

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
15 December 2005 (15.12.2005)

PCT

(10) International Publication Number
WO 2005/118537 A3

(51) International Patent Classification:
A61K 31/496 (2006.01) A61P 13/08 (2006.01)
C07D 211/88 (2006.01)

(74) Common Representative: RANBAXY LABORATORIES LIMITED; c/o DESHMUKH, Jay, R., 600 College Road East, Suite 2100, Princeton, NJ 08540 (US).

(21) International Application Number:
PCT/IB2005/001534

(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, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, 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, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(22) International Filing Date: 31 May 2005 (31.05.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
992/DEL/2004 31 May 2004 (31.05.2004) IN

(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).

(71) Applicant (for all designated States except US): RANBAXY LABORATORIES LIMITED [IN/IN]; Plot No. 90, Sector -32, Gurgaon, Haryana 122001 (IN).

(72) Inventors; and

(75) Inventors/Applicants (for US only): SALMAN, Mohammad [IN/US]; 12 Jackson Avenue, Princeton, NJ 08540 (US). SHARMA, Somesh [IN/IN]; 76 Pragati Apartments, Pashim Vihar, New Delhi, Delhi 110063 (IN). YADAV, Gyan, Chand [IN/IN]; KA-24, Ground Floor, Ghaziabad, Uttar Pradesh 201010 (IN). KAPKOTI, Gobind Singh [IN/IN]; Lamgara, Almora, Uttaranchal 263670 (IN). MISHRA, Anurag [IN/IN]; WZ/43, Channamal Park, Rampura Bus-Stop, Punjabi Bagh, Delhi 110 026 (IN). GUPTA, Praful [IN/IN]; 119 Mahaveer Colony, Jain Bag, Saharanpur 247001, Uttar Pradesh (IN). ANAND, Nitya [IN/IN]; B-62 Nirala Nagar, Lucknow, Uttar Pradesh 226007 (IN). CHUGH, Anita [IN/IN]; RA-36, Inderpuri, New Delhi, Delhi 110012 (IN). NANDA, Kamna [IN/IN]; A-4/46, Moti Nagar, New Delhi, Delhi 110015 (IN).

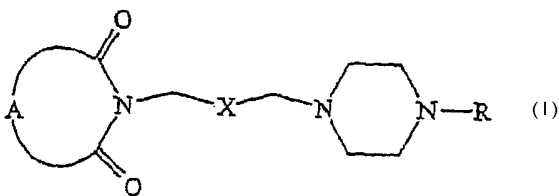
Published:

- 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

(88) Date of publication of the international search report:
1 June 2006

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.

(54) Title: ARYLPIPERAZINE DERIVATIVES AS ADRENERGIC RECEPTOR ANTAGONISTS



(57) Abstract: The present invention relates to α_{1a} and/or α_{1d} adrenergic receptor antagonists of formula (I), which can function as α_{1a} and/or α_{1d} adrenergic receptor antagonist and can be used for the treatment of a disease or disorder mediated through α_{1a} and/or α_{1d} adrenergic receptor. Compounds disclosed herein can be used for the treatment of benign prostatic hyperplasia (BPH) and the related symptoms thereof. Further, compounds disclosed herein can be used for the treatment of lower urinary

tract symptoms associated with or without BPH. Also provided are processes for preparing such compounds, pharmaceutical compositions thereof, and the methods of treating BPH or related symptoms thereof.

WO 2005/118537 A3

INTERNATIONAL SEARCH REPORT

 National application No
 PCT/IB2005/001534

A. CLASSIFICATION OF SUBJECT MATTER
 INV. A61K31/496 C07D211/88 A61P13/08

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED
 Minimum documentation searched (classification system followed by classification symbols)
 C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, CHEM ABS Data, BEILSTEIN Data, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|-----------|--|-----------------------|
| X | WO 00/05205 A (RANBAXY LABORATORIES LIMITED; ANAND, NITYA; SINHA, NEELIMA; JAIN, SANJ) 3 February 2000 (2000-02-03) compounds with rn:255861-56-4; 255861-57-5; 255861-64-4; 255861-65-5; 255861-66-6; 255861-67-7; 255861-68-8; 255861-69-9; 255861-70-2; 255861-71-3; 255861-72-4; 255861-73-5; 255861-82-6; 255861-83-7; compounds with rn: 255861-84-8; 255861-85-9; 255861-86-0; 255861-87-1; 255861-88-2; 255861-89-3; 255861-90-6; 255861-91-7; 255861-92-8; 255861-93-9 page 27 - page 33; claims compounds with rn: 255861-74-6, 255861-94-0 ----- -/-- | 1-13 |

 Further documents are listed in the continuation of Box C.

 See patent family annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

& document member of the same patent family

Date of the actual completion of the international search

14 March 2006

Date of mailing of the international search report

31 03. 2006

 Name and mailing address of the ISA/
 European Patent Office, P.B. 5616 Patentlaan 2
 NL - 2280 HV Rijswijk
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
 Fax: (+31-70) 340-3016

Authorized officer

Gavriliiu, D

INTERNATIONAL SEARCH REPORT

 International application No
 PCT/IB2005/001534

| C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT | | |
|--|--|--------------------------|
| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
| X | WO 03/084928 A (RANBAXY LABORATORIES LIMITED; SALMAN, MOHAMMAD; YADAV, GYAN, CHAND; SH) 16 October 2003 (2003-10-16) compounds with rn: 614746-62-2; 614746-63-3; 614746-73-5; 614746-74-6; 614746-75-7; 614746-86-0; 614746-88-2; 614746-89-3; 614747-06-7; 614747-07-8; page 40 - page 45; claims compounds with rn: 614746-82-6, 614746-53-1, 614746-83-7, 614746-84-8, 614746-85-9, 614746-87-1, 614747-15-6 compound with: 614747-29-4 ----- | 1-13 |
| X | FR 2 167 355 A (SYNTHELABO,FR) 24 August 1973 (1973-08-24) compounds with rn: 50845-98-2; 50845-99-3; 50845-98-2; 50846-04-3; 50845-05-4; 50845-07-6; page 7, line 29 - page 10, line 22; claims ----- | 1-13 |
| X | DATABASE CA [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; SAMANT, S. D. ET AL: "Synthesis and pharmacology of 1-(4-aryl-1-piperazinylalkyl)-4-(4- methoxyphenyl)piperidine-2,6-diones: tranquilizers" XP002355328 retrieved from STN Database accession no: 1981:550591 compounds with rn: 79323-01-6; 79323-02-7; 79323-03-8; 79323-04-9; 79323-05-9; 79323-05-0; 79323-06-1; 79323-07-2; abstract & JOURNAL OF THE INDIAN CHEMICAL SOCIETY , 58(7), 692-4 CODEN: JICSAH; ISSN: 0019-4522, 1981, ----- | 1-13 |
| X | US 4 479 954 A (HIROSE ET AL) 30 October 1984 (1984-10-30) ----- compounds with rn: 84916-63-2, 84916-93-8, 84916-65-4, 84916-75-6, 84916-77-8, 84916-84-7, 84916-86-9, 84916-85-8, 84916-95-0, 84917-09-9, 84916-65-4, 84916-78-9, 84917-09-9 column 13, line 15 - column 15, line 25; claims compounds with rn: 84916-69-8, 84916-80-3, 84917-11-3 compounds with rn: 84916-67-6, 84917-08-8 ----- -/-- | 1-13, 15-20, 24-29 |

INTERNATIONAL SEARCH REPORT

In International application No
 PCT/IB2005/001534

| C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT | | |
|--|--|---|
| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
| X | <p>EP 0 111 226 A (EISAI CO., LTD) 20 June 1984 (1984-06-20)</p> <p>compounds with rn: 92993-77-6, 92993-15-2, 92993-16-3, 92993-28-7, 92993-31-2, 92993-72-1, 92993-76-5, page 3, line 21 - page 8, line 12; claims compounds with rn: 84916-69-8, 92993-25-4, 92993-65-2, 92993-70-9</p> | <p>1-13, 15-20, 24-29</p> |
| X | <p>WO 02/44151 A (RANBAXY LABORATORIES LIMITED; ANAND, NITYA; JAIN, SANJAY; SINHA, NEELI) 6 June 2002 (2002-06-06) the whole document</p> | <p>1-13, 15-20, 24-29</p> |
| X | <p>US 5 932 584 A (CHERN ET AL) 3 August 1999 (1999-08-03) compounds with rn: 180959-06-2, 180959-07-3 column 5, line 45 - column 6, line 22 compounds with rn: 84916-69-8, 92993-65-2, 92993-25-4,</p> | <p>1-13</p> |
| X | <p>CHERN J-W ET AL: "Studies on Quinazolines IX: Fluorination versus 1,2-Migration in the Reaction of 1,3-Bifunctionalized amino-2-propanol with DAST" TETRAHEDRON LETTERS, ELSEVIER, AMSTERDAM, NL, vol. 39, no. 46, 12 November 1998 (1998-11-12), pages 8483-8486, XPO04139449 ISSN: 0040-4039 compounds with rn: 217170-69-9, 217170-73-5</p> | <p>1-13</p> |
| X | <p>US 5 663 173 A (JEGHAM ET AL) 2 September 1997 (1997-09-02) compound with rn: 186348-45-8 column 10, line 50 - column 13, line 25; claims</p> | <p>1-13</p> |
| | -/-- | |

INTERNATIONAL SEARCH REPORT

 II
 onal application No
 PCT/IB2005/001534

| C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT | | |
|--|--|-----------------------|
| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
| X | DATABASE CA [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; KHADIKAR, B. M. ET AL: "Synthesis and pharmacology of 2-[3-(4-aryl-1-piperazinyl)-2- hydroxypropyl/3-oxopropyl/propoxy]-1H-iso- ndole-1,3(2H)-diones" XP002371915 retrieved from STN Database accession no. 1994:270316 compounds with rn: 71484-33-8, 71484-35-0, 71484-37-2, 154501-26-5, 154501-27-6, 154501-28-7; 154501-29-8 abstract & INDIAN JOURNAL OF CHEMISTRY, SECTION B: ORGANIC CHEMISTRY INCLUDING MEDICINAL CHEMISTRY, 32B(11), 1137-42 CODEN: IJSBDB; ISSN: 0376-4699, 1993, ----- | 1-13 |
| X | US 5 244 901 A (GEORGE ET AL) 14 September 1993 (1993-09-14) compounds with rn: 148857-38-9, 148857-46-9, 148857-48-1. column 10, line 50 - column 11, line 55 ----- | 1-13 |
| X | US 4 818 756 A (SEIDEL ET AL) 4 April 1989 (1989-04-04) compound with rn: 95847-81-7 column 28, line 23 - column 32, line 45 ----- | 1-13 |
| A | WO 98/51298 A (ORTHO-MCNEIL PHARMACEUTICAL INC) 19 November 1998 (1998-11-19) table b claims ----- | 1-13 |
| X | DATABASE CA CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; ICHIKAWA, KAICHIRO: "Reactions of aliphatic amines with epoxypropane derivatives and their products. III" XP002371916 Database accession no. 1964:454851 compound with rn: 96070-60-9 abstract & ICHIKAWA KAICHIRO: "Reactions of aliphatic amines with epoxypropane derivatives and their products. III" JUKI GOSEI KAGAKU KYOKAISHI, vol. 22, no. 8, 1964, pages 649-653, CODEN: YGKKAE ; ISSN: 0037-9980 ----- -/-- | 1-13 |

INTERNATIONAL SEARCH REPORT

 International application No
 PCT/IB2005/001534

| C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT | | |
|--|--|-----------------------|
| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
| X | DATABASE CA CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; ZAJDEL, PAWEL ET AL.: "Preliminary study on application of impregnated synthetic peptide TLC stationary phases for the pre-screening of 5HT1A ligands" XP002371917 retrieved from STN Database accession no. 2003:624903 compounds with rn: 650616-98-1, 650616-99-2, 650617-00-8, 650617-01-9, 650617-02-0, 650617-03-1 abstract & ZAJDEL, PAWEL ET AL.: "Preliminary study on application of impregnated synthetic peptide TLC stationary phases for the pre-screening of 5HT1A ligands" BIOMEDICAL CHROMATOGRAPHY, vol. 17, no. 5, 2003, pages 312-317, CODEN: BICHE2; ISSN: 0269-3879 ----- | 1-29 |
| X | DATABASE CA CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; PAWLOWSKI, MACIEJ ET AL.: "Synthesis, 5-HT1A and 5-HT2A receptor affinity of new 1-phenylpiperazinypropyl derivatives of purine-2,6 and pyrrolidine-2,5-diones" XP002371918 retrieved from STN Database accession no. 2000:779927 compounds with rn: 315663-18-4, 315663-19-5, 315663-20-8, 315663-21-9, 315663-22-0, 315663-23-1 abstract & PAWLOWSKI, MACIEJ ET AL.: "Synthesis, 5-HT1A and 5-HT2A receptor affinity of new 1-phenylpiperazinypropyl derivatives of purine-2,6 and pyrrolidine-2,5-diones" FARMACO, vol. 55, no. 6-7, 2000, pages 461-468, CODEN: FRMCE8; ISSN: 0014-827X ----- -/-- | 1-29 |

INTERNATIONAL SEARCH REPORT

 International application No
 PCT/IB2005/001534

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|-----------|---|-----------------------|
| X | DATABASE CA CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; OBNISKA, JOLANTA ET AL.: "Synthesis and anticonvulsant properties of new N.piperazinylalkyl imides of succinic acid" XP002371919 retrieved from STN Database accession no. 1998:616973 compounds with rn: 216143-74-7, 216143-81-6, 216143-89-4 abstract & OBNISKA, JOLANTA ET AL.: "Synthesis and anticonvulsant properties of new N.piperazinylalkyl imides of succinic acid" ACTA POLONIAEPHARMACEUTICA, vol. 55, no. 3, 1998, pages 223-231, CODEN: APPHAX; ISSN: 0001-6837 ----- | 1-29 |
| X | DATABASE CA CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; KHADILKAR, B.M. ET AL.: "SYNTHESIS AND HYPOTHENSIVE ACTIVITY OF SOME SUCCINIMIDE DERIVATIVES" XP002371920 retrieved from STN Database accession no. 1993:427951 compounds with rn: 148304-47-6, 148304-48-7, 148304-49-8, 148304-50-1, 148304-51-2, 148304-52-3, 148304-53-4, 148304-54-5, 148304-55-6, 148304-56-7, 148304-57-8, 148304-58-9, 148304-59-0, 148304-60-3 abstract & KHADILKAR, B.M. ET AL.: "SYNTHESIS AND HYPOTHENSIVE ACTIVITY OF SOME SUCCINIMIDE DERIVATIVES" INDIAN JOURNAL OF CHEMISTRY, SECTION B: ORGANIC CHEMISTRY INCLUDING MEDICINAL CHEMISTRY, vol. 32B, no. 3, 1993, pages 338-342, CODEN: IJSBDB, ISSN: 0376-4699 ----- | 1-29 |
| X | NEW J S ET AL: "BUSPIRONE ANALOGUES. 2. STRUCTURE-ACTIVITY RELATIONSHIPS OF AROMATIC IMIDE DERIVATIVES" JOURNAL OF MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY. WASHINGTON, US, vol. 29, no. 8, 1986, pages 1476-1482, XP002939655 ISSN: 0022-2623 compounds with rn: 98054-89-8, 102492-98-8 ----- -/-- | 1-29 |

INTERNATIONAL SEARCH REPORT

In International application No
PCT/IB2005/001534

| C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT | | |
|--|--|-----------------------|
| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
| X | <p>DATABASE CA CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; ZEJC, ALFRED ET AL.: "N-piperazinyl and N-(3-piperazinylpropyl)imides of phenyl- and chlorophenylsuccinic acids" XP002371921 retrieved from STN Database accession no. 1985:454036 compounds with rn: 97310-22-0, 97310-23-1, 97310-24-2, 97310-25-3, 97310-27-5, 97310-29-7 abstract: & ZEJC, ALFRED ET AL.: "N-piperazinyl and N-(3-piperazinylpropyl)imides of phenyl- and chlorophenylsuccinic acids": ACTA POLONIAE PHARMACEUTICA, vol. 41, no. 5, 1984, pages 529-533, CODEN: APPHAX; ISSN: 0001-6837</p> | 1-29 |
| X | <p>JP 59 036661 A (EISAI KK) 28 February 1984 (1984-02-28) compounds with rn: 84916-67-6, 81450-50-9 abstract</p> | 1-29 |
| X | <p>GB 788 868 A (SOCIETE DES USINES CHIMIQUES RHONE-POULENC) 8 January 1958 (1958-01-08) compounds with rn: 102666-58-0, 124158-09-4</p> | 1-29 |
| X | <p>WO 03/061577 A (BIOGEN, INC; LIN, KOCHUNG; PEPINSKY, R.; BLAKE; CHEN, LING, LING; HESS) 31 July 2003 (2003-07-31) compounds with rn: 569361-48-4 claims</p> | 1-29 |
| X | <p>SALMON L ET AL: "A general approach to the synthesis of polyamine linked-monoindolylmaleimides, a new series of trypanothione reductase inhibitors" CHEMICAL AND PHARMACEUTICAL BULLETIN, PHARMACEUTICAL SOCIETY OF JAPAN, TOKYO, JP, vol. 46, no. 4, April 1998 (1998-04), pages 707-710, XP002902554 ISSN: 0009-2363 compounds with rn: 207449-33-0, 207449-34-1</p> | 1-29 |

-/--

INTERNATIONAL SEARCH REPORT

 In International application No
 PCT/IB2005/001534

| C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT | | |
|--|--|-----------------------|
| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
| X | DATABASE CA CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; MOKROSZ, JERZY L.; DUSZYNSKA, BEATA; PALUCHOWSKA, MARIA H.; CHARAKCHIEVA-MINOL, S.; MOKROSZ, MARIA J: "Structure-activity relationship studies of CNS agents. Part 22. A search for new trazodone-like antidepressants: synthesis and preliminary receptor binding studies" XP002371922 retrieved from STN Database accession no. 1995:801125 compound with rn: 171112-94-0 abstract & MOKROSZ, JERZY L.; DUSZYNSKA, BEATA; PALUCHOWSKA, MARIA H.; CHARAKCHIEVA-MINOL, S.; MOKROSZ, MARIA J.: "Structure-activity relationship studies of CNS agents. Part 22. A search for new trazodone-like antidepressants: synthesis and preliminary receptor binding studies" ARCHIV DER PHARMAZIE (WEINHEIM, GERMANY), vol. 328, no. 7-8, 1995, pages 623-625, CODEN: ARPMAS; ISSN: 0365-6233 | 1-29 |
| X | FERNANDEZ BRANA ET AL: "Synthesis, structure and cytostatic activity of a series of N-substituted 3,4-diphenyl-1H- pyrrole -2,5-diones" CHEMICAL AND PHARMACEUTICAL BULLETIN, PHARMACEUTICAL SOCIETY OF JAPAN, TOKYO, JP, vol. 37, no. 10, 1989, pages 2710-2712, XP002130577 ISSN: 0009-2363 compound with rn: 128143-38-4 | 1-29 |
| X | DATABASE CA [Online] CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; POPOV-PERGAL, KATARINA ET AL: "Synthesis of some bismaleimides and polyimides" XP002371923 retrieved from STN Database accession no. 1988:529759 compound with rn: 116421-49-9 abstract & HEMIJSKA INDUSTRIJA , 42(1), 6-9 CODEN: HMIDA8; ISSN: 0367-598X, 1988, | 1-29 |

INTERNATIONAL SEARCH REPORT

 International application No
 PCT/IB2005/001534

| C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT | | |
|--|---|-----------------------|
| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
| P,X | DATABASE CA CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; ZAJDEL, PAWEL ET AL.: "A New Classs of Arylpiperazine Derivates: the Library Synthesis on Synphase Lanterns and Biological Evaluation on Serotonin 5-HT1A and 5-HT2A Receptors" XP002371924 retrieved from STN Database accession no. 141:207170 compounds with rn: 742115-32-8, 742115-33-9, 742115-35-1, 742115-37-3, 742115-38-4, 742115-40-8, 742115-41-9, 743458-97-1, 743458-98-2 abstract: & ZAJDEL, PAWEL ET AL.: "A New Classs of Arylpiperazine Derivates: the Library Synthesis on Synphase Lanterns and Biological Evaluation on Serotonin 5-HT1A and 5-HT2A Receptors" JOURNAL OF COMBINATORIAL CHEMISTRY, vol. 6, no. 5, 2004, pages 761-767, CODEN: JCCHFF; ISSN: 1520-4766 | 1-29 |
| P,X | WO 2005/018643 A (RANBAXY LABORATORIES LIMITED; SALMAN, MOHAMMAD; YADAV, GYAN, CHAND; SH) 3 March 2005 (2005-03-03) compounds with rn: 846595-34-4; 846595-35-5; 846595-36-6; 846595-37-7; 846595-38-8; 846595-39-9; 846595-40-2; 846595-41-3; 846595-23-1claims compounds with rn: 25861-56-4; 754183-78-3; 766506-33-6; 846595-18-4; 846595-19-5; 846595-20-8; 846595-21-9; 846595-22-0; 846595-26-4; 846595-28-6; 846595-29-7; 846595-30-0; 846595-31-1; 846595-33-3; | 1-13 |
| P,X | WO 2005/037282 A (RANBAXY LABORATORIES LIMITED; ANAND, NITYA; SALMAN, MOHAMMAD; SHARMA,) 28 April 2005 (2005-04-28) the whole document | 1-29 |
| P,X | WO 2005/037281 A (RANBAXY LABORATORIES LIMITED; ANAND, NITYA; SALMAN, MOHAMMAD; SHARMA,) 28 April 2005 (2005-04-28) the whole document | 1-29 |
| E | WO 2005/092341 A (RANBAXY LABORATORIES LIMITED) 6 October 2005 (2005-10-06) compounds with rn: 764645-88-7; 866097-12-3; 866097-17-8 claims | 1-13 |

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB2005/001534

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
- No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-13(part.)

Compounds of formula (I), wherein A is a 2,6-piperidiny1 moiety, their pharmaceutical composition and their uses.

2. claims: 1-14(part.), 15-19, 20(part.), 24-29

Compounds of formula (I), wherein A is a hydrogenated 1,3-dioxo-isoindole ring, their pharmaceutical composition and their uses.

3. claims: 1-13(part.)

Compounds of formula (I), wherein A is a 1,3-dioxo-isoindole ring, their pharmaceutical compositions and their uses.

4. claims: 1-13(part.), 14-29

Compounds of formula (I), wherein A is a 2,5-pyrrolidiny1 ring(which can be further condensed), their pharmaceutical composition and their uses.

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No
PCT/IB2005/001534

| Patent document cited in search report | | Publication date | Patent family member(s) | Publication date |
|--|------------|------------------|-------------------------|------------------|
| WO 0005205 | A | 03-02-2000 | AU 763541 B2 | 24-07-2003 |
| | | | AU 4641099 A | 14-02-2000 |
| | | | BR 9912318 A | 02-05-2001 |
| | | | CA 2338317 A1 | 03-02-2000 |
| | | | EP 1097134 A1 | 09-05-2001 |
| | | | HU 0102980 A2 | 28-12-2001 |
| | | | MX PA01000637 A | 08-04-2002 |
| | | | NZ 509388 A | 19-12-2003 |
| | | | PL 345562 A1 | 17-12-2001 |
| | | | SK 932001 A3 | 06-08-2001 |
| WO 03084928 | A | 16-10-2003 | AU 2002253429 A1 | 20-10-2003 |
| | | | BR 0215685 A | 09-02-2005 |
| | | | CA 2481888 A1 | 16-10-2003 |
| | | | EP 1495000 A1 | 12-01-2005 |
| | | | JP 2005527578 T | 15-09-2005 |
| | | | US 2005228180 A1 | 13-10-2005 |
| FR 2167355 | A | 24-08-1973 | NONE | |
| US 4479954 | A | 30-10-1984 | BE 893378 A1 | 01-12-1982 |
| | | | CA 1211436 A1 | 16-09-1986 |
| | | | CH 649287 A5 | 15-05-1985 |
| | | | DE 3220262 A1 | 16-12-1982 |
| | | | DK 241982 A | 30-11-1982 |
| | | | ES 8308548 A1 | 01-12-1983 |
| | | | ES 8503343 A1 | 01-06-1985 |
| | | | ES 8601156 A1 | 16-02-1986 |
| | | | FR 2506771 A1 | 03-12-1982 |
| | | | GB 2101590 A | 19-01-1983 |
| | | | IT 1151781 B | 24-12-1986 |
| | | | JP 1603541 C | 04-04-1991 |
| | | | JP 2029671 B | 02-07-1990 |
| | | | JP 57197265 A | 03-12-1982 |
| | | | KR 8701027 B1 | 25-05-1987 |
| | | | NL 8202173 A | 16-12-1982 |
| | | | PH 19837 A | 22-07-1986 |
| | | | PH 19291 A | 04-03-1986 |
| PH 19276 A | 21-02-1986 | | | |
| PH 19272 A | 21-02-1986 | | | |
| SE 450894 B | 10-08-1987 | | | |
| SE 8203272 A | 30-11-1982 | | | |
| EP 0111226 | A | 20-06-1984 | CA 1257596 A1 | 18-07-1989 |
| | | | DE 3373652 D1 | 22-10-1987 |
| | | | JP 1720039 C | 14-12-1992 |
| | | | JP 4009782 B | 21-02-1992 |
| | | | JP 59095267 A | 01-06-1984 |
| | | | US 4567180 A | 28-01-1986 |
| WO 0244151 | A | 06-06-2002 | AU 2231502 A | 11-06-2002 |
| | | | BG 107943 A | 31-08-2004 |
| | | | BR 0115865 A | 23-12-2003 |
| | | | CA 2430343 A1 | 06-06-2002 |
| | | | CN 1486300 A | 31-03-2004 |
| | | | CZ 20031698 A3 | 12-11-2003 |
| | | | EE 200300250 A | 15-10-2003 |
| | | | EP 1339682 A1 | 03-09-2003 |

INTERNATIONAL SEARCH REPORT

information on patent family members

International application No
PCT/IB2005/001534

| Patent document cited in search report | Publication date | Patent family member(s) | Publication date | |
|--|------------------|-------------------------|------------------|------------|
| WO 0244151 | A | HU 0400545 A2 | 28-07-2004 | |
| | | JP 2004514711 T | 20-05-2004 | |
| | | MA 26064 A1 | 01-04-2004 | |
| | | MX PA03004850 A | 26-01-2004 | |
| | | NZ 526226 A | 28-05-2004 | |
| | | PL 362210 A1 | 18-10-2004 | |
| | | SK 8052003 A3 | 02-12-2003 | |
| | | US 2002156085 A1 | 24-10-2002 | |
| | | ZA 200304242 A | 02-03-2004 | |
| US 5932584 | A | 03-08-1999 | NONE | |
| US 5663173 | A | 02-09-1997 | AU 704388 B2 | 22-04-1999 |
| | | | AU 5591296 A | 02-01-1997 |
| | | | CA 2178849 A1 | 14-12-1996 |
| | | | CN 1143644 A | 26-02-1997 |
| | | | CZ 9601716 A3 | 15-01-1997 |
| | | | EP 0748807 A1 | 18-12-1996 |
| | | | FR 2735475 A1 | 20-12-1996 |
| | | | HU 9601620 A2 | 28-01-1997 |
| | | | IL 118644 A | 17-02-2000 |
| | | | JP 9118680 A | 06-05-1997 |
| | | | NO 962477 A | 16-12-1996 |
| | | | NZ 286805 A | 25-03-1998 |
| | | | PL 314745 A1 | 23-12-1996 |
| | | | SK 75296 A3 | 07-05-1997 |
| | | | ZA 9604985 A | 23-01-1997 |
| | | | US 5244901 | A |
| AU 645698 B2 | 20-01-1994 | | | |
| AU 1859092 A | 07-01-1993 | | | |
| CA 2072528 A1 | 28-12-1992 | | | |
| CN 1067884 A | 13-01-1993 | | | |
| CZ 9202002 A3 | 13-01-1993 | | | |
| DE 69208955 D1 | 18-04-1996 | | | |
| DE 69208955 T2 | 24-10-1996 | | | |
| DK 522915 T3 | 22-07-1996 | | | |
| EP 0522915 A1 | 13-01-1993 | | | |
| ES 2087477 T3 | 16-07-1996 | | | |
| FI 922983 A | 28-12-1992 | | | |
| FR 2678271 A1 | 31-12-1992 | | | |
| GR 3020055 T3 | 31-08-1996 | | | |
| HU 61996 A2 | 29-03-1993 | | | |
| IE 922093 A1 | 30-12-1992 | | | |
| JP 3160371 B2 | 25-04-2001 | | | |
| JP 5186434 A | 27-07-1993 | | | |
| MX 9203331 A1 | 01-12-1992 | | | |
| NO 922524 A | 28-12-1992 | | | |
| PL 295021 A1 | 08-03-1993 | | | |
| ZA 9204787 A | 31-03-1993 | | | |
| US 4818756 | A | 04-04-1989 | AU 569086 B2 | 21-01-1988 |
| | | | AU 2929384 A | 20-12-1984 |
| | | | CA 1300624 C | 12-05-1992 |
| | | | DE 3321969 A1 | 20-12-1984 |
| | | | DK 31092 A | 06-03-1992 |
| | | | DK 295984 A | 19-12-1984 |

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/IB2005/001534

| Patent document cited in search report | Publication date | Patent family member(s) | Publication date |
|--|------------------|-------------------------|------------------|
| | | EP 0129128 A2 | 27-12-1984 |
| US 4818756 | A | ES 8600275 A1 | 01-01-1986 |
| | | ES 8607285 A1 | 01-11-1986 |
| | | ES 8603464 A1 | 16-04-1986 |
| | | ES 8603465 A1 | 16-04-1986 |
| | | ES 8603466 A1 | 16-04-1986 |
| | | ES 8603467 A1 | 16-04-1986 |
| | | FI 842419 A | 19-12-1984 |
| | | GR 82211 A1 | 13-12-1984 |
| | | HU 34746 A2 | 28-04-1985 |
| | | IL 72120 A | 28-09-1989 |
| | | JP 1932158 C | 26-05-1995 |
| | | JP 6060165 B | 10-08-1994 |
| | | JP 60023373 A | 05-02-1985 |
| | | KR 9200761 B1 | 21-01-1992 |
| | | NZ 208529 A | 27-01-1989 |
| | | PH 22960 A | 03-02-1989 |
| | | PT 78751 A | 01-07-1984 |
| | | US 4937343 A | 26-06-1990 |
| | | US 4988809 A | 29-01-1991 |
| | | ZA 8404585 A | 27-02-1985 |
| WO 9851298 | A | 19-11-1998 | |
| | | AT 250033 T | 15-10-2003 |
| | | AU 7366998 A | 08-12-1998 |
| | | BR 9809804 A | 27-06-2000 |
| | | CA 2289987 A1 | 19-11-1998 |
| | | CN 1515556 A | 28-07-2004 |
| | | CN 1264300 A | 23-08-2000 |
| | | CN 1515563 A | 28-07-2004 |
| | | DE 69818255 D1 | 23-10-2003 |
| | | DE 69818255 T2 | 23-12-2004 |
| | | DK 984777 T3 | 08-12-2003 |
| | | EA 1904 B1 | 22-10-2001 |
| | | EP 0984777 A1 | 15-03-2000 |
| | | ES 2206928 T3 | 16-05-2004 |
| | | HK 1024630 A1 | 21-01-2004 |
| | | HU 0100048 A2 | 30-07-2001 |
| | | JP 2002511065 T | 09-04-2002 |
| | | NO 995518 A | 11-01-2000 |
| | | NZ 500992 A | 28-02-2003 |
| | | PL 342518 A1 | 18-06-2001 |
| | | PT 984777 T | 30-01-2004 |
| | | TR 9902971 T2 | 21-03-2001 |
| | | ZA 9803968 A | 11-11-1999 |
| JP 59036661 | A | 28-02-1984 | NONE |
| GB 788868 | A | 08-01-1958 | GB 802244 A |
| | | | 01-10-1958 |
| WO 03061577 | A | 31-07-2003 | |
| | | BG 108839 A | 30-04-2005 |
| | | BR 0306993 A | 06-09-2005 |
| | | CA 2473526 A1 | 31-07-2003 |
| | | CN 1630530 A | 22-06-2005 |
| | | CZ 20040877 A3 | 15-12-2004 |
| | | EE 200400105 A | 15-12-2004 |
| | | EP 1476181 A2 | 17-11-2004 |
| | | HU 0500457 A2 | 29-08-2005 |

INTERNATIONAL SEARCH REPORT
 information on patent family members

International application No
 PCT/IB2005/001534

| Patent document cited in search report | Publication date | Patent family member(s) | Publication date |
|--|------------------|-------------------------|------------------|
| | | JP 2005526151 T | 02-09-2005 |
| | | MX PA04006855 A | 19-04-2005 |
| WO 03061577 A | | SK 3102004 A3 | 03-01-2005 |
| WO 2005018643 A | 03-03-2005 | AU 2003259391 A1 | 10-03-2005 |
| WO 2005037282 A | 28-04-2005 | AU 2003278403 A1 | 05-05-2005 |
| | | WO 2005037281 A1 | 28-04-2005 |
| WO 2005037281 A | 28-04-2005 | AU 2003278403 A1 | 05-05-2005 |
| | | WO 2005037282 A1 | 28-04-2005 |
| WO 2005092341 A | 06-10-2005 | WO 2005092342 A1 | 06-10-2005 |