

ANNEX I

1. A combination comprising (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol or a physiologically functional derivative thereof, with the exception of the succinate salt thereof and of solvates of that succinate salt, and (2R,cis)-4-amino-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one or a physiologically functional derivative thereof.
2. A combination as claimed in claim 1 wherein the physiologically functional derivative of (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol or (2R,cis)-4-amino-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one is a physiologically acceptable salt, ether, ester, salt of such ester, or solvate thereof.
3. A combination according to claim 1 comprising (1 S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol or a physiologically functional derivative thereof, zidovudine or a physiologically functional derivative thereof, and (2R,cis)-4-amino-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one or a physiologically functional derivative thereof.
4. A combination according to claim 3 wherein the physiologically functional derivative of (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol, zidovudine, or (2R,cis)-4-amino-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one is a physiologically acceptable salt, ether, ester, salt of such ester, or solvate thereof.
5. A combination according to claim 3 or 4 wherein the ratio of (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol:zidovudine:(2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one is in the ratio of 1 to 20: 1 to 20: 1 to 10 by weight.
6. A combination according to any claim from 1 to 5 for use in medical therapy.
7. A pharmaceutical formulation comprising a combination according to claims 1 to 5 in association with one or more pharmaceutically acceptable carriers therefor.
8. A formulation according to claim 7 in unit dosage form.
9. Use of (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol and (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one in the manufacture of a medicament for the treatment and/or prophylaxis of an HIV infection.
10. Use of (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol, zidovudine and (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one in the manufacture of a medicament for the treatment and/or prophylaxis of an HIV infection.
11. Use as claimed in claim 9 or 10 for the treatment and for prophylaxis of an HIV infection resistant to nucleoside or non-nucleoside inhibitors
12. Use as claimed in claim 9 or 10 in the treatment of AIDS.

13. Use as claimed in claim 9 or 10 in the treatment of AIDS related conditions or AIDS dementia complex.
14. A product comprising (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol, and (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one as a combined preparation for simultaneous, separate or sequential use in the treatment and/or prophylaxis of an HIV infection.
15. A product comprising (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol, zidovudine and (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one as a combined preparation for simultaneous, separate or sequential use in the treatment and/or prophylaxis of an HIV infection.
16. A product as claimed in claim 15 wherein the components are present in the ratio of 1 to 20 : 1 to 20 : 1 to 10 by weight respectively.
17. A product comprising (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol as a preparation for simultaneous, separate or sequential use together with (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one in the treatment and/or prophylaxis of an HIV infection.
18. A product comprising (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one as a preparation for simultaneous, separate or sequential use together with (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol in the treatment and/or prophylaxis of an HIV infection.
19. A product comprising (1 S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol as a preparation for simultaneous, separate or sequential use together with zidovudine and (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one in the treatment and/or prophylaxis of an HIV infection.
20. A product comprising zidovudine as a preparation for simultaneous, separate or sequential use together with (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol and (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one in the treatment and/or prophylaxis of an HIV infection.
21. A product comprising (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one as a preparation for simultaneous, separate or sequential use together with zidovudine and (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol in the treatment and/or prophylaxis of an HIV infection.
22. A product comprising zidovudine and (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one as a preparation for simultaneous, separate or sequential use together with (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol in the treatment and/or prophylaxis of an HIV infection.

ANNEX II

1. A combination of two active ingredients consisting of comprising (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol or a physiologically functional derivative thereof and (2R,cis)-4-amino-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one or a physiologically functional derivative thereof.
2. A combination as claimed in claim 1 wherein the physiologically functional derivative of (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol or (2R,cis)-4-amino-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one is a physiologically acceptable salt, ether, ester, salt of such ester, or solvate thereof.
3. A combination according to ~~claim 1~~ comprising (1 S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cy-clopentene-1-methanol or a physiologically functional derivative thereof, zidovudine or a physiologically functional derivative thereof, and (2R,cis)-4-amino-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one or a physiologically functional derivative thereof.
4. A combination according to claim 3 wherein the physiologically functional derivative of (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol, zidovudine, or (2R,cis)-4-amino-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one is a physiologically acceptable salt, ether, ester, salt of such ester, or solvate thereof.
5. A combination according to claim 3 or 4 wherein the ratio of (1S,4R)-cis-4-[2-amino-6(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol:zidovudine: (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-y1)-(1H)-pyrimidin-2-one is in the ratio of 1 to 20: 1 to 20: 1 to 10 by weight.
6. A combination according to any claim from 1 to 5 for use in medical therapy.
7. A pharmaceutical formulation ~~comprising~~ consisting of a combination according to claims 1 to 5 in association with one or more pharmaceutically acceptable carriers therefor.
8. A formulation according to claim 7 in unit dosage form.
9. Use of (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol and (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one a combination according to claims 1 or 2 in the manufacture of a medicament formulation according to claims 7 or 8 for the treatment and/or prophylaxis of an HIV infection.
10. Use of (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol, zidovudine and (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one in the manufacture of a medicament for the treatment and/or prophylaxis of an HIV infection.
11. Use as claimed in claim 9 or 10 for the treatment and for prophylaxis of an HIV infection resistant to nucleoside or non-nucleoside inhibitors
12. Use as claimed in claim 9 or 10 in the treatment of AIDS.

13. Use as claimed in claim 9 or 10 in the treatment of AIDS related conditions or AIDS dementia complex.
14. A combination according to claim 1 product comprising (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol, and (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one as a combined preparation for simultaneous, separate or sequential use in the treatment and/or prophylaxis of an HIV infection.
15. A product comprising (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol, zidovudine and (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one as a combined preparation for simultaneous, separate or sequential use in the treatment and/or prophylaxis of an HIV infection.
16. A product as claimed in claim 15 wherein the components are present in the ratio of 1 to 20 : 1 to 20 : 1 to 10 by weight respectively.
17. A product ~~comprising~~ consisting of (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol as a preparation for simultaneous, separate or sequential use together with (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one in the treatment and/or prophylaxis of an HIV infection.
18. A product ~~comprising~~ consisting of (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one as a preparation for simultaneous, separate or sequential use together with (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol in the treatment and/or prophylaxis of an HIV infection.
19. A product comprising (1 S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol as a preparation for simultaneous, separate or sequential use together with zidovudine and (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one in the treatment and/or prophylaxis of an HIV infection.
20. A product comprising zidovudine as a preparation for simultaneous, separate or sequential use together with (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol and (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one in the treatment and/or prophylaxis of an HIV infection.
21. A product comprising (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one as a preparation for simultaneous, separate or sequential use together with zidovudine and (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol in the treatment and/or prophylaxis of an HIV infection.
22. A product comprising zidovudine and (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one as a preparation for simultaneous, separate or sequential use together with (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol in the treatment and/or prophylaxis of an HIV infection.

ANNEX III

1. A combination of two active ingredients consisting of comprising (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol or a physiologically functional derivative thereof and (2R,cis)-4-amino-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one or a physiologically functional derivative thereof.
2. A combination as claimed in claim 1 wherein the physiologically functional derivative of (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol or (2R,cis)-4-amino-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one is a physiologically acceptable salt, ether, ester, salt of such ester, or solvate thereof.
3. ~~A combination according to claim 1 comprising (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol or a physiologically functional derivative thereof, zidovudine or a physiologically functional derivative thereof, and (2R,cis)-4-amino-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one or a physiologically functional derivative thereof.~~
4. ~~A combination according to claim 3 wherein the physiologically functional derivative of (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol, zidovudine, or (2R,cis)-4-amino-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one is a physiologically acceptable salt, ether, ester, salt of such ester, or solvate thereof.~~
5. ~~A combination according to claim 3 or 4 wherein the ratio of (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol:zidovudine:(2R,cis)-4-amino-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one is in the ratio of 1 to 20: 1 to 20: 1 to 10 by weight.~~
- 6.3. ~~A combination according to any claims from 1 or 2 to 5 for use in medical therapy.~~
- 7.4. ~~A pharmaceutical formulation comprising consisting of a combination according to claims 1 to 5 or 2 in association with one or more pharmaceutically acceptable carriers therefor.~~
- 8.5. ~~A formulation according to claim 47 in unit dosage form.~~
- 9.6. ~~Use of (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol and (2R,cis)-4-amino-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one a combination according to claims 1 or 2 in the manufacture of a medicament formulation according to claims 4 or 5 for the treatment and/or prophylaxis of an HIV infection.~~
10. ~~Use of (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol, zidovudine and (2R,cis)-4-amino-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one in the manufacture of a medicament for the treatment and/or prophylaxis of an HIV infection.~~
- 11.7. ~~Use as claimed in claim 9 or 106 for the treatment and for prophylaxis of an HIV infection resistant to nucleoside or non-nucleoside inhibitors~~
- 12.8. ~~Use as claimed in claim 9 or 106 in the treatment of AIDS.~~

- 13.9. Use as claimed in claim 9 or 106 in the treatment of AIDS related conditions or AIDS dementia complex.
- 14.10. A combination according to claim 1 product comprising (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol, and (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one as a combined preparation for simultaneous, separate or sequential use in the treatment and/or prophylaxis of an HIV infection.
15. A product comprising (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol, zidovudine and (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one as a combined preparation for simultaneous, separate or sequential use in the treatment and/or prophylaxis of an HIV infection.
16. A product as claimed in claim 15 wherein the components are present in the ratio of 1 to 20 : 1 to 20 : 1 to 10 by weight respectively.
17. A product comprising (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol as a preparation for simultaneous, separate or sequential use together with (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one in the treatment and/or prophylaxis of an HIV infection.
18. A product comprising (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one as a preparation for simultaneous, separate or sequential use together with (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol in the treatment and/or prophylaxis of an HIV infection.
19. A product comprising (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol as a preparation for simultaneous, separate or sequential use together with zidovudine and (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one in the treatment and/or prophylaxis of an HIV infection.
20. A product comprising zidovudine as a preparation for simultaneous, separate or sequential use together with (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol and (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one in the treatment and/or prophylaxis of an HIV infection.
21. A product comprising (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one as a preparation for simultaneous, separate or sequential use together with zidovudine and (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol in the treatment and/or prophylaxis of an HIV infection.
22. A product comprising zidovudine and (2R,cis)-4-amino-1-(2-hydroxymethyl-1,3-oxathiolan-5-yl)-(1H)-pyrimidin-2-one as a preparation for simultaneous, separate or sequential use together with (1S,4R)-cis-4-[2-amino-6-(cyclopropylamino)-9H-purin-9-yl]-2-cyclopentene-1-methanol in the treatment and/or prophylaxis of an HIV infection.

Claim No: HP-2015-00024

IN THE HIGH COURT OF JUSTICE
CHANCERY DIVISION
PATENTS COURT

BETWEEN:

GENERICS [U.K.] LIMITED
(trading as MYLAN)

Claimant

-and-

VIIV HEALTHCARE UK LIMITED

Defendant

STATEMENT OF REASONS

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