Moreover, in case of a pharmaceutical combination according to embodiment 6) where the first and/or the second active ingredient is admistered according to a dose up-titration regimen (see for example the up-titration regimen disclosed in WO 2009/115954 for COMPOUND 1) the pharmaceutical compositions needed for the dose up-titration will contain the amounts of active ingredient required for the different steps of the dose up-titration regimen.

7) A further embodiment of the invention relates to a pharmaceutical combination according to any one of embodiments 1) to 5), wherein the first and the second active ingredient are comprised in separated pharmaceutical compositions.

In case the first and the second active ingredient are comprised in separated pharmaceutical compositions, they can be administered simultaneously, sequentially or separately; preferably the separated pharmaceutical compositions are administered simultaneously or sequentially, especially sequentially. In case the first active ingredient is for example administered once daily and the second active ingredient twice daily, then the separated pharmaceutical compositions are preferably administered one time per day simultaneously or sequentially, especially sequentially. If administered sequentially or separately, the separated pharmaceutical compositions may be administered in one or the other order. The number of administrations per day may be the same or different for the separated pharmaceutical compositions. For instance, one pharmaceutical composition may be administered twice daily and the other pharmaceutical composition may be administered once or twice daily. Preferably the pharmaceutical composition comprising COMPOUND 1 is administered once daily and the pharmaceutical composition comprising the second active ingredient is administered twice daily. Further, the separated pharmaceutical compositions may be administered by the same or different routes of administration, preferably by the same route of administration. Most preferably the separated pharmaceutical compositions are administered orally.

8) A further embodiment of the invention relates to a pharmaceutical combination according to any one of embodiments 1) to 7) for use as a medicament.

9) A further embodiment of the invention relates to the use of a pharmaceutical combination according to any one of embodiments 1) to 7) in the manufacture of a medicament for the prevention and/or treatment of a disease or disorder associated with an activated immune system.

10) A further embodiment of the invention relates to the use of a pharmaceutical combination according to any one of embodiments 1) to 7) in the manufacture of a medicament for the prevention and/or treatment of a disease or disorder selected from the group consisting of rejection of transplanted organs such as kidney, liver, heart, lung, pancreas, cornea, and skin; graft-versus-host disease; autoimmune syndromes including rheumatoid arthritis, multiple sclerosis, inflammatory bowel diseases such as Crohn's disease and ulcerative colitis, psoriasis, psoriatic arthritis, thyroiditis such as Hashimoto's thyroiditis, and uveo-retinitis; atopic diseases such as rhinitis, conjunctivitis, and dermatitis; asthma; type I diabetes; post-infectious autoimmune diseases including rheumatic fever and post-infectious glomerulonephritis; solid cancers; and tumor metastasis.

11) A further embodiment of the invention relates to the use of a pharmaceutical combination according to any one of embodiments 1) to 7) in the manufacture of a medicament for the prevention and/or treatment of a disease or disorder selected from the group consisting of rejection of transplanted organs selected from kidney, liver, heart and lung; graft-versus-host disease; autoimmune syndromes selected from rheumatoid arthritis, multiple sclerosis, psoriasis, psoriatic arthritis, Crohn's disease, and Hashimoto's thyroiditis; and atopic dermatitis.

12) A preferred embodiment of the invention relates to the use of a pharmaceutical combination according to any one of embodiments 1) to 7) in the manufacture of a medicament for the prevention and/or treatment of graft-versus-host disease.

13) A most preferred embodiment of the invention relates to the use of a pharmaceutical combination according to any one of embodiments 1) to 7) in the manufacture of a medicament for the prevention and/or treatment of multiple sclerosis.

14) Another very preferred embodiment of the invention relates the use of a pharmaceutical combination according to any one of embodiments 1) to 7) in the manufacture of a medicament for the prevention and/or treatment of relapsing multiple sclerosis.

15) Another very preferred embodiment of the invention relates to the use of a pharmaceutical combination according to any one of embodiments 1) to 7) in the manufacture of a medicament for the prevention and/or treatment of relapsing-remitting multiple sclerosis.

The present invention also relates to a method for the prevention or treatment of a disease or disorder listed in any one of embodiments 9) to 15) comprising administering to a subject

(preferably a human subject) in need thereof a pharmaceutically active amount of a pharmaceutical combination according to any one of embodiments 1) to 7).

16) A further embodiment of the invention relates to a pharmaceutical composition containing, as active principle, (R)-5-[3-chloro-4-(2,3-dihydroxy-propoxy)-benz[Z]ylidene]-2-([Z]-propylimino)-3-o-tolyl-thiazolidin-4-one and at least one therapeutically inert excipient, wherein the pharmaceutical composition is to be administered in combination with a second pharmaceutical composition containing, as active principle, methyl fumarate, dimethyl fumarate, (N,N-diethylcarbamoyl)methyl methyl (2E)but-2-ene-1,4-dioate, or 2-(2,5-dioxopyrrolidin-1-yl)ethyl methyl (2E)but-2-ene-1,4-dioate, or a pharmaceutically acceptable salt thereof and at least one therapeutically inert excipient.

17) A further embodiment of the invention relates to a pharmaceutical composition containing, as active principle, (R)-5-[3-chloro-4-(2,3-dihydroxy-propoxy)-benz[Z]ylidene]-2-([Z]-propylimino)-3-o-tolyl-thiazolidin-4-one and at least one therapeutically inert excipient, wherein the pharmaceutical composition is to be administered in combination with a second pharmaceutical composition containing, as active principle, dimethyl fumarate and at least one therapeutically inert excipient.

18) A further embodiment of the invention relates to a pharmaceutical composition according to embodiment 16) or 17) for use as a medicament.

19) A further embodiment of the invention relates to the use of a pharmaceutical composition according to embodiment 16) or 17) in the manufacture of a medicament for the prevention and/or treatment of a disease or disorder listed in any one of embodiments 9) to 15).

20) A further embodiment of the invention relates to a pharmaceutical composition containing, as active principle, methyl fumarate, dimethyl fumarate, (N,N-diethylcarbamoyl)methyl methyl (2E)but-2-ene-1,4-dioate, or 2-(2,5-dioxopyrrolidin-1-yl)ethyl methyl (2E)but-2-ene-1,4-dioate, or a pharmaceutically acceptable salt thereof, and at least one therapeutically inert excipient, wherein the pharmaceutical composition is to be administered in combination with a second pharmaceutical composition containing, as active principle, (R)-5-[3-chloro-4-(2,3-dihydroxy-propoxy)-benz[Z]ylidene]-2-([Z]-propylimino)-3-o-tolyl-thiazolidin-4-one and at least one therapeutically inert excipient.

21) A further embodiment of the invention relates to a pharmaceutical composition containing, as active principle, dimethyl fumarate and at least one therapeutically inert excipient, wherein the pharmaceutical composition is to be administered in combination with a second pharmaceutical composition containing, as active principle, (R)-5-[3-chloro-4-(2,3-dihydroxy-propoxy)-benz[Z]ylidene]-2-([Z]-propylimino)-3-o-tolyl-thiazolidin-4-one and at least one therapeutically inert excipient.

22) A further embodiment of the invention relates to a pharmaceutical composition according to embodiment 20) or 21) for use as a medicament.

23) A further embodiment of the invention relates to the use of a pharmaceutical composition according to embodiment 20) or 21) in the manufacture of a medicament for the prevention and/or treatment of a disease or disorder listed in any one of embodiments 9) to 15).

24) A further embodiment of the invention relates to a kit of parts comprising a first pharmaceutical composition containing, as active principle, (R)-5-[3-chloro-4-(2,3-dihydroxy-propoxy)-benz[Z]ylidene]-2-([Z]-propylimino)-3-o-tolyl-thiazolidin-4-one and at least one therapeutically inert excipient; and a second pharmaceutical composition containing, as active principle, methyl fumarate, dimethyl fumarate, (N,N-diethylcarbamoyl)methyl methyl (2E)but-2-ene-1,4-dioate, or 2-(2,5-dioxopyrrolidin-1-yl)ethyl methyl (2E)but-2-ene-1,4-dioate, or a pharmaceutically acceptable salt thereof, and at least one therapeutically inert excipient.

25) A further embodiment of the invention relates to a kit of parts according to embodiment 24), wherein the second pharmaceutical composition contains, as active principle, dimethyl fumarate and at least one therapeutically inert excipient.

26) A further embodiment of the invention relates to a kit of parts according to embodiment 24) or 25) further comprising instructions for the simultaneous, sequential or separate administration of the pharmaceutical compositions.

27) A further embodiment of the invention relates to a kit of parts according to any one of embodiments 24) to 26) for use as a medicament.

Claims:

1. A pharmaceutical combination comprising a first active ingredient which is (R)-5-[3-chloro-4-(2,3-dihydroxy-propoxy)-benz[Z]ylidene]-2-([Z]-propylimino)-3-o-tolyl-thiazolidin-4-one or a pharmaceutically acceptable salt thereof and a second active ingredient which is selected from the group consisting of methyl fumarate, dimethyl fumarate, (N,N-diethylcarbamoyl)methyl methyl (2E)but-2-ene-1,4-dioate, and 2-(2,5-dioxopyrrolidin-1-yl)ethyl methyl (2E)but-2-ene-1,4-dioate, or a pharmaceutically acceptable salt thereof.

2. A pharmaceutical combination according to claim 1, wherein the first active ingredient is (R)-5-[3-chloro-4-(2,3-dihydroxy-propoxy)-benz[Z]ylidene]-2-([Z]-propylimino)-3-o-tolyl-thiazolidin-4-one and the second active ingredient is methyl fumarate or a pharmaceutically acceptable salt thereof.

3. A pharmaceutical combination according to claim 1, wherein the first active ingredient is (R)-5-[3-chloro-4-(2,3-dihydroxy-propoxy)-benz[Z]ylidene]-2-([Z]-propylimino)-3-o-tolyl-thiazolidin-4-one and the second active ingredient is dimethyl fumarate.

4. A pharmaceutical combination according to claim 1, wherein the first active ingredient is (R)-5-[3-chloro-4-(2,3-dihydroxy-propoxy)-benz[Z]ylidene]-2-([Z]-propylimino)-3-o-tolyl-thiazolidin-4-one and the second active ingredient is (N,N-diethylcarbamoyl)methyl methyl (2E)but-2-ene-1,4-dioate.

5. A pharmaceutical combination according to claim 1, wherein the first active ingredient is (R)-5-[3-chloro-4-(2,3-dihydroxy-propoxy)-benz[Z]ylidene]-2-([Z]-propylimino)-3-o-tolyl-thiazolidin-4-one and the second active ingredient is 2-(2,5-dioxopyrrolidin-1-yl)ethyl methyl (2E)but-2-ene-1,4-dioate.

6. A pharmaceutical combination according to any one of claims 1 to 5, wherein the first and the second active ingredient are comprised in a single pharmaceutical composition.

7. A pharmaceutical combination according to any one of claims 1 to 5, wherein the first and the second active ingredient are comprised in separated pharmaceutical compositions.

8. A pharmaceutical combination according to any one of claims 1 to 7 for use as a medicament.

9. Use of a pharmaceutical combination according to any one of claims 1 to 7 in the manufacture of a medicament for the prevention and/or treatment of a disease or disorder associated with an activated immune system.

10. Use of a pharmaceutical combination according to any one of claims 1 to 7 in the manufacture of a medicament for the prevention and/or treatment of a disease or disorder selected from the group consisting of rejection of transplanted organs such as kidney, liver, heart, lung, pancreas, cornea, and skin; graft-versus-host disease; autoimmune syndromes including rheumatoid arthritis, multiple sclerosis, inflammatory bowel diseases such as Crohn's disease and ulcerative colitis, psoriasis, psoriatic arthritis, thyroiditis such as Hashimoto's thyroiditis, and uveo-retinitis; atopic diseases such as rhinitis, conjunctivitis, and dermatitis; asthma; type I diabetes; post-infectious autoimmune diseases including rheumatic fever and post-infectious glomerulonephritis; solid cancers; and tumor metastasis.

11. Use of a pharmaceutical combination according to any one of claims 1 to 7 in the manufacture of a medicament for the prevention and/or treatment of a disease or disorder selected from the group consisting of rejection of transplanted organs selected from kidney, liver, heart and lung; graft-versus-host disease; autoimmune syndromes selected from rheumatoid arthritis, multiple sclerosis, psoriasis, psoriatic arthritis, Crohn's disease, and Hashimoto's thyroiditis; and atopic dermatitis.

12. Use of a pharmaceutical combination according to any one of claims 1 to 7 in the manufacture of a medicament for the prevention and/or treatment of graft-versus-host disease.

13. Use of a pharmaceutical combination according to any one of claims 1 to 7 in the manufacture of a medicament for the prevention and/or treatment of multiple sclerosis.

14. Use of a pharmaceutical combination according to any one of claims 1 to 7 in the manufacture of a medicament for the prevention and/or treatment of relapsing multiple sclerosis.

15. Use of a pharmaceutical combination according to any one of claims 1 to 7 in the manufacture of a medicament for the prevention and/or treatment of relapsing-remitting multiple sclerosis.

16. A pharmaceutical composition containing, as active principle, (R)-5-[3-chloro-4-(2,3-dihydroxy-propoxy)-benz[Z]ylidene]-2-([Z]-propylimino)-3-o-tolyl-thiazolidin-4-one and at

least one therapeutically inert excipient, wherein the pharmaceutical composition is to be administered in combination with a second pharmaceutical composition containing, as active principle, methyl fumarate, dimethyl fumarate, (N,N-diethylcarbamoyl)methyl methyl (2E)but-2-ene-1,4-dioate, or 2-(2,5-dioxopyrrolidin-1-yl)ethyl methyl (2E)but-2-ene-1,4-dioate, or a pharmaceutically acceptable salt thereof and at least one therapeutically inert excipient.

17. A pharmaceutical composition containing, as active principle, (R)-5-[3-chloro-4-(2,3-dihydroxy-propoxy)-benz[Z]ylidene]-2-([Z]-propylimino)-3-o-tolyl-thiazolidin-4-one and at least one therapeutically inert excipient, wherein the pharmaceutical composition is to be administered in combination with a second pharmaceutical composition containing, as active principle, dimethyl fumarate and at least one therapeutically inert excipient.

18. A pharmaceutical composition according to claim 16 or 17 for use as a medicament.

19. Use of a pharmaceutical composition according to claim 16 or 17 in the manufacture of a medicament for the prevention and/or treatment of a disease or disorder listed in any one of claims 9 to 15.

20. A pharmaceutical composition containing, as active principle, methyl fumarate, dimethyl fumarate, (N,N-diethylcarbamoyl)methyl methyl (2E)but-2-ene-1,4-dioate, or 2-(2,5-dioxopyrrolidin-1-yl)ethyl methyl (2E)but-2-ene-1,4-dioate, or a pharmaceutically acceptable salt thereof, and at least one therapeutically inert excipient, wherein the pharmaceutical composition is to be administered in combination with a second pharmaceutical composition containing, as active principle, (R)-5-[3-chloro-4-(2,3-dihydroxy-propoxy)-benz[Z]ylidene]-2-([Z]-propylimino)-3-o-tolyl-thiazolidin-4-one and at least one therapeutically inert excipient.

21. A pharmaceutical composition containing, as active principle, dimethyl fumarate and at least one therapeutically inert excipient, wherein the pharmaceutical composition is to be administered in combination with a second pharmaceutical composition containing, as active principle, (R)-5-[3-chloro-4-(2,3-dihydroxy-propoxy)-benz[Z]ylidene]-2-([Z]-propylimino)-3-o-tolyl-thiazolidin-4-one and at least one therapeutically inert excipient.

22. A pharmaceutical composition according to claim 20 or 21 for use as a medicament.

23. Use of a pharmaceutical composition according to claim 20 or 21 in the manufacture of a medicament for the prevention and/or treatment of a disease or disorder listed in any one of claims 9 to 15.

24. A kit of parts comprising a first pharmaceutical composition containing, as active principle, (R)-5-[3-chloro-4-(2,3-dihydroxy-propoxy)-benz[Z]ylidene]-2-([Z]-propylimino)-3-o-tolyl-thiazolidin-4-one and at least one therapeutically inert excipient; and a second pharmaceutical composition containing, as active principle, methyl fumarate, dimethyl fumarate, (N,N-diethylcarbamoyl)methyl methyl (2E)but-2-ene-1,4-dioate, or 2-(2,5-dioxopyrrolidin-1-yl)ethyl methyl (2E)but-2-ene-1,4-dioate, or a pharmaceutically acceptable salt thereof, and at least one therapeutically inert excipient.

25. A kit of parts according to claim 24, wherein the second pharmaceutical composition contains, as active principle, dimethyl fumarate and at least one therapeutically inert excipient.

26. A kit of parts according to claim 24 or 25 further comprising instructions for the simultaneous, sequential or separate administration of the pharmaceutical compositions.

27. A kit of parts according to any one of claims 24 to 26 for use as a medicament.

28. A kit of parts according to any one of claims 24 to 26 for use in the prevention and/or treatment of a disease or disorder listed in any one of claims 9 to 15.

29. Use of (R)-5-[3-chloro-4-(2,3-dihydroxy-propoxy)-benz[Z]ylidene]-2-([Z]-propylimino)-3-o-tolyl-thiazolidin-4-one and a second active ingredient which is selected from the group consisting of methyl fumarate, dimethyl fumarate, (N,N-diethylcarbamoyl)methyl methyl (2E)but-2-ene-1,4-dioate, and 2-(2,5-dioxopyrrolidin-1-yl)ethyl methyl (2E)but-2-ene-1,4-dioate, or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for use in the prevention and/or treatment of a disease or disorder listed in any one of claims 9 to 15.

30. The use according to claim 29, wherein the second active ingredient is dimethyl fumarate.

31. Use of (R)-5-[3-chloro-4-(2,3-dihydroxy-propoxy)-benz[Z]ylidene]-2-([Z]-propylimino)-3-o-tolyl-thiazolidin-4-one for the manufacture of a medicament for use, in combination with a

second medicament comprising methyl fumarate, dimethyl fumarate, (N,N-diethylcarbamoyl)methyl methyl (2E)but-2-ene-1,4-dioate, or 2-(2,5-dioxopyrrolidin-1-yl)ethyl methyl (2E)but-2-ene-1,4-dioate, or a pharmaceutically acceptable salt thereof, in the prevention and/or treatment of a disease or disorder listed in any one of claims 9 to 15.

32. The use according to claim 31, wherein the second medicament comprises dimethyl fumarate.

33. Use of methyl fumarate, dimethyl fumarate, (N,N-diethylcarbamoyl)methyl methyl (2E)but-2-ene-1,4-dioate, or 2-(2,5-dioxopyrrolidin-1-yl)ethyl methyl (2E)but-2-ene-1,4-dioate, or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for use, in combination with a second medicament comprising (R)-5-[3-chloro-4-(2,3-dihydroxy-propoxy)-benz[Z]ylidene]-2-([Z]-propylimino)-3-o-tolyl-thiazolidin-4-one, in the prevention and/or treatment of a disease or disorder listed in any one of claims 9 to 15.

34. Use of dimethyl fumarate for the manufacture of a medicament for use, in combination with a second medicament comprising (R)-5-[3-chloro-4-(2,3-dihydroxy-propoxy)-benz[Z]ylidene]-2-([Z]-propylimino)-3-o-tolyl-thiazolidin-4-one, in the prevention and/or treatment of a disease or disorder listed in any one of claims 9 to 15.