



## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<b>(51) International Patent Classification<sup>5</sup> :</b> <b>A61K 31/00, 31/14, 31/405</b> <b>A61K 31/435, 31/44, 31/55</b> <b>A61K 31/66</b>	<b>A3</b>	<b>(11) International Publication Number:</b> <b>WO 92/20328</b> <b>(43) International Publication Date:</b> 26 November 1992 (26.11.92)
<b>(21) International Application Number:</b> PCT/DK92/00161 <b>(22) International Filing Date:</b> 14 May 1992 (14.05.92) <b>(30) Priority data:</b> 3706 14 May 1991 (14.05.91) IS 3706 31 July 1991 (31.07.91) IS 0182/92 13 February 1992 (13.02.92) DK <b>(71)(72) Applicant and Inventor:</b> SNORRASON, Ernir [IS/IS]; Stigahlid 80, IS-105 Reykjavik (IS). <b>(74) Agent:</b> PLOUGMANN & VINGTOFT; Sankt Annæ Plads 11, DK-1250 Copenhagen K (DK).	<b>(81) Designated States:</b> AT, AT (European patent), AU, BB, BE (European patent), BF (OAPI patent), BG, BJ (OAPI patent), BR, CA, CF (OAPI patent), CG (OAPI patent), CH, CH (European patent), CI (OAPI patent), CM (OAPI patent), CS, DE, DE (European patent), DK, DK (European patent), ES, ES (European patent), FI, FR (European patent), GA (OAPI patent), GB, GB (European patent), GN (OAPI patent), GR (European patent), HU, IT (European patent), JP, KP, KR, LK, LU, LU (European patent), MC (European patent), MG, ML (OAPI patent), MN, MR (OAPI patent), MW, NL, NL (European patent), NO, PL, RO, RU, SD, SE, SE (European patent), SN (OAPI patent), TD (OAPI patent), TG (OAPI patent).  <b>Published</b> <i>With international search report.  Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>  <b>(88) Date of publication of the international search report:</b> 15 April 1993 (15.04.93)	
<b>(54) Title:</b> IMPROVEMENTS IN BENZODIAZEPINE TREATMENT BY CHOLINESTERASE INHIBITORS		
<b>(57) Abstract</b>		
<p>The use of a pharmaceutically acceptable cholinesterase inhibitor or a prodrug thereof for counteracting the sedative, hypnotic or respiratory depressive effects of benzodiazepines, substantially without interfering with the anxiolytic, antipsychotic, anticonvulsant, and muscle relaxant activity of benzodiazepines, especially the benzodiazepines used for treatment of diseases where the sedative, hypnotic or respiratory depressive effects are undesirable, such as diseases selected from the group consisting of anxiety, anxiety neurosis, anxiety reactions, panic reactions, schizophrenia, affective or schizoaffective type schizophrenia, borderline psychosis, agitating endogene depressions, hyperactivity in children, and muscle spasms; the use of a pharmaceutically acceptable cholinesterase inhibitor or a prodrug thereof for the treatment of schizophrenia, in particular affective or schizoaffective type schizophrenia. The acetyl cholinesterase is preferably one that acts substantially selectively at nicotinic receptor sites, and which has selectively for acetyl cholinesterase opposed to butyryl cholinesterase, e.g. galanthamine or a galanthamine derivative.</p>		

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III. DOCUMENTS CONSIDERED TO BE RELEVANT (CONTINUED FROM THE SECOND SHEET)		
Category °	Citation of Document, with indication, where appropriate, of the relevant passages	Relevant to Claim No.
X	Anesthesia and Analgesia, vol. 54, no. 5, September-October 1975, C.D. BLITT et al.: "Reversal of lorazepam delirium by physostigmine", pages 607-608, see complete article <p style="text-align: center;">---</p>	1-4,8, 15
X	Resuscitation, vol. 16/suppl., 1988, Elsevier Scientific Publishers Ireland Ltd, (IE), P.M. LAUVEN et al.: "Flumazenil (Ro 15-1788) and physostigmine", pages S41-S48, see pages S42-S48 <p style="text-align: center;">---</p>	1-4,8, 15
A	Anesthesia and Analgesia, vol. 65, no. 6, June 1986, The International Anesthesia Research Society, W.E. HOFFMAN et al.: "Cerebrovascular and cerebral metabolic effects of physostigmine, midazolam, and a benzodiazepine antagonist", pages 639-644 <p style="text-align: center;">---</p>	
A	Anesthesia and Analgesia, vol. 62, no. 7, July 1983, The International Anesthesia Research Society, U.A. PANDIT et al.: "Physostigmine fails to reverse clinical, psychomotor, or EEG effects of lorazepam", pages 679-685 <p style="text-align: center;">---</p>	
A	W. FORTH et al.: "Allgemeine und spezielle Pharmakologie und Toxikologie", 5th edition, pages 106-109, Wissenschaftsverlag, Mannheim, DE <p style="text-align: center;">---</p>	
A	Biological Psychiatry, vol. 18, no. 12, December 1983, Society of Biological Psychiatry, S.I. DEUTSCH et al.: "Acetylcholinesterase activity in CSF in schizophrenia, depression, Alzheimer's disease, and normals", pages 1363-1373 <p style="text-align: center;">-----</p>	

## INTERNATIONAL SEARCH REPORT

international application No.

PCT/DK92/00161

**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.:  
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 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:

FOR FURTHER INFORMATION PLEASE SEE FORM PCT/ISA/206 DATED 23.09.92.

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.:  
  1. Claims 1-5, 8 partially, 9-16, 31-34, 35 partially, 38 partially.
  2. Claims 8 partially, 17-18, 21-30, 38 and 39 partially.
  3. Claims 6, 7, 19 and 20
  
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.