharmaceutical formulation disclosed herein, for use in treating RA, Ps, GenPs, Pruritus, AS, PA, PPP, HS or MM.

In a further aspect of the present disclosure, there is provided an aqueous pharmaceutical formulation disclosed herein, for use in reducing injection-associated pain experienced by a patient, wherein the formulation is to be ~~at the time of, or shortly after,~~ SQ, IP and/or IM administered to the patient and the reduction in injection-associated pain experienced by a patient is upon administration of ~~an aqueous pharmaceutical~~ the formulation ~~comprising an anti-IL17A antibody~~.

WE CLAIM:

1. A~~n~~ bufferless aqueous pharmaceutical formulation comprising:

(i) an anti-IL-17A antibody at a concentration of 80 mg/mL +/- 10%;

(ii) sucrose in a concentration of 234mM +/- 10%; and

(iii) a surfactant in a concentration of between 0.005% w/v +/- 10% to 0.05% w/v +/- 10%,

wherein, the pharmaceutical formulation is an aqueous solution at a pH between 5.2 to 6.5, the pharmaceutical formulation is substantially free of an ionic tonicity excipient and the anti-IL17A antibody comprises a light chain variable region (LCVR) and a heavy chain variable region (HCVR), wherein the LCVR comprises complementarity determining regions (CDRs) LCDR1, LCDR2, and LCDR3 and the HCVR comprises CDRs HCDR1, HCDR2, and HCDR3, wherein:

LCDR1 comprises the amino acid sequence of SEQ ID NO. 1,
LCDR2 comprises the amino acid sequence of SEQ ID NO. 2,
LCDR3 comprises the amino acid sequence of SEQ ID NO. 3,
HCDR1 comprises the amino acid sequence of SEQ ID NO. 4,
HCDR2 comprises the amino acid sequence of SEQ ID NO. 5, and
HCDR3 comprises the amino acid sequence of SEQ ID NO. 6.

2. The pharmaceutical formulation of claim 1, wherein the surfactant is polysorbate 20 or polysorbate 80.

3. The pharmaceutical formulation of claim 2, wherein the surfactant is polysorbate 80.

4. The pharmaceutical formulation of claim 1, wherein the pharmaceutical formulation is substantially free of ionic tonicity excipient.

~~4~~5. The pharmaceutical formulation of claim 1, wherein the pharmaceutical formulation is substantially free of L-amino acid excipients.

~~5~~6. The pharmaceutical formulation of claim 1, wherein the LCVR comprises the amino acid sequence of SEQ ID NO. 7 and the HCVR comprises the amino acid sequence of SEQ ID NO. 8.

~~6~~7. The pharmaceutical formulation of claim ~~5~~6, wherein anti-IL17A antibody comprises a light chain (LC) and a heavy chain (HC), wherein the LC comprises the amino acid sequence of SEQ ID NO. 9 and the HC comprises the amino acid sequence of SEQ ID NO. 10.

~~7~~8. The pharmaceutical formulation of claim 1, wherein the anti-IL17A antibody is ixekizumab.

~~8~~9. Use of a bufferless pharmaceutical formulation of claim 1, in the manufacture of a medicament for treating RA, Ps, GenPs, Pruritus, AS, PA, PPP, HS or MM.

~~9~~10. The use of claim ~~8~~9, wherein:
an initial dose of the pharmaceutical formulation is to be subcutaneously administered to a patient on day 0, and the pharmaceutical formulation is to be subsequently subcutaneously administered to the patient at every four week interval thereafter,
wherein the pharmaceutical formulation to be administered to the patient at every four week interval after the initial dose comprises the anti-IL17A antibody at a concentration of about 80 mg/mL.

~~10~~11. The use of claim ~~8~~9, wherein:
an initial dose of the pharmaceutical formulation is to be subcutaneously administered to a patient on day 0, and the pharmaceutical formulation is to be subsequently subcutaneously administered to the patient at every two week interval thereafter,
wherein the pharmaceutical formulation to be administered to the patient at every two week interval after the initial dose comprises the anti-IL17A antibody at a concentration of about 80 mg/mL.

~~11~~12. The use of claim ~~8~~9, wherein:

an initial dose of the pharmaceutical formulation is to be subcutaneously administered to a patient on day 0, the pharmaceutical formulation to be subsequently subcutaneously administered to the patient on each of days 14, 28, 42, 56, 70 and 84, and the pharmaceutical formulation is to be subsequently subcutaneously administered to the patient at every four week interval thereafter,
wherein the pharmaceutical formulation, to be administered to the patient at each of days 14, 28, 42, 56, 70 and 84, and every four week interval thereafter, comprises the anti-IL17A antibody at a concentration of about 80 mg/mL.

~~12~~13. The use of claim ~~11~~12, wherein the initial dose of the pharmaceutical formulation comprises about 160 mg of the anti-IL17A antibody.

~~13~~14. The use of claim ~~12~~13, wherein the ~~about 160 mg initial dose of the~~ pharmaceutical formulation comprises two doses of ~~the pharmaceutical formulation, each dose comprising~~ about 80 mg of the anti-IL17A antibody.

~~14~~15. Use of a~~n~~ bufferless aqueous pharmaceutical formulation of claim 1, in the manufacture of a medicament for reducing injection-associated pain experienced by a patient ~~at the time of, or shortly after~~, wherein the formulation is to be SQ, IP and/or IM ~~administration of an aqueous pharmaceutical formulation comprising an anti-IL17A antibody, wherein the pharmaceutical formulation is to be~~ administered to the patient~~,~~ and the reduction in injection-associated pain experienced by a patient is upon administration of the formulation,
wherein the administration provides a therapeutically favorable level of injection-associated pain comprising a VAS score of less than 30 mm or less than 20mm.

~~15. The use of claim 14, wherein the therapeutically favorable level of injection-associated pain comprises a VAS score of less than 30 mm or less than 20 mm.~~

16. The use of claim 14, wherein the anti-IL17A antibody is ixekizumab.

~~17. The pharmaceutical formulation of claim 1, wherein the pharmaceutical formulation is bufferless.~~

~~18~~17. The use ~~pharmaceutical formulation~~ of claim ~~17~~15 or claim 16, wherein the pharmaceutical formulation is substantially free of L-amino acid excipients.

~~19~~18. The use ~~pharmaceutical formulation~~ of claim ~~18~~17, wherein the surfactant is polysorbate 80 and wherein the anti-IL17A antibody is ixekizumab.

~~20~~19. The use of claim 8, wherein the pharmaceutical formulation is bufferless, substantially free of L-amino acid excipients and the surfactant is polysorbate 80.

~~21~~20. A pharmaceutical formulation of claim 1, for use in treating RA, Ps, GenPs, Pruritus, AS, PA, PPP, HS or MM.

~~22~~21. An aqueous pharmaceutical formulation of claim 1, for use in reducing injection-associated pain experienced by a patient, wherein the formulation is to be ~~at the time of, or shortly after,~~ SQ, IP and/or IM administered to the patient and the reduction in injection-associated pain experienced by a patient is upon administration of ~~an aqueous pharmaceutical~~the formulation ~~comprising an anti-IL17A antibody~~.