CLAIMS

1. A pre-filled syringe, the syringe comprising a glass body, a stopper and a plunger, the body comprising an outlet at an outlet end and the stopper being arranged within the body such that a front surface of the stopper and the body define a variable volume chamber from which a fluid can be expelled though the outlet, the plunger comprising a plunger contact surface at a first end and a rod extending between the plunger contact surface and a rear portion, the plunger contact surface arranged to contact the stopper, such that the plunger can be used to force the stopper towards the outlet end of the body, reducing the volume of the variable volume chamber, characterised in that the fluid is an ophthalmic solution which comprises a VEGF-antagonist wherein:

(a) the syringe has a nominal maximum fill volume of between about 0.5ml and about 1ml,

(b) the syringe is filled a dosage volume of between about 0.03ml and about 0.05ml of said VEGF antagonist solution,

(c) the syringe barrel comprises less than about 500µg silicone oil, and

(d) the VEGF antagonist solution comprises no more than 2 particles ≥50µm in diameter per ml.

2. A pre-filled syringe according to claim 1, wherein the syringe is filled with between about 0.15ml and about 0.175ml of a VEGF antagonist solution.

3. A pre-filled syringe according to claim 1 or claim 2, wherein the syringe is filled with about 0.165ml of said VEGF antagonist solution.

4. A pre-filled syringe according to any previous claim, wherein the syringe is filled with dosage volume of about 0.05ml of a VEGF antagonist solution.

5. A pre-filled syringe according to any previous claim, in which the dosage volume is determined by the volume of the variable volume chamber when a predetermined part of the stopper is aligned with a priming mark on the syringe.

6. A pre-filled syringe according to any previous claim, wherein the syringe barrel has an internal coating of silicone oil that has an average thickness of about 450nm or less, preferably 400nm or less, preferably 350nm or less, preferably 300nm or less, preferably 200nm or less, preferably 100nm or less, preferably 50nm or less, preferably 20nm or less.

7. A pre-filled syringe according to any previous claim, wherein the syringe barrel has an internal coating of less than about 500μg silicone oil, preferably less than about 100μg silicone oil, preferably less than about 50μg silicone oil, preferably less than about 25μg silicone oil, preferably less than about 10μg silicone oil.

8. A pre-filled syringe according to any previous claim, wherein the syringe barrel has an internal coating of more than about 1μg, more than about 3μg, more than about 5μg, more than about 7μg or more than about 10μg silicone oil.

9. A pre-filled syringe according to any previous claim, wherein the syringe barrel has an internal coating of about 1μg-about 500μg, about 3μg-about 200μg, about 5μg-about 100μg or about 10μg-about 50μg silicone oil.

10. A pre-filled syringe according to any previous claim, wherein the silicone oil is DC365 emulsion.

11. A pre-filled syringe according to any one of claims 1-5, wherein the syringe is silicone oil free.

12. A pre-filled syringe according to any previous claim, wherein the VEGF antagonist solution further comprises one or more of (i) no more than 5 particles ≥25μm in diameter per ml, and (ii) no more than 50 particles ≥10μm in diameter per ml.

13. A pre-filled syringe according to any previous claim, wherein the VEGF antagonist solution meets USP789.

14. A pre-filled syringe according to any previous claim, wherein the VEGF antagonist is an anti-VEGF antibody.

15. A pre-filled syringe according to claim 14, wherein the anti-VEGF antibody is ranibizumab.

16. A pre-filled syringe according to claim 15, wherein the ranibizumab is at a concentration of 10mg/ml.

17. A pre-filled syringe according to any one of claims 1-13 wherein the VEGF antagonist is a non-antibody VEGF antagonist.

18. A pre-filled syringe according to claim 17, wherein the non-antibody VEGF antagonist is aflibercept or conbercept.

19. A pre-filled syringe according to claim 18, wherein the non-antibody VEGF antagonist is aflibercept at a concentration of 40mg/ml.

20. A pre-filled syringe according to any previous claim, wherein the syringe has a stopper break loose force of less than about 11N.

21. A pre-filled syringe according to claim 20, wherein the syringe has a stopper break loose force of less than about 5N.

22. A pre-filled syringe according to any previous claim, wherein the syringe has a stopper slide force of less than about 11N.

23. A pre-filled syringe according to claim 22, wherein the syringe has a stopper slide force of less than about 5N.

24. A pre-filled syringe according to any of claims 20-23, wherein the stopper break loose force or stopper slide force is measured using a filled syringe, at a stopper travelling speed of 190mm/min, with a 30G x 0.5 inch needle attached to the syringe.

25. A blister pack comprising a pre-filled syringe according to any previous claim, wherein the syringe has been sterilised using H_2O_2 or EtO.

26. A blister pack comprising a pre-filled syringe according to claim 25, wherein the outer surface of the syringe has ≤1ppm EtO or H_2O_2 residue.

27. A blister pack comprising a pre-filled syringe according to claim 25, wherein the syringe has been sterilised using EtO or H_2O_2 and the total EtO or H_2O_2 residue found on the outside of the syringe and inside of the blister pack is ≤0.1mg.

28. A blister pack comprising a pre-filled syringe according to any one of claims 25-27, wherein ≤5% of the VEGF antagonist is alkylated.

29. A blister pack comprising a pre-filled syringe according to any of claims 25-28, wherein the syringe has been sterilised using EtO or H_2O_2 with a Sterility Assurance Level of at least 10^{-6}.

30. A blister pack according to any of claims 25-29, wherein the pre-filled syringe has a shelf life of up to 6 months, 9 months, 12 months, 15 months, 18 months, 24 months or longer.

31. A kit comprising: (i) a pre-filled syringe according to any one of claims 1-24, or a blister pack comprising a pre-filled syringe according to any one of claims 25-30, (ii) a needle, and optionally (iii) instructions for administration.

32. A kit according to claim 31, wherein the needle is a 30-gauge x ½ inch needle.

33. A pre-filled syringe according to any one of claims 1-24 for use in therapy.

34. A pre-filled syringe according to any one of claims 1-24 for use in the treatment of an ocular disease selected from choroidal neovascularisation, wet age-related macular degeneration, macular edema secondary to retinal vein occlusion (RVO) including both branch RVO (bRVO) and central RVO (cRVO), choroidal neovascularisation secondary to pathologic myopia (PM), diabetic macular edema (DME), diabetic retinopathy, and proliferative retinopathy.

35. A method of treating a patient suffering from of an ocular disease selected from choroidal neovascularisation, wet age-related macular degeneration, macular edema secondary to retinal vein occlusion (RVO) including both branch RVO (bRVO) and central RVO (cRVO), choroidal neovascularisation secondary to pathologic myopia (PM), diabetic macular edema (DME), diabetic retinopathy, and proliferative retinopathy, comprising the step of administering an ophthalmic solution to the patient using a pre-filled syringe according to any one of claims 1-24.

36. The method of claim 35, further comprising an initial priming step in which the physician depresses the plunger of the pre-filled syringe to align the pre-determined part of the stopper with the priming mark.

37. A method according to claim 35 or 36, wherein the VEGF antagonist administered is a non-antibody VEGF antagonist and wherein the patient has previously received treatment with an antibody VEGF antagonist.

CLAIMS

1. A pre-filled syringe, the syringe comprising a glass body, a stopper and a plunger, the body comprising an outlet at an outlet end and the stopper being arranged within the body such that a front surface of the stopper and the body define a variable volume chamber from which a fluid can be expelled though the outlet, the plunger comprising a plunger contact surface at a first end and a rod extending between the plunger contact surface and a rear portion, the plunger contact surface arranged to contact the stopper, such that the plunger can be used to force the stopper towards the outlet end of the body, reducing the volume of the variable volume chamber, characterised in that the fluid is an ophthalmic solution which comprises a VEGF-antagonist wherein:

(a) the syringe has a nominal maximum fill volume of between about 0.5ml and about 1ml,

(b) the syringe is filled a dosage volume of between about 0.03ml and about 0.05ml of said VEGF antagonist solution,

(c) the syringe barrel comprises less than about 100µg silicone oil,

(d) the VEGF antagonist solution comprises no more than 2 particles ≥50µm in diameter per ml, and

(e) the syringe has a stopper break loose force of less than about 11 N.

2. A pre-filled syringe according to any previous claim, wherein the syringe barrel has an internal coating of silicone oil that has an average thickness of about 450nm or less, preferably 400nm or less, preferably 350nm or less, preferably 300nm or less, preferably 200nm or less, preferably 100nm or less, preferably 50nm or less, preferably 20nm or less.

3. A pre-filled syringe according to any previous claim, wherein the syringe barrel has an internal coating of about 5µg-about 100µg or about 10µg-about 50µg silicone oil.

4. A pre-filled syringe according to any previous claim, wherein the VEGF antagonist solution further comprises one or more of (i) no more than 5 particles ≥25µm in diameter per ml, and (ii) no more than 50 particles ≥10µm in diameter per ml.

5. A pre-filled syringe according to any previous claim, wherein the VEGF antagonist is an anti-VEGF antibody.

6. A pre-filled syringe according to claim 5, wherein the anti-VEGF antibody is ranibizumab.

7. A pre-filled syringe according to any one of claims 1-4 wherein the VEGF antagonist is a non-antibody VEGF antagonist.

8. A pre-filled syringe according to claim 7, wherein the non-antibody VEGF antagonist is aflibercept or conbercept.

9. A pre-filled syringe according to any previous claim, wherein the syringe has a stopper slide force of less than about 11N.

10. A blister pack comprising a pre-filled syringe according to any previous claim, wherein the syringe has been sterilised using H_2O_2 or EtO and

wherein the outer surface of the syringe has $\leq$1ppm EtO or H_2O_2 residue.

11. A blister pack comprising a pre-filled syringe according to claim 10, wherein the syringe has been sterilised using EtO or H_2O_2 and the total EtO or H_2O_2 residue found on the outside of the syringe and inside of the blister pack is $\leq$0.1mg.

12. A blister pack comprising a pre-filled syringe according to claim 10 or 11, wherein $\leq$5% of the VEGF antagonist is alkylated.

13. A kit comprising: (i) a pre-filled syringe according to any one of claims 1-9, or a blister pack comprising a pre-filled syringe according to any one of claims 10-11, (ii) a needle, and optionally (iii) instructions for administration.

14. A pre-filled syringe according to any one of claims 1-9 for use in therapy.

15. A pre-filled syringe according to any one of claims 1-9 for use in the treatment of an ocular disease selected from choroidal neovascularisation, wet age-related macular degeneration, macular edema secondary to retinal vein occlusion (RVO) including both branch RVO (bRVO) and central RVO (cRVO), choroidal neovascularisation secondary to pathologic myopia (PM), diabetic macular edema (DME), diabetic retinopathy, and proliferative retinopathy.