

CLAIMS

1. An ophthalmic composition comprising from about 0.001 wt% to about 0.5 wt% of a muscarinic antagonist and deuterated water, at a pH of from about 4.2 to about 7.9, wherein the ophthalmic composition is substantially free of a benzalkonium chloride preservative.
2. The ophthalmic composition of claim 1, wherein the ophthalmic composition is substantially free of a preservative selected from cetrimonium, sodium perborate, stabilized oxychloro complex, SofZia, polyquaternium-1, chlorobutanol, edetate disodium, polyhexamethylene biguanide, or combinations thereof.
3. The ophthalmic composition of any of claims 1 or 2, wherein the ophthalmic composition has no detectable amount of a benzalkonium chloride preservative.
4. The ophthalmic composition of any of claims 1-3, wherein the ophthalmic composition has no detectable amount of benzalkonium chloride.
5. The ophthalmic composition of any of claims 1-4, wherein the ophthalmic composition has no detectable amount of a preservative.
6. The ophthalmic composition of any of claims 1-5, wherein the muscarinic antagonist comprises atropine, atropine sulfate, noratropine, atropine-N-oxide, tropine, tropic acid, hyoscine, scopolamine, tropicamide, cyclopentolate, pirenzepine, homatropine, or a combination thereof.
7. The ophthalmic composition of claim 1, wherein the muscarinic antagonist is atropine or a pharmaceutically acceptable salt of atropine.
8. The ophthalmic composition of claim 1, wherein the muscarinic antagonist is present in the ophthalmic composition at a concentration of one of: from about 0.001 wt% to about 0.40 wt%, from about 0.001 wt% to about 0.30 wt%, from about 0.001 wt% to about 0.20 wt%, from about 0.001 wt% to about 0.10 wt%, from about 0.001 wt% to about 0.09 wt%, from about 0.001 wt% to about 0.08 wt%, from about 0.001 wt% to about 0.07 wt%, from about 0.001 wt% to about 0.06 wt%, from about 0.001 wt% to about 0.05 wt%, from about 0.001 wt% to about 0.04 wt%, from about 0.001 wt% to about 0.03 wt%, from about 0.001 wt% to about 0.025 wt%, from about 0.001 wt% to about 0.02 wt%, from about 0.001 wt% to about 0.01 wt%, from about 0.001 wt% to about 0.008 wt%, or from about 0.001 wt% to about 0.005 wt%.
9. The ophthalmic composition of claim 1, wherein the muscarinic antagonist is present in the ophthalmic composition at a concentration from about 0.001 wt% to about 0.10 wt%.
10. The ophthalmic composition of any of claims 1-8, wherein the ophthalmic composition further comprises 0.004 wt% to about 0.20 wt% citrate.
11. The ophthalmic composition of any of claims 1-8, wherein the ophthalmic composition further comprises an osmolarity adjusting agent.
12. The ophthalmic composition of claim 11, wherein the osmolarity adjusting agent is sodium chloride.
13. The ophthalmic composition of claim 12, wherein the sodium chloride is present in the ophthalmic composition at a concentration of one of: from about 0.01 wt% to about 1.0 wt%,

- from about 0.05 wt% to about 1.5 wt%, from about 0.075 wt% to about 2.0 wt%, or from about 0.1 wt% to about 3.0 wt%.
14. The ophthalmic composition of any of claims 1-13, wherein the ophthalmic composition further comprises a buffering agent.
 15. The ophthalmic composition of claim 14, wherein the buffering agent is selected from borates, borate-polyol complexes, phosphate buffering agents, citrate buffering agents, acetate buffering agents, carbonate buffering agents, organic buffering agents, amino acid buffering agents, or combinations thereof.
 16. The ophthalmic composition of any of claims 1-15, wherein the ophthalmic composition is essentially free of procaine and benactyzine, or pharmaceutically acceptable salts thereof.
 17. The ophthalmic composition of any of claims 1-16, wherein the ophthalmic composition further comprises a pH adjusting agent.
 18. The ophthalmic composition of claim 17, wherein the pH adjusting agent comprises DCl, HCl, NaOH, NaOD, CD₃COOD, C₆D₈O₇, CH₃COOH, C₆H₈O₇, or combinations thereof.
 19. The ophthalmic composition of claim 1, wherein the ophthalmic composition comprises less than about 10% of a degradant of the muscarinic antagonist formed from degradation of the muscarinic antagonist.
 20. An ophthalmic composition comprising from about 0.001 wt% to about 0.5 wt% of a muscarinic antagonist, deuterated water, at a pH of from about 4.2 to about 7.9, and one or more sodium phosphate buffers, wherein at least one sodium phosphate buffer of the one or more sodium phosphate buffers is present in the ophthalmic composition at a concentration of about 0.004 wt% to about 0.20 wt%.
 21. The ophthalmic composition of claim 20, wherein the muscarinic antagonist comprises atropine, atropine sulfate, noratropine, atropine-N-oxide, tropine, tropic acid, hyoscine, scopolamine, tropicamide, cyclopentolate, pirenzepine, homatropine, or a combination thereof.
 22. The ophthalmic composition of claim 20, wherein the muscarinic antagonist is atropine or a pharmaceutically acceptable salt of atropine.
 23. The ophthalmic composition of claim 20, wherein a first sodium phosphate buffer of the one or more sodium phosphate buffers is monosodium phosphate anhydrous.
 24. The ophthalmic composition of claim 23, wherein the monosodium phosphate anhydrous is present in the ophthalmic composition at a concentration of about 0.004 wt% to about 0.20 wt%.
 25. The ophthalmic composition of claim 23, wherein a second sodium phosphate buffer of the one or more sodium phosphate buffers is disodium phosphate anhydrous.
 26. The ophthalmic composition of claim 25, wherein the disodium phosphate anhydrous is present in the ophthalmic composition at a concentration of about 0.050 wt% to about 2.0 wt%.
 27. The ophthalmic composition of claim 20, wherein the muscarinic antagonist is present in the ophthalmic composition at a concentration of one of: from about 0.001 wt% to about 0.40 wt%, from about 0.001 wt% to about 0.30 wt%, from about 0.001 wt% to about 0.20 wt%, from about

- 0.001 wt% to about 0.10 wt%, from about 0.001 wt% to about 0.09 wt%, from about 0.001 wt% to about 0.08 wt%, from about 0.001 wt% to about 0.07 wt%, from about 0.001 wt% to about 0.06 wt%, from about 0.001 wt% to about 0.05 wt%, from about 0.001 wt% to about 0.04 wt%, from about 0.001 wt% to about 0.03 wt%, from about 0.001 wt% to about 0.025 wt%, from about 0.001 wt% to about 0.02 wt%, from about 0.001 wt% to about 0.01 wt%, from about 0.001 wt% to about 0.008 wt%, or from about 0.001 wt% to about 0.005 wt%.
28. The ophthalmic composition of claim 20, wherein the muscarinic antagonist is present in the ophthalmic composition at a concentration from about 0.001 wt% to about 0.10 wt%.
 29. The ophthalmic composition of claim 20, wherein the ophthalmic composition is essentially free of citrate and acetate buffering agents.
 30. The ophthalmic composition of any of claims 20-29, wherein the ophthalmic composition further comprises an osmolarity adjusting agent.
 31. The ophthalmic composition of claim 30, wherein the osmolarity adjusting agent is sodium chloride.
 32. The ophthalmic composition of claim 31, wherein the sodium chloride is present in the ophthalmic composition at a concentration of one of: from about 0.01 wt% to about 1.0 wt%, from about 0.05 wt% to about 1.5 wt%, from about 0.075 wt% to about 2.0 wt%, or from about 0.1 wt% to about 3.0 wt%.
 33. The ophthalmic composition of any of claims 20-32, wherein the ophthalmic composition is free of a preservative selected from benzalkonium chloride, cetrimonium, sodium perborate, stabilized oxychloro complex, SofZia, polyquaternium-1, chlorobutanol, edetate disodium, polyhexamethylene biguanide, or combinations thereof.
 34. The ophthalmic composition of claim 33, wherein the ophthalmic composition is substantially free of a benzalkonium chloride preservative.
 35. The ophthalmic composition of any of claims 20-34, wherein the ophthalmic composition is substantially free of any preservative.
 36. The ophthalmic composition of any of claims 20-35, wherein the ophthalmic composition further comprises a buffering agent.
 37. The ophthalmic composition of claim 36, wherein the buffering agent is selected from borates, borate-polyol complexes, phosphate buffering agents, citrate buffering agents, acetate buffering agents, carbonate buffering agents, organic buffering agents, amino acid buffering agents, or combinations thereof.
 38. The ophthalmic composition of any of claims 20-37, wherein the ophthalmic composition further comprises EDTA.
 39. The ophthalmic composition of claim 38, wherein the EDTA is present in the ophthalmic composition at a concentration of 0.01 wt% to about 0.50 wt%.
 40. The ophthalmic composition of any of claims 20-39, wherein the ophthalmic composition is essentially free of procaine and benactyzine, or pharmaceutically acceptable salts thereof.

41. The ophthalmic composition of any of claims 20-40, wherein the ophthalmic composition further comprises a pH adjusting agent.
42. The ophthalmic composition of claim 41, wherein the pH adjusting agent comprises DCl, HCl, NaOH, NaOD, CD₃COOD, C₆D₈O₇, CH₃COOH, C₆H₈O₇, or combinations thereof.
43. An ophthalmic composition comprising from about 0.001 wt% to about 0.5 wt% of a muscarinic antagonist, deuterated water, at a pH of from about 4.2 to about 7.9, and 0.01 wt% to about 0.50 wt% EDTA.
44. The ophthalmic composition of claim 43, wherein the muscarinic antagonist comprises atropine, atropine sulfate, noratropine, atropine-N-oxide, tropine, tropic acid, hyoscine, scopolamine, tropicamide, cyclopentolate, pirenzepine, homatropine, or a combination thereof.
45. The ophthalmic composition of claim 43, wherein the muscarinic antagonist is atropine or pharmaceutically acceptable salt of atropine.
46. The ophthalmic composition of any of claims 43-45, wherein the ophthalmic composition further comprises one or more sodium phosphate buffers.
47. The ophthalmic composition of claim 46, wherein a first sodium phosphate buffer of the one or more sodium phosphate buffers is monosodium phosphate anhydrous.
48. The ophthalmic composition of claim 47, wherein the sodium phosphate anhydrous is present in the ophthalmic composition at a concentration of about 0.004 wt% to about 0.20 wt%.
49. The ophthalmic composition of claim 46, wherein a second sodium phosphate of the one or more sodium phosphate buffers is disodium phosphate anhydrous.
50. The ophthalmic composition of claim 49, wherein the disodium phosphate anhydrous is present in the ophthalmic composition at a concentration of about 0.050 wt% to about 2.0 wt%.
51. The ophthalmic composition of claim 43, wherein the muscarinic antagonist is present in the ophthalmic composition at a concentration of one of: from about 0.001 wt% to about 0.40 wt%, from about 0.001 wt% to about 0.30 wt%, from about 0.001 wt% to about 0.20 wt%, from about 0.001 wt% to about 0.10 wt%, from about 0.001 wt% to about 0.09 wt%, from about 0.001 wt% to about 0.08 wt%, from about 0.001 wt% to about 0.07 wt%, from about 0.001 wt% to about 0.06 wt%, from about 0.001 wt% to about 0.05 wt%, from about 0.001 wt% to about 0.04 wt%, from about 0.001 wt% to about 0.03 wt%, from about 0.001 wt% to about 0.025 wt%, from about 0.001 wt% to about 0.02 wt%, from about 0.001 wt% to about 0.01 wt%, from about 0.001 wt% to about 0.008 wt%, or from about 0.001 wt% to about 0.005 wt%.
52. The ophthalmic composition of claim 43, wherein the muscarinic antagonist is present in the ophthalmic composition at a concentration from about 0.001 wt% to about 0.10 wt%.
53. The ophthalmic composition of any of claims 43-52, wherein the ophthalmic composition further comprises 0.004 wt% to about 0.20 wt% citrate.
54. The ophthalmic composition of any of claims 43-53, wherein the ophthalmic composition further comprises an osmolarity adjusting agent.

55. The ophthalmic composition of claim 54, wherein the osmolarity adjusting agent is sodium chloride.
56. The ophthalmic composition of claim 55, wherein the sodium chloride is present in the ophthalmic composition at a concentration of one of: from about 0.01 wt% to about 1.0 wt%, from about 0.05 wt% to about 1.5 wt%, from about 0.075 wt% to about 2.0 wt%, or from about 0.1 wt% to about 3.0 wt%.
57. The ophthalmic composition of any of claims 43-56, wherein the ophthalmic composition is free of a preservative selected from benzalkonium chloride, cetrimonium, sodium perborate, stabilized oxychloro complex, SofZia, polyquaternium-1, chlorobutanol, edetate disodium, polyhexamethylene biguanide, or combinations thereof.
58. The ophthalmic composition of claim 57, wherein the ophthalmic composition is substantially free of a benzalkonium chloride preservative.
59. The ophthalmic composition of any of claims 43-58, wherein the ophthalmic composition is substantially free of any preservative.
60. The ophthalmic composition of any of claims 43-59, wherein the ophthalmic composition further comprises a buffering agent.
61. The ophthalmic composition of claim 60, wherein the buffering agent is selected from borates, borate-polyol complexes, phosphate buffering agents, citrate buffering agents, acetate buffering agents, carbonate buffering agents, organic buffering agents, amino acid buffering agents, or combinations thereof.
62. The ophthalmic composition of any of claims 43-61, wherein the ophthalmic composition is essentially free of procaine and benactyzine, or pharmaceutically acceptable salts thereof.
63. The ophthalmic composition of any of claims 43-62, wherein the ophthalmic composition further comprises a pH adjusting agent.
64. The ophthalmic composition of claim 63, wherein the pH adjusting agent comprises DCl, HCl, NaOH, NaOD, CD₃COOD, C₆D₈O₇, CH₃COOH, C₆H₈O₇, or combinations thereof.
65. An ophthalmic composition comprising from about 0.001 wt% to about 0.5 wt% of a muscarinic antagonist, deuterated water, at a pH of from about 4.2 to about 7.9, and water, wherein a ratio of the water to the deuterated water is in a range of 60:40 to 99:1.
66. The ophthalmic composition of claim 65, wherein the muscarinic antagonist comprises atropine, atropine sulfate, noratropine, atropine-N-oxide, tropine, tropic acid, hyoscine, scopolamine, tropicamide, cyclopentolate, pirenzepine, homatropine, or a combination thereof.
67. The ophthalmic composition of claim 65, wherein the muscarinic antagonist is atropine or pharmaceutically acceptable salt of atropine.
68. The ophthalmic composition of claim 65, wherein the muscarinic antagonist is present in the ophthalmic composition at a concentration of one of: from about 0.001 wt% to about 0.40 wt%, from about 0.001 wt% to about 0.30 wt%, from about 0.001 wt% to about 0.20 wt%, from about 0.001 wt% to about 0.10 wt%, from about 0.001 wt% to about 0.09 wt%, from about 0.001 wt%

- to about 0.08 wt%, from about 0.001 wt% to about 0.07 wt%, from about 0.001 wt% to about 0.06 wt%, from about 0.001 wt% to about 0.05 wt%, from about 0.001 wt% to about 0.04 wt%, from about 0.001 wt% to about 0.03 wt%, from about 0.001 wt% to about 0.025 wt%, from about 0.001 wt% to about 0.02 wt%, from about 0.001 wt% to about 0.01 wt%, from about 0.001 wt% to about 0.008 wt%, or from about 0.001 wt% to about 0.005 wt%.
69. The ophthalmic composition of claim 65, wherein the muscarinic antagonist is present in the ophthalmic composition at a concentration from about 0.001 wt% to about 0.10 wt%.
70. The ophthalmic composition of claim 65, wherein a ratio of the water to the deuterated water is in a range of about 80:20 to about 60:40.
71. The ophthalmic composition of claim 65, wherein a ratio of the water to the deuterated water is about 65:35.
72. The ophthalmic composition of claim 65, wherein a ratio of the water to the deuterated water is about 90:10.
73. The ophthalmic composition of claim 65, wherein the muscarinic antagonist is present in the ophthalmic composition at a concentration of from about 0.01 wt% to about 0.05 wt%.
74. The ophthalmic composition of claim 65, wherein the muscarinic antagonist is present in the ophthalmic composition at a concentration of from about 0.01 wt% to about 0.03 wt%.
75. The ophthalmic composition of claim 65, wherein the muscarinic antagonist is present in the ophthalmic composition at a concentration of about 0.01 wt%.
76. The ophthalmic composition of claim 65, wherein the muscarinic antagonist is present in the ophthalmic composition at a concentration of about 0.03 wt%.
77. The ophthalmic composition of any one of claims 65-76, wherein the ophthalmic composition is substantially free of a benzalkonium chloride preservative.
78. The ophthalmic composition of any one of claims 65-76, wherein the ophthalmic composition has no detectable amount of a benzalkonium chloride preservative.
79. The ophthalmic composition of any one of claims 65-76, wherein the ophthalmic composition has no detectable amount of a preservative.
80. The ophthalmic composition of claim 65, wherein the ophthalmic composition has a pH from about 5.1 to about 6.0.
81. The ophthalmic composition of claim 65, wherein the ophthalmic composition has a pH from about 5.54 to about 5.59.
82. The ophthalmic composition of any of claims 65-81, wherein the ophthalmic composition further comprises 0.004 wt% to about 0.20 wt% citrate.
83. The ophthalmic composition of any of claims 65-82, wherein the ophthalmic composition further comprises one or more sodium phosphate buffers.
84. The ophthalmic composition of claim 83, wherein a first sodium phosphate buffer of the one or more sodium phosphate buffers is monosodium phosphate anhydrous.

85. The ophthalmic composition of claim 84, wherein the monosodium phosphate anhydrous is present in the ophthalmic composition at a concentration of about 0.004 wt% to about 0.20 wt%.
86. The ophthalmic composition of claim 85, wherein a second sodium phosphate of the one or more sodium phosphate buffers is disodium phosphate anhydrous.
87. The ophthalmic composition of claim 86, wherein the disodium phosphate anhydrous is present in the ophthalmic composition at a concentration of about 0.050 wt% to about 2.0 wt%.
88. The ophthalmic composition of any of claims 65-87, wherein the ophthalmic composition further comprises an osmolarity adjusting agent.
89. The ophthalmic composition of any of claims 65-88, wherein the osmolarity adjusting agent is sodium chloride.
90. The ophthalmic composition of claim 89, wherein the sodium chloride is present in the ophthalmic composition at a concentration of one of: from about 0.01 wt% to about 1.0 wt%, from about 0.05 wt% to about 1.5 wt%, from about 0.075 wt% to about 2.0 wt%, or from about 0.1 wt% to about 3.0 wt%.
91. The ophthalmic composition of any of claims 65-90, wherein the ophthalmic composition is free of a preservative selected from benzalkonium chloride, cetrimonium, sodium perborate, stabilized oxychloro complex, SofZia, polyquaternium-1, chlorobutanol, edetate disodium, polyhexamethylene biguanide, or combinations thereof.
92. The ophthalmic composition of claim 91, wherein the ophthalmic composition is substantially free of a benzalkonium chloride preservative.
93. The ophthalmic composition of any of claims 65-92, wherein the ophthalmic composition is substantially free of any preservative.
94. The ophthalmic composition of any of claims 65-93, wherein the ophthalmic composition further comprises a buffering agent.
95. The ophthalmic composition of claim 94, wherein the buffering agent is selected from borates, borate-polyol complexes, phosphate buffering agents, citrate buffering agents, acetate buffering agents, carbonate buffering agents, organic buffering agents, amino acid buffering agents, or combinations thereof.
96. The ophthalmic composition of any of claims 65-95, wherein the ophthalmic composition further comprises EDTA.
97. The ophthalmic composition of claim 96, wherein the EDTA is present in the ophthalmic composition at a concentration of 0.01 wt% to about 0.50 wt%.
98. The ophthalmic composition of any of claims 65-97, wherein the ophthalmic composition is essentially free of procaine and benactyzine, or pharmaceutically acceptable salts thereof.
99. The ophthalmic composition of any of claims 65-98, wherein the ophthalmic composition further comprises a pH adjusting agent.
100. The ophthalmic composition of claim 99, wherein the pH adjusting agent comprises DCl, HCl, NaOH, NaOD, CD₃COOD, C₆D₈O₇, CH₃COOH, C₆H₈O₇, or combinations thereof.

101. The ophthalmic composition of claim 65, wherein the ophthalmic composition comprises less than about 10% of a degradant of the muscarinic antagonist formed from degradation of the muscarinic antagonist.
102. The ophthalmic composition of 1-101, wherein the ophthalmic composition is formulated as an ophthalmic solution for treatment of pre-myopia, myopia, progression of myopia, or slowing progression of myopia.