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AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

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4 December 2014

(54) Title: PHARMACEUTICAL DOSAGE FORM

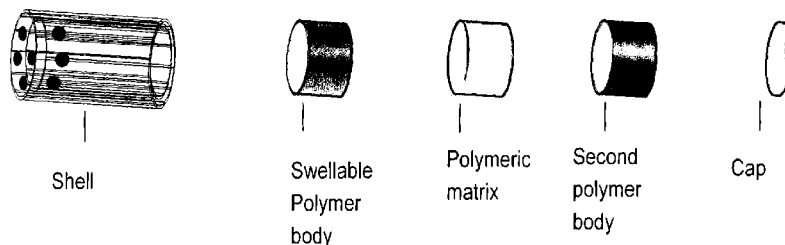


FIG 1

(57) Abstract: The invention relates to a pharmaceutical dosage form for delivery of, at a target site in a human or animal body, an active pharmaceutical ingredient (API), said pharmaceutical dosage form comprising a shell defining therein an outlet; a polymeric matrix having at least one API, the polymeric matrix received within the shell; and a swellable polymer body located within the shell, wherein the swellable polymer body is pH responsive, such that in use, exposure of the body to a medium of increasing pH causes an increase in swelling and an increase in volume of the swellable polymer body, which in turn, facilitates displacement of the matrix through the outlet toward the target site for delivery of the API.



WO 2014/102741 A3

INTERNATIONAL SEARCH REPORT

International application No PCT/IB2013/061366

A. CLASSIFICATION OF SUBJECT MATTER INV. A61K9/24 A61K38/00 A61K9/32 ADD.				
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				
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 practicable, search terms used) EPO-Internal, BIOSIS, EMBASE, WPI 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 4 904 474 A (THEEUWES FELIX [US] ET AL) 27 February 1990 (1990-02-27)	1-4,6-8, 13, 17-19, 22,24, 25,31-35 26,27		
Y	column 1, line 5 - line 11 column 4, line 51 - line 56 column 5, line 13 - line 34 column 6, line 46 - column 7, line 48 column 8, line 19 - line 21 examples 1-8 claims 1-22 ----- -/--			
<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C. <input checked="" type="checkbox"/> See patent family annex.				
* Special categories of cited documents : <table style="width: 100%; border: none;"> <tr> <td style="width: 50%; border: none; vertical-align: top;"> "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier application or patent 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 </td> <td style="width: 50%; border: none; vertical-align: top;"> "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 </td> </tr> </table>			"A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier application or patent 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
"A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier application or patent 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	Date of mailing of the international search report			
8 September 2014	17/09/2014			
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Authorized officer Marchand, Petra			

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2013/061366

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>WO 2007/044234 A1 (ALZA CORP [US]; REYES IRAN [US]; LEE JULIE [US]; BARCLAY BRIAN L [US];) 19 April 2007 (2007-04-19)</p> <p>paragraph [0001] example 2 figure 2 claims</p>	<p>1-4,6-8, 13, 17-19, 22,24, 25,28, 31-35</p>
A	<p>US 6 524 305 B1 (PETERSON LEWIS L [US] ET AL) 25 February 2003 (2003-02-25)</p> <p>column 1, line 13 - line 15 figures 1-9 column 13, line 7 - line 39 column 16, line 24 - line 65 column 19, line 20 - line 26 column 21, line 13 - line 40 claims</p>	<p>1-8,13, 17-19, 22, 24-28, 31-35</p>
A	<p>WO 2007/140416 A2 (ALZA CORP [US]; LAUTENBACH SCOTT D [US]; DE LA SERNA PEDRO E [US]; ZAM) 6 December 2007 (2007-12-06)</p> <p>figures claims paragraph [0040]</p>	<p>1-8,13, 17-19, 22, 24-28, 31-35</p>
A	<p>MALATERRE V ET AL: "Oral osmotically driven systems: 30 years of development and clinical use", EUROPEAN JOURNAL OF PHARMACEUTICS AND BIOPHARMACEUTICS, ELSEVIER SCIENCE PUBLISHERS B.V., AMSTERDAM, NL, vol. 73, no. 3, 1 November 2009 (2009-11-01), pages 311-323, XP026736254, ISSN: 0939-6411, DOI: 10.1016/J.EJPB.2009.07.002 [retrieved on 2009-07-12] the whole document figure 1 paragraph 3.2 "Multilayer-core osmotic systems"</p>	<p>1-8,13, 17-19, 22, 24-28, 31-35</p>

INTERNATIONAL SEARCH REPORT

International application No
PCT/IB2013/061366

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>US 6 004 582 A (FAOUR JOAQUINA [AR] ET AL) 21 December 1999 (1999-12-21) column 1, line 4 - line 10 column 3, line 40 - line 24 figure 2 column 7, line 17 - column 8, line 57 claims 1,16,18,19</p> <p style="text-align: center;">-----</p>	26,27
X	<p>US 4 959 218 A (ECKENHOFF JAMES B [US] ET AL) 25 September 1990 (1990-09-25)</p> <p>column 1, line 14 - line 24 column 3, line 28 - line 42 figure 3 examples 1,2 claims 1,2</p> <p style="text-align: center;">-----</p>	1-4,7,8, 13,18, 19,22, 24,28
X	<p>WO 2004/010981 A1 (ALZA CORP [US]) 5 February 2004 (2004-02-05)</p> <p>paragraph [0001] paragraph [0090] - paragraph [0096] paragraph [0109] paragraph [0115] - paragraph [0116] paragraph [0119] - paragraph [0121] paragraph [0141] figures 1,3 examples 1,2 claims 1,24-26,33-37,</p> <p style="text-align: center;">-----</p>	1-4,8, 13,18, 19,22,28

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No PCT/IB2013/061366

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 4904474	A	27-02-1990	NONE

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB2013/061366

Box No. 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 No. 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 fees, this Authority did not invite payment of additional fees.

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.:
1-8, 13, 17-19, 22, 24-26, 28, 31-34(completely); 27, 35(partially)

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 and, where applicable, the payment of a protest fee.
- The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- 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: 1-8, 13, 17-19, 22, 24, 25, 31, 34(completely); 32, 33, 35(partially)

A pharmaceutical dosage form for delivery of, at a target site in a human or animal body, an active pharmaceutical ingredient (API), said pharmaceutical dosage form comprising: a shell defining therein an outlet; a polymeric matrix having at least one API, the polymeric matrix received within the shell; and a swellable polymer body located within the shell, wherein the swellable polymer body is pH responsive, such that in use, exposure of the body to a medium of increasing pH causes an increase in swelling and an increase in volume of the swellable polymer body, which in turn, facilitates displacement of the polymeric matrix through the outlet toward the target site for delivery of the API; in particular also those wherein the synthetic polymer is selected from the group consisting of: polyetheretherketone, high density polyethylene (HDPE), ultra high molecular weight polyethylene (UHMWPE), polytetrafluoroethylene, polymethmethacrylate, polydimethylsiloxane, and poly(sulphone); or wherein the shell defines an inlet at a region proximate the location of the swellable polymer body; or those having an elongate cylindrical shell defining an outlet and an inlet at opposing first and second end regions of the shell, a mucoadhesive polymeric matrix having at least one API, the polymeric matrix received within and in register with the shell

2. claim: 9

Dosage forms wherein the polymeric matrix is at least one polymer selected from the group consisting of: chitosan, trimethyl chitosan, trimethyl chitosan chloride (TMC:Cl), EDTA-g-chitosan, 2-mercaptoethylamine-g-chitosan, and polyacrylic acid-cysteine

3. claims: 10-12, 20, 21(completely); 27, 30(partially)

Dosage forms wherein the compositions contain a permeation enhancer or metal chelator

4. claim: 14

Dosage forms wherein the polymeric matrix further includes a glidant

5. claim: 15

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Dosage forms wherein the polymeric matrix is cross-linked by microwave radiation, ultraviolet radiation or chemical crosslinking

6. claim: 16

Dosage forms wherein the at least one drug is a peptide and/or protein selected from salmon calcitonin, eel calcitonin, chicken calcitonin, rat calcitonin, human calcitonin, porcine calcitonin or any gene-variant of calcitonin, parathyroid hormone, parathyroid hormone analogue PTH 1-31NH₂, parathyroid hormone analogue PTH 1-34NH₂, insulin of any gene variant, vasopressin, desmopressin, luteinizing hormone-releasing factor, erythropoietin, tissue plasminogen activators, human growth factor, adrenocorticotropin, various interleukins, and enkephalin

7. claim: 23

Dosage forms wherein the swellable polymer body further includes at least one drug

8. claims: 26(completely); 27, 33, 35(partially)

Dosage forms which further include a cap closing the outlet of the shell, whereby said cap is stable in acidic conditions of the stomach and degraded in neutral or alkaline conditions (enteric cap)

9. claims: 28(completely); 32(partially)

Dosage forms which further comprise a spacer between the swellable polymer body and the polymeric matrix

10. claims: 29(completely); 30, 35(partially)

Dosage forms which further comprise a second polymeric body located proximal the outlet inside the shell

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No PCT/IB2013/061366

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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