

(19) World Intellectual Property Organization
International Bureau(43) International Publication Date
9 March 2006 (09.03.2006)

PCT

(10) International Publication Number
WO 2006/024627 A2

(51) International Patent Classification:

A61K 31/165 (2006.01) A61P 3/10 (2006.01)
C07C 235/22 (2006.01) A61P 9/00 (2006.01)
C07D 307/85 (2006.01) A61P 19/10 (2006.01)
C07D 311/66 (2006.01) A61P 25/28 (2006.01)
C07D 319/20 (2006.01) A61P 27/06 (2006.01)
A61P 3/04 (2006.01)

(21) International Application Number:

PCT/EP2005/054197

(22) International Filing Date: 26 August 2005 (26.08.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

04104152.6 30 August 2004 (30.08.2004) EP
60/607,851 8 September 2004 (08.09.2004) 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): JAROSKOVA, Libuse [CZ/BE]; Janssen Pharmaceutica N.V., Turnhoutseweg 30, B-2340 Beerse (BE). LINDERS, Joannes, Theodorus, Maria [NL/NL]; Janssen Pharmaceutica N.V., Turnhoutseweg 30, B-2340 Beerse (BE). VAN DER VEKEN, Louis, Jozef, Elisabeth [BE/BE]; Janssen Pharmaceutica N.V., Turnhoutseweg 30, B-2340 Beerse (BE). WILLEMSSENS, Gustaaf, Henri, Maria [BE/BE]; Janssen Pharmaceutica N.V., Turnhoutseweg 30, B-2340 Beerse (BE). BISCHOFF, François Paul [FR/BE]; Janssen Pharmaceutica N.V., Turnhoutseweg 30, B-2340 Beerse (BE).

(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, 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.

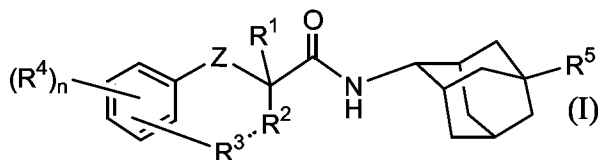
(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, 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, 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, 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, LV, MC, NL, PL, PT, RO,

[Continued on next page]

(54) Title: N-2 ADAMANTANYL-2-PHENOXY-ACETAMIDE DERIVATIVES AS 11-BETA HYDROXYSTEROID DEHYDROGENASE INHIBITORS



(57) Abstract: The N-oxide forms, the pharmaceutically acceptable addition salts and the stereochemically isomeric forms thereof, wherein n is 1, 2, 3, or 4; Z represents O, S, NR⁶, SO or SO₂; R¹ represent hydrogen, cyano, hydroxy, or C₁₋₄alkyl optionally substituted with halo, R² represents hydrogen, C₁₋₄alkyl, or C₁₋₄alkyloxy-; R³ represents hydrogen, C₁₋₄alkyl, C₁₋₄alkyloxy- or R³ combined with R² form together a divalent radical selected from the group consist-

ing of -O-CH₂- (a), -NR⁷-CH₂- (b), -(CR⁸R⁹)_m- (c) and -CR¹⁰- (d) wherein m represents 1 or 2 and R⁷, R⁸, R⁹ and R¹⁰ are each independently selected from hydrogen or C₁₋₄alkyl; R⁴ represents hydrogen, halo, hydroxy, cyano, amino, NR¹¹, C₁₋₄alkyloxy- optionally substituted with one or where possible two or three substituents selected from hydroxy and halo or R⁴ represents C₁₋₄alkyl optionally substituted with one or where possible two or three substituents selected from hydroxy and halo; R⁵ represents hydrogen, halo, cyano, amino, phenyl, hydroxy, C₁₋₄alkyloxycarbonyl, hydroxycarbonyl, NR¹³R¹⁴ or C₁₋₄alkyl substituted with one or more substituents selected from hydroxycarbonyl, phenyl, C₁₋₄alkyloxy or NR¹³R¹⁴; R⁶ represents hydrogen; R¹¹ and R¹² each independently represent hydrogen, C₁₋₄alkyl or C₁₋₄alkylcarbonyl-; R¹³ and R¹⁴ each independently represent hydrogen, C₁₋₄alkyl or C₁₋₄alkylcarbonyl-; R¹⁵ and R¹⁶ each independently represent hydrogen, C₁₋₄alkyl or C₁₋₄alkylcarbonyl-; R¹⁷ and R¹⁸ each independently represent hydrogen, C₁₋₄alkyl or C₁₋₄alkylcarbonyl-.



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*
- *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:

- *without international search report and to be republished upon receipt of that 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.