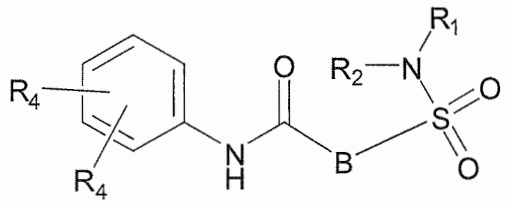
Each R_4 is independently selected from hydrogen, halogen, C_1-C_4alkyloxy, C_1-C_4alkyl, C_1-C_4alkenyl, OH, CN, CFH_2, CF_2H, CF_3 , HC≡C or a 3-5 membered saturated ring optionally containing one or more heteroatoms each independently selected from the group consisting of O and N, such C_1-C_4alkyl optionally substituted with OH;

R_5 represents C_1-C_6alkyl, CFH_2, CF_2H, CF_3, phenyl, pyridyl or a 3-7 membered saturated ring optionally containing one or more heteroatoms each independently selected from the group consisting of O, S and N, such 3-7 membered saturated ring optionally being substituted with one or more substituents each independently selected from the group consisting of hydrogen, halogen, C_1-C_4alkyloxy, C_1-C_4alkyloxycarbonyl, oxo, C(=O)-C_1-C_3alkyl, C_1-C_4alkyl, OH, CN, CFH_2, CF_2H and CF_3;

or a pharmaceutically acceptable salt or a solvate thereof.

In one, there is provided a compound of Formula (Ia)



(Ia)

or a stereoisomer or tautomeric form thereof, wherein:

B represents a monocyclic 5 to 6 membered aromatic ring, ~~optionally~~ containing one or more heteroatoms each independently selected from the group consisting of O, S and N, such 5 to 6 membered aromatic ring optionally being substituted with one or more substituents each independently selected from the group consisting of hydrogen, halo, C_1-C_3alkyl, CN, CFH_2, CF_2H and CF_3;

R_1 represents hydrogen or C_1-C_3alkyl;

R_2 represents C_1-C_6alkyl, C_1-C_3alkyl-R_5, benzyl, C(=O)-R_5, CFH_2, CF_2H, CF_3 or a 3-7 membered saturated ring optionally containing one or more heteroatoms each independently selected from the group consisting of O, S and N, such 3-7 membered saturated ring or C_1-C_6alkyl optionally being substituted with one or more substituents each independently selected from the group consisting of hydrogen, halo, C_1-C_4alkyloxy, oxo, C(=O)-C_1-C_3alkyl, C_1-C_4alkyl, OH, CN, CFH_2, CF_2H and CF_3;

Or R_1 R_2 together with the Nitrogen to which they are attached form a 1,4-dioxa-8-azaspiro[4.5] moiety or a 5-7 membered saturated ring, optionally containing one or more additional heteroatoms each independently selected from the group consisting of O, S and N, such 5-7 membered saturated ring optionally being substituted with one or more substituents each independently selected from the group consisting of hydrogen, halo, C_1-C_4alkyloxy, oxo C(=O)-C_1-C_3alkyl, C_1-C_4alkyl, OH, CN, CFH_2, CF_2H and CF_3;

Each R_4 is independently selected from hydrogen, halo, C_1-C_4alkyloxy, C_1-C_4alkyl, OH, CN, CFH_2, CF_2H, CF_3 or a 3-5 membered saturated ring optionally containing one or more heteroatoms each independently selected from the group consisting of O and N;

R_5 represents C_1-C_6alkyl, CFH_2, CF_2H, CF_3 or a 3-7 membered saturated ring optionally containing one or more heteroatoms each independently selected from the group consisting of O, S and N, such 3-7 membered saturated ring optionally being substituted with one or more substituents each independently selected from the group consisting of hydrogen, halo, C_1-C_4alkyloxy, oxo, C(=O)-C_1-C_3alkyl, C_1-C_4alkyl, OH, CN, CFH_2, CF_2H and CF_3;

or a pharmaceutically acceptable salt or a solvate thereof

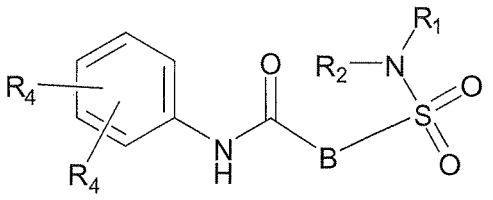
The disclosure further relates to a pharmaceutical composition comprising a compound of Formula (I), and a pharmaceutically acceptable carrier. In another aspect, there is provided a pharmaceutical composition comprising a compound of Formula (Ia), and a pharmaceutically acceptable carrier.

The disclosure also relates to the compounds of Formula (I) for use as a medicament, preferably for use in the prevention or treatment of an HBV infection in a mammal. In another aspect, there is provided a compound of Formula (Ia) for use in the prevention or treatment of an HBV infection in a mammal.

The disclosure also relates to a combination of a compound of Formula (I), and another HBV inhibitor. In another aspect, there is provided a product containing (a) a compound as defined herein, and (b) another HBV inhibitor, as a combined preparation for use simultaneously, separately or sequentially ~~use~~ in the treatment of HBV infections.

Claims

1. A compound of Formula (Ia)



(Ia)

or a stereoisomer or tautomeric form thereof, wherein:

B represents a monocyclic 5 to 6 membered aromatic ring, ~~optionally~~ containing one or more heteroatoms each independently selected from the group consisting of O, S and N, such 5 to 6 membered aromatic ring optionally being substituted with one or more substituents each independently selected from the group consisting of hydrogen, halo, C_1-C_3alkyl, CN, CFH_2, CF_2H and CF_3;

R_1 represents hydrogen or C_1-C_3alkyl;

R_2 represents C_1-C_6alkyl, C_1-C_3alkyl-R_5, benzyl, C(=O)-R_5, CFH_2, CF_2H, CF_3 or a 3-7 membered saturated ring optionally containing one or more heteroatoms each independently selected from the group consisting of O, S and N, such 3-7 membered saturated ring or C_1-C_6alkyl optionally being substituted with one or more substituents each independently selected from the group consisting of hydrogen, halo, C_1-C_4alkyloxy, oxo, C(=O)-C_1-C_3alkyl, C_1-C_4alkyl, OH, CN, CFH_2, CF_2H and CF_3;

Or R_1 R_2 together with the Nitrogen to which they are attached form a 1,4-dioxa-8-azaspiro[4.5] moiety or a 5-7 membered saturated ring, optionally containing one or more additional heteroatoms each independently selected from the group consisting of O, S and N, such 5-7 membered saturated ring optionally being substituted with one or more substituents each independently selected from the group consisting of hydrogen, halo, C_1-C_4alkyloxy, oxo C(=O)-C_1-C_3alkyl, C_1-C_4alkyl, OH, CN, CFH_2, CF_2H and CF_3;

Each R_4 is independently selected from hydrogen, halo, C_1-C_4alkyloxy, C_1-C_4alkyl, OH, CN, CFH_2, CF_2H, CF_3 or a 3-5 membered saturated ring optionally containing

one or more heteroatoms each independently selected from the group consisting of O and N;

R_5 represents C_1-C_6alkyl, CFH_2, CF_2H, CF_3 or a 3-7 membered saturated ring optionally containing one or more heteroatoms each independently selected from the group consisting of O, S and N, such 3-7 membered saturated ring optionally being substituted with one or more substituents each independently selected from the group consisting of hydrogen, halo, C_1-C_4alkyloxy, oxo, C(=O)-C_1-C_3alkyl, C_1-C_4alkyl, OH, CN, CFH_2, CF_2H and CF_3;

or a pharmaceutically acceptable salt or a solvate thereof.

2. The compound according to claim 1, wherein R_2 represents a 3-7 membered saturated ring, containing one or more heteroatoms each independently selected from the group consisting of O, S and N, such 3-7 membered saturated ring optionally being substituted with one or more substituents each independently selected from the group consisting of hydrogen, halo, C_1-C_4alkyloxy, C(=O)- C_1-C_3alkyl, C_1-C_4alkyl, OH, CN, CFH_2, CF_2H and CF_3;

Or R_1 R_2 together with the Nitrogen to which they are attached form a 5-7 membered saturated ring, optionally containing one or more additional heteroatoms each independently selected from the group consisting of O, S and N, such 5-7 membered saturated ring optionally being substituted with one or more substituents each independently selected from the group consisting of hydrogen, halo, C_1 C_4alkyloxy, oxo, C(=O)-C_1-C_3alkyl, C_1-C_4alkyl, OH, CN, CFH_2, CF_2H and CF_3.

3. The compound according to claim 1 or 2, wherein R_2 represents a 4-7 membered saturated ring containing carbon and one or more oxygen atoms, such 4-7 membered saturated ring optionally being substituted with one or more substituents each independently selected from the group consisting of hydrogen, halo, C_1 C_4alkyloxy, C(=O)- C_1-C_3alkyl, C_1-C_4alkyl, OH, CN, CFH_2, CF_2H and CF_3.

~~4. A compound according any one of claims 1 to 3, wherein B represents phenyl or thiophene, optionally being substituted with one or more substituents each independently selected from the group consisting of hydrogen, halogen, C_1-C_3alkyl, CN, CFH_2, CF_2H and CF_3.~~

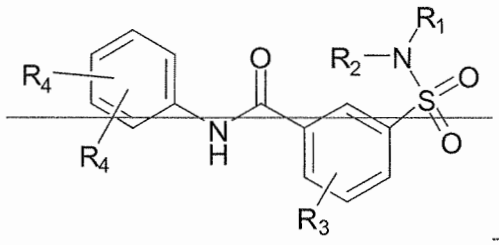
~~5.~~4. A compound ~~of Formula (I)~~ according to any one of the previous claims, wherein

R_2 represents C_1-C_3alkyl-R_{56} or a 4-7 membered saturated ring consisting of carbon atoms and one or more heteroatoms each independently selected from the group consisting of O or S, such 4-7 membered saturated ring optionally being substituted with one or more substituents each independently selected from the group consisting of hydrogen, halo, C_1-C_4alkyloxy, oxo, C(=O)-C_1-C_3alkyl, C_1-C_4alkyl, OH, CN, CFH_2, CF_2H and CF_3;

Each R_4 is independently selected from hydrogen, halo, C_1-C_4alkyloxy, C_1-C_4alkyl, OH, CN, CFH_2, CF_2H, CF_3 or a 3-5 membered saturated ring optionally containing one or more heteroatoms each independently selected from the group consisting of O and N; and

R_{56} represents a 4-7 membered saturated ring optionally containing one or more heteroatoms each independently selected from the group consisting of O or S, such 4-7 membered saturated ring optionally being substituted with one or more substituents each independently selected from the group consisting of hydrogen, halo, C_1-C_4alkyloxy, oxo, C(=O)-C_1-C_3alkyl, C_1-C_4alkyl, OH, CN, CFH_2, CF_2H and CF_3.

~~6. A compound according to any one of the previous claims, which is of Formula (Ib)~~

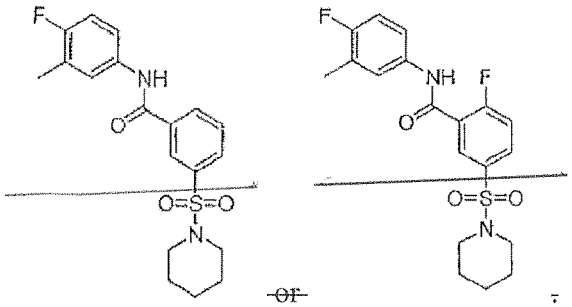


~~(Ib)~~

~~wherein R_1, R_2, R_4 are defined as in any one of the previous claims and R_3 is selected from the group comprising hydrogen, halo, C_1-C_3alkyl, CN, CFH_2, CF_2H, CF_3.~~

~~7.~~5.A compound according to any one of the previous claims, wherein at least one R_4 represents Fluor, C_1-C_3alkyl or cyclopropyl.

~~8.~~6.A compound according to any one of the previous claims, wherein one R_4 on the *para* position represents Fluor and the other one R_4 on the *meta* position represents methyl. ~~and such compound is not~~



~~or~~

~~9.~~7. A compound according to any one of the previous claims, wherein B is substituted with halo, said halo ~~R_3~~ represents Fluor.

~~10.~~8. A compound according to any one of claims 1 to ~~9~~6, wherein B represents ~~phenyl or~~ thiophene, optionally being substituted with one or more substituents each independently selected from the group consisting of hydrogen, halogen, C_1-C_3alkyl, CN, CFH_2, CF_2H and CF_3.

~~11.~~9. A compound according to any one of the previous claims for use in the prevention or treatment of an HBV infection in a mammal.

~~12.~~10. A pharmaceutical composition comprising a compound according to any of claims 1 to ~~10~~8, and a pharmaceutically acceptable carrier.

~~13.~~11. A product containing (a) a compound of formula I as defined in any one of claims 1 to ~~10~~8, and (b) another HBV inhibitor, as a combined preparation for use simultaneously, separately or sequentially ~~use~~ in the treatment of HBV infections.