possible but not alluding to polyethylene as the sole material or as a major resin component (EP 1 829 545).

Furthermore, almost all of PGF2α analogues are practically insoluble in water. It is thus necessary to solve also the problem of solubility to water in order to formulate PGF2α analogues in ophthalmic solutions, especially for unit dose preparations. In EP 1 321 144 and US 2007/248697, a nonionic surfactant has been added to the ophthalmic solution to prevent a prostaglandin derivative from being adsorbed to a resinous container. Other attempts to compensate the difficulties in formulating highly lipophilic prostaglandin analogues in water have been described for example in EP 0 969 846, EP 1 666 043, EP 1 011 728 and WO 2007/042262 but they do not mention any preservative-free composition.

It is therefore an object of the present invention to provide an ophthalmic aqueous solution comprising PGF2α analogues and substantially no preservatives wherein the absorption of PGF2α analogues to the resinous containers consisting essentially of polyethylene is prevented and wherein said analogues remain soluble, stable and bioavailable in a preservative-free preparation. The aqueous ophthalmic solution according to the invention provides a significant clinical advantage as there is currently an unmet clinical need of preservative-free prostaglandin eye drops for glaucoma patients.

Summary

The present disclosure relates to an aqueous ophthalmic solution for treating ocular hypertension and glaucoma comprising PGF2α analogue as an active ingredient thereof which solution contains nonionic surfactant, stabilizing agent, and substantially no preservatives in a container consisting essentially of polyethylene.

In one aspect of the present disclosure, there is provided an ophthalmic aqueous solution comprising

0.0010 – 0.0015% w/v tafluprost;

0.05 – 0.1% w/v polysorbate 80;

0.01 – 0.1% w/v disodium edetate; and

buffering agents, pH adjusters and tonicity agents conventionally used in ophthalmic solutions, and substantially no preservatives, in a container consisting essentially of polyethylene or in contact with container material consisting essentially of polyethylene.

In another aspect of the present disclosure, there is provide an ophthalmic aqueous solution, comprising

0.0015% w/v tafluprost;

0.075% w/v polysorbate 80;

0.05% w/v disodium edetate;

2.25% w/v glycerol;

0.2% w/v sodium dihydrogen phosphate dihydrate;

pH adjusters, and

substantially no preservatives, in a container consisting essentially of polyethylene or in contact with container material consisting essentially of polyethylene.

The present disclosure also relates to a method for treating ocular hypertension and glaucoma, which method comprises administering an aqueous ophthalmic solution comprising PGF2α analogue as an active ingredient thereof to a subject in need of said treatment, wherein the ophthalmic solution contains nonionic surfactant, stabilizing agent, and substantially no preservatives.

Further, the present disclosure relates to the use of PGF2α analogue for manufacturing an ophthalmic aqueous solution for the treatment of ocular hypertension and glaucoma, wherein said solution contains nonionic surfactant, stabilizing agent, substantially no preservatives and is stored in a container consisting essentially of polyethylene.

In a further aspect of the present disclosure, there is provided a use of tafluprost for the manufacture of an ophthalmic aqueous solution for the treatment of ocular hypertension and glaucoma, wherein said ophthalmic solution comprises 0.0010-0.0015% w/v tafluprost, 0.05-0.1% w/v polysorbate 80, 0.01-0.1% w/v disodium edetate, and substantially no preservatives.

Another object of the present disclosure is a method for increasing aqueous solubility and improving stability of PGF2α analogues in an aqueous ophthalmic solution, comprising the steps of preparing an ophthalmic aqueous solution containing

PGF2α analogue, nonionic surfactant, stabilizing agent and substantially no preservatives, and packaging the preservative-free ophthalmic solution in a container consisting essentially of polyethylene.

In yet another aspect of the present disclosure, there is provided a method for increasing aqueous solubility and improving stability of tafluprost in an aqueous ophthalmic solution, comprising the steps of preparing an aqueous ophthalmic solution containing 0.0010-0.0015% w/v tafluprost, 0.05-0.1% w/v polysorbate 80, 0.01-0.1% w/v disodium edetate and substantially no preservatives, and packaging the preservative-free ophthalmic solution in a container consisting essentially of polyethylene or in contact with container material consisting essentially of polyethylene.

Claims

1. An ophthalmic aqueous solution comprising
0.0010 - 0.0015% w/v tafluprost;
0.05 - 0.1% w/v polysorbate 80;
0.01 - 0.1% w/v disodium edetate; and
buffering agents, pH adjusters and tonicity agents conventionally used in ophthalmic solutions, and substantially no preservatives, in a container consisting essentially of polyethylene or in contact with container material consisting essentially of polyethylene.

2. An ophthalmic aqueous solution, comprising
0.0015% w/v tafluprost;
0.075% w/v polysorbate 80;
0.05% w/v disodium edetate;
2.25% w/v glycerol;
0.2% w/v sodium dihydrogen phosphate dihydrate;
pH adjusters; and
substantially no preservatives, in a container consisting essentially of polyethylene or in contact with container material consisting essentially of polyethylene.

3. The ophthalmic aqueous solution according to claim 1 or 2 in a container containing no more than 10% of any material other than polyethylene,
wherein the material other than polyethylene is selected from the group consisting of polypropylene, polyethylene terephthalate, polyvinyl chloride, acrylic resins, polystyrene, polymethyl methacrylate and nylon 6.

4. The ophthalmic aqueous solution according to claim 1 or 2 in a single dose or unit dose form.

5. The ophthalmic aqueous solution according to claim 1 or 2 in a fluid dispenser form.

6. The ophthalmic aqueous solution according to claim 1 or 2 further comprising timolol.

7. A method for increasing aqueous solubility and improving stability of tafluprost in an aqueous ophthalmic solution, comprising the steps of preparing an aqueous ophthalmic solution containing 0.0010-0.0015% w/v tafluprost, 0.05-0.1% w/v polysorbate 80, 0.01-0.1% w/v disodium edetate and substantially no preservatives, and packaging the preservative-free ophthalmic solution in a container consisting essentially of polyethylene or in contact with container material consisting essentially of polyethylene.

8. Use of tafluprost for the manufacture of an ophthalmic aqueous solution for the treatment of ocular hypertension and glaucoma, wherein said ophthalmic solution comprises 0.0010-0.0015% w/v tafluprost, 0.05-0.1% w/v polysorbate 80, 0.01-0.1% w/v disodium edetate, and substantially no preservatives.

9. The use according to claim 8, wherein the ophthalmic aqueous solution is packaged in a container consisting essentially of polyethylene or in contact with container material consisting essentially of polyethylene.