



US008673927B2

(12) **United States Patent**
Dugi et al.

(10) **Patent No.:** US 8,673,927 B2
(45) **Date of Patent:** *Mar. 18, 2014

(54) **USES OF DPP-IV INHIBITORS**

(75) Inventors: **Klaus Dugi**, Dresden (DE); **Frank Himmelsbach**, Mittelbiberach (DE); **Michael Mark**, Biberach (DE)

(73) Assignee: **Boehringer Ingelheim International GmbH**, Ingelheim am Rhein (DE)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 111 days.

This patent is subject to a terminal disclaimer.

(21) Appl. No.: **12/946,193**

(22) Filed: **Nov. 15, 2010**

(65) **Prior Publication Data**

US 2011/0065731 A1 Mar. 17, 2011

5,234,897 A	8/1993	Findeisen et al.
5,258,380 A	11/1993	Janssens et al.
5,266,555 A	11/1993	Findeisen et al.
5,273,995 A	12/1993	Roth
5,284,967 A	2/1994	Macher
5,300,298 A	4/1994	LaNoue
5,329,025 A	7/1994	Wong et al.
5,332,744 A	7/1994	Chakravarty et al.
5,389,642 A	2/1995	Dorsch et al.
5,399,578 A	3/1995	Buhlmayer et al.
5,407,929 A	4/1995	Takahashi et al.
5,470,579 A	11/1995	Bonte et al.
5,591,762 A	1/1997	Hauel et al.
5,594,003 A	1/1997	Hauel et al.
5,602,127 A	2/1997	Hauel et al.
5,614,519 A	3/1997	Hauel et al.
5,719,279 A	2/1998	Kufner-Muhl et al.
5,728,849 A	3/1998	Bouchard et al.
5,753,635 A	5/1998	Buckman et al.
5,830,908 A	11/1998	Grunenberg et al.
5,958,951 A	9/1999	Ahrndt et al.
5,965,555 A	10/1999	Gebert et al.
5,965,592 A	10/1999	Buhlmayer et al.
6,011,049 A	1/2000	Whitcomb
6,107,302 A	8/2000	Carter et al.
6,166,063 A	12/2000	Villhauer

(Continued)

Related U.S. Application Data

(63) Continuation of application No. 11/744,703, filed on May 4, 2007, now Pat. No. 8,232,281.

(30) **Foreign Application Priority Data**

May 4, 2006 (EP) 06009203

(51) **Int. Cl.**

A6IK 31/52 (2006.01)
A6IK 31/155 (2006.01)

(52) **U.S. Cl.**

USPC **514/263.21; 514/635; 514/868**

(58) **Field of Classification Search**

USPC 514/263.21, 635, 866
See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

2,056,046 A	9/1936	Fourneau
2,375,138 A	5/1945	Victors
2,629,736 A	2/1953	Krimmel
2,730,544 A	1/1956	Sahyun
2,750,387 A	6/1956	Krimmel
2,928,833 A	3/1960	Leake et al.
3,174,901 A	3/1965	Sterne
3,236,891 A	2/1966	Seemuller
3,454,635 A	7/1969	Muth
3,673,241 A	6/1972	Marxer
3,925,357 A	12/1975	Okada et al.
4,005,208 A	1/1977	Bender et al.
4,061,753 A	12/1977	Bodor et al.
4,599,338 A	7/1986	Regnier et al.
4,639,436 A	1/1987	Junge et al.
4,687,777 A	8/1987	Meguro et al.
4,816,455 A	3/1989	Schickaneder et al.
4,873,330 A	10/1989	Lindholm
4,968,672 A	11/1990	Jacobson et al.
5,041,448 A	8/1991	Janssens et al.
5,051,517 A	9/1991	Findeisen et al.
5,084,460 A	1/1992	Munson, Jr. et al.

FOREIGN PATENT DOCUMENTS

AU	2003280680 A1	6/2004
AU	2009224546 A1	9/2009

(Continued)

OTHER PUBLICATIONS

Bastin, R.J. et al., "Salt Selection and Optimization Procedures for Pharmaceutical New Chemical Entities". Organic Process Research and Development, 2000, vol. 4, p. 427-435.

Chemical Abstract: No. 211513-37-0—Dalcetrapib. "Propanethioic acid, 2-methyl-S-(2-[{1-(2-ethylbutyl)cyclohexyl}carbonyl}amino}phenyl)ester". Formula: C23 H35 N O2 S. American Chemical Society. Sep. 20, 1998.

Chemical Abstract: No. 875446-37-0—Anacetrapib. "2-Oxazolidinone, 5-[3,5-bis(trifluoromethyl)phenyl]-3[[4'fluoro-2'-methoxy-5'-(1-methylethyl)-4-(trifluoromethyl)[1,1'-biphenyl]-2-yl]methyl]-4-methyl-(4S,5R)-" Formula: C30 H25 F10 N O3. American Chemical Society, Feb. 28, 2006.

(Continued)

Primary Examiner — Kevin E Weddington

(74) *Attorney, Agent, or Firm* — Michael P. Morris; David L. Kershner

(57) **ABSTRACT**

The specification describes the use of selected DPP IV inhibitors for the treatment of physiological functional disorders and for reducing the risk of the occurrence of such functional disorders in at-risk patient groups. In addition, the use of the above-mentioned DPP IV inhibitors in conjunction with other active substances is described, by means of which improved treatment outcomes can be achieved. These applications may be used to prepare corresponding medicaments.

(56)

References Cited**U.S. PATENT DOCUMENTS**

6,248,758 B1	6/2001	Klokkers et al.	2004/0097510 A1	5/2004	Himmelsbach et al.
6,303,661 B1	10/2001	Demuth et al.	2004/0116328 A1	6/2004	Yoshikawa et al.
6,342,601 B1	1/2002	Bantick et al.	2004/0122048 A1	6/2004	Benjamin et al.
6,372,940 B1	4/2002	Cavazza	2004/0166125 A1	8/2004	Himmelsbach et al.
6,548,481 B1	4/2003	Demuth et al.	2004/0180925 A1	9/2004	Matsuno et al.
6,579,868 B1	6/2003	Asano et al.	2004/0259903 A1	12/2004	Boehringer et al.
6,727,261 B2	4/2004	Gobbi et al.	2005/0020574 A1	1/2005	Hauel et al.
6,784,195 B2	8/2004	Hale et al.	2005/0026921 A1	2/2005	Eckhardt et al.
6,821,978 B2	11/2004	Chackalamannil et al.	2005/0032804 A1	2/2005	Cypes et al.
6,869,947 B2	3/2005	Kanstrup et al.	2005/0070562 A1	3/2005	Jones et al.
6,995,183 B2	2/2006	Hamann et al.	2005/0070594 A1	3/2005	Kauschke et al.
7,060,722 B2	6/2006	Kitajima et al.	2005/0130985 A1	6/2005	Himmelsbach et al.
7,074,794 B2	7/2006	Kitajima et al.	2005/0143377 A1	6/2005	Himmelsbach et al.
7,074,798 B2	7/2006	Yoshikawa et al.	2005/0171093 A1	8/2005	Eckhardt et al.
7,074,923 B2	7/2006	Dahanukar et al.	2005/0187227 A1	8/2005	Himmelsbach et al.
7,109,192 B2	9/2006	Hauel et al.	2005/0203095 A1	9/2005	Eckhardt et al.
7,179,809 B2	2/2007	Eckhardt et al.	2005/0234108 A1	10/2005	Himmelsbach et al.
7,183,280 B2	2/2007	Himmelsbach et al.	2005/0234235 A1	10/2005	Eckhardt et al.
7,192,952 B2	3/2007	Kanstrup et al.	2005/0239778 A1	10/2005	Konetzki et al.
7,217,711 B2	5/2007	Eckhardt et al.	2005/0256310 A1	11/2005	Hulin et al.
7,235,538 B2	6/2007	Kanstrup et al.	2005/0261271 A1	11/2005	Feng et al.
7,291,642 B2	11/2007	Kauffmann-Hefner et al.	2005/0261352 A1	11/2005	Eckhardt
7,361,687 B2	4/2008	Barth et al.	2005/0266080 A1	12/2005	Desai et al.
7,393,847 B2	7/2008	Eckhardt et al.	2005/0276794 A1	12/2005	Papas et al.
7,407,955 B2	8/2008	Himmelsbach et al.	2006/0004074 A1	1/2006	Eckhardt et al.
7,432,262 B2	10/2008	Eckhardt et al.	2006/0039974 A1	2/2006	Akiyama et al.
7,439,370 B2	10/2008	Eckhardt	2006/0047125 A1	3/2006	Leonardi et al.
7,470,716 B2	12/2008	Eckhardt et al.	2006/0058323 A1	3/2006	Eckhardt et al.
7,476,671 B2	1/2009	Eckhardt et al.	2006/0063787 A1	3/2006	Yoshikawa et al.
7,482,337 B2	1/2009	Himmelsbach et al.	2006/0074058 A1	4/2006	Holmes et al.
7,495,002 B2	2/2009	Langkopf et al.	2006/0079541 A1	4/2006	Langkopf et al.
7,495,003 B2	2/2009	Eckhardt et al.	2006/0094722 A1	5/2006	Yasuda et al.
7,495,005 B2	2/2009	Himmelsbach et al.	2006/0100199 A1	5/2006	Yoshikawa et al.
7,501,426 B2	3/2009	Himmelsbach et al.	2006/0106035 A1	5/2006	Hendrix et al.
7,550,455 B2	6/2009	Himmelsbach et al.	2006/0111372 A1	5/2006	Hendrix et al.
7,560,450 B2	7/2009	Eckhardt et al.	2006/0111379 A1	5/2006	Guillemont et al.
7,566,707 B2	7/2009	Eckhardt et al.	2006/0142310 A1	6/2006	Pfrenge et al.
7,569,574 B2	8/2009	Maier et al.	2006/0154866 A1	7/2006	Chu et al.
7,579,449 B2	8/2009	Eckhardt et al.	2006/0159746 A1	7/2006	Troup et al.
7,610,153 B2	10/2009	Carter, Jr. et al.	2006/0173056 A1	8/2006	Kitajima et al.
7,645,763 B2	1/2010	Himmelsbach et al.	2006/0205711 A1	9/2006	Himmelsbach et al.
7,718,666 B2	5/2010	Boehringer et al.	2006/0205943 A1	9/2006	Dahanukar et al.
7,799,782 B2	9/2010	Munson et al.	2006/0247226 A1	11/2006	Himmelsbach et al.
7,820,815 B2	10/2010	Pfrenge et al.	2006/0270668 A1	11/2006	Chew et al.
7,838,529 B2	11/2010	Himmelsbach et al.	2006/0270701 A1	11/2006	Kroth et al.
8,039,477 B2	10/2011	Hendrix et al.	2007/0027168 A1	2/2007	Pfrenge et al.
8,071,583 B2	12/2011	Himmelsbach	2007/0060530 A1	3/2007	Christopher et al.
8,106,060 B2	1/2012	Pfrenge et al.	2007/0072803 A1	3/2007	Chu et al.
8,119,648 B2 *	2/2012	Himmelsbach et al.	2007/0072810 A1	3/2007	Asakawa
8,158,633 B2	4/2012	Hendrix et al.	2007/0088038 A1	4/2007	Eckhardt et al.
8,178,541 B2 *	5/2012	Himmelsbach et al.	2007/0093659 A1	4/2007	Bonfanti et al.
8,232,281 B2 *	7/2012	Dugi et al.	2007/0142383 A1	6/2007	Eckhardt et al.
2001/0020006 A1	9/2001	Demuth et al.	2007/0185091 A1	8/2007	Himmelsbach et al.
2001/0051646 A1	12/2001	Demuth et al.	2007/0196472 A1	8/2007	Kiel et al.
2002/0019411 A1	2/2002	Robl et al.	2007/0219178 A1	9/2007	Muramoto
2002/0137903 A1	9/2002	Ellsworth et al.	2007/0259900 A1	11/2007	Sieger et al.
2002/0161001 A1	10/2002	Kanstrup et al.	2007/0259925 A1	11/2007	Boehringer et al.
2002/0169174 A1	11/2002	Chackalamannil et al.	2007/0259927 A1	11/2007	Suzuki et al.
2002/0198205 A1	12/2002	Himmelsbach et al.	2007/0281940 A1	12/2007	Dugi et al.
2003/0078269 A1	4/2003	Pearson et al.	2007/0299076 A1	12/2007	Piotrowski et al.
2003/0100563 A1	5/2003	Edmondson et al.	2008/0039427 A1	2/2008	Ray et al.
2003/0105077 A1	6/2003	Kanstrup et al.	2008/0107731 A1	5/2008	Kohlräusch et al.
2003/0114390 A1	6/2003	Washburn et al.	2008/0108816 A1	5/2008	Zutter
2003/0149071 A1	8/2003	Gobbi et al.	2008/0249089 A1	10/2008	Himmelsbach et al.
2003/0166578 A1	9/2003	Arch et al.	2008/0255159 A1	10/2008	Himmelsbach et al.
2003/0199528 A1	10/2003	Kanstrup et al.	2008/0312243 A1	12/2008	Eckhardt et al.
2003/0224043 A1	12/2003	Appel et al.	2008/0318922 A1	12/2008	Nakahira et al.
2003/0232987 A1	12/2003	Dahanukar et al.	2009/0023920 A1	1/2009	Eckhardt
2003/0236272 A1	12/2003	Carr	2009/0088408 A1	4/2009	Meade et al.
2004/0023981 A1	2/2004	Ren et al.	2009/0088569 A1	4/2009	Eckhardt et al.
2004/0034014 A1	2/2004	Kanstrup et al.	2009/0093457 A1	4/2009	Himmelsbach et al.
2004/0063725 A1	4/2004	Barth et al.	2009/0131432 A1	5/2009	Himmelsbach et al.
2004/0077645 A1	4/2004	Himmelsbach et al.	2009/0136596 A1	5/2009	Munson et al.

(56)	References Cited		
U.S. PATENT DOCUMENTS			
2009/0186086 A1	7/2009	Shankar et al.	DE 102004024454 A1 12/2005
2009/0192314 A1	7/2009	Pfrengle et al.	DE 102004044221 A1 3/2006
2009/0297470 A1	12/2009	Franz	DE 102004054054 A1 5/2006
2009/0301105 A1	12/2009	Loerting	EP 0023032 A1 1/1981
2009/0325926 A1	12/2009	Himmelsbach	EP 0149578 A2 7/1985
2010/0074950 A1	3/2010	Sesha	EP 0223403 A2 5/1987
2010/0092551 A1	4/2010	Nakamura et al.	EP 0237608 A1 9/1987
2010/0173916 A1	7/2010	Himmelsbach et al.	EP 0248634 A2 12/1987
2010/0183531 A1	7/2010	Johncock et al.	EP 0389282 A2 9/1990
2010/0204250 A1	8/2010	Himmelsbach et al.	EP 0399285 A1 11/1990
2011/0009391 A1	1/2011	Braun et al.	EP 0400974 A2 12/1990
2011/0046076 A1	2/2011	Eickelmann et al.	EP 409281 A1 1/1991
2011/0065731 A1	3/2011	Dugi et al.	EP 0412358 A1 2/1991
2011/0092510 A1	4/2011	Klein et al.	EP 443983 A1 8/1991
2011/0098240 A1	4/2011	Dugi et al.	EP 0524482 A1 1/1993
2011/0112069 A1	5/2011	Himmelsbach et al.	EP 0657454 A1 6/1995
2011/0144083 A1	6/2011	Himmelsbach et al.	EP 0775704 A1 5/1997
2011/0144095 A1	6/2011	Himmelsbach et al.	EP 0950658 A1 10/1999
2011/0190322 A1	8/2011	Klein et al.	EP 1054012 A1 11/2000
2011/0195917 A1	8/2011	Dugi et al.	EP 1066265 A1 1/2001
2011/0206766 A1	8/2011	Friedl et al.	EP 1333033 8/2003
2011/0263493 A1	10/2011	Dugi et al.	EP 1338595 A2 8/2003
2011/0263617 A1	10/2011	Mark et al.	EP 1406873 A2 4/2004
2011/0275561 A1	11/2011	Graefe-Mody et al.	EP 1500403 A1 1/2005
2011/0301182 A1	12/2011	Dugi	EP 1514552 A1 3/2005
2012/0003313 A1	1/2012	Kohlrausch et al.	EP 1537880 A1 6/2005
2012/0035158 A1	2/2012	Himmelsbach et al.	EP 1557165 A1 7/2005
2012/0040982 A1	2/2012	Himmelsbach et al.	EP 1586571 A1 10/2005
2012/0053173 A1	3/2012	Banno et al.	EP 1743655 A1 1/2007
2012/0094894 A1	4/2012	Graefe-Mody et al.	EP 1760076 3/2007
2012/0107398 A1	5/2012	Schneider et al.	EP 1829877 A1 9/2007
2012/0121530 A1	5/2012	Klein et al.	EP 1852108 A1 11/2007
2012/0122776 A1	5/2012	Graefe-Mody et al.	EP 2143443 A1 1/2010
2012/0129874 A1	5/2012	Sieger et al.	ES 385302 A1 4/1973
2012/0142712 A1	6/2012	Pfrengle et al.	ES 2256797 T3 7/2006
2012/0165251 A1	6/2012	Klein et al.	ES 2263057 T3 12/2006
2012/0208831 A1	8/2012	Himmelsbach et al.	FR 2707641 A1 1/1995
2012/0219622 A1	8/2012	Kohlrausch et al.	GB 2084580 A 4/1982
2012/0219623 A1	8/2012	Meincke	HU 9003243 5/1990
2012/0252782 A1	10/2012	Himmelsbach et al.	HU 9902308 A2 7/2000
2012/0252783 A1	10/2012	Himmelsbach et al.	JP S374895 A 6/1962
2012/0296091 A1	11/2012	Sieger et al.	JP 770120 3/1995
2013/0172244 A1	7/2013	Klein et al.	JP 2000502684 A 3/2000
2013/0184204 A1	7/2013	Pfrengle et al.	JP 2001213770 A 8/2001
2013/0196898 A1	8/2013	Dugi et al.	JP 2003300977 A 10/2003
FOREIGN PATENT DOCUMENTS			
CA 1123437 A1	5/1982		JP 2006045156 A 2/2006
CA 2136288 A1	5/1995		JP 2010053576 A 3/2010
CA 2418656 A1	2/2002		KR 20070111099 A 11/2007
CA 2496249 A1	3/2004		WO 9107945 A1 6/1991
CA 2496325 A1	3/2004		WO 9205175 A1 4/1992
CA 2498423 A1	4/2004		WO 9219227 A2 11/1992
CA 2505389 A1	5/2004		WO 9402150 A1 2/1994
CA 2508233 A1	6/2004		WO 9403456 A1 2/1994
CA 2529729 A1	12/2004		WO 9532178 A1 11/1995
CA 2543074 A1	6/2005		WO 9609045 A1 3/1996
CA 2555050 A1	9/2005		WO 9636638 A1 11/1996
CA 2556064 A1	9/2005		WO 9723447 A1 7/1997
CA 2558067 A1	10/2005		WO 9723473 A1 7/1997
CA 2561210 A1	10/2005		WO 9746526 A1 12/1997
CA 2562859 A1	11/2005		WO 9807725 2/1998
CA 2576294 A1	3/2006		WO 9811893 A1 3/1998
CA 2590912 A1	6/2006		WO 9818770 A1 5/1998
CA 2651019 A1	11/2007		WO 9822464 A1 5/1998
CA 2651089 A1	11/2007		WO 9828007 A1 7/1998
CN 101234105 A	8/2008		WO 9840069 A2 9/1998
DE 2205815 A1	8/1973		WO 9856406 A1 12/1998
DE 2758025 A1	7/1979		WO 9929695 A1 6/1999
DE 10109021 A1	9/2002		WO 9950248 A1 10/1999
DE 10117803 A1	10/2002		WO 0073307 A2 12/2000

(56)	References Cited						
FOREIGN PATENT DOCUMENTS							
WO	02053516	A2	7/2002	WO	2007017423	A1	
WO	02068420	A1	9/2002	WO	2007033350	A1	
WO	03000241	A2	1/2003	WO	2007035355	A2	
WO	03002531	A2	1/2003	WO	2007035665	A1	
WO	03004496	A1	1/2003	WO	2007041053	A2	
WO	03024965	A2	3/2003	WO	2007071738	6/2007	
WO	03037327	A1	5/2003	WO	2007072083	A1	
WO	03055881	A1	7/2003	WO	2007078726	A2	
WO	03057200	A2	7/2003	WO	2007093610	A1	
WO	03064454	A1	8/2003	WO	2007099345	A1	
WO	03088900	A2	10/2003	WO	2007120702	A2	
WO	03099279	A1	12/2003	WO	2007120936	A2	
WO	03099836	A1	12/2003	WO	2007128721	A	
WO	03104229	A1	12/2003	WO	2007128724	A1	
WO	03106428	A1	12/2003	WO	2007128761	A2	
WO	2004002924	A1	1/2004	WO	2007149797	A2	
WO	2004011416	A1	2/2004	WO	2008005569	A2	
WO	2004018467	A2	3/2004	WO	2008005576	A1	
WO	2004018468	A2	3/2004	WO	2008017670	2/2008	
WO	2004018469	A1	3/2004	WO	2008022267	A2	
WO	2004028524	A1	4/2004	WO	2008055870	A1	
WO	2004033455	A1	4/2004	WO	2008055940	A2	
WO	2004035575	A1	4/2004	WO	2008070692	A2	
WO	2004041820	A1	5/2004	WO	2008081205	A1	
WO	2004046148	A1	6/2004	WO	2008083238	A2	
WO	2004048379	A1	6/2004	WO	2008087198	A1	
WO	2004050658	A1	6/2004	WO	2008093878	A1	
WO	2004052362	A1	6/2004	WO	2008093882	A1	
WO	2004058233	A1	7/2004	WO	2008113000	A1	
WO	2004062689	A1	7/2004	WO	2008131149	A2	
WO	2004065380	A	8/2004	WO	2009011451	A	
WO	2004081006	A1	9/2004	WO	2009022007	A1	
WO	2004082402	A1	9/2004	WO	2009022008	A1	
WO	2004096806	A1	11/2004	WO	20090222010	A1	
WO	2004096811	A1	11/2004	WO	2009024542	A2	
WO	2004106279	A2	12/2004	WO	2009063072	A2	
WO	2004108730	A1	12/2004	WO	2009064399	A1	
WO	2004111051	A1	12/2004	WO	2009099734	A1	
WO	2005000846	A1	1/2005	WO	2009112691	A2	
WO	2005000848	A1	1/2005	WO	2009121945	A2	
WO	2005007647	A1	1/2005	WO	2009123992	A1	
WO	2005012288	A1	2/2005	WO	2009147125	A1	
WO	2005023179	A2	3/2005	WO	2010015664	A1	
WO	2005049022	A2	6/2005	WO	2010018217	A2	
WO	2005051950	A1	6/2005	WO	2010029089	A2	
WO	2005058901	A1	6/2005	WO	2010043688	A1	
WO	2005061489	A1	7/2005	WO	2010045656	A2	
WO	2005063750	A1	7/2005	WO	2010072776	A1	
WO	2005082906	A1	9/2005	WO	2010079197	A1	
WO	2005085246	A1	9/2005	WO	2010086411	A1	
WO	2005092870	A1	10/2005	WO	2010092125	A1	
WO	2005092877	A1	10/2005	WO	2010096384	A2	
WO	2005095343	A1	10/2005	WO	20100092163	A2	
WO	2005097798	A	10/2005	WO	2010106457	A2	
WO	2005116000	A1	12/2005	WO	2010147768	A1	
WO	2005116014	A1	12/2005	WO	2011039367	A2	
WO	2005117861	A1	12/2005	WO	2011064352	A1	
WO	2005117948	A1	12/2005	WO	2011113947	A1	
WO	2006005613	A1	1/2006	WO	2011138380	A1	
WO	2006027204	A1	3/2006	WO	2011138421	A1	
WO	2006029769	A1	3/2006	WO	2011161161	A1	
WO	2006036664	A1	4/2006	WO	2012065993	A1	
WO	2006040625	A1	4/2006	WO	2013103629	A1	
WO	2006047248	A1	5/2006	OTHER PUBLICATIONS			
WO	2006048209	A1	5/2006	Clinical Trials: NCT00954447, View on Jun. 14, 2010. "Efficacy and Safety of Linagliptin in Combination with Insulin in Patients with Type 2 Diabetes". < http://clinicaltrials.gov/archive/NCT00954447/2010_06_14 >.			
WO	2006048427	A1	5/2006	Demuth, H-U. et al., "Type 2 diabetes—Therapy with dipeptidyl peptidase IV inhibitors". <i>Biochimica et Biophysica Acta</i> , vol. 1751(1), 2005, p. 33-44.			
WO	2006068163	A1	6/2006	Gallwitz, B. "Sitagliptin with Metformin: Profile of a Combination			
WO	2006071078	A1	7/2006				
WO	2006076231	A2	7/2006				
WO	2006083491	A2	8/2006				
WO	2006135693	A2	12/2006				
WO	2006137085	A1	12/2006				
WO	2007007173	A2	1/2007				

(56)

References Cited**OTHER PUBLICATIONS**

- Graefe-Mody, et al; Evaluation of the Potential for Steady-State Pharmacokinetic and Pharmacodynamic Interactions Between the DPP-4 Inhibitor Linagliptin and Metformin in Healthy Subjects; Currents Medical Research and Opinion (2009) vol. 25, No. 8 pp. 1963-1972.
- He, Y. L. et al., "Bioequivalence of Vildagliptin/Metformin Combination Tablets and Coadministration of Vildagliptin and Metformin as Free Combination in Healthy Subjects". J. Clinical Pharmacology, 2007, vol. 47, No. 9, Abstracts of the 36th Annual Meeting of the American College of Clinical Pharmacology, San Francisco, CA, Abstract 116, p. 1210.
- Hunziker, D. et al, "Inhibitors of DPP IV-recent advances and structural views", Current Topics in Medicinal Chemistry, 2005, vol. 5 issue 16, pp. 1623-1637.
- Knorr, M. et al., "Comparison of Direct and Indirect Antioxidant Effects of Linagliptin (BI 1356, Ondero) with other Gliptins—Evidence for Anti-Inflammatory Properties of Linagliptin". Free Radical Biology and medicine, Elsevier Science, U.S. vol. 49, Oct. 23, 2010, p. S197.
- Levien,T.L. et al, "New drugs in development for the treatment of diabetes", Diabetes Spectrum, American Diabetes Association, US, vol. 22, No. 2, Jan. 1, 2009, pp. 92-106.
- Meece, J. "When Oral Agents Fail: Optimizing Insulin Therapy in the Older Adult". Consultant Pharmacist, The Society, Arlington, VA US. vol. 24, No. Suppl B, Jun. 1, 2009, p. 11-17.
- Rosenstock, J. et al., "Alogliptin added to insulin therapy in patients with type 2 diabetes reduces HbA1c without causing weight gain or increased hypoglycaemia". Diabetes, Obesity and Metabolism, Dec. 2009, vol. 11, No. 12, p. 1145-1152.
- Sune Negre, J. M. "New Galenic Contributions to Administration Forms". Continued Training for Hospital Pharmacists 3.2. [retrieved on Feb. 23, 2011]. Retrieved from the internet <<http://www.ub.es/legmh/capitols/sunyenegre.pdf>>.
- Thomas, L., "Chronic treatment with the Dipeptidyl Peptidase-4 Inhibitor BI 1356[9R]-8-(3-Amino-piperidin-1-yl)-7-but-2-ynyl-3-methyl-1(4-methyl-quinazolin-2-ylmethyl)-3,7-dihydro-purine-2,6-dione] Increases Basal Glucagon-Like Peptide-1 and Improves Glycemic Control in Diabetic Rodent Models" The Journal of Pharmacology and Experimental Therapeutics, Feb. 2009, vol. 328, No. 2, pp. 556-563.
- Conarello, S.L. et al; "Mice lacking dipeptidyl peptidase IV are protected against obesity and insulin resistance," PNAS 2003; 100:6825-6830; originally published online May 14, 2003; information current as of Dec. 2006. www.pnas.org/cgi/content/full/100/11/6825.
- European Search Report for EP 08 15 9141 mailed Apr. 6, 2009 [European counterpart of U.S. Appl. No. 12/143,128].
- Uhlig-Laske, B. et al., "Linagliptin, a Potent and Selective DPP-4 Inhibitor, is Safe and Efficacious in Patients with Inadequately Controlled Type 2 Diabetes Despite Metformin Therapy". 535-P Clinical Therapeutics/New Technology—Pharmacologic Treatment of Diabetes or Its Complications, Posters, vol. 58, Jun. 5, 2009, p. A143. Abstract in English for German DE2205815, 1972.
- Abstract in English for German EP0023032, 1981.
- Abstract in English, for KR20070111099, Nov. 11, 2007.
- Augeri, D.J. "Discovery and Preclinical Profile of Saxagliptin (GMB-477118): A Highly Potent, Long-Acting, Orally Active Dipeptidyl Peptidase IV Inhibitor for the Treatment of Type 2 Diabetes". Journal Med. Chem, 2005, vol. 48, No. 15, p. 5025-5037.
- Augustyns, K. et al., The Unique Properties of Dipeptidyl-peptidase IV (DPP IV/CD 26) and the Therapeutic Potential of DPP-IV Inhibitors, Current Medicinal Chemistry, vol. 6, No. 4, 1999, pp. 311-327.
- Aulinger, B.A. et al., "Ex-4 and the DPP-IV Inhibitor Vildagliptin have Additive Effects to Suppress Food Intake in Rodents". Abstract No. 1545-P, 2008.
- Balaban, Y.H. et al., "Dipeptidyl peptidase IV (DDP IV) in NASH Balkan, B. et al, "Inhibition of dipeptidyl peptidase IV with NVP-DPP728 increases plasma GLP-1 (7-36 amide) concentrations and improves oral glucose tolerance in obes Zucker rats". Diabetologia, 1999, 42, p. 1324-1331.
- Beljean-Leymarie et al., Hydrazines et hydrazenes heterocycliques. IV. Syntheses de derives de l'hydrazine dans la serie des imidazo[4,5-d]pyridazinones-4, Can. J. Chem., vol. 61, No. 11, 1983, pp. 2563-2566.
- Bollag, R.J. et al; "Osteoblast-Derived Cells Express Functional Glucose-Dependent Insulinotropic Peptide Receptors," Endocrinology, vol. 141, No. 3, 2000, pp. 1228-1235.
- Brazg, R. et al: "Effect of adding sitagliptin, a dipeptidyl peptidase-4 inhibitor, to metformin on 24-h glycemic control and beta-cell function in patients with type 2 diabetes." Diabetes, Obesity and Metabolism, Mar. 2007, vol. 9, No. 2, pp. 18-193.
- Brittain, H.G., "Methods for the Characterization of Polymorphs: X-Ray Powder Diffraction," Polymorphism in Pharmaceutical Solids, 1999, p. 235-238.
- Busso et al., "Circulating CD26 is Negatively Associated with Inflammation in Human and Experimental Arthritis," Am. J. Path., vol. 166, No. 2, Feb. 2005, pp. 433-442.
- Caira, M.R., "Crystalline polymorphism of organic compounds" Topics in Current Chemistry, Springer, Berlin, vol. 198, 1998, p. 163-208.
- Chemical Abstract. EP412358, 1991:185517, Findeisen.
- Chemical Abstract: FR2707641, 1995:543545, Dodey.
- Chemical Abstracts Accession No. 106:95577 Romanenko et al., "Synthesis and Biological Activity of 3-Methyl, 7- or 8-alkyl-7,8-dialkyl, heterocyclic, and cyclohexylaminoxanthines," Zaporozh. Med. Institute (1986).
- Chemical Abstracts Accession No. 1987:95577: Abstract of Romanenko et al., "Synthesis and biological activity of 3-methyl, 7- or 8-alkyl, 7,8-dialkyl, heterocyclic, and cyclohexylaminoxanthines," Zaporozh, USSR, Farmatsevtichnii Zhurnal, 1986, (Kiev), vol. 5, 1986, pp. 41-44.
- Clinical Trials. NCT00622284. "Efficacy and safety of BI 1356 in combination with metformin in patients with type 2 diabetes" ClinicalTrials.gov (Online) No. NCT00622284, Feb. 13, 2008, p. 1-5, URL:<http://clinicaltrials.gov/ct2/show/>.
- Clinical Trials. "View of NCT00601250 on 1008-01-25: Efficacy and Safety of BI 1356 vs Placebo added to Metformin Background Therapy in Patients with Type 2 Diabetes" Clinical Trials. Gov Archive, [Online] Jan. 25, 2008 URL:http://clinicaltrials.gov/archive/NCT00601250/2008_01_25 [retrieved on Feb. 27, 2009].
- Clinical Trials. View of NCT00730275 on Aug. 7, 2008. "A study to assess the pharmacokinetics, safety and tolerability of Sitagliptin in adolescents".
- Conarello, S.L. et al., "Mice lacking dipeptidyl peptidase IV are protected against obesity and insulin resistance". PNAS, May 27, 2003, vol. 100, No. 11, p. 6825-6830.
- Cygankiewicz, Andrzej et al., Investigations into the Piperazine Derivatives of Dimethylxanthine:, Acta Polon. Pharm. [Papers of Polish Pharmacology], XXXIX, No. 5, pp. 607-612, 1977.
- Deacon, C.F. et al; "Dipeptidyl peptidase IV inhabitation as an approach to the treatment and prevention of type 2 diabetes: a historical perspective," Biochemical and Biophysical Research Communications (BBRC) 294 (2002) 1-4.
- Deacon, C.F. et al. Inhibitors of dipeptidyl peptidase IV: a novel approach for the prevention and treatment of Type 2 diabetes? Expert Opinion on Investigational Drugs, 2004, September, vol. 13, No. 9, p. 1091-1102.
- DeMeester, I. et al.; "CD26, let it cut or cut it down", Review: Immunology Today; Aug. 1999, vol. 20, No. 8 pp. 367-375.
- Dugi, K.A. et al., "BI 1356, a novel xanthine-based DPP-IV inhibitor, exhibits high potency with a wide therapeutic window and significantly reduces postprandial glucose excursions after an OGTT". Diabetologia, vol. 50, No. Suppl 1, Sep. 2007, p. S367, and 43rd Annual Meeting of the European Association for the Study of Diabetes; Amsterdam, Netherlands, Sep. 18-21, 2007.
- Eckhardt Matthias et al: 8-(3-(R)-aminopiperidin-1-yl)-7-but-2-ynyl-1-3-methyl-1-(4-methyl-quinolin-2-ylmethyl)-3,7-

Explore Litigation Insights



Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts



Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research



With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips



Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS

Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS

Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS

Sync your system to PACER to automate legal marketing.