In another aspect, the present invention relates to a compound of formula I or a pharmaceutically-acceptable salt thereof for use in increasing standing time in a human patient having symptomatic neurogenic orthostatic hypotension.

In another aspect, the present invention relates to a compound of formula I or a pharmaceutically-acceptable salt thereof for use in the treatment orthostatic dizziness or lightheadedness in a human patient caused by symptomatic neurogenic orthostatic hypotension.

In another aspect, the present invention relates to a pharmaceutical composition comprising a pharmaceutically-acceptable carrier and a compound of formula I or a pharmaceutically-acceptable salt thereof for use in the treatment of neurogenic orthostatic hypotension and the symptoms thereof in a human patient; wherein the composition is administered to the patient to provide an amount of the compound ranging from about 1 mg/day to about 20 mg/day and wherein the use is characterized by (a) an increase in the patient's seated systolic blood pressure; (b) an increase in the patient's standing time; or (c) a decrease in dizziness or lightheadedness experienced by the patient.

In another aspect, the present invention relates to use of a compound of formula I or a pharmaceutically-acceptable salt thereof for the manufacture of a medicament for the treatment of neurogenic orthostatic hypotension in a human patient and the symptoms thereof; wherein the compound is to be administered to the patient in an amount ranging from about 1 mg/day to about 20 mg/day and wherein the use is characterized by (a) an increase in the patient's seated systolic blood pressure; (b) an increase in the patient's standing time; or (c) a decrease in dizziness or lightheadedness experienced by the patient.

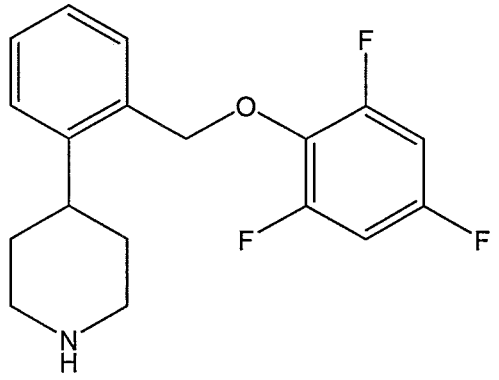
In another aspect, there is provided a use of a pharmaceutical composition comprising a pharmaceutically-acceptable carrier and a compound of formula I or a pharmaceutically-acceptable salt thereof in the manufacture of a medicament for the treatment of neurogenic orthostatic hypotension and the symptoms thereof in a human patient; wherein the composition is to be administered to the patient to provide an amount of the compound ranging from about 1 mg/day to about 20 mg/day and wherein the use is characterized by (a) an increase in the patient's seated systolic blood pressure; (b) an increase in the patient's standing time; or (c) a decrease in dizziness or lightheadedness experienced by the patient.

In another aspect, the present invention relates to a method for treating neurogenic orthostatic hypotension and the symptoms thereof in a human patient, the method comprising administering to the patient a compound of formula I or a pharmaceutically-acceptable salt thereof.

In another aspect, the present invention relates to a method for treating neurogenic orthostatic hypotension and the symptoms thereof in a human patient, the method comprising administering to the patient a compound of formula I or a pharmaceutically-acceptable salt thereof; wherein the compound is administered to the patient in an amount ranging from about 1 mg/day to about 20 mg/day and wherein the method is characterized by (a) an increase in the patient's seated systolic blood pressure; (b) an increase in the

WHAT IS CLAIMED IS:

1. Use of a compound of formula I:



I

or a pharmaceutically-acceptable salt thereof in the manufacture of a medicament for the treatment of neurogenic orthostatic hypotension and symptoms thereof in a human patient; wherein the compound is to be administered to the patient in an amount ranging from about 1 mg/day to about 20 mg/day and wherein the use is characterized by: (a) an increase in the patient's seated systolic blood pressure; (b) an increase in the patient's standing time; or (c) a decrease in dizziness or lightheadedness experienced by the patient.

2. The use according to Claim 1, wherein the compound is 4-[2-(2,4,6-trifluorophenoxymethyl)phenyl]piperidine hydrochloride.

3. The use according to Claim 1, wherein the compound is a crystalline hydrochloride salt of 4-[2-(2,4,6-trifluorophenoxymethyl)phenyl]piperidine characterized by a powder x-ray diffraction pattern comprising diffraction peaks at 2θ values of 4.44±0.20, 10.22±0.20, 17.16±0.20 and 21.78±0.20.

4. The use according to Claim 3, wherein the crystalline hydrochloride salt of 4-[2-(2,4,6-trifluorophenoxymethyl)phenyl]piperidine is further characterized by having one or more additional diffraction peaks at 2θ values selected from 8.11±0.20, 13.18±0.20, 16.06±0.20, 18.38±0.20, 23.76±0.20, 26.32±0.20, 27.24±0.20, 29.60±0.20 and 31.94±0.20.

5. The use according to Claim 1, wherein the compound is a crystalline hydrochloride salt of 4-[2-(2,4,6-trifluorophenoxymethyl)phenyl]piperidine characterized by a differential scanning calorimetry trace having a melting point of about 197±2 °C.

6. The use according to any one of Claims 1 to 5, wherein the patient has multiple system atrophy, pure autonomic failure, or Parkinson's disease.

7. The use according to any one of Claims 1 to 5, wherein the patient has multiple system atrophy.

8. The use according to any one of Claims 1 to 7, wherein the use is characterized by an increase in the patient's seated systolic blood pressure.

9. The use according to any one of Claims 1 to 7, wherein the use is characterized by an increase in the patient's standing time.

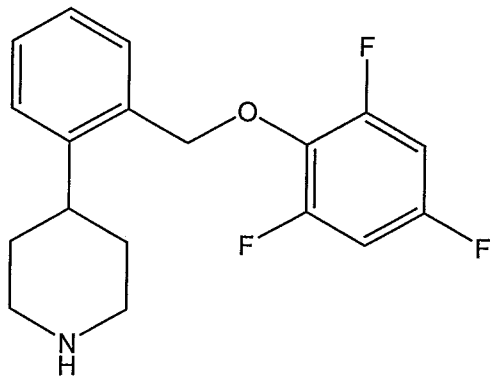
10. The use according to any one of Claims 1 to 7, wherein the use is characterized by a decrease in dizziness or lightheadedness experienced by the patient.

11. The use according to any one of Claims 1 to 7, wherein the compound is to be administered with an agent selected from an α1-adrenoceptor agonist, an α-2 adrenergic receptor antagonist, a corticosteroid, a norepinephrine precursor and a cholinesterase inhibitor; or a combination thereof.

12. The use according to any one of Claims 1 to 7, wherein the compound is to be administered with midodrine, fludrocortisone acetate, droxidopa or pyridostigmine, or, in each case, a pharmaceutically-acceptable salt thereof.

13. The use according to any one of Claims 1 to 7, wherein the compound is to be administered with midodrine hydrochloride, fludrocortisone acetate, droxidopa or pyridostigmine bromide.

14. Use of a pharmaceutical composition comprising a pharmaceutically-acceptable carrier and a compound of formula I:



I

or a pharmaceutically-acceptable salt thereof in the manufacture of a medicament for the treatment of neurogenic orthostatic hypotension and the symptoms thereof in a human patient; wherein the composition is to be administered to the patient to provide an amount of the compound ranging from about 1 mg/day to about 20 mg/day and wherein the use is characterized by (a) an increase in the patient's seated systolic blood pressure; (b) an increase in the patient's standing time; or (c) a decrease in dizziness or lightheadedness experienced by the patient.

15. The use according to Claim 14, wherein the compound is 4-[2-(2,4,6-trifluorophenoxymethyl)phenyl]piperidine hydrochloride.

16. The use according to Claim 14, wherein the compound is a crystalline hydrochloride salt of 4-[2-(2,4,6-trifluorophenoxymethyl)phenyl]piperidine characterized by a powder x-ray diffraction pattern comprising diffraction peaks at 2θ values of 4.44±0.20, 10.22±0.20, 17.16±0.20 and 21.78±0.20.

17. The use according to Claim 16, wherein the crystalline hydrochloride salt of 4-[2-(2,4,6-trifluorophenoxymethyl)phenyl]piperidine is further characterized by having one or more additional diffraction peaks at 2θ values selected from 8.11±0.20, 13.18±0.20, 16.06±0.20, 18.38±0.20, 23.76±0.20, 26.32±0.20, 27.24±0.20, 29.60±0.20 and 31.94±0.20.

18. The use according to Claim 14, wherein the compound is a crystalline hydrochloride salt of 4-[2-(2,4,6-trifluorophenoxymethyl)phenyl]piperidine characterized by a differential scanning calorimetry trace having a melting point of about 197±2 °C.

19. The use according to any one of Claims 14 to 18, wherein the patient has multiple system atrophy, pure autonomic failure, or Parkinson's disease.

20. The use according to any one of Claims 14 to 18, wherein the patient has multiple system atrophy.