

CLAIMS

WHAT IS CLAIMED IS:

1. Use of varenicline, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of dry eye or ocular discomfort, wherein the medicament is to be administered into a nasal cavity of an individual in need thereof; and

wherein between 5 micrograms and 1000 micrograms of varenicline, or a pharmaceutically acceptable salt thereof, are to be administered in alternating nostrils of the individual.

2. Use of varenicline, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for increasing tear production, wherein the medicament is to be administered into a nasal cavity of an individual in need thereof; and

wherein between 5 micrograms and 1000 micrograms of varenicline, or a pharmaceutically acceptable salt thereof, are to be administered in alternating nostrils of the individual.

3. The use according to claim 1, wherein the treatment is the treatment of dry eye.

4. The use according to claim 1, wherein the treatment is the treatment of ocular discomfort.

5. The use according to any one of claims 1 to 4, wherein the medicament is to be administered to the individual prior to or after LASIK eye surgery.

6. The use according to any one of claims 1 to 5, wherein the varenicline, or a pharmaceutically acceptable salt thereof, does not cross the blood-brain barrier in a pharmacologically relevant concentration.

7. The use according to any one of claims 1 to 6, wherein the varenicline, or a pharmaceutically acceptable salt thereof, is to be administered in an amount that is not systemically bioavailable.

8. The use according to any one of claims 1 to 7, wherein the varenicline, or a pharmaceutically acceptable salt thereof, is to be administered in an amount that does not result in undesired psychoactive side effects.
9. The use according to any one of claims 1 to 8, wherein the varenicline, or a pharmaceutically acceptable salt thereof, is to be administered in an amount that does not result in undesired systemic side effects.
10. The use according to any one of claims 1 or 3 to 9, wherein the treatment further comprises local administration of one or more substances that prevent entry or reduce entry of a nicotinic acetylcholine receptor into a desensitized state, or facilitate recovery of the nicotinic acetylcholine receptor from the desensitized state.
11. The use according to any one of claims 2 or 5 to 9, wherein the method further comprises local administration of one or more substances that prevent entry or reduce entry of a nicotinic acetylcholine receptor into a desensitized state, or facilitate recovery of the nicotinic acetylcholine receptor from the desensitized state.
12. The use according to claim 10 or 11, wherein the one or more substances are selected from protein kinase C (PKC) or factors that upregulate or up-modulate PKC, cAMP-dependent protein kinase (PKA) or factors that upregulate or up-modulate PKA, and calcineurin inhibitors.
13. The use according to claim 12, wherein the calcineurin inhibitor is selected from cyclosporine, pimecrolimus, and tacrolimus.
14. The use according to any one of claims 1 to 13, wherein between 5 micrograms and 100 micrograms of varenicline or a pharmaceutically acceptable salt thereof are to be administered in alternating nostrils of the individual.
15. The use according to any one of claims 1 to 13, wherein between 5 micrograms and 50 micrograms of varenicline, or a pharmaceutically acceptable salt thereof, are to be administered in alternating nostrils of the individual.

16. The use according to any one of claims 1 to 15, wherein between 5 micrograms and 600 micrograms of varenicline or a pharmaceutically acceptable salt thereof are to be administered in alternating nostrils of the individual.
17. The use according to any one of claims 1 to 15, wherein between 100 micrograms and 750 micrograms of varenicline or a pharmaceutically acceptable salt thereof are to be administered in alternating nostrils of the individual.
18. The use according to any one of claims 1 to 15, wherein between 150 micrograms and 600 micrograms of varenicline or a pharmaceutically acceptable salt thereof are to be administered in alternating nostrils of the individual.
19. The use according to any one of claims 1 to 18, wherein the varenicline, or a pharmaceutically acceptable salt thereof, is to be administered at least once daily.
20. The use according to any one of claims 1 to 18, wherein the varenicline, or a pharmaceutically acceptable salt thereof, is to be administered at least twice daily.
21. The use according to any one of claims 1 to 18, wherein the varenicline, or a pharmaceutically acceptable salt thereof, is to be administered at least once weekly.
22. The use according to any one of claims 1 to 21, wherein the varenicline, or a pharmaceutically acceptable salt thereof, is to be administered into the nasal cavity as a liquid, suspension, aerosol, gel, ointment, dry powder, cream, paste, lotion, or balm.
23. The use according to any one of claims 1 to 22, wherein the varenicline, or a pharmaceutically acceptable salt thereof, is to be administered into the nasal cavity by a syringe, dropper, bottle nebulizer, atomization pump, inhaler, powder spray device, vaporizer, patch, medicated stick, pipette, or jet of liquid.
24. The use according to any one of claims 1 to 22, wherein the varenicline, or a pharmaceutically acceptable salt thereof, is to be administered in combination with use of a medical device.

25. The use according to claim 24, wherein the varenicline, or a pharmaceutically acceptable salt thereof, is to be administered in combination with use of a punctal plug.
26. The use according to any one of claims 1 to 25, wherein a trigeminal nerve is activated.
27. The use according to any one of claims 1 to 26, wherein an anterior ethmoidal nerve is activated.
28. The use according to any one of claims 1 to 27, wherein a nasolacrimal reflex is activated.
29. The use according to any one of claims 1 to 28, wherein the individual has a Schirmer tear test score of ≤ 10 mm/5 minutes in at least one eye prior to the administration of varenicline.
30. The use according to claim 29, wherein the Schirmer tear test is performed with topical anesthetic.
31. The use according to claim 29, wherein the Schirmer tear test is performed without nasal stimulation.
32. The use according to claim 29, wherein the Schirmer tear test is performed with nasal stimulation.
33. A pharmaceutical formulation comprising varenicline, or a pharmaceutically acceptable salt thereof, comprising between 5 micrograms and 100 micrograms of varenicline, or a pharmaceutically acceptable salt thereof, per dose; and
- wherein the pharmaceutical formulation is a nasal formulation.
34. The pharmaceutical formulation of claim 33, further comprising one or more substances selected from protein kinase C (PKC) or factors that upregulate or up-modulate PKC, cAMP-dependent protein kinase (PKA) or factors that upregulate or up-modulate PKA, and calcineurin inhibitors.

35. The pharmaceutical formulation of claim 34, wherein the calcineurin inhibitor is selected from cyclosporine, pimecrolimus, and tacrolimus.
36. The pharmaceutical formulation of any one of claims 33 to 35, wherein the pharmaceutical formulation comprises about 0.5 mg/mL of varenicline, or a pharmaceutically acceptable salt thereof.
37. The pharmaceutical formulation of any one of claims 33 to 35, wherein the pharmaceutical formulation comprises about 1 mg/mL of varenicline, or a pharmaceutically acceptable salt thereof.
38. The pharmaceutical formulation of any one of claims 33 to 35, wherein the pharmaceutical formulation comprises about 10 mg/mL of varenicline, or a pharmaceutically acceptable salt thereof.
39. The pharmaceutical formulation of any one of claims 33 to 35, wherein the pharmaceutical formulation comprises about 20 mg/mL of varenicline, or a pharmaceutically acceptable salt thereof.
40. The pharmaceutical formulation of any one of claims 33 to 39, comprising between 5 micrograms and 50 micrograms of varenicline, or a pharmaceutically acceptable salt thereof, per dose.
41. The pharmaceutical formulation of any one of claims 33 to 40, wherein the formulation is a liquid, suspension, aerosol, gel, ointment, dry powder, cream, paste, lotion, or balm.
42. The pharmaceutical formulation of any one of claims 33 to 41, wherein the formulation is present in a syringe, dropper, bottle nebulizer, atomization pump, inhaler, powder spray device, vaporizer, patch, medicated stick, pipette, or jet of liquid.
43. Use of the pharmaceutical formulation of any one of claims 33 to 42 in the manufacture of a medicament for the treatment of dry eye.
44. Use of the pharmaceutical formulation of any one of claims 33 to 42 in the manufacture of a medicament for the treatment of ocular discomfort.

45. Use of the pharmaceutical formulation of any one of claims 33 to 42 in the manufacture of a medicament for a method for increasing tear production.

46. Products containing varenicline, or a pharmaceutically acceptable salt thereof, and one or more substances that prevent entry or reduce entry of a nicotinic acetylcholine receptor into a desensitized state, or facilitate recovery of the nicotinic acetylcholine receptor from the desensitized state as a combined preparation for use in therapy;

wherein the product comprises between 5 micrograms and 100 micrograms of varenicline, or a pharmaceutically acceptable salt thereof, per dose; and

wherein the product comprises a nasal formulation of varenicline.

47. Products containing varenicline, or a pharmaceutically acceptable salt thereof, and one or more substances that prevent entry or reduce entry of a nicotinic acetylcholine receptor into a desensitized state, or facilitate recovery of the nicotinic acetylcholine receptor from the desensitized state as a combined preparation for use in the treatment of dry eye or ocular discomfort;

wherein the product comprises between 5 micrograms and 100 micrograms of varenicline, or a pharmaceutically acceptable salt thereof, per dose; and

wherein the product comprises a nasal formulation of varenicline.

48. Products containing varenicline, or a pharmaceutically acceptable salt thereof, and one or more substances that prevent entry or reduce entry of a nicotinic acetylcholine receptor into a desensitized state, or facilitate recovery of the nicotinic acetylcholine receptor from the desensitized state as a combined preparation for use in increasing tear production;

wherein the product comprises between 5 micrograms and 100 micrograms of varenicline, or a pharmaceutically acceptable salt thereof, per dose; and

wherein the product comprises a nasal formulation of varenicline.

49. The products in accordance with any one of claims 46 to 48, wherein the one or more substances are selected from protein kinase C (PKC) or factors that upregulate or up-modulate PKC, cAMP-dependent protein kinase (PKA) or factors that upregulate or up-modulate PKA, and calcineurin inhibitors.

50. The products in accordance with claim 49, wherein the calcineurin inhibitor is selected from cyclosporine, pimecrolimus, and tacrolimus.