

Propylene glycol but no alcohol and uses the surfactant blend of polysorbate 80 and polyoxyl 40 stearate to form the foam lamella. The latest advance in topical pharmaceutical foam technology is Amzeeq® topical minocycline foam for the treatment of acne and rosacea. This product does not contain solvents but uses a blend of multiple natural oils to dissolve minocycline combined with hydrogenated castor oil as the surfactant to form foam lamella.

Brief Summary

There is provided an aerosol foam composition comprising roflumilast. The aerosol foam composition is preferably an oil in water emulsion in combination with a propellant. The propellant is a mixture of liquefied hydrocarbon gases preferably a propane/isobutane/butane blend. The hydrocarbon propellant results in a roflumilast aerosol foam which is stable, has consistent physical properties, excellent aesthetics, and no discernable roflumilast degradation after long term (storage at ambient temperature for more than 24 months) or accelerated storage conditions (storage at 40°C and 75% relative humidity for 6 months). Preferably, the roflumilast aerosol foam does not contain alcohol or propylene glycol.

In one aspect, there is provided an aerosol foam comprising roflumilast, cetearyl alcohol, dicetyl phosphate, cetareth-10 phosphate in an oil in water emulsion and a propane/isobutane/butane propellant blend, wherein said oil in water emulsion has a viscosity of 4,000-11,000 cP, wherein said propellant and oil in water emulsion are in a ratio of about 1:8 to 1:6, and wherein said aerosol foam is emitted from a container but collapses after application to a subject's skin.

In another aspect, there is provided an aerosol foam comprising an oil in water emulsion and a propane/isobutane/butane propellant blend, wherein the oil in water emulsion consists of:

Roflumilast	0.3% w/w
White Petrolatum	5.0% w/w
Isopropyl Palmitate	2.5% w/w
Emulsifier blend comprising cetearyl alcohol, dicetyl phosphate, and ceteth-10 phosphate	2.0% w/w
Hexylene glycol	2.0% w/w
Diethylene glycol monoethyl ether	25.0% w/w
Methylparaben	0.2% w/w
Propylparaben	0.05% w/w
pH Modifier	q.s. ad pH 5.5
Purified Water	q.s. ad 100.

In another aspect, there is provided an aerosol foam comprising an oil in water emulsion and a propane/isobutane/butane propellant blend, wherein the oil in water emulsion consists of:

Roflumilast	0.3% w/w
White Petrolatum	5.0% w/w
Isopropyl Palmitate	2.5% w/w
Emulsifier blend comprising cetearyl alcohol, dicetyl phosphate, and cetareth-10 phosphate	2.0% w/w
Diethylene glycol monoethyl ether	25.0% w/w
Methylparaben	0.2% w/w
Propylparaben	0.05% w/w
pH Modifier	q.s. ad pH 5.5
Purified Water	q.s. ad 100.

In another aspect, there is provided use of a composition comprising roflumilast, cetearyl alcohol, dicetyl phosphate, cetearth-10 phosphate in an oil in water emulsion and a propane/isobutane/butane propellant blend in the manufacture of a medicament for inhibiting phosphodiesterase 4, wherein the medicament is in a form of an aerosol foam and is to be topically administered to a patient, wherein said oil in water emulsion has a viscosity of 4,000-11,000 cP, wherein said propellant and oil in water emulsion are in a ratio of about 1:8 to 1:6, wherein said aerosol foam is emitted from a container but collapses after application to the patient's skin.

In another aspect, there is provided an aerosol foam comprising roflumilast, cetearyl alcohol, dicetyl phosphate, cetearth-10 phosphate and diethylene glycol monoethyl ether in an oil in water emulsion, and a propane/isobutane/butane propellant blend, wherein said oil in water emulsion has a viscosity of 4,000-11,000 cP, wherein said foam does not include hexylene glycol, wherein said diethylene glycol monoethyl ether is in an amount of 25% w/w to 35% w/w, wherein said aerosol foam is emitted from a container but collapses after application to the skin, and wherein said aerosol foam has a foam half-life of 30 seconds or more.

Brief Description of the Drawings

Figures 1A- 1E show acceptable and unacceptable foams. Figures 1A-1D show acceptable foam structures including an expanding foam, a quick breaking foam, a stiff foam and a stout foam immediately after dispensing and 5 minutes after dispensing. Figure 1E shows an unacceptable foam with inadequate mixing of the propellant and the concentrate, resulting in sputtering during dispensing.

Detailed Description of the Invention

Claims

1. An aerosol foam comprising roflumilast, cetearyl alcohol, dicetyl phosphate, cetareth-10 phosphate in an oil in water emulsion and a propane/isobutane/butane propellant blend, wherein said oil in water emulsion has a viscosity of 4,000-11,000 cP, wherein said propellant and oil in water emulsion are in a ratio of about 1:8 to 1:6, and wherein said aerosol foam is emitted from a container but collapses after application to a subject's skin.

2. An aerosol foam comprising an oil in water emulsion and a propane/isobutane/butane propellant blend, wherein the oil in water emulsion consists of:

Roflumilast	0.3% w/w
White Petrolatum	5.0% w/w
Isopropyl Palmitate	2.5% w/w
Emulsifier blend comprising cetearyl alcohol, dicetyl phosphate, and ceteth-10 phosphate	2.0% w/w
Hexylene glycol	2.0% w/w
Diethylene glycol monoethyl ether	25.0% w/w
Methylparaben	0.2% w/w
Propylparaben	0.05% w/w
pH Modifier	q.s. ad pH 5.5
Purified Water	q.s. ad 100.

3. An aerosol foam comprising an oil in water emulsion and a propane/isobutane/butane propellant blend, wherein the oil in water emulsion consists of:

Roflumilast	0.3% w/w
White Petrolatum	5.0% w/w
Isopropyl Palmitate	2.5% w/w
Emulsifier blend comprising cetearyl alcohol, dicetyl phosphate, and ceteareth-10 phosphate	2.0% w/w
Diethylene glycol monoethyl ether	25.0% w/w
Methylparaben	0.2% w/w
Propylparaben	0.05% w/w
pH Modifier	q.s. ad pH 5.5
Purified Water	q.s. ad 100.

4. The aerosol foam according to claim 1, further comprising hexylene glycol in an amount of 0% w/w to 4.00% w/w and/or diethylene glycol monoethyl ether in an amount of 25% w/w to 35% w/w.

5. The aerosol foam according to claim 4, wherein said hexylene glycol is in an amount of 2.00% w/w to 4.00% w/w and/or said diethylene glycol monoethyl ether is in an amount of 25% w/w to 35% w/w.

6. The aerosol foam according to claim 1, further comprising at least one additional component selected from the group consisting of a solvent, moisturizer, surfactant or emulsifier, polymer or thickener, preservative, antioxidant, sequestering agent,

stabilizer, buffer, pH adjusting solution, skin penetration enhancer, film former, dye, pigment, and fragrance.

7. The aerosol foam according to claim 1, further comprising an additional active agent selected from the group consisting of anthralin, azathioprine, tacrolimus, coal tar, methotrexate, methoxsalen, salicylic acid, ammonium lactate, urea, hydroxyurea, 5-fluorouracil, propylthiouracil, 6-thioguanine, sulfasalazine, mycophenolate mofetil, fumaric acid esters, corticosteroids, corticotropin, vitamin D analogues, acitretin, tazarotene, cyclosporine, resorcinol, colchicine, adalimumab, ustekinumab, infliximab, bronchodilators, and antibiotics.

8. The aerosol foam according to claim 1, wherein said roflumilast is in an amount of 0.05-2% by weight of the total composition.

9. The aerosol foam according to claim 1, wherein said propane/isobutane/butane propellant blend is AP-70.

10. Use of a composition comprising roflumilast, cetearyl alcohol, dicetyl phosphate, cetareth-10 phosphate in an oil in water emulsion and a propane/isobutane/butane propellant blend in the manufacture of a medicament for inhibiting phosphodiesterase 4, wherein the medicament is in a form of an aerosol foam and is to be topically administered to a patient, wherein said oil in water emulsion has a viscosity of 4,000-11,000 cP, wherein said propellant and oil in water emulsion are in

a ratio of about 1:8 to 1:6, wherein said aerosol foam is emitted from a container but collapses after application to the patient's skin.

11. The use according to claim 10, wherein said patient is suffering from a proliferative, inflammatory and/or allergic dermatoses.

12. The use according to claim 11, wherein said proliferative, inflammatory and allergic dermatoses is selected from the group consisting of psoriasis (vulgaris), eczema, acne, lichen simplex, lichen sclerosus, prurigo nodularis, sunburn, pruritus, alopecia areata, hypertrophic scars, discoid lupus erythematosus, and pyodermias.

13. The use according to claim 11, wherein said patient is suffering from an inflammatory dermatoses.

14. The use according to claim 13, wherein said patient is suffering from atopic dermatitis.

15. The use according to claim 10, wherein said aerosol foam further comprises at least one component selected from the group consisting of hexylene glycol and diethylene glycol monoethyl ether.

16. The use according to claim 13, wherein said aerosol foam is to be administered one or more times per day.

17. The use according to claim 16, wherein said aerosol foam is to be administered 1-2 times per day.

18. The use according to claim 10, wherein said aerosol foam does not include hexylene glycol.

19. The use according to claim 10, wherein said aerosol foam further comprises diethylene glycol monoethyl ether in an amount of 25% w/w to 35% w/w.

20. An aerosol foam comprising roflumilast, cetearyl alcohol, dicetyl phosphate, cetareth-10 phosphate and diethylene glycol monoethyl ether in an oil in water emulsion, and a propane/isobutane/butane propellant blend, wherein said oil in water emulsion has a viscosity of 4,000-11,000 cP, wherein said foam does not include hexylene glycol, wherein said diethylene glycol monoethyl ether is in an amount of 25% w/w to 35% w/w, wherein said aerosol foam is emitted from a container but collapses after application to the skin, and wherein said aerosol foam has a foam half-life of 30 seconds or more.

21. The aerosol foam according to claim 20, wherein said aerosol foam has a half-life of 5 minutes or more.