22 April 2003

PCT

WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 7 :
C07D 217/22, 401/12, A61K 31/47, C07D 237/34, 239/94

A1

(11) International Publication Number: WO 00/24718

(43) International Publication Date: 4 May 2000 (04.05.00)

(21) International Application Number: PCT/EP99/07928

(22) International Filing Date: 19 October 1999 (19.10.99)

(30) Priority Data:
98203559.4 23 October 1998 (23.10.98) EP

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(81) Designated States: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, 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.

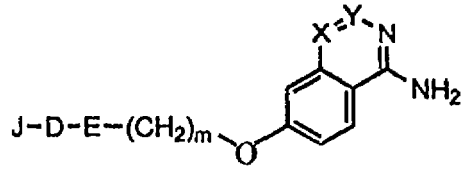


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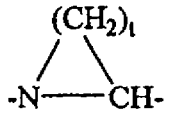
(54) Title: SERINE PROTEASE INHIBITOR

(57) Abstract

The invention relates to a serine protease inhibitor having formula (I), in which J is H, R^1, R^1-O-C(O)-, R^1-C(O)-, R^1-SO_2-, R^3OOC-$(CHR^2)_p$-, (R^{2a}, R^{2b})N-CO-$(CHR^2)_p$- or Het-CO-$(CHR^2)_p$-; D is an amino-acid of the formula -NH-CHR^1-C(O)-, -NR^4-CH[$(CH_2)_q$C(O)OR^1]-C(O)-, -NR^4-CH[$(CH_2)_q$C(O)N(R^{2a},R^{2b})]-C(O)-, -NR^4-CH[$(CH_2)_q$C(O)Het]-C(O)-, D-1-Tiq, D-3-Tiq, D-Atc, Aic, D-1-Piq or D 3-Piq; E is -NR^2-CH_2 or the fragment (a), optionally substituted with (1-6C)alkyl, (1-6C)alkoxy or benzyloxy; R^1 is selected from (1-12C)alkyl, (2-12C)alkenyl, (2-12C)alkynyl, (3-12C)cycloalkyl and (3-12C)cycloalkyl(1-6C)alkylene, which groups may optionally be substituted with (3-12C)cycloalkyl, (1-6C)alkoxy, oxo, OH, CF_3 or halogen, and from (6-14C)aryl, (7-15C)aralkyl, (8-16C)aralkenyl and (14-20C)(bisaryl)alkyl, whereby the aryl groups may optionally be substituted with (1-6C)alkyl, (3-12C)cycloalkyl, (1-6C)alkoxy, OH, CF_3 or halogen; R^2, R^{2a} and R^{2b} are each independently selected from H, (1-8C)alkyl, (3-8C)alkenyl, (3-8C)alkynyl, (3-8C)cycloalkyl and (3-6C)cycloalkyl(1-4C)alkylene, which can each be optionally substituted with (3-6C)cycloalkyl, (1-6C)alkoxy, CF_3 or halogen, and from (6-14C)aryl and (7-15C)aralkyl whereby the aryl groups may optionally be substituted with (1-6C)alkyl, (3-6C)cycloalkyl, (1-6C)alkoxy, CF_3 or halogen; R^3 is defined for R^2 or Het-(1-6C)alkyl; R^4 is H or (1-3C)alkyl; X and Y are CH or N with the proviso that they are not both N; Het is a 4-, 5- or 6-membered heterocycle containing one or more heteroatoms selected from O, N and S; m is 1 or 2; p is 1, 2 or 3; q is 1, 2 or 3; t is 2, 3 or 4; or a prodrug; or a pharmaceutically acceptable addition salt and/or solvate thereof and its use in therapy and manufacture of a medicament for treating or preventing thrombin-mediated and thrombin-associated diseases.



(I)



(a)



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