

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
13 February 2003 (13.02.2003)

PCT

(10) International Publication Number  
**WO 03/011274 A3**

- (51) International Patent Classification<sup>7</sup>: **A61K 31/192**, 31/46, 45/08, A61P 11/00, 11/06 // (A61K 31/46, 31:192)
- (21) International Application Number: PCT/EP02/08322
- (22) International Filing Date: 25 July 2002 (25.07.2002)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:  
0118373.0 27 July 2001 (27.07.2001) GB
- (71) Applicant (for all designated States except US): **GLAXO GROUP LIMITED** [GB/GB]; Glaxo Wellcome House, Berkeley Avenue, Greenford, Middlesex UB6 0NN (GB).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): **KNOWLES, Richard, Graham** [GB/GB]; GlaxoSmithKline, Gunnels Wood Road, Stevenage, Hertfordshire SG1 2NY (GB). **WARD, Peter** [GB/GB]; GlaxoSmithKline, Gunnels Wood Road, Stevenage, Hertfordshire SG1 2NY (GB).
- (74) Agent: **GIDDINGS, Peter, John**; Corporate Intellectual Property, GlaxoSmithKline, 98 Great West Road (CN925.1), Brentford, Middlesex TW8 9GS (GB).
- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, 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, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW.
- (84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
- Published:  
— with international search report
- (88) Date of publication of the international search report:  
18 September 2003
- 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.



**WO 03/011274 A3**

(54) Title: USE OF A PDE4 INHIBITOR IN COMBINATION WITH AN ANTICHOLINERGIC AGENT FOR THE TREATMENT OF PULMONARY DISEASE SUCH AS ASTHMA

(57) Abstract: This invention relates to treating pulmonary diseases such as obstructive pulmonary disease or asthma by administering a phosphodiesterase 4 inhibitor in combination with an anticholinergic agent.

## INTERNATIONAL SEARCH REPORT

International Application No  
PCT/EP 02/08322

<b>A. CLASSIFICATION OF SUBJECT MATTER</b>		
IPC 7	A61K31/192 A61K31/46	A61K45/08 A61P11/00 A61P11/06
	//((A61K31/46, 31:192))	
According to International Patent Classification (IPC) or to both national classification and IPC		
<b>B. FIELDS SEARCHED</b>		
Minimum documentation searched (classification system followed by classification symbols)		
IPC 7	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)		
PAJ, EPO-Internal, BIOSIS, EMBASE, MEDLINE, WPI Data		
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 1 040 829 A (PFIZER) 4 October 2000 (2000-10-04) page 37, line 42,43; claim 10 ---	2,6
E	WO 02 069945 A (BOEHRINGER INGELHEIM PHARMA ;PIEPER MICHAEL PAUL (DE); PAIRET MICH) 12 September 2002 (2002-09-12) page 1, line 1-3,32 page 2, line 14 page 7, line 5,6; claims 1,3 ---	1-9
E	EP 1 270 577 A (TAKEDA CHEMICAL INDUSTRIES LTD) 2 January 2003 (2003-01-02) page 82, line 1-10; claim 47 --- -/--	1-4,6-9
<input checked="" type="checkbox"/> Further documents are listed in the continuation of box C. <input checked="" type="checkbox"/> 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		Date of mailing of the international search report
24 February 2003		03/03/2003
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  Allnutt, S

## INTERNATIONAL SEARCH REPORT

 International Application No  
 PCT/EP 02/08322

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	WO 02 053564 A (ALMIRALL PRODESFARMA AG ;BUIL ALBERO MARIA ANTONIA (ES); FERNANDEZ) 11 July 2002 (2002-07-11) page 1, line 7,8,27-31; claim 36 ---	1-4,8,9
P,X	WO 01 57036 A (MARFAT ANTHONY ;PFIZER PROD INC (US); CHAMBER ROBERT JAMES (US)) 9 August 2001 (2001-08-09) page 22, line 20 page 36, line 4,5,32,33 page 35, line 28,29 ---	1-9
P,X	WO 02 09689 A (EDELSON JEFFREY D ;SMITHKLINE BEECHAM CORP (US)) 7 February 2002 (2002-02-07) page 6, line 23,24; claims 1,2 page 7, line 7-9 ---	1-6,8,9
A	TAVAKKOLI A ET AL: "DRUG TREATMENT O ASTHMA IN THE 1990S ACHIEVEMENTS AND NEW STRATEGIES" DRUGS, ADIS INTERNATIONAL LTD, AT, vol. 57, no. 1, January 1999 (1999-01), pages 1-8, XP001098314 ISSN: 0012-6667 page 3, column 2, line 4-23 page 4, column 2, line 29-34 -----	1-9

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/EP 02/08322

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 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.: 1, 5-9  
because they relate to subject matter not required to be searched by this Authority, namely:  
see FURTHER INFORMATION sheet PCT/ISA/210
  
2.  Claims Nos.: 1-9  
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:  
see FURTHER INFORMATION sheet PCT/ISA/210
  
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 II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

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

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

Continuation of Box I.1

Although claims 1 and 5-9 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

---

Continuation of Box I.1

Claims Nos.: 1,5-9

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

---

Continuation of Box I.2

Claims Nos.: 1-9

In claims 1-4, 6, 8 and 9, the expression "PDE 4 inhibitor" is defined by reference to a desirable characteristic or property. This leads to a lack of clarity (Article 6 PCT) and is such as to render a meaningful search over the whole claimed scope impossible. Consequently, a search has been carried out for those clear, supported and concise claims i.e. the compounds defined in claim 5 and the description (pg 4, l. 13-27). In addition, this term encompasses a very large number of possible compounds which may have this characteristic and a complete search is therefore not possible.

The applicants attention is drawn to the fact that some compounds may be already known to treat the diseases/disorders claimed by the applicant but are as yet not identified as PDE 4 inhibitors.

The same reasoning applies to the term "anticholinergic agent" in claims 1-4, 5, 8 and 9. The search has been carried out based on the compounds disclosed in claim 7 and in the description (pg 5, l. 9-31).

Present claims 1-7 relate to an extremely large number of possible disorders due to the broadness of the term "exacerbations associated with a pulmonary disease". Consequently, the search has been restricted to those disorders which are clear, concise and supported by the description (on pg 2, l. 11-12) and in claims 8 and 9.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

## INTERNATIONAL SEARCH REPORT

 International Application No  
 PCT/EP 02/08322

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
EP 1040829	A	04-10-2000	EP 1040829 A2	04-10-2000
			JP 2000198734 A	18-07-2000
WO 02069945	A	12-09-2002	DE 10110772 A1	12-09-2002
			WO 02069945 A2	12-09-2002
			US 2002193393 A1	19-12-2002
EP 1270577	A	02-01-2003	AU 3955001 A	03-10-2001
			EP 1270577 A1	02-01-2003
			WO 0170746 A1	27-09-2001
			JP 2001335579 A	04-12-2001
WO 02053564	A	11-07-2002	WO 02053564 A2	11-07-2002
WO 0157036	A	09-08-2001	AU 2700201 A	14-08-2001
			BR 0107964 A	29-10-2002
			EP 1252158 A1	30-10-2002
			WO 0157036 A1	09-08-2001
			NO 20023613 A	30-09-2002
			TR 200201880 T2	21-11-2002
WO 0209689	A	07-02-2002	AU 7902301 A	13-02-2002
			WO 0209689 A1	07-02-2002