USE OF PRAMIPEXOLE IN THE TREATMENT OF RESTLESS LEGS SYNDROME

FIELD OF THE INVENTION

The present invention relates to the use of pramipexole or 2-amino-6-n-propylamino-4,5,6,7-tetrahydrobenzo-thiazole or the (-)-enantiomers thereof, and the pharmacologically acceptable salts thereof, in the treatment of restless leg syndrome.

BACKGROUND OF THE INVENTION

Restless leg syndrome (RLS) is a neurosensorimotor disorder with parestethesias, sleep disturbances and, in most cases, periodic limb movements of sleep (PLMS).

Pramipexole is a dopamine-D_3/D_2 agonist the synthesis of which is described in European Patent 186 087 and its counterpart, U.S. Patent 4,886,812. It is known primarily for the treatment of schizophrenia and Parkinson's disease. It is known from German patent application DE 38 43 227 that pramipexole lowers the plasma level of prolactin. Also, this European patent application discloses the use of pramipexole in the treatment of drug dependency. Further, it is known from German patent application DE 39 33 738 that pramipexole can be used to decrease abnormal high levels of thyroid stimulating hormone (TSH). U.S. patent 5,112,842 discloses the transdermal administration of the compounds and transdermal systems containing these active compounds. The WO patent application PCT/EP 93/03389 describes pramipexole as an antidepressant agent, while the PCT application PCT/US95/15618 discloses the neuroprotective effects of pramipexole.

Surprisingly and unexpectedly, it has been found that pramipexole and the pharmacologically acceptable salts thereof can be used in the treatment of restless leg syndrome.

SUMMARY OF THE INVENTION

The present invention particularly provides a method for treatment of restless legs syndrome in a patient suffering from or susceptible to such condition comprising the administration of an effective amount of pramipexole. By pramipexole is meant 2-amino-6-n-propylamino-4,5,6,7-tetrahydrobenzothiazole, its (-)-enantiomer thereof, and pharmacologically acceptable salts thereof especially (-)-2-amino-6-n-propylamino-4,5,6,7-tetrahydrobenzothiazole dihydrochloride (H_2O).

2-Amino-6-n-propyl-amino-4,5,6,7-tetrahydrobenzothiazole, particularly the (-)-enantiomer thereof, and the pharmacologically acceptable acid addition salts thereof can be given for treating RSL. The form of conventional galenic

preparations consist essentially of an inert pharmaceutical carrier and an effective dose of the active substance; e.g., plain or coated tablets, capsules, lozenges, powders, solutions, suspensions, emulsions, syrups, suppositories, etc.

Preferred are tablets comprising 0.88 (0.125), 0.18 (0.25), 0.7 (1.0), 088 (1.25) and 1.1 (1.5) mg of Pramipexole base (mg Pramipexole 2HCl), respectively, and further comprising mannitol, maize starch, colloidal silica, polividone and magnesium stearate as excipients.

The effective dose range is 0.001 to 10.0 mg/day and patient, preferred between 0.001 and 6, more preferred between 0.01 to 6 and especially preferred between 0.75 and 4.5 mg/day and patient p.o. In addition to being administered by oral or intravenous route pramipexole may also be administered transdermally or by inhalation.

Dosages should be increased gradually from a starting dose of about 0.264 mg of base per day and then increased every 5-7 days. Providing patients do not experience intolerable side effects, the dosage should be titrated to achieve a maximal therapeutic effect.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

The present invention is seen more fully by the examples given below:

In a pilot study on Restless Leg Syndrome, 10 patients have been treated with pramipexole in a crossover design. The patients received up to 1.5 mg a day of pramipexole over 4 weeks. After the first treatment period there is a two week wash-out period and an additional 4-week treatment period.

Since the symptoms of RLS are quite obvious, their improvement from treatment was obvious to the investigator.

CLAIMS

1. A method for treating restless legs syndrome in a patient suffering from comprising the administration of an effective amount of the compound 2-amino-6-n-propylamino-4,5,6,7-tetrahydrobenzothiazole, its (-)-enantiomer thereof, and pharmacologically acceptable salts thereof.

2. A method for treating restless legs syndrome in a patient suffering from comprising the administration of an effective amount of Pramipexole, its dihydrochloride, or its dihydrochloride-(H_2O) thereof.

3. A method of claim 2, wherein the dose of Pramipexole is about 0.01-10.0 mg/day.

4. Use of 2-amino-6-n-propylamino-4,5,6,7-tetrahydrobenzothiazole, its (-)-enantiomer thereof, or a pharmacologically acceptable salt thereof, to prepare a medicament for treating restless legs syndrome in a patient suffering from or susceptible to such condition.

5. A use of claim 4, wherein the compound is Pramipexole, its dihydrochloride, or its dihydrochloride-(H_2O) thereof.

6. A use of claim 5, wherein the dose of Pramipexole is about 0.01-10.0 mg/day.

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