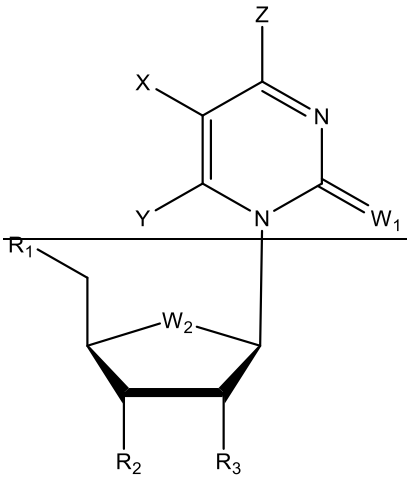
CLAIMS

1. A compound of Formula (I):



Formula (I)

or a stereoisomer, solvate, tautomer or pharmaceutically acceptable salt thereof for use in therapy;

wherein:

X is a group containing from 1 to 20 non-hydrogen atoms, which contains at least one functional group selected from an aldehyde, an alcohol, a protected alcohol, an ether, an ester and a carboxylic acid, with the proviso that X is not -COOH;

W_1 and W_2 are each independently O, S or NH;

Y is H or a group containing from 1 to 15 non-hydrogen atoms;

Z is -OPG, $-OR_z$ or $-N(R_xR_y)$, where R_x, R_y and R_z are independently H or a group containing from 1 to 10 non-hydrogen atoms;

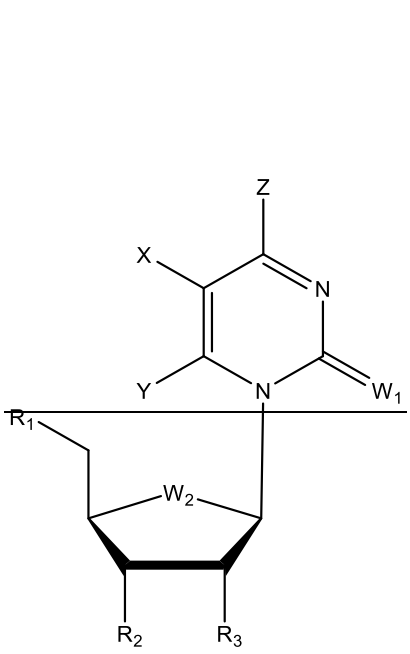
~~R_1 is H or a group containing from 1 to 15 non-hydrogen atoms;~~

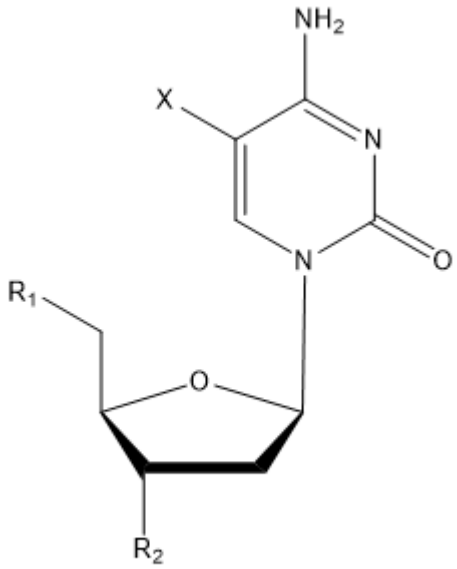
~~R_2 is H, -OH, -OPG, -F, -Cl, -Br, -I, or -N_3; and~~

~~R_3 is H, -F, -Cl, -Br, -I, or -N_3;~~

~~where PG is an alcohol protecting group, such as acetyl (Ac), benzyl (Bn) or benzoyl (Bz).~~

~~2.~~1. A compound of Formula (IIa):





Formula (IIa)

~~Formula (I)~~

or a stereoisomer, solvate, tautomer or pharmaceutically acceptable salt thereof for use in the treatment or prevention of cancer of the central nervous system;

wherein:

X is -$(CH_2)_n$-X', wherein n is from 0 to 6 and X' is -CHO, -OH, -OR or -OC(=O)R, where R is methyla group containing from 1 to 20 non-hydrogen atoms, which contains at least one functional group selected from an aldehyde, an alcohol, a protected alcohol, an ether, an ester and a carboxylic acid, with the proviso that X is not -COOH;

W_1 and W_2 are each independently O, S or NH;

Y is H or a group containing from 1 to 15 non-hydrogen atoms;

Z is -OPG, $-OR_z$ or $-N(R_xR_y)$, where R_x, R_y and R_z are independently H or a group containing from 1 to 10 non-hydrogen atoms;

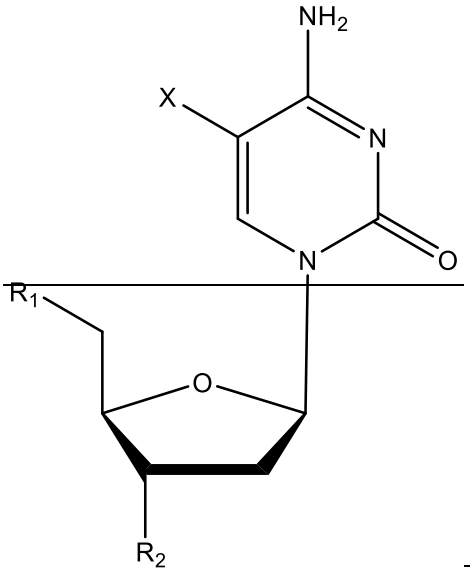
R_1 is -OH or $-O(P(=O)(OH)O)_nH$ where n is from 1 to 3H or a group containing from 1 to 15 non-hydrogen atoms; and

R_2 is H, -OH, -OPG, -F, -Cl, -Br, -I, or $-N_3$; and

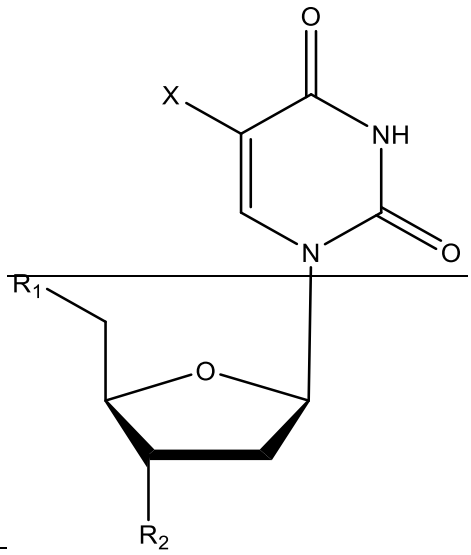
R_3 is H, -F, -Cl, -Br, -I, or $-N_3$;

where PG is an alcohol protecting group, such as acetyl (Ac), benzyl (Bn) or benzoyl (Bz).

3. The compound for use of claim 1 or claim 2, wherein the compound is a compound of Formula (IIa) or Formula (IIb), preferably Formula (IIa), or a stereoisomer, solvate, tautomer or pharmaceutically acceptable salt thereof:



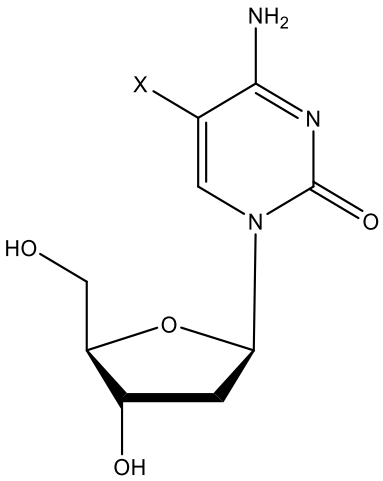
Formula (IIa)



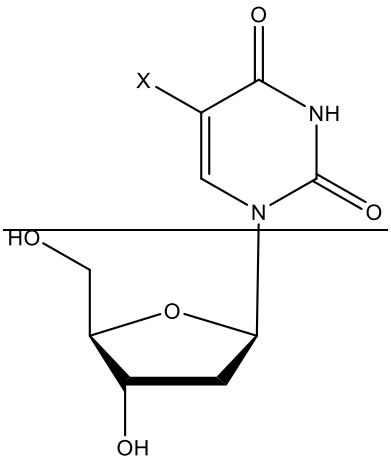
Formula (IIb)

wherein X, R_1 and R_2 are as defined in claim 1 or claim 2.

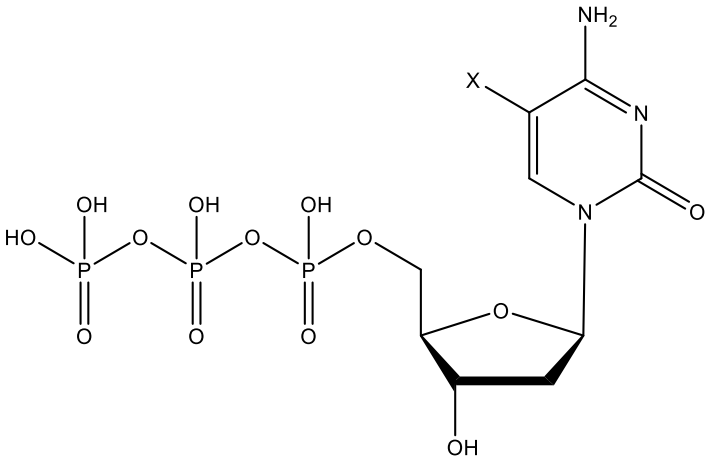
4.2. The compound for use of any one of claims 1 to 3, wherein the compound is a compound of Formula (IIIa), (IIIb), (IIIc) or (IIId), preferably Formula (IIIa) or (IIIc), or a stereoisomer, solvate, tautomer or pharmaceutically acceptable salt thereof:



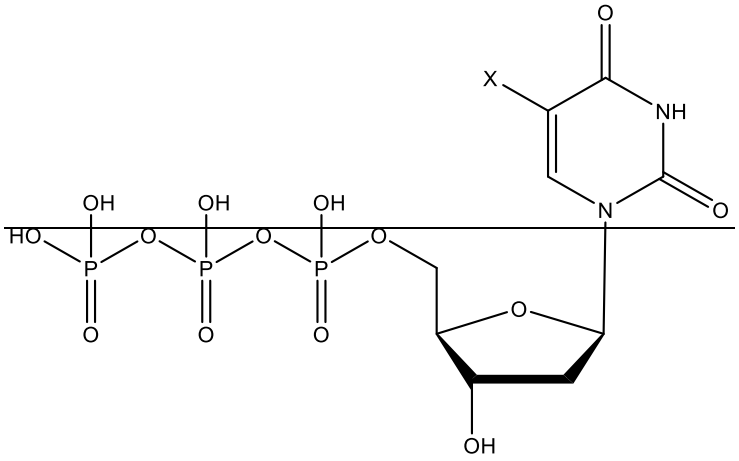
Formula (IIIa)



Formula (IIIb)



Formula (IIIc)



~~Formula (IIId)~~

wherein X is as defined in claim 1~~ or claim 2~~.

~~5. The compound for use of any one of claims 1 to 4, wherein X is -$(CH_2)_n$-X', wherein n is from 0 to 6 and X' is -CHO, -OH, -OR or -OC(=O)R, where R is methyl.~~

~~6. The compound for use of any one of claims 1 to 5, wherein X is a group containing from 2 to 20 non-hydrogen atoms.~~

~~7. The compound for use of any one of claims 1 to 5, wherein X is not -COOH or -OH.~~

~~8.~~3. The compound for use of ~~any one of~~ claim~~s~~ 1 ~~to~~ or claim 2~~7~~, wherein X is

~~a)~~ -CHO, ~~or~~ -CH_2OH~~; or~~,

~~b)~~ -CH_2OCH_3~~-~~, or -$CH_2OC(=O)CH_3$.

~~9.~~4. The compound for use of any one of claims 1 to ~~8~~3, wherein X is -CHO or -CH_2OH.

~~10.~~5. The compound for use of any one of claims 1 to ~~9~~4, wherein X is CH_2OH.

~~11. The compound for use of any one of claims 1 to 10, wherein Z is is -NH_2.~~

~~12.~~6. The compound for use of any one of claims 1 to ~~8~~5, wherein the compound is 5-formyl-2’-deoxycytidine, 5-hydroxymethyl-2’-deoxycytidine, ~~5-methoxymethyl-2’-deoxyuridine, 5-acetoxymethyl-2’-deoxyuridine,~~ 5-formyl-2'-deoxycytidine-5'-triphosphate or 5-hydroxymethyl-2'-deoxycytidine-5'-triphosphate, or a stereoisomer, solvate, tautomer or pharmaceutically acceptable salt thereof.

~~13.~~7. The compound for use of claim ~~12~~6, wherein the compound is 5-formyl-2’-deoxycytidine or 5-hydroxymethyl-2’-deoxycytidine, or a stereoisomer, solvate, tautomer or pharmaceutically acceptable salt thereof.~~,~~

~~14.~~8. The compound for use of claim ~~13~~7, wherein the compound is 5-hydroxymethyl-2’-deoxycytidine or a stereoisomer, solvate, tautomer or pharmaceutically acceptable salt thereof.

~~15. The compound for use of any one of claims 2 to 14, wherein the cancer is a cancer of a tissue derived from the ectoderm, paraxial mesoderm, or lateral plate mesoderm, preferably from the ectoderm.~~

~~16.~~9. The compound for use of any one of claims ~~2~~ 1 to ~~15~~8, wherein the cancer is ~~a cancer of the central nervous system, preferably~~ a brain cancer.

~~17.~~10. The compound for use of any one of claims ~~2~~1 to ~~16~~9, wherein the cancer is glioma~~, preferably glioblastoma~~.

11. The compound for use of claim 10, wherein the cancer is glioblastoma.

~~18. The compound for use of any one of claims 2 to 17, wherein the cancer is a cancer in which CDA is not over-expressed, preferably wherein the cancer expresses CDA at a level of ≤140 transcripts per million (TPM).~~

~~19. The compound for use of any one of claims 2 to 18, wherein the CDA expression level in the cancer is not greater than 90% of the CDA expression level in a reference cancer cell line as determined using the same method under the same conditions, wherein said reference cancer cell line is MDA-MB-231.~~

~~20~~12. The compound for use of any one of claims ~~2~~ 1 to ~~19~~11, wherein the cancer is resistant to treatment with gemcitabine, cytarabine, temozolomide or 5-fluorouracil.

~~21~~13. The compound for use of any one of claims ~~2~~ 1 to ~~20~~12, wherein said treatment comprises administering said compound at a dose between 10 mg/kg and 405 mg/kg.

~~22~~14. The compound for use of any one of claims ~~2~~ 1 to ~~21~~13, wherein said treatment further comprises the administration of a further anticancer agent.

~~23~~15. A kit comprising a compound as defined in any one of claims 1 to ~~14~~ 8 and a further anticancer agent for using in the treatment or prevention of a cancer of the central nervous system.

~~24~~16. A pharmaceutical composition comprising a compound as defined in any one of claims 1 to ~~14~~ 8 and optionally a further anticancer agent, together with one or more pharmaceutically acceptable excipients.

~~25~~17. The composition for use of claim ~~22~~14 or~~,~~ the kit of claim ~~23~~ 15, or the pharmaceutical ~~product~~ composition of claim ~~24~~16, wherein the further anticancer agent is selected from the group consisting of gemcitabine, cytarabine, Temozolomide, 5-fluorouracil and gliadel (RTM).

~~26. A method of treating or preventing cancer in a subject which method comprises administering a compound as defined in any one of claims 1 to 14 to said subject, wherein said cancer is as defined in any one of claims 2 or 15 to 17, and wherein said treatment is as defined in any one of claims 2, 21, 22 or 25.~~