(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
27 February 2003 (27.02.2003)

PCT

(10) International Publication Number
WO 03/015776 A1

(51) International Patent Classification[7]: A61K 31/426, 31/427, 31/506, 31/497, C07D 417/04, 417/14, A61P 31/12, 37/02, 37/08, 29/00, C07D 277/24

(21) International Application Number: PCT/EP02/08956

(22) International Filing Date: 9 August 2002 (09.08.2002)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
01203088.8 13 August 2001 (13.08.2001) EP

(71) Applicant *(for all designated States except US)*: **JANSSEN PHARMACEUTICA N.V.** [BE/BE]; Turnhoutseweg 30, B-2340 Beerse (BE).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **LOVE, Christopher, John** [GB/BE]; Janssen Pharmaceutica N.V., Turnhoutseweg 30, B-2340 Beerse (BE). **VAN WAUWE, Jean, Pierre, Frans** [BE/BE]; Janssen Pharmaceutica N.V., Turnhoutseweg 30, B-2340 Beerse (BE). **DE BRABANDER, Marc, J.** [BE/BE]; Valerialaan 2, B-2980 Zoersel (BE). **MOSES, Roger, Clive** [GB/GB]; 18 Fernleigh Road, Walebridge, Cornwall PL27 7AX (GB). **GONCHARENKO, Mykhalyo** [UA/CA]; 875 Wonderland Road South, Apt. #1202, London, Ontario N6K 3N1 (CA). **COOYMANS, Ludwig, Paul** [BE/BE]; Janssen Pharmaceutica N.V., Turnhoutseweg 30, B-2340 Beerse (BE). **VANDERMAESEN, Nele** [BE/BE]; Janssen Pharmaceutica N.V., Turnhoutseweg 30, B-2340 Beerse (BE). **DIELS, Gaston, Stanislas, Marcella** [BE/BE]; Janssen Pharmaceutica N.V., Turnhoutseweg 30, B-2340 Beerse (BE). **SIBLEY, Anthony, William** [GB/GB]; 1 Camelot View, Camelford, Cornwall PL32 9TU (GB). **NOULA, Caterina** [GR/GB]; 3 Beech Drive, St. Columb Major, Cornwall TR9 6SZ (GB).

(74) Common Representative: **JANSSEN PHARMACEUTICA N.V.**; Lies Vervoort, Johnson & Johnson Patent Law Department, Turnhoutseweg 30, B-2340 Beerse (BE).

(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)*

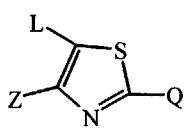
— *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for all designations*

— *of inventorship (Rule 4.17(iv)) for US only*

[Continued on next page]

WO 03/015776 A1

(54) Title: 2,4,5-TRISUBSTITUTED THIAZOLYL DERIVATIVES AND THEIR ANTIINFLAMMATORY ACTIVITY



(I)

(57) Abstract: This invention concerns the use of a compound of formula (I), a *N*-oxide, a pharmaceutically acceptable addition salt, a quaternary amine and a stereochemically isomeric form thereof, wherein Z is halo; C_{1-6}alkyl; C_{1-6}alkyl substituted with hydroxy, carboxyl, cyano, amino, mono -or di(C_{1-6}alkyl)amino, aminocarbonyl, mono -or di(C_{1-6}alkyl)aminocarbonyl, C_{1-6}alkyloxycarbonyl or C_{1-6}alkyloxy; polyhaloC_{1-4}alkyl; C_{1-4}alkyloxy; cyano; amino; aminocarbonyl; mono -or di(C_{1-6}alkyl)aminocarbonyl; C_{1-6}alkyloxycarbonyl; C_{1-6}alkylcarbonyloxy; H_2N-S(=O)$_2$-; mono -or di(C_{1-6}alkyl)amino-S(=O)$_2$; -C(=N-R^x)NR^yR^z; Q is an optionally substituted carbocycle or an optionally substituted heterocycle; L is substituted phenyl or an optionally substituted monocyclic 5 or 6-membered partially saturated or aromatic heterocycle or a bicyclic partially saturated or aromatic heterocycle; aryl is optionally substituted phenyl; for the manufacture of a medicament for the prevention or the treatment of diseases mediated through TNF-α and/or IL-12.

Published:
— *with international search report*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.