

Claims:

1. A method of making an auto injector that is configured to dispense a therapeutic fluid comprising fremanezumab contained in an operative prefilled syringe, the operative prefilled syringe including an operative barrel and an operative stopper movably positioned within the operative barrel, the operative stopper configured to move axially within the operative barrel along an operative path of travel from a first operative position to a second operative position, the auto injector comprising a piston rod configured to abut the operative stopper and an injection spring having a spring force, the injection spring configured to apply, via the piston rod, a dispensing force to the operative stopper upon actuation of the auto injector, the dispensing force being at least a portion of the spring force, the method comprising:

aging a syringe prefilled with the therapeutic fluid at an accelerated rate to form an aged reference prefilled syringe, the aged reference prefilled syringe including a reference barrel and a reference stopper movably positioned within the reference barrel;

moving the reference stopper of the aged reference prefilled syringe axially within the reference barrel along a reference path of travel from at least a first reference position to at least a second reference position;

measuring, as the reference stopper moves within the reference barrel along the reference path of travel, a plurality of exertion forces applied to the reference stopper and a plurality of reference stopper positions;

generating an exertion force profile, the exertion force profile including at least some of the plurality of the exertion forces and of the plurality of the reference stopper positions measured while the reference stopper moves between the first and second reference positions, at least one of the plurality of exertion forces correlating to at least one of the plurality of reference stopper positions; and

selecting the injection spring so that the dispensing force applied to the operative stopper as the operative stopper moves along the operative path of travel between the first and second operative positions is greater than an exertion force of the plurality of exertion forces at a corresponding one of the plurality of reference stopper positions, the dispensing force comprising an initial dispensing force of between 20 N and 40 N when

the operative stopper is positioned in the first operative position and a final dispensing force of between 12 N and 20 N when the operative stopper is positioned at the second operative position, the initial dispensing force is greater than the final dispensing force.

2. The method of claim 1, wherein selecting the injection spring comprises selecting an exertion force from the exertion force profile, and selecting at least one spring parameter, the selected at least one spring parameter corresponding to the selected exertion force.

3. The method of claim 2, wherein selecting the at least one spring parameter comprises selecting a spring constant for the injection spring and an uncompressed length for the injection spring.

4. The method of claim 2, wherein selecting the at least one spring parameter comprises selecting a spring constant and a first compressed spring length corresponding to the reference stopper being at the first reference position along the reference path of travel.

5. The method of claim 2, wherein selecting the at least one spring parameter comprises selecting a spring constant and a second compressed spring length corresponding to the reference stopper being at a position along the reference path of travel corresponding to a maximum measured exertion force in the exertion force profile.

6. The method of claim 5, wherein the dispensing force when the operative stopper is at the second operative position is greater than 50% of the dispensing force when the operative stopper is at the first operative position.

7. The method of claim 1, wherein the injection spring is configured to move the operative stopper along the operative path of travel from the first operative position to the second operative position in a period between 5 seconds to 19 seconds.

8. The method of claim 1, wherein the aged reference prefilled syringe holds a volume of the therapeutic fluid between the first reference position and the second reference position, and moving the reference stopper along the reference path of travel from the first reference position to the second reference position ejects the volume of the therapeutic fluid from the aged reference prefilled syringe.

9. The method of claim 8, wherein the volume of the therapeutic fluid in the aged reference prefilled syringe is equal to a volume of the therapeutic fluid held in the operative prefilled syringe.

10. The method of claim 8, wherein the volume is between 1.51 mL and 1.66 mL.

11. The method of claim 1, wherein the reference barrel of the aged reference prefilled syringe comprises an inner surface, and the aged reference prefilled syringe comprises a lubricant on the inner surface.

12. The method of claim 11, wherein the lubricant in the aged reference prefilled syringe comprises between 0.35 mg and 1.1 mg of silicone oil before the aging.

13. The method of claim 12, wherein the silicone oil has a viscosity between 500 cSt at 25° C and 1500 cSt at 25° C before the aging.

14. The method of claim 1, wherein the aging of the aged reference prefilled syringe comprises heating the aged reference prefilled syringe for a period of time.

15. The method of claim 14, wherein:
the period of time is determined according to the Arrhenius equation; and
heating the aged reference prefilled syringe for the period of time comprises heating the aged reference prefilled syringe at a temperature of between 20° C and 60° C.

16. The method of claim 1, wherein the reference barrel of the aged reference prefilled syringe has a volume of 1 mL or 2.25 mL.
17. The method of claim 1, wherein a distance between the first reference position of the reference stopper and the second reference position of the reference stopper is between 25.7 mm and 30 mm.
18. The method of claim 1, wherein the aged reference prefilled syringe comprises a reference needle, the reference needle defining a channel, the channel having a diameter between 0.15 mm and 0.3 mm.
19. The method of claim 18, wherein the channel defined by the reference needle has a length between 15 mm and 25 mm.
20. The method of claim 1, wherein the reference barrel comprises glass.
21. The method of claim 1, wherein the reference stopper comprises ethylene tetrafluoroethylene.
22. The method of claim 1, wherein the operative prefilled syringe is similar to the aged reference prefilled syringe.
23. The method of claim 1, wherein the injection spring comprises at least one of a variable force spring, a constant force spring, a helical spring, a conical spring, a torsion spring, a gas spring, or a hydraulic spring.
24. An auto injector apparatus comprising:
a prefilled syringe including:
a barrel that defines a proximal end and a distal end and that extends along a longitudinal axis between the proximal end and the distal end, the barrel having an inner diameter of 8.65 mm;
a needle disposed at the distal end of the barrel, the needle having an inner

diameter of 0.27 mm and a length of 19.5 mm or less;

a therapeutic fluid held within the barrel, the therapeutic fluid comprising fremanezumab, the therapeutic fluid having a volume of between 1.51 mL and 1.66 mL and a viscosity of 8.8 cSt at 22°C; and

a stopper disposed within the barrel, the stopper is configured to move axially within the barrel along a path of travel between a first position and a second position to expel the volume of the therapeutic fluid from the prefilled syringe, the first position being an initial position of the stopper before a delivery of the therapeutic fluid, and the second position being a final position of the stopper after the delivery of the therapeutic fluid; and

an auto injector that holds the prefilled syringe, the auto injector comprising:

a piston rod configured to abut the stopper; and

an injection spring configured drive the piston rod into abutment with the stopper to apply a dispensing force to the stopper,

wherein, upon an actuation of the auto injector, the injection spring is configured to provide, via the piston rod, an initial dispensing force of between 20 N and 40 N to the stopper when the stopper is positioned at the first position and is configured to provide, via the piston rod, a final dispensing force of between 12 N and 20 N to the stopper when the stopper is positioned at the second position,

wherein the initial dispensing force is greater than the final dispensing force, and

wherein the dispensing force is at least a portion of a spring force for the injection spring.

25. The auto injector apparatus of claim 24, wherein the final dispensing force is at least 12.5 N.

26. The auto injector apparatus of claim 25, wherein the final dispensing force is at least 14 N.

27. The auto injector apparatus of claim 24, wherein the prefilled syringe has an accelerated age of at least 24 months.

28. The auto injector apparatus of claim 24, wherein the initial dispensing force is between 20 N and 30 N.

29. The auto injector apparatus of claim 24, wherein the final dispensing force is between 15 N and 18 N.

30. The auto injector apparatus of claim 24, wherein the prefilled syringe is unaged, and wherein, when the stopper is at the first position, an actual stored spring energy of the injection spring is at least 25% greater than a minimum stored spring energy required to move the stopper from the first position to the second position without stalling the prefilled syringe.

31. The auto injector apparatus of claim 24, wherein the injection spring has a stored energy of between 0.9 J and 2 J when the stopper is positioned in the first position.

32. The auto injector apparatus of claim 31, wherein, when the stopper is positioned in the first position, the injection spring has a spring constant of between 0.2 N/mm and 0.4 N/mm and a compressed length of between 50 mm and 100 mm.

33. The auto injector apparatus of claim 32, wherein the spring constant is between 0.28 N/mm and 0.32 N/mm and the compressed length is between 75 mm and 95 mm.

34. The auto injector apparatus of claim 33, wherein the injection spring is configured to move the stopper, via the piston rod, along the path of travel from the first position to the second position within a period of between 5 seconds and 19 seconds.

35. The auto injector apparatus of claim 24, wherein:
the prefilled syringe is unaged,
the barrel of the prefilled syringe comprises glass and defines an inner surface;
and

the prefilled syringe further comprises between 0.4 mg and 1.1 mg of silicone oil on the inner surface.

36. The auto injector apparatus of claim 35, wherein the silicone oil has a viscosity of 1000 cSt at 25°C.

37. The auto injector apparatus of claim 24, wherein the stopper has a length of between 7.3 mm and 8.1 mm.

38. The auto injector apparatus of claim 37, wherein the stopper is configured to compress to a compressed state and relax to an uncompressed state, and the stopper comprises:

a main body, the main body being cylindrical and having a diameter in the uncompressed state of between 8.85 mm and 9.05 mm; and

at least one annular rib, the annular rib extending radially from the main body, the annular rib having an outer diameter in the uncompressed state of between 9.25 mm and 9.45 mm.

39. The auto injector apparatus of claim 37, wherein a portion of the stopper is coated with ethylene tetrafluoroethylene, and another portion of the stopper is coated with silicone.

40. The auto injector apparatus of claim 24, wherein a distance between the first position and the second position is between 25.7 mm and 30 mm.

41. The auto injector apparatus of claim 24, wherein the injection spring is selected according to the method of claim 1.

42. An auto injector apparatus comprising:

a prefilled syringe, the prefilled syringe comprising:

a barrel comprising glass, the barrel having an inner diameter of 8.65 mm, the

barrel defining an inner surface and a path of travel;

a needle in fluid communication with the barrel, the needle having an inner diameter of 0.27 mm and a length of 19.5 mm or less; and

a stopper positioned within the barrel, the stopper is configured to move axially within the barrel along the path of travel between a first position and a second position;

a therapeutic fluid held within the barrel, the therapeutic fluid having a viscosity of 10 cP or less at 22°C; and

0.35 mg to 1.1 mg of silicone oil on the inner surface of the barrel, the silicone oil having a viscosity in a range from 500 cSt at 25°C to 1500 cSt at 25°C before the prefilled syringe is aged; and

an auto injector that holds the prefilled syringe, the auto injector comprising:

a plunger that is configured to engage with the stopper; and

an injection spring that biases the plunger towards the stopper with a dispensing force, the dispensing force comprising an initial dispensing force of between 20 N and 40 N when the stopper is positioned in the first position and a final dispensing force of between 12 N and 20 N when the stopper is positioned at the second position, the initial dispensing force is greater than the final dispensing force, the dispensing force is sufficient to move the stopper along the path of travel from the first position to the second position within 5 seconds to 25 seconds,

wherein, in the first position, the injection spring:has a spring force between 20 N and 30 N;

has a stored spring energy between 0.9 J and 2 J;

has a spring constant between 0.2 N/mm and 0.4 N/mm,

has a compressed length between 50 mm and 100 mm; and

has a stored energy 25% greater than a minimum spring energy required to move the stopper from the first position to the second position without stalling before the prefilled syringe is aged.

43. An auto injector apparatus comprising:

a prefilled syringe comprising a stopper and a therapeutic fluid including

fremanezumab; and

an auto injector comprising an injection spring and a piston rod, the piston rod is configured to move the stopper from a first position to a second position with a force of 30 N or less and in 19 seconds or less,

wherein a distance between the first and second positions corresponds to one dose of the therapeutic fluid,

wherein, upon an actuation of the auto injector, the injection spring is configured to provide, via the piston rod, an initial dispensing force of between 20 N and 40 N to the stopper when the stopper is positioned at the first position and is configured to provide, via the piston rod, a final dispensing force of between 12 N and 20 N to the stopper when the stopper is positioned at the second position, and

wherein the initial dispensing force is greater than the final dispensing force.