

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

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
28 July 2011 (28.07.2011)

PCT

(10) International Publication Number
WO 2011/090923 A1

(51) International Patent Classification:
A01N 47/06 (2006.01) *A61K 31/265* (2006.01)

(21) International Application Number:
PCT/US2011/021498

(22) International Filing Date:
18 January 2011 (18.01.2011)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
12/691,680 21 January 2010 (21.01.2010) US

(71) Applicant (for all designated States except US):
VALEANT PHARMACEUTICALS INTERNATIONAL-AL [US/US]; One Enterprise, Aliso Viejo, CA 92656 (US).

(72) Inventor; and

(75) Inventor/Applicant (for US only): **NADJSOMBATI, Biljana** [US/US]; One Enterprise, Aliso Viejo, CA 92656 (US).

(74) Agents: **BEHAR, Victor** et al.; Jones Day, 222 East 41st Street, New York, NY 10017-6702 (US).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

— with international search report (Art. 21(3))

(54) Title: MODIFIED RELEASE FORMULATION AND METHODS OF USE

(57) Abstract: A modified release pharmaceutical formulation includes about 30-70% N-(2-amino-4- (fluorobenzylamino)-phenyl) carbamic acid ethyl ester (retigabine), or a pharmaceutically acceptable salt, solvate or hydrate thereof, about 5-30% of a drug delivery matrix including hydroxypropylmethylcellulose (HPMC), and an enteric polymer. The pharmaceutical formulation produces a sustained plasma concentration of retigabine following administration to a subject for 4- 20 hours longer than the time required for in vitro release of 80% of retigabine. The plasma concentration vs. time profile of this formulation is substantially flat over an extended period lasting for about 4 hours to about 36 hours. A method of treating a disorder characterized by nervous system hyperexcitability includes administering to a subject an effective amount of these pharmaceutical formulations.



WO 2011/090923 A1