Title (en)

COMBINATION OF MTP INHIBITORS AND HMG-CoA REDUCTASE INHIBITORS AND THE USE THEREOF IN MEDICAMENTS

Title (de)

KOMBINATION VON MTP-INHIBITOREN UND HMG-CoA-REDUKTASE-INHIBITOREN UND IHRE VERWENDUNG IN ARZNEIMITTELN

Title (fr)

COMBINAISON D'INHIBITEURS DE MTP (PROTEINE DE TRANSFERT MICROSOMALE) ET INHIBITEURS DE HMG-CoA-REDUCTASE ET LEUR UTILISATION DANS DES MEDICAMENTS

Publication

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Application

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Priority

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Abstract (en)

[origin: DE19929065A1] A combination of MTP inhibitor(s) (A), selected from 5 classes of specific bi- or tricyclic aza-heterocyclic compounds, and HMG-CoA reductase inhibitors (B) is used in the treatment or prophylaxis of cardiovascular diseases. The use of a combination of at least one MTP inhibitor (A) and at least one HMG-CoA reductase inhibitor (B) is claimed in the treatment or prophylaxis of diseases. (A) is selected from tricyclic pyrrole derivatives of formula (A1), heterocyclic-substituted phenylacetamide derivatives of formula (A2) or (A3), purine derivatives of formula (A4) and indolo-pyrimidine derivatives of formula (A5) (including isomers and salts). R1a + R2a = group completing a phenyl or pyridyl ring or a dihydropyridone ring of formula (a) (all rings being optionally substituted by 1-3 of halo, CF3, COOH, OH, alkoxy, alkoxycarbonyl or alkyl (itself optionally substituted by OH or 1-4C alkoxy)); R3a + R4a = group completing a pyridyl ring or a 4-8 membered cycloalkene or oxocycloalkene residue (all rings being optionally substituted as in R1a/R2a); Da = H, 4-12C cycloalkyl or 1-12C alkyl; Ea = CO or CS; La = O, S or N(R9a); R9a = H or alkyl (optionally substituted by OH or Ph); R5a = Ph or 5-7 membered (un)saturated heterocycle (both optionally substituted by 1-3 of NO2, COOH, halo, CN, alkenyl, alkoxycarbonyl and alkyl (itself optionally substituted by OH, COOH, alkoxy or alkoxycarbonyl) and/or by OR10a or NR11aR12a); R10a = H, alkyl or alkenyl; R11a, R12a = Ph, H, alkyl or up to 8C acyl (optionally substituted by NR13aR14a); R13a, R14a = H or up to 8C acyl; R6a = H, COOH, (1-5C) alkoxycarbonyl or alkyl (optionally substituted by OH or OCOR15a); R15a = Ph (optionally substituted by 1-3 of halo, OH or 1-5C alkyl); or 1-22C alkyl or 2-22C alkenyl (both optionally substituted by OR16a); R16a = H, CH2Ph, CPh3 or alkyl; R7a = H; or R6a + R7a = =O; Ab = one of 9 specified bicyclic heterocyclic groups; Db, Eb = H, halo, CF3, OH, COOH, alkoxy, alkoxy or alkoxycarbonyl; Zb = O or S; R1b = 3-10C cycloalkyl, 1-10C alkyl or phenyl (optionally substituted by 1 or 2 of halo, NO2, CN, OH, 1-4C alkyl and 1-4C alkoxy); R2b = H or 1-3C alkyl; R3b = H, 1-5C alkyl, 3-7C cycloalkyl, phenyl or 5-7 membered aromatic heterocyclyl (optionally substituted by 1-3 of halo, NO2, Ph, OH, alkyl and alkoxy); R4b = H, CH2OH or CH2OCOR11b; R11b = H, 1-8C alkyl or phenyl (optionally substituted by 1-3 of halo, OH, CN, 1-4C alkyl and 1-4C alkoxy); Dc = imidazolyl, aza-imidazolyl or indolyl group of formula (k) or (l); Tc = N or CH; R6c-R11c = H, CF3, halo, alkyl or alkoxy; R5c, R8c, R9c = H, 3-6C cycloalkyl, Ph, alkoxycarbonyl or alkyl (optionally substituted by halo); or R5c may also be benzyl if Tc = N; Ec, Lc = H, halo, CF3, OH, COOH, alkyl, alkoxy or alkoxycarbonyl; R1c-R4c = as R1b-R4b respectively; Ad = one of 2 specified purinyl residues; Dd, Ed = H, halo, CF3, OH, COOH, alkyl, alkoxy or alkoxycarbonyl; R1d = H or cycloalkyl; 1-8C alkyl or 2-8C alkenyl (both optionally substituted by 3-6C cycloalkyl, Ph or 5- or 6-membered aromatic heterocyclyl); or Ph or 5- or 6-membered aromatic heterocyclyl (where the ring systems are optionally substituted by 1-3 of halo, Ph, CF3, 1-5C alkyl, 1-5C alkoxy, OH or NR9dR10d); R9d, R10d = H, Ph, 1-5C alkyl or 1-5C acyl; Ld = O or S; R2d = SH, OH, 1-8C alkoxy or -N(R13d)-CHR14dR15d; R13d = H or 1-4C alkyl; R14d = H, Ph or 5- or 6-membered aromatic heterocyclyl; R15d = H or 1-8C alkyl (optionally substituted by OH); Ae, De, Ee, Ge, Le, Me = H, halo, CF3, COOH, OH, alkoxy, alkoxycarbonyl or alkyl (optionally substituted by OH or 1-4C alkoxy); R1e, R2e = H, cycloalkyl, 1-10C alkyl (optionally substituted by 3-6C cycloalkyl) or Ph (optionally substituted by halo or CF3); or CR1eR2e = 4-8C cycloalkylidene; R3e = phenyl (optionally substituted by 1-3 of NO2, COOH, halo, CN, alkenyl, alkoxycarbonyl or alkyl (optionally substituted by OH, COOH, 1-4C alkoxy or (1-4C) alkoxycarbonyl and/or by OR4e or NR5eR6e); R4e = H, alkyl or alkenyl; R5e, R6e = Ph, H, alkyl or up to 8C acyl (optionally substituted by NR7eR8e); R7e, R8e = H or up to 8C acyl; unless specified otherwise alkyl moieties have 1-6C, alkenyl moieties 2-6C and cycloalkyl moieties 3-8C; heterocycles contain 1-3 of S, N and/or O as heteroatom(s). The full definitions are given in the DEFINITION (Full Definitions) field. Independent claims are included for: (1) medicaments containing a combination of (A), (B) and optionally one or more further components; and (2) production of the medicaments by converting (A), (B) and optionally further components into a suitable application form with auxiliaries and carriers.

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IPC 8 full level

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