20000615 3-1

**PCT** WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 :
A61K 31/165, C07C 317/40, 317/44, 323/65, C07D 213/89, 295/08

A1

(11) International Publication Number: WO 99/62506

(43) International Publication Date: 9 December 1999 (09.12.99)

(21) International Application Number: PCT/GB99/01669

(22) International Filing Date: 26 May 1999 (26.05.99)

(30) Priority Data:
9811427.5 29 May 1998 (29.05.98) GB

(71) Applicant *(for all designated States except US)*: ZENECA LIMITED [GB/GB]; 15 Stanhope Gate, London W1Y 6LN (GB).

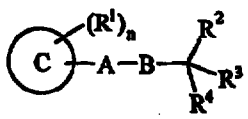
(72) Inventors; and
(75) Inventors/Applicants *(for US only)*: BUTLIN, Roger, John [GB/GB]; Mereside, Alderley Park, Macclesfield, Cheshire SK10 4TG (GB). NOWAK, Thorsten [DE/GB]; Mereside, Alderley Park, Macclesfield, Cheshire SK10 4TG (GB). BURROWS, Jeremy, Nicholas [GB/GB]; Mereside, Alderley Park, Macclesfield, Cheshire SK10 4TG (GB). BLOCK, Michael, Howard [GB/GB]; Mereside, Alderley Park, Macclesfield, Cheshire SK10 4TG (GB).

(74) Agent: BILL, Kevin; ZENECA Pharmaceuticals, Intellectual Property Dept., Mereside, Alderley Park, Macclesfield, Cheshire SK10 4TG (GB).

(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, 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: USE OF COMPOUNDS FOR THE ELEVATION OF PYRUVATE DEHYDROGENASE ACTIVITY




(I)

(57) Abstract

The use of compounds of formula (I), and salts thereof; and pharmaceutically acceptable *in vivo* cleavable prodrugs of said compound of formula (I); and pharmaceutically acceptable salts of said compound or said prodrugs; in formula (I), Ring C is phenyl or a carbon linked heteroaryl ring substituted as defined within; $R^1$ is an ortho substituent as defined within; n is 1 or 2; A–B is a linking group as defined within; $R^2$ and $R^3$ are as defined within; $R^4$ is hydroxy, hydrogen, halo, amino or methyl; in the manufacture of a medicament for use in the elevation of PDH activity in warm–blooded animals such as humans is described. Pharmaceutical compositions, methods and processes for preparation of compounds of formula (I) are also described.