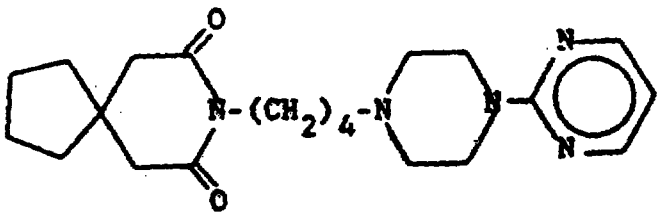
Description

This invention is concerned with the use of the pyrimidine compound 8-[4-(4-(2-pyrimidinyl)-1-piperazinyl]butyl]-8-azaspiro[4.5]decane-7,9-dione or a pharmaceutically acceptable acid addition salt thereof for preparing pharmaceutical compositions for alleviation of phobic anxiety.

The pyrimidine compound with which the present invention is concerned has the following structural formula



and is known as buspirone. The hydrochloride salt has been referred to in the prior art as MJ 9022-1 and as buspirone hydrochloride. Other acid addition salts thereof are named by combining "buspirone" with the appropriate word to define the acid from which it is prepared as in "buspirone hydrochloride". The latter is the United States Adopted Name (USAN); refer to J. American Med. Assoc. 225, 520 (1973).

The synthesis of the compound and the disclosure of its psychotropic properties are described in the following patents and publications.

1. Y. H. Wu, et al., J. Med. Chem., 15, 477 (1972).
2. Y. H. Wu, et al., U.S. Patent No. 3,717,634 which issued February 20, 1973.
3. L. E. Allen, et al., Arzneium. Forsch., 24, No. 6, 917-922 (1974).
4. G. L. Sathananthan, et al., Current Therapeutic Research, 18/5, 701-705 (1975).
5. Y. H. Wu, et al., U.S. Patent No. 3,976,776, issued August 24, 1976.

The use of buspirone hydrochloride as a novel anti-anxiety agent for the treatment of neurotic patients is described in G. P. Casten, et al., U.S. Patent No. 4,182,763, issued January 9, 1980. Currently, a New Drug Application (NDA) is pending before the U.S. Food & Drug Administration for the use of buspirone in treatment of anxiety neurosis. In addition, other clinical studies are being conducted to lend support to the use of buspirone for the therapeutic method of the instant invention.

The present invention can be distinguished from the above prior art in that it is directed to a distinct patient population characterized by a disease state different from that related to the anxiolytic process disclosed in the prior art. Support for this distinction is found in the reference, "The Diagnostic Validity of Anxiety Disorders and Their Relationship to Depressive Illness", by A.B. Boyer, Breier et al., in Am. J. Psychiatry, 142:7 (July, 1985), pages 787-796. The diagnosis and treatment of panic disorders has been recently reviewed; cf: D. V. Sheehan, "Panic Attacks and Phobias", New England Journal of Medicine, 307, pages 156-158, 1982; R. I. Shader, et al., "Panic Disorders: Current Perspectives", J. Clin. Pyschopharmacology, 2/6 Supplement, pages 2S-26S, 1982; and W. Matuzas, et al., "Treatment of Agoraphobia and Panic Attacks", Arch. Gen. Psychiatry, 40, pages 220-222, 1983.

J.Psychiatr.Res. 18 (1), 1984, 73-78 is concerned with the short-term drug treatment of anxiety in primary care. Patients were treated with diazepam, buspirone and a placebo in a double-blinded cross-over study. Patients were admitted to the study if their DSM-III primary diagnosis was generalized anxiety disorder, panic disorder or agoraphobia with panic attacks. No essential efficacy differences were detected between the three test substances and it was shown that buspirone gas little different from placebo.

Although panic disorder and in particular phobic anxiety or panic attacks, is a relatively new diagnosis, the basic diagnostic concepts are well known to those skilled in the art and are clearly differentiated from generalized, persistent anxiety. Although the prior art references concerning buspirone disclose the compounds described in the instant application and their tranquilizing and anti-anxiety effects, none of these prior art buspirone references disclose or suggest that these compounds are useful to treat or prevent phobic anxiety which is the applicants' claimed invention.

An example for comparison which distinguishes use in generalized anxiety from use in panic disorder is the drug alprazolam which was disclosed in U.S. Patent No. 3,987,052, issued Cctober, 1976 to Hester as having sedative, tranquilizing and muscle relaxant effects and could be used to alleviate tension and anxiety in mammals. U.S. Patent No. 4,508,726, issued April, 1985, to Coleman discloses and claims the treatment of panic disorders with alprazolam. Further, U.S. Patent No. 4,508,726 admits that alprazolam had been

previously disclosed for the management of anxiety disorders. Alprazolam, a benzodiazepine compound, bears no structural or biochemical relationship to buspirone and would not suggest its usefulness in panic disorders.

In summary, buspirone and its pharmaceutically acceptable salts bear no structural resemblance to any therapeutic agent alleged to be useful in the treatment of panic disorders and in particular phobic anxiety. It is now appreciated by those skilled in the art that generalized anxiety and panic disorders and in particular phobic anxiety are distinguishable disease states with differently defined patient populations. There also exists nothing in the prior art which teaches or suggests that the instant compounds would be useful in alleviation of panic disorder and in particular phobic anxiety.

The use of the present invention is intended for the alleviation of phobic anxiety. The use essentially involves administration of buspirone, or a pharmaceutically acceptable acid addition salt thereof, to one in need of such treatment.

Oral administration of buspirone hydrochloride from 10 to 60 mg per day in divided doses is anticipated as being the preferred dosage regimen.

The treatment of phobic anxiety essentially involves administration of buspirone, or a pharmaceutically acceptable acid addition salt thereof, to a patient in need of such treatment. Pharmaceutically acceptable acid addition salts of buspirone and methods of pharmaceutical formulation are described in the above patents of Wu, et al., U.S. Patent No. 3,717,634 and Casten, et al., U.S. Patent No. 4,182,763.

Administration of buspirone according to the present invention may be made by the parenteral, oral, or rectal routes. The oral route is preferred, however. The clinical dosage range for alleviation of a phobic anxiety is expected to be about the same to slightly higher compared with that for anti-anxiety usage, but can vary to some extent. In general, the expected amount of buspirone administered would be less than 100 mg per day, generally in the 20 mg to 60 mg range, and preferably in the range of 30-60 mg per day. Since the dosage should be tailored to the individual patient, the usual practice is to commence with a dose of 5 mg administered two or three times per day and then to increase the dose every two or three days by 5 mg at each dosage time until the desired response is observed or until the patient exhibits side effects. Single daily dosage may be applicable in some instances.

Claims

1. The use of buspirone or a pharmaceutically acceptable acid addition salt thereof for preparing pharmaceutical compositions for alleviation of phobic anxiety.

2. The use according to claim 1 wherein buspirone hydrochloride is employed for preparing pharmaceutical compositions for oral administration.

Patentansprüche

1. Verwendung von Buspiron oder eines pharmazeutisch verträglichen Säureadditionssalzes davon zur Herstellung pharmazeutischer Mittel zur Linderung von phobischer Angst.

2. Verwendung nach Anspruch 1, wobei Buspiron-Hydrochlorid zur Herstellung pharmazeutischer Mittel zur oralen Verabreichung verwendet wird.

Revendications

1. Utilisation de buspirone ou de son sel d'addition d'acide acceptable en pharmacie pour la préparation de compositions pharmaceutiques pour l'atténuation de l'anxiété phobique.

2. Utilisation selon la revendication 1, où on emploie le chlorhydrate de buspirone pour la préparation de compositions pharmaceutiques pour une administration orale.

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