

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
27 January 2005 (27.01.2005)

PCT

(10) International Publication Number
WO 2005/007620 A3

(51) International Patent Classification⁷: A61K 31/42,
C07D 231/12

PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM,
ZW.

(21) International Application Number:
PCT/HU2004/000077

(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, IT, LU, 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).

(22) International Filing Date: 16 July 2004 (16.07.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
P 0302219 16 July 2003 (16.07.2003) HU

Declaration 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, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,
MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM,
PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, 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,
IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI patent
(BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
SN, TD, TG)

(71) Applicant (for all designated States except US):
RICHTER GEDEON VEGYÉSZETI GYÁR RT.
[HU/HU]; Gyömrői út 19-21, H-1103 Budapest (HU).

(72) Inventors; and

(75) Inventors/Applicants (for US only): FISCHER, János
[HU/HU]; Úri u. 33, H-1014 Budapest (HU). FODOR,
Tamás [HU/HU]; Andrásy út 3, H-1061 Budapest (HU).
KÁRPÁTI, Egon [HU/HU]; Tövis u. 7/D, H-1022
Budapest (HU). KIS-VARGA, Istvánné [HU/HU]; Május
1 út 1, H-2366 Kakucs (HU). LÉVAL, Sándor [HU/HU];
Ipar u. 20, H-2051 Biatorbágy (HU). ERDÉLYI, Péter
[HU/HU]; Medveszőlő u. 5, H-1103 Budapest (HU).
ZÁJERNÉ BALÁZS, Mária [HU/HU]; Csombor u. 6/1,
H-1103 Budapest (HU). GERE, Anikó [HU/HU]; Egy
József u. 40, H-1111 Budapest (HU).

(74) Common Representative: RICHTER GEDEON VEG-
YÉSZETI GYÁR RT.; Gyömrői út 19-21, H-1103 Bu-
dapest (HU).

Published:

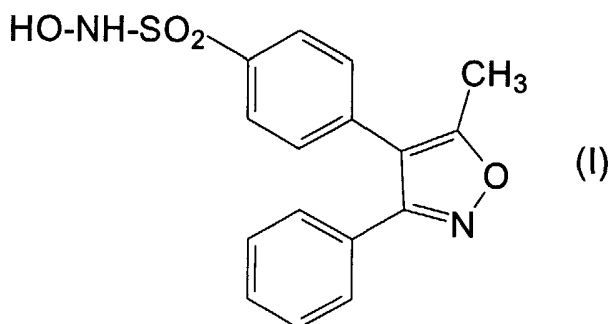
— with international search report
— before the expiration of the time limit for amending the
claims and to be republished in the event of receipt of
amendments

(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, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,
MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG,

(88) Date of publication of the international search report:
10 March 2005

For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: NEW N-HYDROXY-4-(3-PHENYL-5-METHYL-ISOXAZOLE-4-YL)-BENZENESULFONAMIDE SOLVATES



(57) Abstract: The invention relates to new
N-hydroxy-4-(3-phenyl-5-methyl-isoxazole-4-yl)-benzene-
sulfonamide solvates of formula (I), wherein n represents
0 or 1 mol, [solvate] represents water, C₁-C₄ alcohol,
C₁-C₄ alkylester of C₁-C₃ carboxylic acid or dioxane, and
the mixture of solvated (wherein n=1) and solvat-free
forms (wherein n=0). Furthermore, the invention relates
their process for production and use for the treatment of
osteoarthritis and rheumatoid arthritis and surgical and
primary dysmenorrheal pains, based on anti-inflammatory
and analgesic pharmacological model experiments.



WO 2005/007620 A3

INTERNATIONAL SEARCH REPORT

International Application No
PCT/HU2004/000077

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K31/42 C07D231/12

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K C07D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, BEILSTEIN Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	JOSH J. YUAN ET AL.: "Disposition of a specific cyclooxygenase-2 inhibitor, valdecoxib, in human" DRUG METABOLISM AND DISPOSITION, vol. 30, no. 9, 2002, pages 1013-1021, XP002311618 cited in the application abstract; figure 5	1,2,6,7
Y	page 1018, column 2, paragraph 2 ----- -/--	1-7, 14-21

Further documents are listed in the continuation of box C. Patent family members are listed in annex.

° Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed
- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- * & * document member of the same patent family

Date of the actual completion of the international search 21 December 2004	Date of mailing of the international search report 20/01/2005
---	--

Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer Molina de Alba, J
--	---

INTERNATIONAL SEARCH REPORT

International Application No
PCT/HU2004/000077

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	<p>JOHN J. TALLEY ET AL.: "4-'5-Methyl-3-phenylisoxazol-4-yl!-benzen esulfonamide, Valdecoxib: A potent and selective inhibitor of COX-2" J.MED.CHEM., vol. 43, 2000, pages 775-777, XP002311619 page 776, column 2, paragraph 2 - paragraph 3; compounds 2,3</p>	1-21
Y	<p>HERBERT T. NAGASAWA ET AL.: "Carbethoxylating agents as inhibitors of aldehyde dehydrogenase" J.MED.CHEM., vol. 38, 1995, pages 1872-1876, XP002311620 page 1875, column 1, last paragraph</p>	8-13
Y	<p>MAURICE L. MOORE ET AL.: "Substituted sulfanilamides. III. N4-Acyl-N1-hydroxy derivatives" J.AM.CHEM.SOC., vol. 62, 1940, pages 2097-2099, XP002311621 page 2098, column 1, paragraph 2 - paragraph 3</p>	8-13
A	<p>JI Y. ZHANG ET AL.: "Pharmacokinetics and metabolism of a COX-2 inhibitor, valdecoxib, in mice" DRUG METABOLISME AND DISPOSITION, vol. 31, no. 4, April 2003 (2003-04), pages 491-501, XP002311622 page 501, column 1, last paragraph - column 2, paragraph 1; figure 8</p>	1-21
A	<p>DATABASE CAPLUS 'Online! CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; SARAPA, NENAD ET AL: "Valdecoxib, a COX-2-specific inhibitor, does not affect cardiac repolarization" XP002311623 retrieved from STN Database accession no. 2003:753917 abstract & JOURNAL OF CLINICAL PHARMACOLOGY , 43(9), 974-982 CODEN: JCPCBR; ISSN: 0091-2700, 2003,</p>	14-21