that no weight gain was noted on a six week study with paroxetine. *Am. J. Psychiatry*, 160, 749-756, 2003 reports a small weight loss in a 566 patients, eight weeks study with paroxetine. *J Clin. Psychiatry*, 62, 350-536, 2001 that no substantial effects on weight was observed in a 324 patients, eight weeks trial with paroxetine.

Am.J. Psychiatry, 156, 1170-1176, 1999 reports on a long-term (one year) study on the body weight effects of fluoxetine. While fluoxetine in the acute phase induce a slight weight decrease, the long-term effect on weight is similar to placebo.

Finally, *Clin. Therapeutics*, 24, 662-672, 2002 reports on the long-term (52 weeks) body weight effects of bupropion. Bupripion gives rise to a modest, but significant decrease in body weight.

The above literature references show that it is difficult to predict the effects on weight associated with treatment with antidepressants. Many antidepressants do have weight gain as an adverse event, others don't. Also, it appears that it is difficult to predict the weight effects associated with long-term treatment with an antidepressant from results reported from short-term studies. This unpredictability is likely to be explained by at least two factors. Firstly, notwithstanding the severity of weight gain related to treatment with antidepressants, it is normally of a smaller magnitude than for treatment with antipsychotics. Thus, any changes in weight may take longer time to develop and become evident. Secondly, weight loss or gain may in itself be a symptom of depression. Therefore, treatment emergent weight gain (i.e. weight gain associated with the compound as such) may be confounded with weight changes resulting from the treatment of the disease; hence it may take longer time to separate the two effects. These observations seem to be supported by a recently published meta-analysis of 116 clinical studies on the effect of antidepressants on body weight [*J.lin.Psych.*71, 1259-1272, 2010].

Given the important implications treatment emergent weight gain may have on patients, it is important to be able to provide treatments with antidepressants associated with no or only few weight related adverse events.

Summary ~~of the invention~~

The present inventors have surprisingly found that long-term treatment with 1-[2-(2,4-dimethyl-phenylsulfanyl)phenyl]piperazine and pharmaceutically acceptable salts thereof (Compound I) is not associated with weight increase. Thus, in one embodiment, the disclosure~~invention~~ relates to Compound I for use in the treatment of a CNS disease in a patient who has previously

received medication (or is still receiving it) for the treatment of said disease which medication was ceased or reduced (or has to be ceased or reduced) due to weight related adverse events.

In one embodiment, the disclosure~~invention~~ provides Compound I for use in the treatment of a CNS disease in a patient, which patient is overweight.

In one embodiment, the disclosure~~invention~~ provides Compound I for use in the treatment of a CNS disease in a patient, which patient suffers from a further disease wherein weight increase should be avoided.

In one embodiment, the disclosure~~invention~~ provides a method for the treatment of a CNS disease in a patient who has previously received medication (or is still receiving it) for the treatment of said disease which medication was ceased or reduced (or has to be ceased or reduced) due to weight related adverse events, the method comprising the administration of a therapeutically effective amount of Compound I to a patient in need thereof.

In one embodiment, the disclosure~~invention~~ relates to a method of treating a CNS disease in a patient who is overweight, which method comprises the administration of a therapeutically effective amount of Compound I to a patient in need thereof.

In one embodiment, the disclosure~~invention~~ relates to a method for the treatment of a CNS disease in a patient who suffers from a further disease wherein weight increase should be avoided the method comprising the administration of a therapeutically effective amount of Compound I to a patient in need thereof.

In one embodiment, the disclosure~~invention~~ provides Compound I for use in the manufacture of a medicament for the treatment of a CNS disease in a patient who has previously received medication (or is still receiving it) for the treatment of said disease which medication was ceased or reduced (or has to be ceased or reduced) due to weight related adverse events.

In one embodiment, the disclosure~~invention~~ relates to the use of Compound I in the manufacture of a medicament for the treatment of a CNS disease in a patient who is overweight.

In one embodiment, the disclosure~~invention~~ relates to the use of Compound I in the manufacture of a medicament for the treatment of a CNS disease in a patient who suffers from a further disease wherein weight increase should be avoided.

In one aspect of the invention, there is provided the use of 1-[2-(2,4-dimethyl-phenylsulfanyl)phenyl]piperazine and pharmaceutically acceptable salts thereof in the manufacture of a medicament for the treatment of depression or anxiety in a patient who has previously received medication (or is still receiving it) for the treatment of said disease which medication was ceased (or has to be ceased) due to weight related adverse events, wherein said medicament is intended for administration for a treatment period above 12 weeks.

Detailed description of the invention

The molecular structure of 1-[2-(2,4-dimethyl-phenylsulfanyl)phenyl]piperazine is shown below