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

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
21 August 2003 (21.08.2003)

PCT

(10) International Publication Number
WO 03/068752 A1

(51) International Patent Classification[7]: C07D 223/16, 409/10, 407/10, 401/10, 413/10, 403/10, 217/04, 209/44, A61K 31/40, 31/47, 31/55, A61P 3/04, 25/30, 25/24, 25/22

(21) International Application Number: PCT/EP03/01545

(22) International Filing Date: 13 February 2003 (13.02.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

0203438.7	13 February 2002 (13.02.2002)	GB
0203437.9	13 February 2002 (13.02.2002)	GB
0204784.3	28 February 2002 (28.02.2002)	GB
0204758.7	28 February 2002 (28.02.2002)	GB
0212548.2	30 May 2002 (30.05.2002)	GB
0219711.9	23 August 2002 (23.08.2002)	GB
0224466.3	21 October 2002 (21.10.2002)	GB

(71) Applicant *(for all designated States except US)*: **GLAXO GROUP LIMITED** [GB/GB]; Glaxo Wellcome House, Berkeley Avenue, Greenford, Middlesex UB6 ONN (GB).

(72) Inventors; and

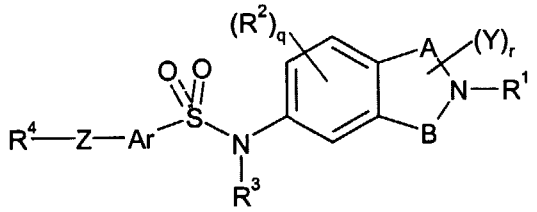
(75) Inventors/Applicants *(for US only)*: **BROMIDGE, Steven, Mark** [GB/IT]; GlaxoSmithKline SpA, Via Alessandro Fleming 2, I-37135 Verona (IT). **COOPER, David, Gwyn** [GB/GB]; GlaxoSmithKline, New Frontiers Science Park South, Third Avenue, Harlow, Essex CM19 5AW (GB). **FORBES, Ian, Thomson** [GB/GB]; GlaxoSmithKline, New Frontiers Science Park South, Third Avenue, Harlow, Essex CM19 5AW (GB). **GRIBBLE, Andrew, Derrick** [GB/GB]; GlaxoSmithKline, New Frontiers Science Park South, Third Avenue, Harlow, Essex CM19 5AW (GB). **JOHNSON, Christopher, Norbert** [GB/GB]; GlaxoSmithKline, New Frontiers Science Park South, Third Avenue, Harlow, Essex CM19 5AW (GB). **LIGHTFOOT, Andrew, P.** [GB/GB]; GlaxoSmithKline, New Frontiers Science Park South, Third Avenue, Harlow, Essex CM19 5AW (GB). **MOSS, Stephen, Frederick** [GB/GB]; GlaxoSmithKline, New Frontiers Science Park South, Third Avenue, Harlow, Essex CM19 5AW (GB). **PAYNE, Andrew, H.** [GB/GB]; GlaxoSmithKline, New Frontiers Science Park South, Third Avenue, Harlow, Essex CM19 5AW (GB). **RAHMAN, Shahzad, Sharooq** [GB/GB]; GlaxoSmithKline, New Frontiers Science Park South, Third Avenue, Harlow, Essex CM19 5AW (GB). **WITTY, David, R.** [GB/GB]; GlaxoSmithKline, New Frontiers Science Park South, Third Avenue, Harlow, Essex CM19 5AW (GB).

(74) Agent: **MCKINNELL, Denise**; GlaxoSmithKline, CN925.1, 980 Great West Road, Brentford, Middlesex TW8 9GS (GB).

(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,

[Continued on next page]

(54) Title: BENZENESULFONAMIDE DERIVATIVES AS ANTIPSYCHOTIC AGENTS



(I)

(57) Abstract: The invention provides compounds of formula (I)wherein A and B represent the groups $-(CH_2)m-$ and $-(CH_2)n-$respectively; R^1 represents hydrogen or C_{1-6}alkyl; R^2 represents hydrogen, halogen, hydroxy, cyano, nitro, hydroxyC_{1-6}alkyl, trifluoromethyl, trifluoromethoxy, C_{1-6}alkyl, C_{1-6}alkoxy, C_{1-6}alkoxyC_{1-6}alkyl, C_{3-7}cycloalkylC_{1-6}alkoxy, $-(CH_2)pC_{3-6}$cycloalkyl, $-(CH_2)pC_{3-6}$cycloalkyloxy, $-COC_{1-6}$alkyl, $-SO_2C_{1-6}$alkyl, $-SOC_{1-6}$alkyl, $-S-C_{1-6}$alkyl, C_{1-6}alkylsulfonyloxy, C_{1-6}alkylsulfonylC_{1-6}alkyl, $-CO_2C_{1-6}$alkyl, $-CO_2NR^7R^8$, $-SO_2NR^7R^8$, C_{1-6}alkylsulfonamido, C_{1-6}alkylsulfonamidoC_{1-6}alkyl, $-(CH_2)_pNR^7R^8$, C_{1-6}alkylamidoC_{1-6}alkyl, $-(CH_2)pNR^7COR^8$, arylsulfonyl, arylsulfonyloxy, arylsulfonylC_{1-6}alkyl, arylsulfonamido, arylcarboxamido, arylsulfonamidoC_{1-6}alkyl, arylcarboxamidoC_{1-6}alkyl, aroyl, aroylC_{1-6}alkyl, arylC_{1-6}alkanoyl, $-SO_2NR^7R^8$, optionally substituted aryl, optionally substituted heteroaryl or optionally substituted heterocyclyl, or a group $CONR^7R^8$ or $SO_2NR^7R^8$ wherein R^7 and R^8 together may be fused to form a 5- 7-membered aromatic or non-aromatic heterocyclic ring optionally interrupted by an O or S atom; R^3 represents hydrogen or C_{1-6}alkyl; Ar represents optionally substituted phenyl or optionally substituted monocyclic heteroaryl group; R^4 represents optionally substituted aryl or optionally substituted heteroaryl; R^7 and R^8 each independently represent hydrogen, C_{1-6}alkyl or together form a 5- to 7-membered heterocyclic ring; Z represents a bond, an oxygen atom or C_{1-6}alkyl:Y represents hydrogen or C_{1-6}alkyl; m and n independently represent an integer selected from 1 and 2; p independently represents an integer selected from 0, 1, 2 and 3; q represents an integer from 1 to 3; r represents an integer from 1 to 4; or a pharmaceutically acceptable salt or solvate thereof. The compounds are useful in therapy, in particular as antipsychotic agents.

WO 03/068752 A1

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, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, 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, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— *with international search report*

— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

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.