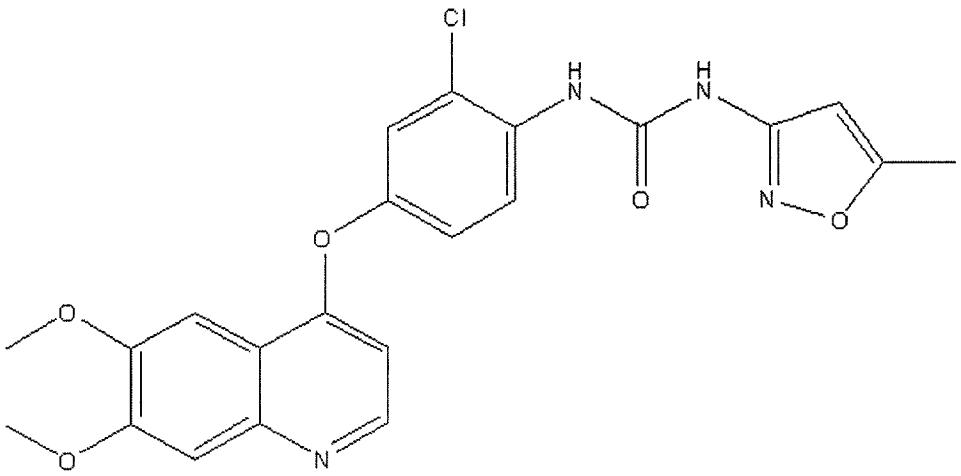
Claims

1. A therapeutic agent for an ophthalmic disease comprising a vascular endothelial growth factor (VEGF) receptor inhibitor in a nanoparticle form, wherein the VEGF receptor inhibitor is a compound represented by formula (II):



(II)

or a pharmaceutically acceptable salt thereof, or a hydrate or a solvate of the compound or the salt, and the therapeutic agent for the ophthalmic disease is eye drops.

2. The therapeutic agent for the ophthalmic disease according to claim 1, wherein the VEGF receptor inhibitor has a mean particle size of 40 nm or smaller.

3. The therapeutic agent for the ophthalmic disease according to claim 1 or 2, further comprising one or more

components selected from a thickening agent, a surfactant and a dispersion media.

4. The therapeutic agent for the ophthalmic disease according to claim 3, wherein the thickening agent is one or more substances selected from carboxyvinyl polymer, carboxymethylcellulose calcium, carboxymethylcellulose sodium, povidone, partially hydrolyzed polyvinyl alcohol, hydroxypropylcellulose, hydroxypropylmethylcellulose, hydroxypropylmethylcellulose phthalate, hydroxyethylcellulose, amorphous cellulose, methylcellulose, magnesium aluminum silicate and triethanolamine.

5. The therapeutic agent for the ophthalmic disease according to claim 3 or 4, wherein the surfactant is one or more substances selected from polyoxyethylene castor oil, polyoxyl 40 stearate, sucrose stearate, polyoxyethylene sorbitan monolaurate, polyoxyethylene sorbitan monostearate, polyoxyethylene sorbitan tristearate, polyoxyethylene sorbitan monooleate, polyoxyethylene sorbitan trioleate, sorbitan monolaurate, sodium lauryl sulfate, L-α-phosphatidylcholine (PC), 1,2-dipalmitoylphosphatidylcholine (DPPC), oleic acid, natural lecithin, synthetic lecithin, polyoxyethylene oleyl ether, polyoxyethylene lauryl ether, diethylene glycol dioleate, tetrahydrofurfuryl oleate, ethyl oleate,

isopropyl myristate, glyceryl monooleate, glyceryl monostearate, glyceryl monoricinoleate, cetyl alcohol, stearyl alcohol, polyethylene glycol, tyloxapol, octylphenol ethoxylate, alkyl glucoside and poloxamer.

6. The therapeutic agent for the ophthalmic disease according to any of claims 3 to 5, wherein the dispersion media is water, an alcohol, liquid paraffin, water containing a solute, an alcohol containing a solute or liquid paraffin containing a solute.

7. The therapeutic agent for the ophthalmic disease according to any of claims 3 to 5, wherein the dispersion media is water containing a solute.

8. The therapeutic agent for the ophthalmic disease according to claim 6 or 7, wherein the solute is one or more substances selected from sodium chloride, glucose, glycerol, mannitol, sodium dihydrogen phosphate, dibasic sodium phosphate hydrate, sodium bicarbonate, trishydroxymethylaminomethane, citric acid hydrate, boric acid, borax, and phosphoric acid.

9. The therapeutic agent for the ophthalmic disease according to any of claims 1 to 8, further comprising one or more components selected from a preservative and an inclusion substance.

10. The therapeutic agent for the ophthalmic disease according to claim 9, wherein the preservative is one or more substances selected from benzalkonium chloride, methyl parahydroxybenzoate, propyl parahydroxybenzoate, chlorobutanol, disodium edetate hydrate, chlorhexidine gluconate and sorbic acid.

11. The therapeutic agent for the ophthalmic disease according to claim 9 or 10, wherein the inclusion substance is one or more substances selected from α-cyclodextrin, β-cyclodextrin, 2-hydroxypropyl-β-cyclodextrin and γ-cyclodextrin.

12. The therapeutic agent for the ophthalmic disease according to any of claims 1 to 11, wherein the ophthalmic disease is a vascular endothelial growth factor (VEGF)-related disease.

13. The therapeutic agent for the ophthalmic disease according to claim 12, wherein the VEGF-related disease is wet age-related macular degeneration, dry age-related macular degeneration, choroidal neovascularization, myopic choroidal neovascularization, branch retinal vein occlusion, macular edema, macular edema following central retinal vein occlusion, diabetic macular edema, proliferative diabetic retinopathy, neovascular glaucoma, angioid streaks of the retina, retinopathy of

prematurity, Coats disease, branch retinal vein occlusion, central retinal vein occlusion, cystoid macular edema, vitreous hemorrhage caused by diabetic retinopathy, Eales disease, central serous chorioretinopathy, epiretinal membrane, uveitis, multifocal choroiditis, anterior ischemic optic neuropathy, corneal neovascularization, pterygium, intraocular melanoma, vasoproliferative tumor of the retina, radiation retinopathy, tuberous sclerosis, vasoproliferative tumor of the retina, conjunctival squamous cell carcinoma or ocular hypertension.

14. The therapeutic agent for the ophthalmic disease according to claim 12 or 13, wherein the VEGF-related disease is wet age-related macular degeneration, myopic choroidal neovascularization, branch retinal vein occlusion, central retinal vein occlusion, macular edema following central retinal vein occlusion, diabetic macular edema, proliferative diabetic retinopathy or neovascular glaucoma.

15. A method for producing a therapeutic agent for an ophthalmic disease according to any of claims 1 to 14, comprising the step of milling a vascular endothelial growth factor (VEGF) receptor inhibitor into a nanoparticle form.

16. The method according to claim 15, wherein the milling step further comprises adding one or more components selected from a thickening agent, a surfactant and a dispersion media, followed by the milling.

17. The method according to claim 15 or 16, wherein the milling step further comprises adding one or more components selected from a preservative and an inclusion substance, followed by the milling.

18. The method according to any of claims 15 to 17, wherein the milling is wet milling.

19. The method according to claim 18, wherein the wet milling comprises the step of adding a dispersion media to the vascular endothelial growth factor (VEGF) receptor inhibitor, followed by the milling.