

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
24 February 2005 (24.02.2005)

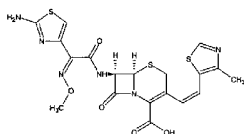
PCT

(10) International Publication Number
WO 2005/016936 A3

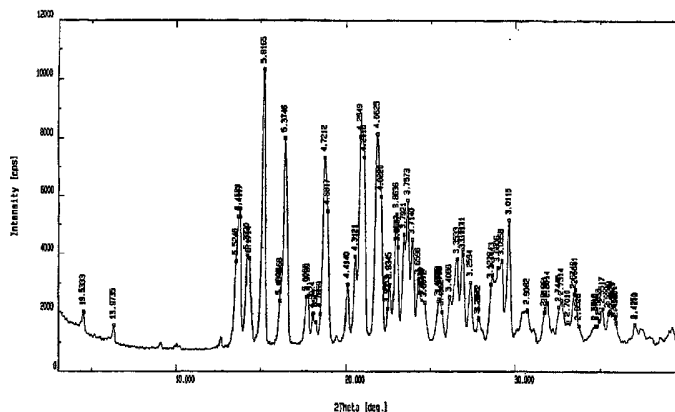
- (51) International Patent Classification⁷: **C07D 501/00**,
A61K 31/545
- (21) International Application Number:
PCT/IB2004/002648
- (22) International Filing Date: 13 August 2004 (13.08.2004)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
1004/DEL/2003 14 August 2003 (14.08.2003) IN
- (72) Inventors; and
(75) Inventors/Applicants (for US only): **KUMAR, Yatendra**
[IN/IN]; U-26/5, Phase - III, DLF Qutab Enclave, Gur-
gaon, Haryana 122001 (IN). **SINGH, Kaptan** [IN/IN];
Flat No. B-02, Saket Enclave, Rajendra Nagar, Sahibabad,
Ghaziabad, Uttar Pradesh 201005 (IN). **PRASAD, Ashok**
[IN/IN]; 147/9, Dr. Gupta's Flats, Kishangarh, Vasant
Kunj, New Delhi, Delhi 110070 (IN). **RICHHARIYA,**
Santosh [IN/IN]; House No. 26, Ganesh Ward, Bina
District, Sagar, Madhya Pradesh 470002 (IN).
- (74) Common Representative: **RANBAXY LABORATO-**
RIES LIMITED; c/o DESHMUKH, Jay, R., 600 College
Road East, Suite 2100, Princeton, NJ 08540 (US).
- (71) Applicant (for all designated States except US): **RAN-**
BAXY LABORATORIES LIMITED [IN/IN]; 19, Nehru
Place, New Delhi, Delhi 110019 (IN).
- (71) Applicant and
(72) Inventor: **PRASAD, Mohan** [IN/IN]; House No. P-3/3,
Phase - II, DLF Qutab Enclave, Gurgaon, Haryana 122001
(IN).
- (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,
PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,

[Continued on next page]

(54) Title: PROCESS FOR SELECTIVE PREPARATION OF Z-ISOMER OF CEFDITOREN AND PHARMACEUTICALLY AC-
CEPTABLE SALTS AND ESTERS THEREOF



(I)



(57) Abstract: The present invention relates to a selective process for preparation of Z-isomer of cefditoren of Formula I and phar-
maceutically acceptable salts and esters thereof. cefditoren possesses a wide spectrum of antibacterial activity against Gram-positive
and Gram-negative bacteria.



TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(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).

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*

(88) Date of publication of the international search report:

11 August 2005

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

INTERNATIONAL SEARCH REPORT

International Application No

PCT/IB2004/002648

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D501/00 A61K31/545

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 C07D A61K

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, BEILSTEIN Data, WPI Data, PAJ, 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	US 4 839 350 A (ATSUMI KUNIO ET AL) 13 June 1989 (1989-06-13) the whole document	1-31, 34
X	column 24; example 18	16-21
A	Reference Example 1	32, 33
X	EP 0 658 558 A (BIOCHEMIE GMBH) 21 June 1995 (1995-06-21) the whole document	1-15, 22-31, 34, 37, 38
P, A	WO 03/091230 A (DESHPANDE PANDURANG BALWANT ; KAMMA RAMAKRISHNA (IN); LUTHRA PARVEN KU) 6 November 2003 (2003-11-06) - the whole document	1-15, 22-34
	-/--	

☒ 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

15 June 2005

Date of mailing of the international search report

24. 06. 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

Deutsch, W

INTERNATIONAL SEARCH REPORT

International Application No

PCT/IB2004/002648

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP 1 016 665 A (MEIJI SEIKA KAISHA) 5 July 2000 (2000-07-05) the whole document	1-15, 22-31, 34
X	page 4, reaction scheme and paragraph '0008!	32, 33
X	US 4 918 068 A (YAMAMOTO ET AL) 17 April 1990 (1990-04-17) example 4	16-21
A	EP 0 597 429 A (BIOCHEMIE GESELLSCHAFT M.B.H) 18 May 1994 (1994-05-18) the whole document	32, 33
X	SAKAGAMI K ET AL: "SYNTHESIS AND ORAL ACTIVITY OF PIVALOYL OXYMETHYL 7-Ä(Z)-2-(2-AMINOTHIA ZOL-4-YL)-2-METHOXYIMINOACETAMIDOÜ-3-(Z)-(4-METHYLTHIAZOL-5-YL)VINYL- 3-CEPHEM-4-CARBOXYLATE (ME1207) AND ITS RELATED COMPOUND" CHEMICAL AND PHARMACEUTICAL BULLETIN, PHARMACEUTICAL SOCIETY OF JAPAN, TOKYO, JP, vol. 39, no. 9, September 1991 (1991-09), pages 2433-2436, XP009042230 ISSN: 0009-2363 the whole document	32, 33, 35, 36
A	EP 0 723 965 A (MEIJI SEIKA KAISHA LTD; MEIJI SEIKA KAISHA, LTD) 31 July 1996 (1996-07-31) the whole document	32, 33
X	page 7, line 35, ME1206 (sodium salt)	16-23
X	US 2002/002279 A1 (YASUI KIYOSHI ET AL) 3 January 2002 (2002-01-03) the whole document	35, 36
X	KENJI SAKAGAMI ET AL.: "Synthesis and Oral Activity of ME1207, a New Orally Active Cephalosporin" THE JOURNAL OF ANTIBIOTICS, vol. XLIII, no. 8, 1990, pages 1047-1050, XP009049100 the whole document	32, 33, 35, 36
X	US 5 233 035 A (HARA ET AL) 3 August 1993 (1993-08-03) example 38	32, 33

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB2004/002648

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☒ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☒ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-15,22-31,34

Claims 1-15:

Subject matter relating to the preparation of cefditoren,
pharmaceutically acceptable salts or ester thereof

2. claims: 16-21

Subject matter relating to a crystalline hydrates of
ceftidoren sodium and crystalline hydrate of ceftidoren
potassium

3. claims: 32-33

Process for the preparation of 7-ATCA (formula IX)

4. claims: Claims 35-38

Subject matter relating to Z-isomers of cefditoren pivoxil
and the Z isomer of 7-ATCA

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/IB2004/002648

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
US 4839350	A	13-06-1989	JP 62019593 A	28-01-1987
			JP 1698887 C	28-09-1992
			JP 3064503 B	07-10-1991
			JP 61178991 A	11-08-1986
			AT 56017 T	15-09-1990
			CA 1272714 A1	14-08-1990
			CN 85106733 A ,C	14-01-1987
			DE 3579399 D1	04-10-1990
			EP 0175610 A2	26-03-1986
			ES 8704955 A1	01-07-1987
			IE 58487 B1	22-09-1993
			KR 8901196 B1	27-04-1989
EP 0658558	A	21-06-1995	AT 400844 B	25-03-1996
			AT 400843 B	25-03-1996
			AT 233093 A	15-08-1995
			AT 198892 T	15-02-2001
			CN 1107850 A ,C	06-09-1995
			CN 1248581 A	29-03-2000
			DE 69427312 D1	28-06-2001
			DE 69427312 T2	23-08-2001
			DK 658558 T3	17-04-2001
			EP 0658558 A1	21-06-1995
			ES 2155839 T3	01-06-2001
			GR 3035535 T3	29-06-2001
			JP 7188250 A	25-07-1995
			PT 658558 T	29-06-2001
			SI 658558 T1	31-08-2001
			US 5616703 A	01-04-1997
			US 2001016581 A1	23-08-2001
			US 6235897 B1	22-05-2001
			AT 232993 A	15-08-1995
WO 03091230	A	06-11-2003	WO 03091230 A1	06-11-2003
EP 1016665	A	05-07-2000	AT 221890 T	15-08-2002
			AU 731265 B2	29-03-2001
			AU 7933198 A	04-01-1999
			BR 9810313 A	19-09-2000
			CA 2294178 A1	30-12-1998
			DE 69807093 D1	12-09-2002
			DE 69807093 T2	27-03-2003
			EA 2449 B1	25-04-2002
			EP 1016665 A1	05-07-2000
			IL 133681 A	31-10-2003
			NZ 502234 A	29-06-2001
			PL 339361 A1	18-12-2000
			SK 185799 A3	11-07-2000
			US 6288223 B1	11-09-2001
			CN 1107679 C	07-05-2003
			ES 2182330 T3	01-03-2003
			HU 0002458 A2	28-02-2001
			ID 24210 A	13-07-2000
			WO 9858932 A1	30-12-1998
			PT 1016665 T	31-12-2002
			TR 200000310 T2	21-08-2000
US 4918068	A	17-04-1990	JP 62205088 A	09-09-1987

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/IB2004/002648

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
US 4918068	A		DE 3789720 D1	09-06-1994
			DE 3789720 T2	18-08-1994
			EP 0236231 A2	09-09-1987
EP 0597429	A	18-05-1994	AT 400436 B	27-12-1995
			AT 221292 A	15-05-1995
			AT 233267 T	15-03-2003
			DE 69332707 D1	03-04-2003
			DE 69332707 T2	16-10-2003
			EP 0597429 A2	18-05-1994
			ES 2193140 T3	01-11-2003
			JP 2662176 B2	08-10-1997
			JP 6247973 A	06-09-1994
			SG 64379 A1	27-04-1999
			US 2001007029 A1	05-07-2001
			US 6248881 B1	19-06-2001
EP 0723965	A	31-07-1996	DE 69427365 D1	05-07-2001
			DE 69427365 T2	28-02-2002
			EP 0723965 A1	31-07-1996
			US 5827845 A	27-10-1998
			ES 2157989 T3	01-09-2001
			WO 9509171 A1	06-04-1995
US 2002002279	A1	03-01-2002	AT 238310 T	15-05-2003
			AU 714735 B2	13-01-2000
			AU 4222297 A	14-04-1998
			BR 9712072 A	24-08-1999
			CA 2265686 A1	26-03-1998
			CN 1234036 A ,C	03-11-1999
			CZ 9900975 A3	11-08-1999
			DE 69721290 D1	28-05-2003
			DE 69721290 T2	22-01-2004
			EA 1526 B1	23-04-2001
			EP 0937083 A1	25-08-1999
			ES 2198593 T3	01-02-2004
			HK 1022912 A1	12-12-2003
			HU 9903454 A2	28-03-2000
			ID 22064 A	26-08-1999
			IL 129016 A	12-01-2003
			WO 9812200 A1	26-03-1998
			JP 3403206 B2	06-05-2003
			JP 2001500521 T	16-01-2001
			KR 2000048496 A	25-07-2000
			NZ 334883 A	29-09-2000
			PL 332314 A1	30-08-1999
			PT 937083 T	29-08-2003
			SK 35499 A3	13-03-2000
			TR 9900614 T2	21-06-1999
			US 6294669 B1	25-09-2001
US 5233035	A	03-08-1993	AU 6314890 A	11-04-1991
			CA 2026204 A1	27-03-1991
			EP 0420608 A2	03-04-1991
			IE 903455 A1	10-04-1991
			NZ 235391 A	25-06-1992
			PT 95403 A	22-05-1991
			CN 1050717 A	17-04-1991

INTERNATIONAL SEARCH REPORT

Information on patent family members

Internal Application No

PCT/IB2004/002648

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5233035	A	JP 3264590 A DD 298104 A5	25-11-1991 06-02-1992