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 along an ejection path from the syringe, allowing the pharmaceutically acceptable solution to contact the ion exchange material before being ejected from the syringe, 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, and wherein the pharmaceutically acceptable solution comprises a drug and an acidic buffer solution, wherein the ion exchange material is loaded with positive ions selected from Na^+ and/or Ca^{2+}.

In another aspect, the present disclosure refers to a method for manufacturing a pre-filled syringe according to the above aspect 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 upstream of the ion exchange material.

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 along an ejection path from the syringe, allowing the pharmaceutically acceptable solution to contact the ion exchange material before being ejected from the syringe, 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, and wherein the pharmaceutically acceptable solution comprises a drug and an acidic buffer solution, wherein the ion exchange material is loaded with positive ions selected from Na^+ and/or Ca^{2+}.

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.

The zeolite material may in embodiments of the invention be a microporous zeolite. The term microporous supposed to indicate that the pore diameters in the zeolite material is less than 2 nm. Other pore systems may also be contemplated, such as mesoporous (pore diameter between 2 nm and 50 nm) and macroporous (pore diameter larger than 50 nm).

A number of different zeolites may be contemplated, such as the zeolites marketed under the names Zeoflair, faujasite and Zeolite Y.

Other ion exchange materials may also be contemplated, such as mesoporous silica. The mesoporous silica may optionally be functionalized to improve the ion exchange properties.

The ion exchange material may comprise a polymer, such as a polystyrene material. The polystyrene material may be acidic, such as strongly acidic typically comprising sulfonic acid groups, e.g. sodium polystyrene sulfonate or polyAMPS. The polystyrene material may also be weakly acidic, typically comprising carboxylic acid groups.

In some examples, basic polystyrenes may also be contemplated. The basic polystyrenes may be strongly basic polystyrenes such as polystyrenes comprising quaternary amino groups, for example, trimethylammonium groups, e.g. polyAPTAC). The polystyrenes may also be weakly basic, typically comprising featuring primary, secondary, and/or tertiary amino groups, e.g. polyethylene amine groups.

In embodiments where the ion exchange material is contained in the barrel of the syringe, the ion exchange material may have the shape of a cylinder, such as in the shape of a plug. The diameter of the cylinder is typically chosen so that the plug conforms to inner periphery of the barrel, and fills a cross-sectional area of the barrel. Preferably, the dimensions, including diameter, of the cylinder may be chosen such that substantially all of the pharmaceutically acceptable solution passes through the ion exchange