

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
26 January 2006 (26.01.2006)

PCT

(10) International Publication Number
WO 2006/008091 A3

(51) International Patent Classification:

C07D 498/14 (2006.01) *C07D 207/40* (2006.01)
C07D 493/04 (2006.01) *A61K 31/40* (2006.01)
C07D 303/48 (2006.01) *A61P 9/00* (2006.01)

(21) International Application Number:

PCT/EP2005/007739

(22) International Filing Date: 15 July 2005 (15.07.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

P200400209 16 July 2004 (16.07.2004) SI
P200400348 24 December 2004 (24.12.2004) SI

(71) Applicant (for all designated States except US): **LEK PHARMACEUTICALS D.D.** [SI/SI]; Verovskova 57, 1526 Ljubljana (SI).

(72) Inventors; and

(75) Inventors/Applicants (for US only): **GRAHEK, Rok** [SI/SI]; Zoisova 17, 4000 Kranj (SI). **KOCJAN, Darko** [SI/SI]; Maroltova ulica 3, 1000 Ljubljana (SI). **BAS-TARDA, Andrej** [SI/SI]; Podlipa 79, 1360 Vrhnika (SI). **KOCIJAN, Andrej** [SI/SI]; Ulica Metoda Mikuza 16, 1000 Ljubljana (SI). **KRACUN, Matjaz** [SI/SI]; Rusjanov trg 1, 1000 Ljubljana (SI).

(74) Agent: **DIETZ, Jörg**; Novartis AG, Corporate Intellectual Property, CH-4002 Basel (CH).

(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, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, 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, IS, IT, LT, LU, LV, 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:
8 September 2006

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.

(54) Title: OXIDATIVE DEGRADATION PRODUCTS OF ATORVASTATIN CALCIUM

(57) Abstract: The present invention relates to oxidative degradation products of atorvastatin calcium and the process of the preparation thereof. The present invention also relates to atorvastatin calcium substantially free of oxidative degradation products and the pharmaceutical compositions containing such atorvastatin calcium.

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INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2005/007739

A. CLASSIFICATION OF SUBJECT MATTER
 INV. C07D498/14 C07D493/04 C07D303/48 C07D207/40 A61K31/40
 A61P9/00

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)
 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, 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	HURLEY T R ET AL: "Photodecomposition of CI-981, an HMG-CoA reductase inhibitor" TETRAHEDRON, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL, vol. 49, no. 10, 5 March 1993 (1993-03-05), pages 1979-1984, XP002363647 ISSN: 0040-4020 cited in the application page 1979, scheme 1; pages 1980-1981, Experimental Section; page 1981, table 1; page 1981, text below table 1; page 1982, lines 1-8	7-10, 15-19
A	page 1979, scheme 1 ----- --/--	1-6

Further documents are listed in the continuation of Box C. See patent family 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
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 - * & * document member of the same patent family

Date of the actual completion of the international search 19 July 2006	Date of mailing of the international search report 27/07/2006
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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 Hass, C
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INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2005/007739

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 03/011826 A (DR. REDDY'S LABORATORIES LTD; CORD, JANET, I; REDDY, M., SATYANARAYANA) 13 February 2003 (2003-02-13) page 2, line 33 - page 3, line 12 page 6, line 34 - page 7, line 7 examples 1-3	15-24
X	WO 03/018547 A (MOREPEN LABORATORIES LTD; SURI, SANJAY; SINGH, J; SARIN, G., S; BANSAL) 6 March 2003 (2003-03-06) examples I,II	15-19
A	US 2003/114497 A1 (ALANI LAMAN ET AL) 19 June 2003 (2003-06-19) paragraphs [0106] - [0109]; claims 67-74,78,79	1-3, 15-24
A	US 5 686 104 A (MILLS ET AL) 11 November 1997 (1997-11-11) column 2, line 12 - line 63 column 10, lines 1-33	15-24
A	US 5 273 995 A (ROTH ET AL) 28 December 1993 (1993-12-28) cited in the application example 10	15-19

INTERNATIONAL SEARCH REPORT

International application No.
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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: 1-14

Degradation products of atorvastatin calcium and processes
for their preparation

2. claims: 15-24

Atorvastatin calcium of a certain purity and pharmaceutical
compositions containing this compound

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2005/007739

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 03011826	A	13-02-2003	BG 108518 A	31-08-2004
			BR 0211488 A	17-08-2004
			CA 2454500 A1	13-02-2003
			CN 1537098 A	13-10-2004
			CZ 20040126 A3	15-12-2004
			EE 200400048 A	15-04-2004
			EP 1414796 A1	06-05-2004
			HR 20040077 A2	30-06-2004
			JP 2005500351 T	06-01-2005
			MX PA04000889 A	03-06-2004
			NZ 530785 A	28-10-2005
WO 03018547	A	06-03-2003	CA 2456095 A1	06-03-2003
			EP 1572638 A2	14-09-2005
			US 2005119493 A1	02-06-2005
US 2003114497	A1	19-06-2003	US 2005107446 A1	19-05-2005
US 5686104	A	11-11-1997	AT 178794 T	15-04-1999
			CA 2150372 A1	04-08-1994
			CY 2128 A	21-06-2002
			DE 69324504 D1	20-05-1999
			DE 69324504 T2	26-08-1999
			DK 680320 T3	25-10-1999
			EP 0680320 A1	08-11-1995
			ES 2133158 T3	01-09-1999
			GR 3030359 T3	30-09-1999
			JP 3254219 B2	04-02-2002
			JP 8505640 T	18-06-1996
			MX 9400281 A1	29-07-1994
			SG 45369 A1	16-10-1998
			WO 9416693 A1	04-08-1994
			US 5273995	A
AT 207896 T	15-11-2001			
AU 628198 B2	10-09-1992			
AU 5972490 A	24-01-1991			
CA 2021546 A1	22-01-1991			
CY 2357 A	04-06-2004			
DE 1061073 T1	03-05-2001			
DE 69033840 D1	06-12-2001			
DE 69033840 T2	16-05-2002			
DE 69034153 D1	05-08-2004			
DE 69034153 T2	14-07-2005			
DK 409281 T3	25-02-2002			
EP 0409281 A1	23-01-1991			
ES 2153332 T1	01-03-2001			
ES 2167306 T3	16-05-2002			
FI 94339 B	15-05-1995			
IE 902659 A1	27-02-1991			
IE 20040325 A1	30-06-2004			
JP 3058967 A	14-03-1991			
JP 3506336 B2	15-03-2004			
JP 2002234871 A	23-08-2002			
JP 2003201236 A	18-07-2003			
KR 167101 B1	15-01-1999			
NO 903251 A	22-01-1991			
NZ 234576 A	23-12-1992			

INTERNATIONAL SEARCH REPORT

Information on patent family members

national application No

PCT/EP2005/007739

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5273995	A	PT 94778 A	20-03-1991
		SG 46495 A1	20-02-1998
		ZA 9005742 A	25-03-1992
