### ${\bf (19) \ World \ Intellectual \ Property \ Organization}$

International Bureau



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- (71) Applicant (for all designated States except US): ARAKIS LTD. [GB/GB]; Chesterford Research Park, Little Chesterford, Saffron Walden, Essex CB10 1XL (GB).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): BAXTER, Andrew, Douglas [GB/GB]; Arakis Ltd., Chesterford Research Park, Little Chesterford, Saffron Walden, Essex CB10 1XL (GB). BREW, John [GB/GB]; Arakis Ltd., Chesterford Research Park, Little Chesterford, saffron Walden, Essex CB10 1XL (GB).

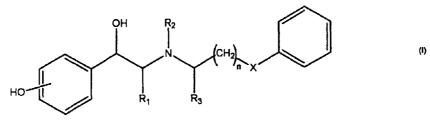
- (74) Agent: GILL JENNINGS & EVERY; Broadgate Hosue, 7 Eldon Street, London EC2M 7LH (GB).
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- (84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, 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, 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).

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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: THE TREATMENT OF INFLAMMATORY DISORDERS AND PAIN USING BETA-AMINOALCOHOLS



(57) Abstract: A compound (preferably bufeniode, denopamine, fenoterol, ifenprodil, isoxsuprine, labetol, medroxalol, mesuprine, nylidrin, protokylol, ractopamine, ritodrine, salmefamol or sulfinalol) that has utility in the treatment or prevention of a condition associated with T-cell proliferation or that is mediated by pro- and/or anti-inflammatory cytokines, and in particular a disease selected from the group consisting of rheumatoid arthritis, osteoarthritis, or osteoporosis, chronic demyelinating disease such as multiple sclerosis, respiratory diseases such as asthma or chronic obstructive pulmonary disease, inflammatory bowel disease (IBD) such as ulcerative colitis or Crohn's disease, dermatological conditions such as psoriasis, scleroderma or atopic dermatitis, dental diseases such as periodontal disease or gingivitis, diabetic nephropathy, lupus nephritis, IgA nephropathy or glomerulonephritis, systemic iupus erythomatosus (SLE), graft vs host disease, a pain condition, is of formula (I), wherein R<sub>1</sub> is H or Me; R<sub>2</sub> is H or alkyl and R<sub>3</sub> is H or Me, or R<sub>2</sub> and R<sub>3</sub> are -CH<sub>2</sub>- thereby forming a ring; n is 0 to 2; X is CH<sub>2</sub> or O; and the two benzene rings are each optionally substituted with OH, OMe, halogen, NHCHO, NHSO<sub>2</sub>Me, CONH<sub>2</sub>, SOMe, OCH<sub>2</sub>O, or CH<sub>2</sub>OH.



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χ Furt	ther documents are listed in the continuation of box C.	X Patent family	members are listed i	n annex.
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	actual completion of the international search	Date of mailing of	the international sea	rch report
	mailing address of the ISA	Authorized officer		
	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	A. Jako	obs	

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C.(Continua	ion) DOCUMENTS CONSIDERED TO BE RELEVANT  Relevant to Claim No.					
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#### INTERNATIONAL SEARCH REPORT

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. X Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
Although claims 1-17 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.
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. X 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.:
1-17 (partially) as far as relating to inventions 1,4,12
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.
χ 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: 1-17 (partially)

Use of bufeniode for the manufacture of a medicament for the treatment or prevention of a condition associated with T-cell proliferation or that is mediated by pro- and/or anti-inflammatory cytokines, and in particular a disease selected from the group consisting of rheumatoid arthritis, osteoarthritis or osteoporosis, chronic demyelinating disease such as multiple sclerosis, respiratory diseases such as asthma or chronic obstructive pulmonary disease, inflammatory bowel disease (IBD) such as ulcerative colitis or Crohn's disease, dermatological conditions such as psoriasis, scleroderma or atopic dermatitis, dental diseases such as periodontal disease or gingivitis, diabetic nephrophathy, lupus nephritis, IgA nephrophathy or glomerulonephritis, systemic lupus erythomatosus (SLE), graft vs host disease, a pain condition is chronic pain such as chronic back pain, malignant pain, chronic headache (including migraine and cluster headaches) or arthritic pain, pain conditions including acute pain such as post-operative pain, post-traumatic pain or acute disease-induced pain and neuropathic pain.

2. claims: 1-17 (partially)

Use of denopamine for the manufacture of a medicament for the treatment or prevention of a condition as specified under invention 1.

3. claims: 1-17 (partially)

Use of fenoterol for the manufacture of a medicament for the treatment or prevention of a condition as specified under invention 1.

4. claims: 1-17 (partially)

Use of ifenprodil for the manufacture of a medicament for the treatment or prevention of a condition as specified under invention 1.

5. claims: 1-17 (partially)

Use of isoxsuprine for the manufacture of a medicament for the treatment or prevention of a condition as specified under invention 1.

#### FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

6. claims: 1-17 (partially)

Use of labetalol for the manufacture of a medicament for the treatment or prevention of a condition as specified under invention 1.

7. claims: 1-17 (partially)

Use of medroxalol for the manufacture of a medicament for the treatment or prevention of a condition as specified under invention 1.

8. claims: 1-17 (partially)

Use of mesuprine for the manufacture of a medicament for the treatment or prevention of a condition as specified under invention 1.

9. claims: 1-17 (partially)

Use of nylidrin for the manufacture of a medicament for the treatment or prevention of a condition as specified under invention 1.

10. claims: 1-17 (partially)

Use of protokylol for the manufacture of a medicament for the treatment or prevention of a condition as specified under invention 1.

11. claims: 1-17 (partially)

Use of ractopramine for the manufacture of a medicament for the treatment or prevention of a condition as specified under invention  ${\bf 1}.$ 

12. claims: 1-17 (partially)

Use of ritodrine for the manufacture of a medicament for the treatment or prevention of a condition as specified under invention 1.

13. claims: 1-17 (partially)

Use of salmefamol for the manufacture of a medicament for the treatment or prevention of a condition as specified under invention 1.

#### FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

14. claims: 1-17 (partially)

Use of sulfinalol for the manufacture of a medicament for the treatment or prevention of a condition as specified under invention  $1. \,$ 

information on patent family members

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