CLAIMS

1. A DGAT1 inhibitor, or a pharmaceutically acceptable salt or ester thereof; for use in the prevention, delay of progression or treatment of a disease or condition which is selected from chylomicronemia syndrome, familial chylomicronemia syndrome, and Type V hyperlipoproteinemia.

2. A DGAT1 inhibitor, or a pharmaceutically acceptable salt or ester thereof, for use in the reduction of postprandial triglyceride levels in patients suffering from a disease or condition which is selected from chylomicronemia syndrome, familial chylomicronemia syndrome, and Type V hyperlipoproteinemia.

3. A DGAT1 inhibitor, or a pharmaceutically acceptable salt or ester thereof, for use in the prevention, delay of progression or treatment of a symptom selected from recurrent episodes of deposition of triglycerides in the skin in the form of eruptive xanthomas, hepatosplenomegaly, milky white triglyceride in the blood vessels in the back of the eye (lipemia retinalis), and mild neuro-cognitive deficits.

4. A DGAT1 inhibitor for use according to any one of claims 1-3 wherein the DGAT1 inhibitor is a compound having the following structure

A-L1-B-C-D-L2-E

wherein

- A is a substituted or unsubstituted alkyl, cycloalkyl, aryl, or heterocyclyl group,
- L1 is selected from the group consisting of:
  * an amine group –NH-
  * a substituted amine group of the formula $–N(CH_3)-$, $-CH_2-NH-$ or $-CH_2-CH_2-NH-$,
  * an amide group –C(O)-NH- ,
  * a sulphonamide group $–S(O)_2-NH-$, or
  * a urea group –NHC(O)-NH-,

- B is a substituted or unsubstituted, monocyclic, 5- or 6-membered divalent heteroaryl group,

- C-D is selected from the following cyclic structures:

* C-D together is a substituted or unsubstituted divalent biphenyl group,

* C is a substituted or unsubstituted divalent phenyl group and D is a single bond,

* C is a substituted or unsubstituted divalent phenyl group, and D is a substituted or unsubstituted divalent non-aromatic monocyclic ring which is selected from a saturated or unsaturated divalent cycloalkyl group or a saturated or unsaturated divalent heterocycloalkyl group,

* C-D together is a spiro residue, wherein

• the first cyclic component is a benzo-fused cyclic component wherein the ring which is fused to the phenyl part is a 5- or 6-membered ring, optionally comprising one or more heteroatoms, the first cyclic component being attached to the moiety B via its phenyl part, and

• the second cyclic component is a cycloalkyl or cycloalkylidenyl residue which is attached to L2,

- L2 is selected from the group consisting of:

* a single bond,

* a divalent residue having the following structure:

$-[R^1]_a-[R^2]_b-[C(O)]_c-[N(R^3)]_d-[R^4]_e-[R^5]_f-$

wherein

a is 0 or 1,

b is 0 or 1,

c is 0 or 1,

d is 0 or 1,

e is 0 or 1,

f is 0 or 1,

with the proviso that (a+b+c+d+e+f) > 0, and c=1 if d=1,

R^1, R^2, R^4 and R^5, which can be the same or different, are a substituted or unsubstituted divalent alkyl, cycloalkyl, alkenyl, alkynyl, alkylene, aryl or heterocyclyl residue,

R^3 is H or hydrocarbyl,

or R^3 and R^4 form together with the nitrogen atom to which they are attached a 5- or 6-membered heterocycloalkyl group,

with the proviso that R^1 and R^2 are not both alkyl if c=1 and d=e=f=0 and the carbonyl carbon atom is attached to the moiety E,

* an alkylidenyl group which is linked to the moiety D via a double bond, and

- E is selected from the group consisting of:

    * a sulphonic acid group and derivatives thereof,

    * a carboxyl group and derivatives thereof, wherein the carboxyl carbon atom is attached to L2,

    * a phosphonic acid group and derivatives thereof,

    * an alpha-keto hydroxyalkyl group,

    * a hydroxyalkyl group wherein the carbon atom bonded to the hydroxyl group is further substituted with one or two trifluoro-methyl groups,

    * a substituted or unsubstituted five-membered heterocyclyl residue having in the ring at least two heteroatoms and at least one carbon atom, wherein

        • the at least one carbon atom of the ring is bonded to two heteroatoms;

        • at least one of the heteroatoms to which the carbon atom of the ring is bonded is a member of the ring;

        • and at least one of the heteroatoms to which the carbon atom of the ring is bonded or at least one of the heteroatoms of the ring is bearing a hydrogen atom;

with the provisos that

- L2 is not a single bond or a divalent alkyl group if the moiety D is a single bond,
- L2 is not a single bond if the moiety D is an unsubstituted divalent phenyl group and E is a carboxylic acid or a derivative thereof,
- E is not a carboxamide group if L2 comprises an amide group,
- E is not a –COOH group if D is a single bond and L2 is a $-N(CH_3)-C(O)-$ group wherein the carbonyl carbon atom is attached to the moiety E,
- L2 is not a divalent N-methyl piperidinyl group if the moiety E is a pyridinyl-1,2,4-triazolyl group,

- L2 is not $-C(O)-[R^4]_e-[R^5]_f-$ when C is a substituted or unsubstituted divalent phenyl group and D is a single bond,

or a pharmaceutically acceptable salt, or ester thereof.

5. A DGAT1 inhibitor for use according to any one of claims 1-4, wherein the DGAT1 inhibitor is a compound which is selected from:

trans-4-[4-[5-[[6-(Trifluoromethyl)-3-pyridinyl]amino]-2-pyridinyl]phenyl]cyclohexane acetic acid,

(4-{6-[5-(4-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-1H-benzoimidazol-2-yl}-3,5-dimethyl-phenoxy)-acetic acid,

(3,5-Dichloro-4-{6-[5-(4-chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-1H-benzoimidazol-2-yl}-phenoxy)-acetic acid,

3-(4-{6-[5-(4-Methoxy-phenyl)-[1,3,4]oxadiazol-2-yl]-1H-benzoimidazol-2-yl}-3,5-dimethyl-phenyl)-propionic acid,

3-(4-{6-[5-(3-Chlorophenylamino)-[1,3,4]oxadiazol-2-yl]-1H-benzoimidazol-2-yl}-3,5-dimethylphenyl)-propionic acid,

3-(4-{6-[5-(4-methoxyphenylamino)-[1,3,4]oxadiazol-2-yl]-1H-benzimidazol-2-yl}-3,5-dimethylphenyl)-propionic acid,

3-(4-{6-[5-(4-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-1H-benzoimidazol-2-yl}-3,5-dimethyl-phenyl)-propionic acid,

3-(4-{5-[5-(4-Methoxy-phenyl)-[1,3,4]oxadiazol-2-yl]-1H-benzoimidazol-2-yl}-3,5-dimethyl-phenyl)-2,2-dimethyl-propionic acid,

[3-(4-{6-[5-(4-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-1H-benzoimidazol-2-yl}-3,5-dimethyl-phenyl)-propyl]-phosphonic acid,

(3-{3,5-Dimethyl-4-[6-(5-phenyl-[1,3,4]oxadiazol-2-yl)-1H-benzoimidazol-2-yl]-phenyl}-propyl)-phosphonic acid,

[3-(4-{6-[5-(4-Methoxy-phenyl)-[1,3,4]oxadiazol-2-yl]-1H-benzoimidazol-2-yl}-3,5-dimethyl-phenyl)-propyl]-phosphonic acid,

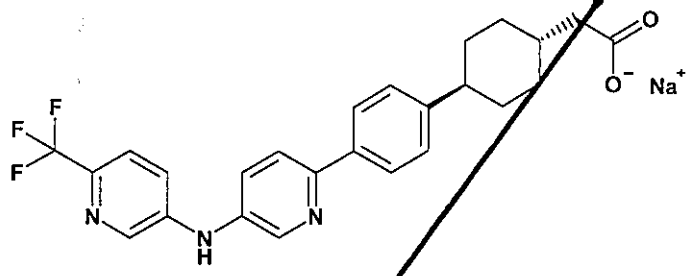
3-{4-[6-(5-methoxy-[1,3,4]oxadiazol-2-yl)-1H-indol-2-yl]-3,5-dimethylphenyl}-propionic acid and

3-(3,5-Dichloro-4-{6-[5-(4-chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-1H-

benzoimidazol-2-yl}-phenyl)-propionic acid,
or a pharmaceutically acceptable salt therof.

6. A DGAT1 inhibitor for use according to any one of claims 1- 5 wherein the DGAT1 inhibitor is *trans*-4-[4-[5-[[6-(trifluoromethyl)-3-pyridinyl]amino]-2-pyridinyl]phenyl]cyclohexane acetic acid, or a pharmaceutically acceptable salt thereof.

7. A DGAT1 inhibitor for use according to any one of claims 1- 6 wherein the DGAT1 inhibitor is *trans*-4-[4-[5-[[6-(trifluoromethyl)-3-pyridinyl]amino]-2-pyridinyl]phenyl]cyclohexane acetic acid, sodium salt:



8. A DGAT1 inhibitor for use according to any one of claims 1- 7 wherein the DGAT1 inhibitor is used at a dose of 5-40 mg.

9. A pharmaceutical composition, comprising a DGAT1 inhibitor, or a pharmaceutically acceptable salt, or ester thereof, for use in the prevention, delay of progression or treatment of a disease or condition which is selected from chylomicronemia syndrome, familial chylomicronemia syndrome, and Type V hyperlipoproteinemia.

10. A pharmaceutical composition, comprising a DGAT1 inhibitor, or a pharmaceutically acceptable salt, or ester thereof, for use in the reduction of postprandial triglyceride levels in patients suffering from a disease or condition which is selected from chylomicronemia syndrome, familial chylomicronemia syndrome, and Type V hyperlipoproteinemia.

11. A pharmaceutical composition, comprising a DGAT1 inhibitor, or a pharmaceutically acceptable salt, or ester thereof, for use in the prevention, delay of progression or treatment of a symptom selected from recurrent episodes of deposition of triglycerides in the skin in the form of eruptive xanthomas, hepatosplenomegaly, milky white triglyceride in the blood vessels in the back of the eye (lipemia retinalis), and mild neuro-cognitive deficits.

12. A pharmaceutical composition, comprising a DGAT1 inhibitor, or a pharmaceutically acceptable salt, or ester thereof, for use according to any one of claims 9-11, wherein the DGAT1 inhibitor is as defined in any one of claims 4-8.

13. A method for the prevention, delay of progression or treatment of a disease or condition which is selected from chylomicronemia syndrome, familial chylomicronemia syndrome, and Type V hyperlipoproteinemia, comprising administration of a therapeutically effective amount of a DGAT1 inhibitor, or a pharmaceutically acceptable salt or ester thereof, to a subject in need of such treatment.

14. A method for the reduction of postprandial triglyceride levels in patients suffering from a disease or condition which is selected from chylomicronemia syndrome, familial chylomicronemia syndrome, and Type V hyperlipoproteinemia, comprising administration of a therapeutically effective amount of a DGAT1 inhibitor, or a pharmaceutically acceptable salt or ester thereof, to a subject in need of such treatment.

15. A method for the the prevention, delay of progression or treatment of a symptom selected from recurrent episodes of deposition of triglycerides in the skin in the form of eruptive xanthomas, hepatosplenomegaly, milky white triglyceride in the blood vessels in the back of the eye (lipemia retinalis), and mild neuro-cognitive deficits, comprising administration of a therapeutically effective amount of a DGAT1 inhibitor, or a pharmaceutically acceptable salt or ester thereof, to a subject in need of such treatment.

16. The method of any one of claims 13-15, wherein the subject is a human.

17. A method according to any one of claims 13-16 wherein the DGAT1 inhibitor is as defined in any one of claims 4-8.

THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. Use of a DGAT1 inhibitor, or a pharmaceutically acceptable salt or ester thereof for the manufacture of a medicament for the prevention, delay of progression or treatment of a disease or condition which is selected from chylomicronemia syndrome, familial chylomicronemia syndrome, and Type V hyperlipoproteinemia.

2. Use of a DGAT1 inhibitor, or a pharmaceutically acceptable salt or ester thereof for the manufacture of a medicament for the reduction of postprandial triglyceride levels in patients suffering from a disease or condition which is selected from chylomicronemia syndrome, familial chylomicronemia syndrome, and Type V hyperlipoproteinemia.

3. Use of a DGAT1 inhibitor, or a pharmaceutically acceptable salt or ester thereof for the manufacture of a medicament for the prevention, delay of progression or treatment of a symptom selected from recurrent episodes of deposition of triglycerides in the skin in the form of eruptive xanthomas, hepatosplenomegaly, milky white triglyceride in the blood vessels in the back of the eye (lipemiaretinalis), and mild neuro-cognitive deficits.

4. A use according to any one of claims 1 to 3 wherein the DGAT1 inhibitor is a compound having the following structure

A-L1-B-C-D-L2-E

wherein

- A is a substituted or unsubstitutedalkyl, cycloalkyl, aryl, or heterocyclylgroup,

- L1 is selected from the group consisting of:
  * an amine group –NH-
  * a substituted amine group of the formula $-N(CH_3)-$, $-CH_2-NH-$ or $-CH_2-CH_2-NH-$,
  * an amide group –C(O)-NH- ,
  * a sulphonamide group $-S(O)_2-NH-$, or
  * a urea group –NHC(O)-NH-,

- B is a substituted or unsubstituted, monocyclic, 5- or 6-membered divalent heteroaryl group,
- C-D is selected from the following cyclic structures:
  * C-D together is a substituted or unsubstituted divalent biphenyl group,
  * C is a substituted or unsubstituted divalent phenyl group and D is a single bond,
  * C is a substituted or unsubstituted divalent phenyl group, and D is a substituted or unsubstituted divalent non-aromatic monocyclic ring which is selected from a saturated or unsaturated divalent cycloalkyl group or a saturated or unsaturated divalent heterocycloalkyl group,
  * C-D together is a spiro residue, wherein
    - the first cyclic component is a benzo-fused cyclic component wherein the ring which is fused to the phenyl part is a 5- or 6-membered ring, optionally comprising one or more heteroatoms, the first cyclic component being attached to the moiety B via its phenyl part, and
    - the second cyclic component is a cycloalkyl or cycloalkylidenyl residue which is attached to L2,
- L2 is selected from the group consisting of:
  * a single bond,
  * a divalent residue having the following structure:

$$-[R^1]_a-[R^2]_b-[C(O)]_c-[N(R^3)]_d-[R^4]_e-[R^5]_f-$$

wherein
a is 0 or 1,
b is 0 or 1,
c is 0 or 1,
d is 0 or 1,
e is 0 or 1,
f is 0 or 1,
with the proviso that (a+b+c+d+e+f) > 0, and c=1 if d=1,
R^1, R^2, R^4 and R^5, which can be the same or different, are a substituted or unsubstituted divalent alkyl, cycloalkyl, alkenyl,

alkynyl, alkylene, aryl or heterocyclyl residue,

R^3 is H or hydrocarbyl,

or R^3 and R^4 form together with the nitrogen atom to which they are attached a 5- or 6-membered heterocycloalkyl group,

with the proviso that R^1 and R^2 are not both alkyl if c=1 and d=e=f=0 and the carbonyl carbon atom is attached to the moiety E,

* analkylidenyl group which is linked to the moiety D via a double bond, and

- E is selected from the group consisting of:
  * a sulphonic acid group and derivatives thereof,
  * a carboxyl group and derivatives thereof, wherein the carboxyl carbon atom is attached to L2,
  * a phosphonic acid group and derivatives thereof,
  * an alpha-ketohydroxyalkyl group,
  * a hydroxyalkyl group wherein the carbon atom bonded to the hydroxyl group is further substituted with one or two trifluoro-methyl groups,
  * a substituted or unsubstituted five-membered heterocyclyl residue having in the ring at least two heteroatoms and at least one carbon atom, wherein
    - the at least one carbon atom of the ring is bonded to two heteroatoms;
    - at least one of the heteroatoms to which the carbon atom of the ring is bonded is a member of the ring;
    - and at least one of the heteroatoms to which the carbon Atom of the ring is bonded or at least one of the heteroatoms of the ring is bearing a hydrogen atom;

with the provisos that

- L2 is not a single bond or a divalent alkyl group if the moiety D is a single bond,
- L2 is not a single bond if the moiety D is an unsubstituted divalent phenyl group and E is a carboxylic acid or a derivative thereof,
- E is not a carboxamide group if L2 comprises an amide group,
- E is not a –COOH group if D is a single bond and L2 is a $–N(CH_3)-C(O)-$ group wherein the carbonyl carbon atom is attached to the moiety E,

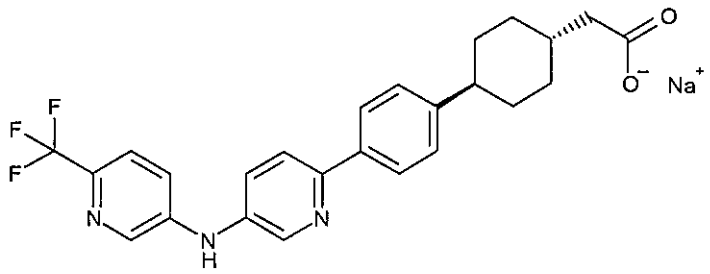
- L2 is not a divalent N-methyl piperidinyl group if the moiety E is a pyridinyl-1,2,4-triazolyl group,
- L2 is not $-C(O)-[R^4]_e-[R^5]_f-$ when C is a substituted or unsubstituted divalent phenyl group and D is a single bond,

or a pharmaceutically acceptable salt, or ester thereof.

5. A use according to any one of claims 1 to 3 wherein the DGAT1 inhibitor is a compound which is selected from:
trans-4-[4-[5-[[6-(Trifluoromethyl)-3-pyridinyl]amino]-2-pyridinyl]phenyl]cyclohexane acetic acid,
(4-{6-[5-(4-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-1H-benzoimidazol-2-yl}-3,5-dimethyl-phenoxy)-acetic acid,
(3,5-Dichloro-4-{6-[5-(4-chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-1H-benzoimidazol-2-yl}-phenoxy)-acetic acid,
3-(4-{6-[5-(4-Methoxy-phenyl)-[1,3,4]oxadiazol-2-yl]-1H-benzoimidazol-2-yl}-3,5-dimethyl-phenyl)-propionic acid,
3-(4-{6-[5-(3-Chlorophenylamino)-[1,3,4]oxadiazol-2-yl]-1H-benzoimidazol-2-yl}-3,5-dimethylphenyl)-propionic acid,
3-(4-{6-[5-(4-methoxyphenylamino)-[1,3,4]oxadiazol-2-yl]-1H-benzimidazol-2-yl}-3,5-dimethylphenyl)-propionic acid,
3-(4-{6-[5-(4-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-1H-benzoimidazol-2-yl}-3,5-dimethyl-phenyl)-propionic acid,
3-(4-{5-[5-(4-Methoxy-phenyl)-[1,3,4]oxadiazol-2-yl]-1H-benzoimidazol-2-yl}-3,5-dimethyl-phenyl)-2,2-dimethyl-propionic acid,
[3-(4-{6-[5-(4-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-1H-benzoimidazol-2-yl}-3,5-dimethyl-phenyl)-propyl]-phosphonic acid,
(3-{3,5-Dimethyl-4-[6-(5-phenyl-[1,3,4]oxadiazol-2-yl)-1H-benzoimidazol-2-yl]-phenyl}-propyl)-phosphonic acid,
[3-(4-{6-[5-(4-Methoxy-phenyl)-[1,3,4]oxadiazol-2-yl]-1H-benzoimidazol-2-yl}-3,5- dimethyl-phenyl)-propyl]-phosphonic acid,
3-{4-[6-(5-methoxy-[1,3,4]oxadiazol-2-yl)-1H-indol-2-yl]-3,5-dimethylphenyl}-propionic acid and
3-(3,5-Dichloro-4-{6-[5-(4-chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-1H-benzoimidazol-2-yl}-phenyl)-propionic acid,
or a pharmaceutically acceptable salt thereof.

6. A use according to any one of claims 1 to 3 wherein the DGAT1 inhibitor is *trans*-4-[4-[5-[[6-(trifluoromethyl)-3-pyridinyl]amino]-2-pyridinyl]phenyl]cyclohexane acetic acid, or a pharmaceutically acceptable salt thereof.

7. A use according to any one of claims 1 to 3 wherein the DGAT1 inhibitor is *trans*-4-[4-[5-[[6-(trifluoromethyl)-3-pyridinyl]amino]-2-pyridinyl]phenyl]cyclohexane acetic acid, sodium salt:



8. A use according to any one of claims 1 to 3 wherein the DGAT1 inhibitor is used at a dose of 5-40 mg.