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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
4 August 2005 (04.08.2005)

PCT

(10) International Publication Number
WO 2005/070924 A1

(51) International Patent Classification[7]: C07D 413/06, 413/14, A61K 31/5355, A61P 31/10

(21) International Application Number: PCT/EP2005/050267

(22) International Filing Date: 21 January 2005 (21.01.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/538,768 23 January 2004 (23.01.2004) US

(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)*: **GUILLEMONT, Jérôme, Emile, Georges** [FR/FR]; c/o Johnson & Johnson, Pharmaceutical, Research and Development, A division of Janssen-Cilag Campus de, Maigremont BP 615 (FR). **PASQUIER, Elisabeth, Therese, Jeanne** [FR/FR]; c/o Johnson & Johnson, Pharmaceutical, Research and Development, A division of Janssen-Cilag Campus de, Maigremont BP 615 (FR).

(74) Common Representative: **JANSSEN PHARMACEUTICA N.V.**; Turnhoutseweg 30, B-2340 Beerse (BE).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, 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, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

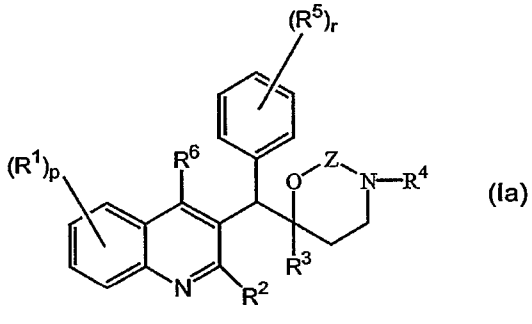
(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT,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

Declarations under Rule 4.17:

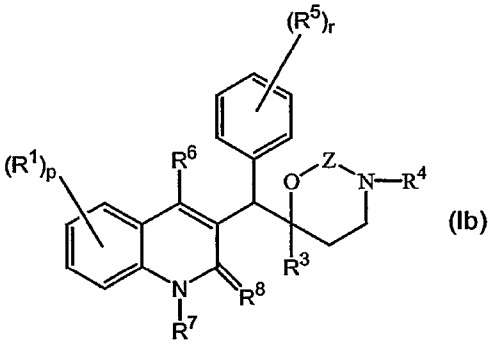
— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE,*

[Continued on next page]

(54) Title: SUBSTITUTED QUINOLINES AND THEIR USE AS MYCOBACTERIAL INHIBITORS



(Ia)



(Ib)

(57) Abstract: The present invention relates to novel substituted quinoline derivatives according to the general formula (Ia) or the general formula (Ib) salts, quaternary amines, stereochemically isomeric forms, tautomeric forms and N-oxide forms thereof, wherein R^1 is hydrogen, halo, haloalkyl, cyano, hydroxy, Ar, Het, alkyl, alkyloxy, alkylthio, alkyloxyalkyl, alkylthioalkyl, Ar-alkyl or di(Ar)alkyl ; p is 1, 2, 3 or 4 ; R^2 is hydrogen, hydroxy, thio, alkyloxy, alkyloxyalkyloxy, alkylthio, mono or di(alkyl)amino or a radical of formula (Ic); R^3 is alkyl, Ar, Ar-alkyl, Het or Het-alkyl; R^4 is hydrogen, alkyl or benzyl; R^5 is hydrogen, halo, haloalkyl, hydroxy, Ar, alkyl, alkyloxy, alkylthio, alkyloxyalkyl, alkylthioalkyl, Ar-alkyl or di(Ar)alkyl ; or two vicinal R^5 radicals may be taken together to form together with the phenyl ring to which they are attached a naphthyl; r is 1, 2, 3, 4 or 5 ; R^6 is hydrogen, alkyl, Ar or Het R^7 is hydrogen or alkyl; R^8 is oxo ; or R^7 and R^8 taken together form the radical - CH=CH-N=; Z is CH_2 or C(=O). The claimed compounds are useful for the treatment of mycobacterial diseases, particularly those diseases caused by pathogenic mycobacteria such as *M. tuberculosis, M. bovis, M. avium, M. smegmatis and M. marinum.* Also claimed is a pharmaceutical composition containing a compound of the present invention, the use of the claimed compounds or compositions for the manufacture of a medicament for the treatment of mycobacterial diseases and a process for preparing the claimed compounds.

WO 2005/070924 A1

EG, 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, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, NA, 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, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, 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*

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.