with a 10 mM sodium citrate buffer (pH 6-7) and sodium chloride (140 mM) as tonicity agent. The choice of pH range was driven by finding the optimal stability of anakinra during long term storage. The human body fluids typically have a pH around 7.4 and injection of solutions having a lower, non-physiological pH may cause discomfort and even pain in the patient.

Injection of a solution having a higher, non-physiological pH may likewise cause discomfort or pain.

Thus, there exists a need in the art today for treatments which avoid or reduce the pain associated with injection of drugs.

Summary

It is an object of the present invention to provide injection instruments that are useful for alleviating some of the problems of the prior art.

According to the present disclosure, this and other objects are met by the invention as defined in the different aspects herein.

Hence, according to a first aspect, there is provided a pre-filled syringe comprising a barrel and a plunger, the barrel having an outlet where a solution can be ejected from the barrel, the barrel containing a pharmaceutically acceptable solution having a non-physiological pH. The syringe further comprises an ion exchange material provided such that the pharmaceutically acceptable solution, when contained within the barrel, does not contact the ion exchange material, wherein the ion exchange material is provided at a position to allow contact with the pharmaceutically acceptable solution upon or just before ejection of the pharmaceutically acceptable solution from the barrel via the outlet, wherein the ion exchange material is adapted to, upon contact with the pharmaceutically acceptable solution, adjust the pH of the pharmaceutically acceptable solution from a first, non-physiological pH to a second pH, wherein the first, non-physiological pH is in the range of 3-6.6 and/or the second pH is in the range of 6.6-8.0, wherein

the second pH is higher than the first non-physiological pH, wherein the ion-exchange material comprises a solid porous material, wherein the solid porous material comprises at least one material selected from the list consisting of a zeolite material, a polystyrene material or a mesoporous silica.

~~According to a second aspect~~As disclosed, there is provided a needle unit adapted to be mounted in fluid communication with a syringe, the needle unit comprising an injection needle adapted for use in injection of a pharmaceutically acceptable solution into the body of a human or animal, and an ion exchange material, wherein the ion exchange material is contained within the needle, wherein the ion exchange material is adapted to, upon contact with a pharmaceutically acceptable solution, adjust the pH of the pharmaceutically acceptable solution from a first, non-physiological pH to a second pH, wherein the first, non-physiological pH is in the range of 3-6.6 and/or the second pH is in the range of 6.6-8.0, such as in the range of 7.0-8.0, preferably 7.1-8.0, wherein the ion-exchange material comprises a solid porous material, wherein the solid porous material comprises at least one material selected from the list consisting of a zeolite material, a polystyrene material or a mesoporous silica.

The present invention is based on the realization that by using a pre-filled syringe with an ion exchange material, the discomfort/and or pain experienced by a patient during injection of a pharmaceutically acceptable

sintered zeolite material matches the inner shape of the barrel and/or needle such that it can be positioned therein and act as an ion exchange material such as disclosed herein.

In some embodiments of the present invention, the method further comprises the step of b1) providing a separator in the barrel. The separator may preferably be a separator such as the separators disclosed above in relation to the first aspect of the invention.

In a third aspect, there is provided a syringe comprising a barrel and a plunger, the barrel having an interior volume adapted to contain a pharmaceutically acceptable solution having a non-physiological pH, wherein the syringe further comprises an ion exchange material provided within the syringe such that it is not in fluid communication with the interior volume of the barrel, and wherein the ion exchange material is provided at a position to, in use, allow contact with the pharmaceutically acceptable solution upon or just before ejection of the pharmaceutically acceptable solution from the barrel, wherein the ion exchange material is adapted to, upon contact with the pharmaceutically acceptable solution, adjust the pH of the solution from a first, non-physiological pH to a second pH, wherein the first, non-physiological pH is in the range of 3-6.6 and/or the second pH is in the range of 6.6-8.0, wherein the second pH is higher than the first non-physiological pH, wherein the ion-exchange material comprises a solid porous material, wherein the solid porous material comprises at least one material selected from the list consisting of a zeolite material, a polystyrene material or a mesoporous silica.

The inventors have realized that by providing a syringe comprising an ion exchange material such that it is not in fluid communication with the interior volume of the barrel, and wherein the ion exchange material is is provided at a position to allow contact with the pharmaceutically acceptable solution upon ejection of the pharmaceutically acceptable solution from the barrel, the syringe can be used to adjust the pH of a pharmaceutically acceptable solution from a first, non-physiological pH to a second, physiological pH, as

described above. The first pH is in the range of 3–6.6 and/or the second pH is in the range of 6.6–8.0.

The syringe is adapted to accommodate a pharmaceutically acceptable solution within its barrel. Before using the syringe to inject a solution into a patient, the patient or a physician operating the syringe fills the barrel with the pharmaceutically acceptable solution upstream the ion exchange material.

CLAIMS

1. A pre-filled syringe comprising a barrel and a plunger, the barrel having an outlet, the barrel containing a pharmaceutically acceptable solution having a non-physiological pH, wherein the syringe further comprises an ion exchange material provided such that the pharmaceutically acceptable solution, when contained within the barrel, does not contact the ion exchange material, and wherein the ion exchange material is provided at a position to allow contact with the pharmaceutically acceptable solution upon or just before ejection of the pharmaceutically acceptable solution from the barrel via the outlet, wherein the ion exchange material is adapted to, upon contact with the pharmaceutically acceptable solution, adjust the pH of the pharmaceutically acceptable solution from a first, non-physiological pH to a second pH, wherein the first, non-physiological pH is in the range of 3-6.6 and/or the second pH is in the range of 6.6-8.0, wherein the second pH is higher than the first non-physiological pH, wherein the ion-exchange material comprises a solid porous material, wherein the solid porous material comprises at least one material selected from the list consisting of a zeolite material, a polystyrene material or a mesoporous silica.

2. The pre-filled syringe according to claim 1, wherein the second pH is in the range of 7.0-8.0.

3. The pre-filled syringe according to claim 2, wherein the second pH is in the range of 7.1-8.0.

4. The pre-filled syringe according to any one of claims claim 1 to 3, wherein the pre-filled syringe comprises a separator arranged at a position along an ejection path from the barrel, and wherein the pharmaceutically acceptable solution is present upstream of said separator along said ejection path, and the ion exchange material is provided downstream of said separator along said ejection path, and the separator is adapted to in a first state prevent the pharmaceutically acceptable solution from contacting the ion

exchange material, and adapted to in a second state allow fluid communication between the pharmaceutically acceptable solution and the ion exchange material, such as to allow contact therebetween.

5. The pre-filled syringe according to claim 4, wherein the separator is selected from the group consisting of a collapsible liquid impermeable membrane, a super-hydrophobic material, a valve, a damper and an air pocket.

6. The pre-filled syringe according to any one of the preceding claims, wherein the syringe comprises an injection needle mounted in fluid communication with said outlet.

7. The pre-filled syringe according to claim 6 wherein the ion exchange material is contained within said needle.

8. The pre-filled syringe according to any one of claims 1–7, wherein the porous solid material comprises a zeolite material, wherein the zeolite is an aluminosilicate zeolite material loaded with Na^+, H^+ and/or Ca^{2+} having

-a SiO_2/Al_2O_3 molar ratio above 1.5; and/or

-a Na_2O content below 10 wt-% of the total zeolite weight.

9. The pre-filled syringe according to any one of the preceding claims, wherein the pharmaceutically acceptable solution comprises an acidic buffer solution.

10. The pre-filled syringe according to claim 9, wherein said acidic buffer solution is a citrate buffer.

11. The pre-filled syringe according to any one of the preceding claims, wherein the pharmaceutically acceptable solution comprises a protein drug or peptide drug.

12. The pre-filled syringe according to claim 11, wherein the protein or peptide drug is an IL-1 receptor antagonist.

13. The pre-filled syringe according to claim 12, wherein the IL-1 receptor antagonist is anakinra.

~~14. A needle unit adapted to be mounted in fluid communication with a syringe, the needle unit comprising an injection needle adapted for use in injection of a pharmaceutically acceptable solution into the body of a human or animal, and an ion exchange material, wherein the ion exchange material is contained within the needle, wherein the ion exchange material is adapted to, upon contact with a pharmaceutically acceptable solution, adjust the pH of the pharmaceutically acceptable solution from a first, non-physiological pH to a second pH, wherein the first, non-physiological pH is in the range of 3-6.6 and/or the second pH is in the range of 6.6-8.0, such as in the range of 7.0-8.0, preferably 7.1-8.0, wherein the ion-exchange material comprises a solid porous material, wherein the solid porous material comprises at least one material selected from the list consisting of a zeolite material, a polystyrene material or a mesoporous silica.~~

~~15. The needle unit according to claim 14, wherein the porous solid material comprises a zeolite material, wherein the zeolite material is an aluminosilicate zeolite material loaded with Na^+, H^+ and/or Ca^{2+} having~~

~~- a SiO_2/Al_2O_3 molar ratio above 1.5; and/or~~

~~- a Na_2O content below 10 wt-% of the total zeolite weight.~~

~~16~~14. A method for manufacturing a pre-filled syringe according to any one of the claims 1 to 13 comprising steps of:

a) providing a syringe having a plunger and a barrel, the barrel having an interior volume;

b) providing the syringe with an ion exchange material at a position that is not in fluid communication with the interior volume of the barrel;

c) placing a pharmaceutically acceptable solution within said barrel.

~~17~~15. The method according to claim ~~16~~14, wherein the ion exchange material is provided within the barrel.

~~18~~16. The method according to claim ~~16~~14, wherein the ion exchange material is contained within a needle unit, and the step b) involves connecting said needle unit to the barrel.

~~19~~17. The method according to claim ~~18~~16, wherein the ion exchange material is a particulate zeolite material and wherein step b) comprises:

b-i) sintering the zeolite material to a shape such that it matches to the inner shape of a needle of the needle unit, and

b-ii) placing the sintered zeolite material within the needle.

~~20~~18. The method according to claim ~~17~~15, wherein the ion exchange material is a particulate zeolite material and wherein step b) comprises:

b-i) sintering a zeolite material to a shape such that it matches to the inner shape of the barrel, and

b-ii) placing the sintered zeolite material within the barrel.

~~21~~19. The method according to any one of the claims ~~17~~ 15 to ~~20~~18, wherein the method further comprises a step of providing a separator in the barrel.

~~22~~20. A syringe comprising a barrel and a plunger, the barrel having an interior volume adapted to contain a pharmaceutically acceptable solution having a non-physiological pH, wherein the syringe further comprises an ion exchange material provided within the syringe such that it is not in fluid communication with the interior volume of the barrel, and wherein the ion exchange material is provided at a position to, in use, allow contact with the pharmaceutically acceptable solution upon or just before ejection of the pharmaceutically acceptable solution from the barrel, wherein the ion exchange material is adapted to, upon contact with the pharmaceutically

acceptable solution, adjust the pH of the solution from a first, non-physiological pH to a second pH, wherein the first, non-physiological pH is in the range of 3-6.6 and/or the second pH is in the range of 6.6-8.0, wherein the second pH is higher than the first non-physiological pH, wherein the ion-exchange material comprises a solid porous material, wherein the solid porous material comprises at least one material selected from the list consisting of a zeolite material, a polystyrene material or a mesoporous silica.

~~23~~21. The syringe according to claim ~~22~~20, wherein the second pH is in the range of 7.0-8.0.

~~24~~22. The syringe according to claim ~~23~~21, wherein the second pH is in the range of 7.1-8.0.

~~25~~23. The syringe according to any one of claims ~~22-24~~20-22, further comprising an injection needle mounted in fluid communication with an outlet of the barrel.

~~26~~24. The syringe according to claim ~~25~~23, wherein the ion exchange material is provided withinin the injection needle.

~~27~~25. A kit comprising:

i) a pre-filled syringe according to any one of the claims 1 to 5; and

ii) a needle unit comprising the needle as defined in any one of claims ~~1-4~~ 6 to ~~15~~7.

~~28~~26. The kit according to claim ~~27~~25, wherein the pre-filled syringe comprises a separator as defined in claim 4.

~~29~~27. The kit according to any one of claims ~~27-28~~25-26, wherein the pharmaceutically acceptable solution is as defined in any one of claims 9-13.

~~30~~28. A kit comprising:

i) a syringe according to any one of claim ~~22-26~~20-24;

ii) a needle unit comprising the needle as defined in any one of claims ~~14-15~~23-24.

~~31~~29. The kit according to claims ~~30~~28, wherein the syringe comprises a separator as defined in claim 4.