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(54) Title: COMBINATION OF SOMATOSTATIN-ANALOGS WITH DOPAMINE- OR GROWTH HORMONE RECEPTOR ANTAGONIST

(57) Abstract: The present invention concerns a product containing Sandostatin® LAR® at 40 mg / 28 days or pasireotide and either a dopamine-agonist, preferably cabergoline, or a growth hormone receptor antagonist, preferably pegvisomant, as a combined preparation for simultaneous, separate or sequential use in acromegalic therapy. In particular, this therapy is useful for treating acromegalic patients not achieving biochemical normalization after at least six-month treatment using at least one somatostatin analogue at conventional regimen.

INTERNATIONAL SEARCH REPORT

International application No
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A. CLASSIFICATION OF SUBJECT MATTER
INV. A61K31/48 A61K38/12 A61K38/16 A61K38/27 A61P5/08

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)
A61K A61P

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, EMBASE, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X,Y	COZZI R ET AL: "Cabergoline addition to depot somatostatin analogues in resistant acromegalic patients: Efficacy and lack of predictive value of prolactin status" CLINICAL ENDOCRINOLOGY 2004 UNITED KINGDOM, vol. 61, no. 2, 2004, pages 209-215, XP002466649 ISSN: 0300-0664 abstract page 209, lines 35-42 page 210, right-hand column, line 5 - page 211, left-hand column, line 12 page 213, left-hand column, line 24 - page 213, right-hand column, line 17 page 241, left-hand column, lines 3-21 page 214, right-hand column, lines 7-21 ----- -/--	1-23

[X] Further documents are listed in the continuation of Box C. [X] See patent family annex.

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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	Tullberg, Erik

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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	JORGENSEN JENS OTTO LUNDE ET AL: "Cotreatment of acromegaly with a somatostatin analog and a growth hormone receptor antagonist" JOURNAL OF CLINICAL ENDOCRINOLOGY AND METABOLISM, ENDOCRINE SOCIETY, CHEVY CHASE, MD, US, vol. 90, no. 10, October 2005 (2005-10), pages 5627-5631, XP002425118 ISSN: 0021-972X abstract page 5628, lines 5-12 page 5630, right-hand column, lines 16-25 page 5630, right-hand column, line 46 - page 5631, left-hand column, line 35	1-23
X,Y	WO 2005/021023 A (UPJOHN CO [US]; BURMAN PIA [SE]; FRIEND KEITH E [US]) 10 March 2005 (2005-03-10) page 1, lines 3-8 page 2, lines 20-30 page 4, line 30 - page 5, line 27 page 9, lines 3-15 page 11, line 6 - page 13, line 27 claims 1-9	1-23
Y	MARZULLO P ET AL: "Efficacy of combined treatment with lanreotide and cabergoline in selected therapy-resistant acromegalic patients." PITUITARY 1999, vol. 1, no. 2, 1999, pages 115-120, XP002466650 ISSN: 1386-341X abstract page 116, right-hand column, lines 10-27 page 119, left-hand column, line 36 - page 119, right-hand column, line 19	1-23
Y	DONANGELO ET AL: "TREATMENT OF ACROMEGALY . FUTURE" ENDOCRINE, MACMILLAN, BASINGSTOKE, GB, vol. 28, no. 1, 2005, pages 123-128, XP009085929 ISSN: 1355-008X abstract page 124, right-hand column, line 52 - page 125, right-hand column, line 14	1-23

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INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2007/055599

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 02/10192 A (NOVARTIS AG [CH]; NOVARTIS ERFIND VERWALT GMBH [AT]; ALBERT RAINER [CH) 7 February 2002 (2002-02-07) cited in the application page 11, lines 5-19 page 20, line 20 claims 1,9	1-23
A	DE MENIS, E.,VISENTIN, A.,BILLECI, D., TRAMONTIN, P.,AGOSTINI, S.,MARTON, E.,CONTE,N.: "Pituitary adenomas in childhood and adolescence. Clinical analysis of 10 Cases" JOURNAL OF ENDOCRINOLOGICAL INVESTIGATION, vol. 24, 2001, pages 92-97, XP009095099 abstract table 2 page 96, left-hand column, lines 47-49	1-23
A	MAHESHWARI HIRALAL G ET AL: "Long-acting peptidomimergic control of gigantism caused by pituitary acidophilic stem cell adenoma" JOURNAL OF CLINICAL ENDOCRINOLOGY AND METABOLISM, vol. 85, no. 9, September 2000 (2000-09), pages 3409-3416, XP002466648 ISSN: 0021-972X abstract page 3413, left-hand column, lines 9-14; figure 1	1-23

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/EP2007/055599

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2005021023 A	10-03-2005	NONE	
WO 0210192 A	07-02-2002	AU 8977801 A	13-02-2002
		BR 0112859 A	01-07-2003
		CA 2416293 A1	07-02-2002
		CN 1446229 A	01-10-2003
		CZ 20030288 A3	14-05-2003
		EP 1307486 A2	07-05-2003
		HU 0300684 A2	29-09-2003
		JP 3829118 B2	04-10-2006
		JP 2004505095 T	19-02-2004
		KR 20060035809 A	26-04-2006
		MX PA03000991 A	09-06-2003
		NO 20030484 A	19-03-2003
		NZ 523836 A	27-08-2004
		PL 358718 A1	09-08-2004
		RU 2287533 C2	20-11-2006
		SK 1212003 A3	05-08-2003
		TW 282341 B	11-06-2007
		US 2005014686 A1	20-01-2005
		ZA 200300406 A	02-04-2004