Claims

[Claim 1]

~~A method for blocking transmission of malaria parasites from a human to a mosquito, comprising administering a pharmaceutically effective amount of~~Use of a combination of I) a pharmaceutical composition and II) a vaccine in the manufacture of a medicament for blocking transmission from a human to a mosquito~~to a human residing in an area in need of blocking malaria transmission~~, wherein:

I) the pharmaceutical composition comprises the following ingredients i) to vi):

i) (4E,8E,12E,16E,20E)-N-{2-[{4-[(2-amino-4-{[(3S)-1-hydroxyhexan-3-yl]amino}-6-methylpyrimidin-5-yl)methyl]benzyl}(methyl)amino]ethyl}-4,8,12,17,21,25-hexamethylhexacosa-4,8,12,16,20,24-hexaeneamide, hereinafter referred to as "Compound A", or a pharmaceutically acceptable salt thereof;

ii) squalane;

iii) an antioxidant agent A selected from the group consisting of ascorbate esters such as L-ascorbyl stearate and ascorbyl palmitate, mineral salts of ascorbic acid such as potassium ascorbate, sodium ascorbate, and calcium ascorbate, and ascorbic acid;

iv) an excipient selected from the group consisting of non-reducing sugars and sugar alcohols, except for mannitol;

v) a hydrophilic surfactant; and

vi) a lipophilic surfactant; and

II) the vaccine is a malaria vaccine comprising an antigen having the sequence represented by SEQ ID NO: 1 or SEQ ID NO: 2.

[Claim 2]

A combination drug comprising:

I) a pharmaceutical composition comprising:

i) (4E,8E,12E,16E,20E)-N-{2-[{4-[(2-amino-4-{[(3S)-1-hydroxyhexan-3-yl]amino}-6-methylpyrimidin-5-

yl)methyl]benzyl}(methyl)amino]ethyl}-4,8,12,17,21,25-hexamethylhexacosa-4,8,12,16,20,24-hexaeneamide or a pharmaceutically acceptable salt thereof;

ii) squalane;

iii) an antioxidant agent A selected from the group consisting of ascorbate esters such as L-ascorbyl stearate and ascorbyl palmitate, mineral salts of ascorbic acid such as potassium ascorbate, sodium ascorbate, and calcium ascorbate, and ascorbic acid;

iv) an excipient selected from the group consisting of non-reducing sugars and sugar alcohols, except for mannitol;

v) a hydrophilic surfactant; and

vi) a lipophilic surfactant; and

II) a malaria vaccine comprising an antigen having the sequence represented by SEQ ID NO: 1 or SEQ ID NO: 2.

[Claim 3]

A vaccine formulation for malaria comprising:

I) a pharmaceutical composition comprising:

i) (4E,8E,12E,16E,20E)-N-{2-[{4-[(2-amino-4-{[(3S)-1-hydroxyhexan-3-yl]amino}-6-methylpyrimidin-5-yl)methyl]benzyl}(methyl)amino]ethyl}-4,8,12,17,21,25-hexamethylhexacosa-4,8,12,16,20,24-hexaeneamide or a pharmaceutically acceptable salt thereof;

ii) squalane;

iii) an antioxidant agent A selected from the group consisting of ascorbate esters such as L-ascorbyl stearate and ascorbyl palmitate, mineral salts of ascorbic acid such as potassium ascorbate, sodium ascorbate, and calcium ascorbate, and ascorbic acid;

iv) an excipient selected from the group consisting of non-reducing sugars and sugar alcohols, except for mannitol;

v) a hydrophilic surfactant; and

vi) a lipophilic surfactant; and

II) a malaria vaccine comprising an antigen having the sequence represented by SEQ ID NO: 1 or SEQ ID NO: 2.

[Claim 4]

A kit comprising:

I) a pharmaceutical composition comprising:

i) (4E,8E,12E,16E,20E)-N-{2-[{4-[(2-amino-4-{[(3S)-1-hydroxyhexan-3-yl]amino}-6-methylpyrimidin-5-yl)methyl]benzyl}(methyl)amino]ethyl}-4,8,12,17,21,25-hexamethylhexacosa-4,8,12,16,20,24-hexaeneamide or a pharmaceutically acceptable salt thereof;

ii) squalane;

iii) an antioxidant agent A selected from the group consisting of ascorbate esters such as L-ascorbyl stearate and ascorbyl palmitate, mineral salts of ascorbic acid such as potassium ascorbate, sodium ascorbate, and calcium ascorbate, and ascorbic acid;

iv) an excipient selected from the group consisting of non-reducing sugars and sugar alcohols, except for mannitol;

v) a hydrophilic surfactant; and

vi) a lipophilic surfactant; and

II) a malaria vaccine comprising an antigen having the sequence represented by SEQ ID NO: 1 or SEQ ID NO: 2.

[Claim 5]

The use, the combination drug, the vaccine formulation, or the kit according to any one of claims 1 to 4~~The method according to claim 1 or the combination drug according to claim 2~~, wherein the pharmaceutical composition is an oil-in-water type emulsion formulation or a lyophilized formulation thereof.

[Claim 6]

The use, the combination drug, the vaccine formulation, or the kit according to any one of claims 1 to 5~~The method according to claim 1 or the combination drug according to~~

~~claim 2~~, wherein the hydrophilic surfactant is polyoxyethylene sorbitan fatty acid esters (e.g., polysorbate 20, polysorbate 40, polysorbate 60, polysorbate 65, and polysorbate 80); polyoxyethylene hydrogenated castor oils (e.g., polyoxyethylene hydrogenated castor oil 10, polyoxyethylene hydrogenated castor oil 20, polyoxyethylene hydrogenated castor oil 40, polyoxyethylene hydrogenated castor oil 50, and polyoxyethylene hydrogenated castor oil 60); or polyoxyethylene polyoxypropylene glycols (e.g., polyoxyethylene (42) polyoxypropylene (67) glycol, polyoxyethylene (54) polyoxypropylene (39) glycol, polyoxyethylene (105) polyoxypropylene (5) glycol, polyoxyethylene (124) polyoxypropylene (39) glycol, polyoxyethylene (160) polyoxypropylene (30) glycol, polyoxyethylene (196) polyoxypropylene (67) glycol, and polyoxyethylene (200) polyoxypropylene (70) glycol).

[Claim 7]

The use, the combination drug, the vaccine formulation, or the kit according to any one of claims 1 to 5~~The method according to claim 1 or the combination drug according to claim 2~~, wherein the hydrophilic surfactant is polysorbate 20, polysorbate 40, or polysorbate 80.

[Claim 8]

The use, the combination drug, the vaccine formulation, or the kit according to any one of claims 1 to 7~~The method according to claim 1 or the combination drug according to claim 2~~, wherein the lipophilic surfactant is sorbitan fatty acid esters (e.g., sorbitan fatty acid ester, sorbitan monolaurate, sorbitan monopalmitate, sorbitan monostearate, sorbitan tristearate, sorbitan monooleate, sorbitan sesquioleate, sorbitan trioleate, and medium-chain triglyceride); glycerin fatty acid esters (e.g., glycerin fatty acid ester, glyceryl monostearate, glyceryl monomyristate, glyceryl monooleate, and glyceryl triisooctanoate); sucrose fatty acid esters (e.g., sucrose fatty acid ester, sucrose stearate, and sucrose palmitate); or propylene glycol fatty acid esters (e.g., propylene glycol fatty acid ester and propylene glycol monostearate).

[Claim 9]

The use, the combination drug, the vaccine formulation, or the kit according to any one

of claims 1 to 7~~The method according to claim 1 or the combination drug according to claim 2~~, wherein the lipophilic surfactant is sorbitan trioleate.

[Claim 10]

The use, the combination drug, the vaccine formulation, or the kit according to any one of claims 1 to 9~~The method according to claim 1 or the combination drug according to claim 2~~, wherein the pharmaceutical composition further comprises an antioxidant agent B selected from the group consisting of tocopherols (e.g., α-tocopherol, β-tocopherol, γ-tocopherol, and δ-tocopherol); tocopherol acetate; and butylhydroxyanisole.

[Claim 11]

The use, the combination drug, the vaccine formulation, or the kit according to any one of claims 1 to 9~~The method according to claim 1 or the combination drug according to claim 2~~, wherein the pharmaceutical composition further comprises an antioxidant B of α-tocopherol.

[Claim 12]

The use, the combination drug, the vaccine formulation, or the kit according to any one of claims 1 to 11~~The method according to claim 1 or the combination drug according to claim 2~~, wherein the antioxidant agent A is ascorbyl palmitate, potassium ascorbate, sodium ascorbate, or ascorbic acid.

[Claim 13]

The use, the combination drug, the vaccine formulation, or the kit according to any one of claims 1 to 11~~The method according to claim 1 or the combination drug according to claim 2~~, wherein the antioxidant agent A is sodium ascorbate or potassium ascorbate.

[Claim 14]

The use, the combination drug, the vaccine formulation, or the kit according to any one of claims 1 to 13~~The method according to claim 1 or the combination drug according to claim 2~~, wherein the excipient is non-reducing sugars (e.g., sucrose and trehalose) or sugar alcohols (e.g., sorbitol, erythritol, xylitol, maltitol, and lactitol).

[Claim 15]

The use, the combination drug, the vaccine formulation, or the kit according to any one of claims 1 to 13~~The method according to claim 1 or the combination drug according to claim 2~~, wherein the excipient is sucrose or trehalose.

[Claim 16]

The use, the combination drug, the vaccine formulation, or the kit according to any one of claims 5 to 15~~The method according to claim 1 or the combination drug according to claim 2~~, wherein the increased amount in the area percentage value of an impurity UK-1.02 after a lyophilized formulation of the pharmaceutical composition is stored for 6 months at 5°C is 5.0% or below.