PCT WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 7 :
A61K 31/505, A61P 3/10, C07D 241/44, 498/04, 401/14, 239/42, 451/02, 451/14, 471/04, 491/10, 487/08, 409/12, 405/12, 491/04, 401/04, 417/12, 409/14, 487/04, 513/10, 417/14 // (C07D 498/04, 213:00, 263:00) (C07D 471/04, 221:00, 231:00) (C07D 491/10, 221:00, 311:00) (C07D 471/04, 221:00, 239:00) (C07D 487/08, 209:00, 209:00) (C07D 491/04, 221:00, 307:00), 487:04) (C07D 241/00, 251:00)

A1

(11) International Publication Number: **WO 00/59510**

(43) International Publication Date: 12 October 2000 (12.10.00)

(21) International Application Number: PCT/IB00/00296

(22) International Filing Date: 16 March 2000 (16.03.00)

(30) Priority Data:
60/127,437 1 April 1999 (01.04.99) US

(71) Applicant *(for all designated States except US)*: PFIZER PRODUCTS INC. [US/US]; Eastern Point Road, Groton, CT 06340 (US).

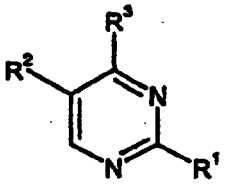
(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: CHU-MOYER, Margaret, Yuhua [US/US]; Pfizer Inc., Central Research Division, Eastern Point Road, Groton, CT 06340 (US). MURRY, Jerry, Anthony [US/US]; Pfizer Inc., Central Research Division, Eastern Point Road, Groton, CT 06340 (US). MYLARI, Banavara, Lakshman [US/US]; Pfizer Inc., Central Research Division, Eastern Point Road, Groton, CT 06340 (US). ZEMBROWSKI, William, James [US/US]; Pfizer Inc., Central Research Division, Eastern Point Road, Groton, CT 06340 (US).

(74) Agents: SPIEGEL, Allen, J. et al.; Simpson, Alison, Urquhart-Dykes & Lord, 91 Wimpole Street, London W1M 8AH (GB).

(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, 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, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published
With international search report.

(54) Title: AMINOPYRIMIDINES AS SORBITOL DEHYDROGENASE INHIBITORS



(I)

(57) Abstract

This invention is directed to sorbitol dehydrogenase inhibitory compounds of formula (I), wherein R^1, R^2 and R^3 are as defined in the specification. This invention is also directed to pharmaceutical compositions containing those compounds and methods of treating or preventing diabetic complications, particularly diabetic neuropathy, diabetic nephropathy, diabetic microangiopathy, diabetic macroangiopathy and diabetic cardiomyopathy by administering such compounds to a mammal suffering from diabetes and therefor at risk for developing such complications. This invention is also directed to pharmaceutical compositions comprising a combination of a compound of formula (I) of this invention with an aldose reductase inhibitor and to methods of treating or preventing diabetic complications therewith. This invention is also directed to pharmaceutical compositions comprising a combination of a compound of formula (I) of this invention with an NHE-1 inhibitor and to methods of treating cardiomyopathy and other heart-related problems therewith. This invention is also directed to certain intermediates used in the synthesis of the compounds of formula (I) and to processes for preparing those intermediates.