Poor sleep can lead to numerous health disturbances including anxiety, depression, irritability, impaired social interactions and psychomotor coordination and the like.

WO 2013/176220 [8] describes circadian rhythm-regulating agents which comprises an inhibitor capable of inhibiting vasopressin receptors V1a and V1b.

V1a antagonists have been described in the prior art, e.g. in EP 0382185, EP 0526348, WO 94/01113, WO 94/18975, WO 95/06035, WO 96/22292, WO 96/22293, WO 97/49707, WO 97/49708, WO 98/24430, WO 99/37637, WO 99/44613, WO 99/55340, WO 99/65525, WO 00/029405, WO 00/066117, WO 01/058880, WO 01/066109, WO 02/002531, WO 02/044179, WO 02/055514, WO 03/031407, WO 03/037901, WO 03/042181, WO 04/074291, WO 04/108138, WO 2005/039565, WO 2005/063754, WO 2006/020491, WO 2006/021213, WO 2006/051851, WO 2006/058705, WO 2006/102283, WO 2006/102308, WO 2007/006688, WO 2007/009906, WO 2007/014851, WO 2007/039438, WO 2007/077122, WO 2007/109615, WO 2008/068159, WO 2008/068183, WO 2008/068184, WO 2008/068185, WO 2008/077810, WO 2008/077811, WO 2008/080842, WO 2008/080844, WO 2008/084005, WO 2010/057795, WO 2010/060836, WO 2011/120877, WO 2011/128265, WO 2011/131596, WO 2011/134877, WO 2011/141396, WO 2012/003436, WO 2012/042534, WO 2013/045373, WO 2013/050334[9], etc.

Detailed description of the invention

~~In one aspect, there is provided the use of a V1a antagonist for the manufacture of a medicament for the treatment and/or prevention of phase shift sleep disorders.~~

~~In another aspect, there is provided a pharmaceutical composition comprising a V1a antagonist in a pharmaceutically acceptable form.~~

~~In another aspect, there is provided a pharmaceutical composition comprising a V1a antagonist as described herein in a pharmaceutically acceptable form.~~

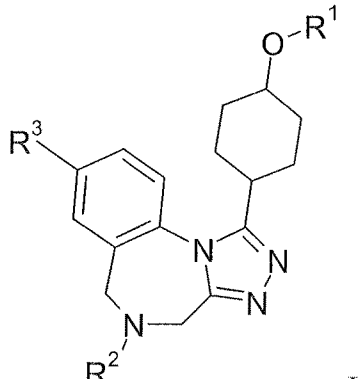
~~In another aspect, there is provided a pharmaceutical composition comprising a V1a antagonist in a pharmaceutically acceptable form for use in the treatment and/or prevention of phase shift sleep disorders.~~

~~In another aspect, there is provided a pharmaceutical composition comprising a V1a antagonist as described herein in a pharmaceutically acceptable form for use in the treatment and/or prevention of phase shift sleep disorders.~~

~~In another aspect, there is provided a V1a antagonist for use in the treatment and/or prevention of phase shift sleep disorders.~~

~~In another aspect, there is provided a V1a antagonist as described herein for use in the treatment and/or prevention of phase shift sleep disorders~~

In one aspect, there is provided use of a ~~a selective~~ V1a antagonist in the manufacture of a medicament for ~~as described herein for use in~~ the treatment and/or prevention of phase shift sleep disorders, wherein the V1a antagonist is a compound of formula I



I

wherein

R^1 is aryl or heteroaryl, unsubstituted or substituted with one or more substituents independently selected from A,

R^2 is H,

C_{1-12}-alkyl, unsubstituted or substituted with one or more OH, halo, cyano or C_{1-12}-alkoxy,

$-(CH_2)_q-R^a$, wherein R^a is phenyl or 5- or 6-membered heteroaryl, each unsubstituted or substituted with one or more substituents independently selected from A,

$-(CH_2)_rNR^iR^{ii}$,

$-C(O)-C_{1-12}$-alkyl, wherein C_{1-12}-alkyl is unsubstituted or substituted with one or more OH, halo, cyano or C_{1-12}-alkoxy,

$-C(O)(CH_2)_qOC(O)-C_{1-12}$-alkyl,

$-C(O)(CH_2)_qNR^iR^{ii}$,

$-C(O)O-C_{1-12}$-alkyl, wherein alkyl is unsubstituted or substituted with one or more OH, halo, cyano or C_{1-12}-alkoxy,

$-S(O)_2-C_{1-12}$-alkyl, or

-S(O)2NRiRii,

R^i and R^{ii} are each independently H, C_{1-12}-alkyl, or form together with the nitrogen to which they are bound a 3- to 7-membered heterocycloalkyl containing one or two heteroatoms selected from N, O or S, which heterocycloalkyl is unsubstituted or substituted by one or more substituents independently selected from B,

q is 1, 2, 3 or 4,

r is 2, 3 or 4,

A is halo, cyano, OH, C_{1-7}-alkyl, halo-C_{1-7}-alkyl, or C_{1-7}-alkoxy, halo-C_{1-7}-alkoxy, or hydroxy-C_{1-7}-alkyl,

B is oxo, halo, OH, C_{1-7}-alkyl or C_{1-7}-alkoxy,

R^3 is Cl or F,

or a pharmaceutically acceptable salt thereof, and wherein said compound is selected from the group consisting of

trans-8-Chloro-1-(4-phenoxy-cyclohexyl)-4H,6H-2,3,5,10b-tetraaza-benzoazulene-5-carboxylic acid tert-butyl ester,
trans-8-Chloro-1-(4-phenoxy-cyclohexyl)-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzoazulene hydrochloride,
trans-8-Chloro-5-methyl-1-(4-phenoxy-cyclohexyl)-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene,
trans-1-[8-Chloro-1-(4-phenoxy-cyclohexyl)-4H,6H-2,3,5,10b-tetraaza-benzoazulen-5-yl]-ethanone,
trans-8-Chloro-5-methanesulfonyl-1-(4-phenoxy-cyclohexyl)-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzoazulene,
trans-2-[8-Chloro-1-(4-phenoxy-cyclohexyl)-4H,6H-2,3,5,10b-tetraaza-benzoazulen-5-yl]-ethanol,
trans-8-Chloro-5-isopropyl-1-(4-phenoxy-cyclohexyl)-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzoazulene,
trans-8-Chloro-1-(4-phenoxy-cyclohexyl)-4H,6H-2,3,5,10b-tetraaza-benzoazulene-5-sulfonic acid dimethylamide,
trans-8-Chloro-1-(4-phenoxy-cyclohexyl)-5-pyridin-2-ylmethyl-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzoazulene,
trans-1-[8-Chloro-1-(4-phenoxy-cyclohexyl)-4H,6H-2,3,5,10b-tetraaza-benzoazulen-5-yl]-2-dimethylamino-ethanone,
trans-8-Fluoro-1-(4-phenoxy-cyclohexyl)-4H,6H-2,3,5,10b-tetraaza-benzo[e]azulene-5-carboxylic acid tert-butyl ester,
trans-8-Fluoro-5-methyl-1-(4-phenoxy-cyclohexyl)-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzoazulene,
cis-8-Chloro-1-(4-phenoxy-cyclohexyl)-4H,6H-2,3,5,10b-tetraaza-benzoazulene-5-carboxylic acid tert-butyl ester,
cis-8-Chloro-5-methyl-1-(4-phenoxy-cyclohexyl)-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzoazulene,
trans-8-Chloro-1-[4-(4-fluoro-phenoxy)-cyclohexyl]-4H,6H-2,3,5,10b-tetraaza-benzoazulene-5-carboxylic acid tert-butyl ester,
trans-8-Chloro-1-[4-(4-fluoro-phenoxy)-cyclohexyl]-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene hydrochloride,

trans-8-Chloro-1-[4-(4-fluoro-phenoxy)-cyclohexyl]-5-methyl-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzoazulene,
trans-8-Chloro-1-[4-(4-cyano-phenoxy)-cyclohexyl]-4H,6H-2,3,5,10b-tetraaza-benzo[e]azulene-5-carboxylic acid tert-butyl ester,
trans-4-[4-(8-Chloro-5-methyl-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulen-1-yl)-cyclohexyloxy]-benzonitrile,
trans-8-Chloro-1-[4-(4-trifluoromethyl-phenoxy)-cyclohexyl]-4H,6H-2,3,5,10b-tetraaza-benzo[e]azulene-5-carboxylic acid tert-butyl ester,
trans-8-Chloro-1-[4-(3-chloro-phenoxy)-cyclohexyl]-4H,6H-2,3,5,10b-tetraaza-benzoazulene-5-carboxylic acid tert-butyl ester,
trans-8-Chloro-1-[4-(3-chloro-phenoxy)-cyclohexyl]-5-methyl-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzoazulene,
trans-8-Chloro-1-[4-(3-methoxy-phenoxy)-cyclohexyl]-4H,6H-2,3,5,10b-tetraaza-benzoazulene-5-carboxylic acid tert-butyl ester,
trans-8-Chloro-1-[4-(3-methoxy-phenoxy)-cyclohexyl]-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene hydrochloride,
trans-8-Chloro-1-[4-(3-methoxy-phenoxy)-cyclohexyl]-5-methyl-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzoazulene,
trans-3-[4-(8-Chloro-5-methyl-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzoazulen-1-yl)-cyclohexyloxy]-benzonitrile,
trans-8-Chloro-1-(4-m-tolyloxy-cyclohexyl)-4H,6H-2,3,5,10b-tetraaza-benzo[e]azulene-5-carboxylic acid tert-butyl ester,
trans-8-Chloro-1-(4-m-tolyloxy-cyclohexyl)-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene hydrochloride,
trans-8-Chloro-5-methyl-1-(4-m-tolyloxy-cyclohexyl)-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene,
trans-1-[4-(3-tert-Butyl-phenoxy)-cyclohexyl]-8-chloro-4H,6H-2,3,5,10b-tetraaza-benzo[e]azulene-5-carboxylic acid tert-butyl ester,
trans-8-Chloro-1-[4-(2-fluoro-phenoxy)-cyclohexyl]-4H,6H-2,3,5,10b-tetraaza-benzo[e]azulene-5-carboxylic acid tert-butyl ester,
trans-8-Chloro-1-[4-(2-fluoro-phenoxy)-cyclohexyl]-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene hydrochloride,
trans-8-Chloro-1-[4-(2-fluoro-phenoxy)-cyclohexyl]-5-methyl-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene,
trans-8-Chloro-1-[4-(2-cyano-phenoxy)-cyclohexyl]-4H,6H-2,3,5,10b-tetraaza-benzoazulene-5-carboxylic acid tert-butyl ester,
trans-2-[4-(8-Chloro-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulen-1-yl)-cyclohexyloxy]-benzonitrile hydrochloride,
trans-2-[4-(8-Chloro-5-methyl-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzoazulen-1-yl)-cyclohexyloxy]-benzonitrile,

trans-8-Chloro-1-(4-o-tolyloxy-cyclohexyl)-4H,6H-2,3,5,10b-tetraaza-benzoazulene-5-carboxylic acid tert-butyl ester,
trans-8-Chloro-5-methyl-1-(4-o-tolyloxy-cyclohexyl)-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzoazulene,
trans-8-Chloro-1-[4-(3,5-difluoro-phenoxy)-cyclohexyl]-4H,6H-2,3,5,10b-tetraaza-benzoazulene-5-carboxylic acid tert-butyl ester,
trans-8-Chloro-1-[4-(3,5-difluoro-phenoxy)-cyclohexyl]-5-methyl-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzoazulene,
trans-8-Chloro-1-[4-(naphthalen-2-yloxy)-cyclohexyl]-4H,6H-2,3,5,10b-tetraaza-benzoazulene-5-carboxylic acid tert-butyl ester,
trans-8-Chloro-5-methyl-1-[4-(naphthalen-2-yloxy)-cyclohexyl]-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzoazulene,
trans-8-Chloro-1-[4-(pyridin-3-yloxy)-cyclohexyl]-4H,6H-2,3,5,10b-tetraaza-benzoazulene-5-carboxylic acid tert-butyl ester,
trans-8-Chloro-5-methyl-1-[4-(pyridin-3-yloxy)-cyclohexyl]-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzoazulene,
trans-8-Chloro-1-[4-(5-chloro-pyridin-3-yloxy)-cyclohexyl]-4H,6H-2,3,5,10b-tetraaza-benzoazulene-5-carboxylic acid tert-butyl ester,
trans-8-Chloro-1-[4-(5-chloro-pyridin-3-yloxy)-cyclohexyl]-5-methyl-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzoazulene,
trans-8-Chloro-1-[4-(pyridin-2-yloxy)-cyclohexyl]-4H,6H-2,3,5,10b-tetraaza-benzoazulene-5-carboxylic acid tert-butyl ester,
trans-8-Chloro-1-[4-(pyridin-2-yloxy)-cyclohexyl]-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzoazulene hydrochloride,
trans-8-Chloro-5-methyl-1-[4-(pyridin-2-yloxy)-cyclohexyl]-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzoazulene,
trans-8-Chloro-1-[4-(6-chloro-pyridin-2-yloxy)-cyclohexyl]-4H,6H-2,3,5,10b-tetraaza-benzo[e]azulene-5-carboxylic acid tert-butyl ester,
trans-8-Chloro-1-[4-(6-chloro-pyridin-2-yloxy)-cyclohexyl]-5-methyl-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene,
trans-8-Chloro-1-[4-(5-chloro-pyridin-2-yloxy)-cyclohexyl]-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene hydrochloride,
trans-8-Chloro-1-[4-(5-chloro-pyridin-2-yloxy)-cyclohexyl]-5-methyl-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene,
trans-8-Chloro-1-[4-(pyrimidin-2-yloxy)-cyclohexyl]-4H,6H-2,3,5,10b-tetraaza-benzo[e]azulene-5-carboxylic acid tert-butyl ester,
cis-8-Chloro-1-[4-(pyrimidin-2-yloxy)-cyclohexyl]-4H,6H-2,3,5,10b-tetraaza-benzo[e]azulene-5-carboxylic acid tert-butyl ester,
trans-8-Chloro-5-methyl-1-[4-(pyrimidin-2-yloxy)-cyclohexyl]-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene,

trans-8-Chloro-1-[4-(pyrazin-2-yloxy)-cyclohexyl]-4H,6H-2,3,5,10b-tetraaza-benzo[e]azulene-5-carboxylic acid tert-butyl ester,
trans- 8-Chloro-5-methyl-1-[4-(pyrazin-2-yloxy)-cyclohexyl]-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene,
trans-8-Chloro-1-[4-(pyrimidin-4-yloxy)-cyclohexyl]-4H,6H-2,3,5,10b-tetraaza-benzo[e]azulene-5-carboxylic acid tert-butyl ester,
trans-8-Chloro-5-methyl-1-[4-(pyrimidin-4-yloxy)-cyclohexyl]-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene,
trans-8-Chloro-1-[4-(pyridazin-3-yloxy)-cyclohexyl]-4H,6H-2,3,5,10b-tetraaza-benzo[e]azulene-5-carboxylic acid tert-butyl ester,
cis-8-Chloro-1-[4-(pyridazin-3-yloxy)-cyclohexyl]-4H,6H-2,3,5,10b-tetraaza-benzo[e]azulene-5-carboxylic acid tert-butyl ester,
trans-8-Chloro-5-methyl-1-[4-(pyridazin-3-yloxy)-cyclohexyl]-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene,
cis-8-Chloro-1-[4-(pyridin-2-yloxy)-cyclohexyl]-4H,6H-2,3,5,10b-tetraaza-benzo[e]azulene-5-carboxylic acid tert-butyl ester ,
cis-8-Chloro-1-[4-(pyridin-2-yloxy)-cyclohexyl]-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene ,
cis-8-Chloro-5-methyl-1-[4-(pyridin-2-yloxy)-cyclohexyl]-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene ,
trans-8-Chloro-1-[4-(3-fluoro-pyridin-2-yloxy)-cyclohexyl]-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene,
trans-8-Chloro-1-[4-(3-fluoro-pyridin-2-yloxy)-cyclohexyl]-5-methyl-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene,
trans-8-Chloro-1-[4-(5-fluoro-pyridin-2-yloxy)-cyclohexyl]-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene
trans-8-Chloro-1-[4-(5-fluoro-pyridin-2-yloxy)-cyclohexyl]-5-methyl-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene,
trans-8-Chloro-1-[4-(6-methyl-pyridin-2-yloxy)-cyclohexyl]-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene,
trans-8-Chloro-5-(2,2-difluoro-ethyl)-1-[4-(6-methyl-pyridin-2-yloxy)-cyclohexyl]-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene,
trans-8-Chloro-5-(2-fluoro-ethyl)-1-[4-(5-fluoro-pyridin-2-yloxy)-cyclohexyl]-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene,
trans-8-Chloro-5-ethyl-1-[4-(3-fluoro-pyridin-2-yloxy)-cyclohexyl]-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene,
trans-8-Chloro-5-ethyl-1-[4-(5-fluoro-pyridin-2-yloxy)-cyclohexyl]-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene,
trans-8-Chloro-5-ethyl-1-[4-(6-methyl-pyridin-2-yloxy)-cyclohexyl]-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene, and

trans-8-Chloro-5-methyl-1-[4-(6-methyl-pyridin-2-yloxy)-cyclohexyl]-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene.

In another aspect, there is provided a pharmaceutical composition comprising a V1a antagonist as defined herein in a pharmaceutically acceptable form for use in the treatment and/or prevention of phase shift sleep disorders.

In another aspect, there is provided a selective V1a antagonist for use in the treatment and/or prevention of phase shift sleep disorders, wherein the V1a antagonist is selected from the group consisting of

trans-8-Chloro-1-(4-phenoxy-cyclohexyl)-4H,6H-2,3,5,10b-tetraaza-benzoazulene-5-carboxylic acid tert-butyl ester,

trans-8-Chloro-1-(4-phenoxy-cyclohexyl)-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzoazulene hydrochloride,

trans-8-Chloro-5-methyl-1-(4-phenoxy-cyclohexyl)-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene,

trans-1-[8-Chloro-1-(4-phenoxy-cyclohexyl)-4H,6H-2,3,5,10b-tetraaza-benzoazulen-5-yl]-ethanone,

trans-8-Chloro-5-methanesulfonyl-1-(4-phenoxy-cyclohexyl)-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzoazulene,

trans-2-[8-Chloro-1-(4-phenoxy-cyclohexyl)-4H,6H-2,3,5,10b-tetraaza-benzoazulen-5-yl]-ethanol,

trans-8-Chloro-5-isopropyl-1-(4-phenoxy-cyclohexyl)-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzoazulene,

trans-8-Chloro-1-(4-phenoxy-cyclohexyl)-4H,6H-2,3,5,10b-tetraaza-benzoazulene-5-sulfonic acid dimethylamide,

trans-8-Chloro-1-(4-phenoxy-cyclohexyl)-5-pyridin-2-ylmethyl-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzoazulene,

trans-1-[8-Chloro-1-(4-phenoxy-cyclohexyl)-4H,6H-2,3,5,10b-tetraaza-benzoazulen-5-yl]-2-dimethylamino-ethanone,

trans-8-Fluoro-1-(4-phenoxy-cyclohexyl)-4H,6H-2,3,5,10b-tetraaza-benzo[e]azulene-5-carboxylic acid tert-butyl ester,

trans-8-Fluoro-5-methyl-1-(4-phenoxy-cyclohexyl)-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzoazulene,

cis-8-Chloro-1-(4-phenoxy-cyclohexyl)-4H,6H-2,3,5,10b-tetraaza-benzoazulene-5-carboxylic acid tert-butyl ester,

cis-8-Chloro-5-methyl-1-(4-phenoxy-cyclohexyl)-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzoazulene,

trans-8-Chloro-1-[4-(4-fluoro-phenoxy)-cyclohexyl]-4H,6H-2,3,5,10b-tetraaza-benzoazulene-5-carboxylic acid tert-butyl ester,

trans-8-Chloro-1-[4-(4-fluoro-phenoxy)-cyclohexyl]-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene hydrochloride,

trans-8-Chloro-1-[4-(4-fluoro-phenoxy)-cyclohexyl]-5-methyl-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzoazulene,

trans-8-Chloro-1-[4-(4-cyano-phenoxy)-cyclohexyl]-4H,6H-2,3,5,10b-tetraaza-benzo[e]azulene-5-carboxylic acid tert-butyl ester,

trans-4-[4-(8-Chloro-5-methyl-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulen-1-yl)-cyclohexyloxy]-benzonitrile,

trans-8-Chloro-1-[4-(4-trifluoromethyl-phenoxy)-cyclohexyl]-4H,6H-2,3,5,10b-tetraaza-benzo[e]azulene-5-carboxylic acid tert-butyl ester,

trans-8-Chloro-1-[4-(3-chloro-phenoxy)-cyclohexyl]-4H,6H-2,3,5,10b-tetraaza-benzoazulene-5-carboxylic acid tert-butyl ester,

trans-8-Chloro-1-[4-(3-chloro-phenoxy)-cyclohexyl]-5-methyl-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzoazulene,

trans-8-Chloro-1-[4-(3-methoxy-phenoxy)-cyclohexyl]-4H,6H-2,3,5,10b-tetraaza-benzoazulene-5-carboxylic acid tert-butyl ester,

trans-8-Chloro-1-[4-(3-methoxy-phenoxy)-cyclohexyl]-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene hydrochloride,

trans-8-Chloro-1-[4-(3-methoxy-phenoxy)-cyclohexyl]-5-methyl-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzoazulene,

trans-3-[4-(8-Chloro-5-methyl-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzoazulen-1-yl)-cyclohexyloxy]-benzonitrile,

trans-8-Chloro-1-(4-m-tolyloxy-cyclohexyl)-4H,6H-2,3,5,10b-tetraaza-benzo[e]azulene-5-carboxylic acid tert-butyl ester,

trans-8-Chloro-1-(4-m-tolyloxy-cyclohexyl)-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene hydrochloride,

trans-8-Chloro-5-methyl-1-(4-m-tolyloxy-cyclohexyl)-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene,

trans-1-[4-(3-tert-Butyl-phenoxy)-cyclohexyl]-8-chloro-4H,6H-2,3,5,10b-tetraaza-benzo[e]azulene-5-carboxylic acid tert-butyl ester,

trans-8-Chloro-1-[4-(2-fluoro-phenoxy)-cyclohexyl]-4H,6H-2,3,5,10b-tetraaza-benzo[e]azulene-5-carboxylic acid tert-butyl ester,

trans-8-Chloro-1-[4-(2-fluoro-phenoxy)-cyclohexyl]-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene hydrochloride,

trans-8-Chloro-1-[4-(2-fluoro-phenoxy)-cyclohexyl]-5-methyl-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene,

trans-8-Chloro-1-[4-(2-cyano-phenoxy)-cyclohexyl]-4H,6H-2,3,5,10b-tetraaza-benzoazulene-5-carboxylic acid tert-butyl ester,

trans-2-[4-(8-Chloro-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulen-1-yl)-cyclohexyloxy]-benzonitrile hydrochloride,

trans-2-[4-(8-Chloro-5-methyl-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzoazulen-1-yl)-cyclohexyloxy]-benzonitrile,

trans-8-Chloro-1-(4-o-tolyloxy-cyclohexyl)-4H,6H-2,3,5,10b-tetraaza-benzoazulene-5-carboxylic acid tert-butyl ester,

trans-8-Chloro-5-methyl-1-(4-o-tolyloxy-cyclohexyl)-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzoazulene,

trans-8-Chloro-1-[4-(3,5-difluoro-phenoxy)-cyclohexyl]-4H,6H-2,3,5,10b-tetraaza-benzoazulene-5-carboxylic acid tert-butyl ester,

trans-8-Chloro-1-[4-(3,5-difluoro-phenoxy)-cyclohexyl]-5-methyl-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzoazulene,

trans-8-Chloro-1-[4-(naphthalen-2-yloxy)-cyclohexyl]-4H,6H-2,3,5,10b-tetraaza-benzoazulene-5-carboxylic acid tert-butyl ester,

trans-8-Chloro-5-methyl-1-[4-(naphthalen-2-yloxy)-cyclohexyl]-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzoazulene,

trans-8-Chloro-1-[4-(pyridin-3-yloxy)-cyclohexyl]-4H,6H-2,3,5,10b-tetraaza-benzoazulene-5-carboxylic acid tert-butyl ester,

trans-8-Chloro-5-methyl-1-[4-(pyridin-3-yloxy)-cyclohexyl]-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzoazulene,

trans-8-Chloro-1-[4-(5-chloro-pyridin-3-yloxy)-cyclohexyl]-4H,6H-2,3,5,10b-tetraaza-benzoazulene-5-carboxylic acid tert-butyl ester,

trans-8-Chloro-1-[4-(5-chloro-pyridin-3-yloxy)-cyclohexyl]-5-methyl-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzoazulene,

trans-8-Chloro-1-[4-(pyridin-2-yloxy)-cyclohexyl]-4H,6H-2,3,5,10b-tetraaza-benzoazulene-5-carboxylic acid tert-butyl ester,

trans-8-Chloro-1-[4-(pyridin-2-yloxy)-cyclohexyl]-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzoazulene hydrochloride,

trans-8-Chloro-5-methyl-1-[4-(pyridin-2-yloxy)-cyclohexyl]-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzoazulene,

trans-8-Chloro-1-[4-(6-chloro-pyridin-2-yloxy)-cyclohexyl]-4H,6H-2,3,5,10b-tetraaza-benzo[e]azulene-5-carboxylic acid tert-butyl ester,

trans-8-Chloro-1-[4-(6-chloro-pyridin-2-yloxy)-cyclohexyl]-5-methyl-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene,

trans-8-Chloro-1-[4-(5-chloro-pyridin-2-yloxy)-cyclohexyl]-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene hydrochloride,

trans-8-Chloro-1-[4-(5-chloro-pyridin-2-yloxy)-cyclohexyl]-5-methyl-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene,

trans-8-Chloro-1-[4-(pyrimidin-2-yloxy)-cyclohexyl]-4H,6H-2,3,5,10b-tetraaza-benzo[e]azulene-5-carboxylic acid tert-butyl ester,

cis-8-Chloro-1-[4-(pyrimidin-2-yloxy)-cyclohexyl]-4H,6H-2,3,5,10b-tetraaza-benzo[e]azulene-5-carboxylic acid tert-butyl ester,

trans-8-Chloro-5-methyl-1-[4-(pyrimidin-2-yloxy)-cyclohexyl]-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene,

trans-8-Chloro-1-[4-(pyrazin-2-yloxy)-cyclohexyl]-4H,6H-2,3,5,10b-tetraaza-benzo[e]azulene-5-carboxylic acid tert-butyl ester,

trans- 8-Chloro-5-methyl-1-[4-(pyrazin-2-yloxy)-cyclohexyl]-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene,

trans-8-Chloro-1-[4-(pyrimidin-4-yloxy)-cyclohexyl]-4H,6H-2,3,5,10b-tetraaza-benzo[e]azulene-5-carboxylic acid tert-butyl ester,

trans-8-Chloro-5-methyl-1-[4-(pyrimidin-4-yloxy)-cyclohexyl]-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene,

trans-8-Chloro-1-[4-(pyridazin-3-yloxy)-cyclohexyl]-4H,6H-2,3,5,10b-tetraaza-benzo[e]azulene-5-carboxylic acid tert-butyl ester,

cis-8-Chloro-1-[4-(pyridazin-3-yloxy)-cyclohexyl]-4H,6H-2,3,5,10b-tetraaza-benzo[e]azulene-5-carboxylic acid tert-butyl ester,

trans-8-Chloro-5-methyl-1-[4-(pyridazin-3-yloxy)-cyclohexyl]-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene,

cis-8-Chloro-1-[4-(pyridin-2-yloxy)-cyclohexyl]-4H,6H-2,3,5,10b-tetraaza-benzo[e]azulene-5-carboxylic acid tert-butyl ester ,

cis-8-Chloro-1-[4-(pyridin-2-yloxy)-cyclohexyl]-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene ,

cis-8-Chloro-5-methyl-1-[4-(pyridin-2-yloxy)-cyclohexyl]-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene ,

trans-8-Chloro-1-[4-(3-fluoro-pyridin-2-yloxy)-cyclohexyl]-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene,

trans-8-Chloro-1-[4-(3-fluoro-pyridin-2-yloxy)-cyclohexyl]-5-methyl-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene,

trans-8-Chloro-1-[4-(5-fluoro-pyridin-2-yloxy)-cyclohexyl]-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene

trans-8-Chloro-1-[4-(5-fluoro-pyridin-2-yloxy)-cyclohexyl]-5-methyl-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene,

trans-8-Chloro-1-[4-(6-methyl-pyridin-2-yloxy)-cyclohexyl]-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene,

trans-8-Chloro-5-(2,2-difluoro-ethyl)-1-[4-(6-methyl-pyridin-2-yloxy)-cyclohexyl]-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene,

trans-8-Chloro-5-(2-fluoro-ethyl)-1-[4-(5-fluoro-pyridin-2-yloxy)-cyclohexyl]-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene,

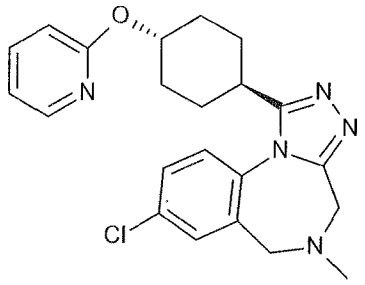
trans-8-Chloro-5-ethyl-1-[4-(3-fluoro-pyridin-2-yloxy)-cyclohexyl]-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene,

trans-8-Chloro-5-ethyl-1-[4-(5-fluoro-pyridin-2-yloxy)-cyclohexyl]-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene,

trans-8-Chloro-5-ethyl-1-[4-(6-methyl-pyridin-2-yloxy)-cyclohexyl]-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene, and

trans-8-Chloro-5-methyl-1-[4-(6-methyl-pyridin-2-yloxy)-cyclohexyl]-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene.

In another aspect, there is provided a selective V1a antagonist for use in the treatment and/or prevention of phase shift sleep disorders, wherein the V1a antagonist is



example 1.

The following definitions of the general terms used in the present description apply irrespectively of whether the terms in question appear alone or in combination with other groups.

The term "phase shift sleep disorders" summarizes conditions classified as disturbances in the circadian rhythm, i.e. the approximately 24-hour cycles that are generated by an organism, e.g. a human being.

Phase shift sleep disorders include, but are not limited to transient disorders like jetlag or or a changed sleep schedule due to work, social responsibilities, or illness, as well as chronic disorders like delayed sleep-phase syndrome (DSPS), delayed sleep-phase type (DSPT), advanced sleep-phase syndrome (ASPS), and irregular sleep-wake cycle.

The term "V1a antagonist" refers to antagonists of the V1a vasopressin receptor subtype. Examples include OPC-21268, OPC-31260, OPC-41061, VPA-985, SR-49059, SR-121463, VP-343, FR-161282, CI-1025, SRX-251, SRX-246, JNJ-17158063, FE-202158, VT-913,

LY307174, Org-52186, PF-184563, YM-218, 1-({(2*R*,3*S*)-5-chloro-3-(2-chlorophenyl)-1-[(3,4-dimethoxyphenyl)sulfonyl]-3-hydroxy-2,3-dihydro-1*H*-indol-2-yl}carbonyl)-L-prolinamide, [6-chloro-1-[2-(dimethylamino)ethyl]indol-3-yl]-spiro[1H-isobenzofuran-3,4'-piperidine]-1'-yl-methanone, 8-Chloro-5-methyl-1-(3,4,5,6-tetrahydro-2H-[1,2']bipyridinyl-4-yl)-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene, trans-8-chloro-5-methyl-1-(4-pyridin-2-yloxycyclohexyl)-4,6-dihydro-[1,2,4]triazolo[4,3-a][1,4]benzodiazepine and the like. The term "selective V1a

Claims

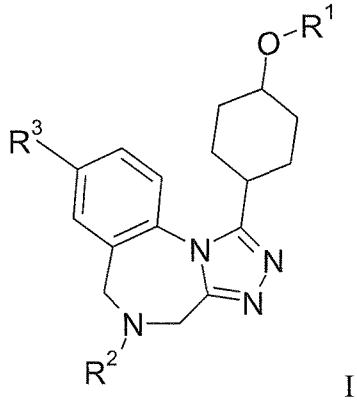
~~1. Use of a V1a antagonist for the manufacture of a medicament for the treatment and/or prevention of phase shift sleep disorders.~~

~~2. Use according to claim 1, for the treatment of phase shift sleep disorders.~~

~~3. Use according to claim 1, for the prevention of phase shift sleep disorders.~~

~~4. Use according to any one of claims 1-3, wherein the phase shift sleep disorder is jetlag.~~

~~5.~~1. Use of a V1a antagonist in the manufacture of a medicament for the treatment and/or prevention of phase-shift sleep disorders, wherein said V1a antagonist ~~according to any one of claims 1-4, wherein the V1a antagonist~~ is a compound of formula I.



I

wherein

R^1 is aryl or heteroaryl, unsubstituted or substituted with one or more substituents independently selected from A,

R^2 is H,

C_{1-12}-alkyl, unsubstituted or substituted with one or more OH, halo, cyano or C_{1-12}-alkoxy,

$-(CH_2)_q-R^a$, wherein R^a is phenyl or 5- or 6-membered heteroaryl, each unsubstituted or substituted with one or more substituents independently selected from A,

$-(CH_2)_rNR^iR^{ii}$,

$-C(O)-C_{1-12}$-alkyl, wherein C_{1-12}-alkyl is unsubstituted or substituted with one or more OH, halo, cyano or C_{1-12}-alkoxy,

$-C(O)(CH_2)_qOC(O)-C_{1-12}$-alkyl,

$-C(O)(CH_2)_qNR^iR^{ii}$,

$-C(O)O-C_{1-12}$-alkyl, wherein alkyl is unsubstituted or substituted with one or more OH, halo, cyano or C_{1-12}-alkoxy,

$-S(O)_2-C_{1-12}$-alkyl, or

-S(O)2NRiRii,

R^i and R^{ii} are each independently H, C_{1-12}-alkyl, or form together with the nitrogen to which they are bound a 3- to 7-membered heterocycloalkyl containing one or two heteroatoms selected from N, O or S, which heterocycloalkyl is unsubstituted or substituted by one or more substituents independently selected from B,

q is 1, 2, 3 or 4,

r is 2, 3 or 4,

A is halo, cyano, OH, C_{1-7}-alkyl, halo-C_{1-7}-alkyl, or C_{1-7}-alkoxy, halo-C_{1-7}-alkoxy, or hydroxy-C_{1-7}-alkyl,

B is oxo, halo, OH, C_{1-7}-alkyl or C_{1-7}-alkoxy,

R^3 is Cl or F,

or a pharmaceutically acceptable salt thereof, and .

~~6. Use according to any one of claims 1-5, wherein the V1a antagonist is a compound of formula I, wherein~~

~~R^1 is a monovalent cyclic aromatic hydrocarbon moiety consisting of a mono- or bicyclic aromatic ring,~~
~~a monovalent 5- or 6-membered aromatic monocyclic or 9- or 10-membered aromatic bicyclic ring containing from one to four ring heteroatoms selected from N, O, or S, the remaining ring atoms being C,~~
~~each unsubstituted or substituted with one or more substituents independently selected from A; and~~

~~A is is halo, cyano, OH, C_{1-7}-alkyl, halo-C_{1-7}-alkyl, C_{1-7}-alkoxy, halo-C_{1-7}-alkoxy, hydroxy-C_{1-7}-alkyl.~~

~~7. Use according to any one of claims 1-6, wherein the V1a antagonist is a compound of formula I, wherein R^1 is a monovalent cyclic aromatic hydrocarbon moiety consisting of a mono-aromatic ring.~~

~~8. Use according to any one of claims 1-7, wherein the V1a antagonist is a compound of formula I, wherein wherein R^1 is pyridinyl.~~

~~9. Use according to any one of claims 1-8, wherein the V1a antagonist is a compound of formula I, wherein R^2 is~~

- ~~H,~~
- ~~C_{1-12}-alkyl, unsubstituted or substituted with one or more OH,~~
- ~~$-(CH_2)_q-R^a$, wherein R^a is phenyl or 5- or 6-membered heteroaryl and q is 1, 2, 3 or 4, preferably 1,~~

- ~~$-C(O)-C_{1-12}$-alkyl,~~
- ~~$-C(O)(CH_2)_qNR^iR^{ii}$, wherein R^i and R^{ii} are each independently H or C_{1-12}-alkyl, preferably C_{1-12}-alkyl, and q is 1, 2, 3 or 4, preferably 1,~~
- ~~$-C(O)O-C_{1-12}$-alkyl,~~
- ~~$-S(O)_2-C_{1-12}$-alkyl, or~~
- ~~$-S(O)_2NR^iR^{ii}$, wherein R^i and R^{ii} are each independently H or C_{1-12}-alkyl, preferably C_{1-12}-alkyl.~~

~~10. Use according to any one of claims 1-9, wherein the V1a antagonist is a compound of formula I, wherein R^2 is methyl.~~

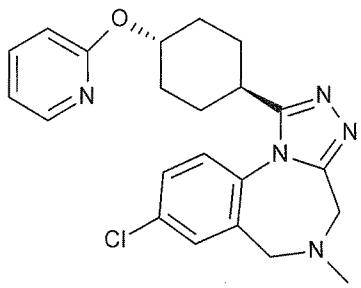
~~11. Use according to any one of claims 1-10, wherein the V1a antagonist is a compound of formula I, wherein R^3 is Cl.~~

~~12. Use according to any one of claims 1-11, wherein the V1a antagonist is a compound of formula I,~~ wherein the compound is selected from the group consisting of

trans-8-Chloro-1-(4-phenoxy-cyclohexyl)-4H,6H-2,3,5,10b-tetraaza-benzoazulene-5-carboxylic acid tert-butyl ester,
trans-8-Chloro-1-(4-phenoxy-cyclohexyl)-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzoazulene hydrochloride,
trans-8-Chloro-5-methyl-1-(4-phenoxy-cyclohexyl)-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene,
trans-1-[8-Chloro-1-(4-phenoxy-cyclohexyl)-4H,6H-2,3,5,10b-tetraaza-benzoazulen-5-yl]-ethanone,
trans-8-Chloro-5-methanesulfonyl-1-(4-phenoxy-cyclohexyl)-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzoazulene,
trans-2-[8-Chloro-1-(4-phenoxy-cyclohexyl)-4H,6H-2,3,5,10b-tetraaza-benzoazulen-5-yl]-ethanol,
trans-8-Chloro-5-isopropyl-1-(4-phenoxy-cyclohexyl)-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzoazulene,
trans-8-Chloro-1-(4-phenoxy-cyclohexyl)-4H,6H-2,3,5,10b-tetraaza-benzoazulene-5-sulfonic acid dimethylamide,
trans-8-Chloro-1-(4-phenoxy-cyclohexyl)-5-pyridin-2-ylmethyl-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzoazulene,
trans-1-[8-Chloro-1-(4-phenoxy-cyclohexyl)-4H,6H-2,3,5,10b-tetraaza-benzoazulen-5-yl]-2-dimethylamino-ethanone,
trans-8-Fluoro-1-(4-phenoxy-cyclohexyl)-4H,6H-2,3,5,10b-tetraaza-benzo[e]azulene-5-carboxylic acid tert-butyl ester,
trans-8-Fluoro-5-methyl-1-(4-phenoxy-cyclohexyl)-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzoazulene,

trans-8-Chloro-5-(2-fluoro-ethyl)-1-[4-(5-fluoro-pyridin-2-yloxy)-cyclohexyl]-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene,
trans-8-Chloro-5-ethyl-1-[4-(3-fluoro-pyridin-2-yloxy)-cyclohexyl]-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene,
trans-8-Chloro-5-ethyl-1-[4-(5-fluoro-pyridin-2-yloxy)-cyclohexyl]-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene,
trans-8-Chloro-5-ethyl-1-[4-(6-methyl-pyridin-2-yloxy)-cyclohexyl]-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene, and
trans-8-Chloro-5-methyl-1-[4-(6-methyl-pyridin-2-yloxy)-cyclohexyl]-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene.

~~13.~~2. Use according to ~~any one of~~ claims 1-~~12~~, wherein the V1a antagonist is



example 1.

3. Use according to claim 1 or 2, wherein the phase shift sleep disorder is jetlag.

~~14. A pharmaceutical composition comprising a V1a antagonist in a pharmaceutically acceptable form.~~

~~15. A pharmaceutical composition comprising a V1a antagonist according to any one of claims 5-13 in a pharmaceutically acceptable form.~~

~~16. A pharmaceutical composition comprising a V1a antagonist in a pharmaceutically acceptable form for use in the treatment and/or prevention of phase shift sleep disorders.~~

~~17.~~4. A pharmaceutical composition comprising a V1a antagonist as defined in ~~according to any one of~~ claims ~~5-13~~1 or 2 in a pharmaceutically acceptable form for use in the treatment and/or prevention of phase shift sleep disorders.

~~18. A V1a antagonist for use in the treatment and/or prevention of phase shift sleep disorders.~~

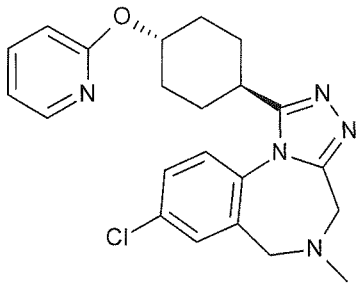
~~19.~~ 5. A V1a antagonist as defined in ~~according to any one of~~ claims ~~5~~1 or 2-~~13~~ 9 for use in the treatment and/or prevention of phase shift sleep disorders.

~~20.~~ 6. A selective V1a antagonist for use in the treatment and/or prevention of phase shift sleep disorders, wherein the V1a antagonist is selected from the group consisting of

trans-8-Chloro-1-(4-phenoxy-cyclohexyl)-4H,6H-2,3,5,10b-tetraaza-benzoazulene-5-carboxylic acid tert-butyl ester,
trans-8-Chloro-1-(4-phenoxy-cyclohexyl)-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzoazulene hydrochloride,
trans-8-Chloro-5-methyl-1-(4-phenoxy-cyclohexyl)-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene,
trans-1-[8-Chloro-1-(4-phenoxy-cyclohexyl)-4H,6H-2,3,5,10b-tetraaza-benzoazulen-5-yl]-ethanone,
trans-8-Chloro-5-methanesulfonyl-1-(4-phenoxy-cyclohexyl)-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzoazulene,
trans-2-[8-Chloro-1-(4-phenoxy-cyclohexyl)-4H,6H-2,3,5,10b-tetraaza-benzoazulen-5-yl]-ethanol,
trans-8-Chloro-5-isopropyl-1-(4-phenoxy-cyclohexyl)-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzoazulene,
trans-8-Chloro-1-(4-phenoxy-cyclohexyl)-4H,6H-2,3,5,10b-tetraaza-benzoazulene-5-sulfonic acid dimethylamide,
trans-8-Chloro-1-(4-phenoxy-cyclohexyl)-5-pyridin-2-ylmethyl-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzoazulene,
trans-1-[8-Chloro-1-(4-phenoxy-cyclohexyl)-4H,6H-2,3,5,10b-tetraaza-benzoazulen-5-yl]-2-dimethylamino-ethanone,
trans-8-Fluoro-1-(4-phenoxy-cyclohexyl)-4H,6H-2,3,5,10b-tetraaza-benzo[e]azulene-5-carboxylic acid tert-butyl ester,
trans-8-Fluoro-5-methyl-1-(4-phenoxy-cyclohexyl)-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzoazulene,
cis-8-Chloro-1-(4-phenoxy-cyclohexyl)-4H,6H-2,3,5,10b-tetraaza-benzoazulene-5-carboxylic acid tert-butyl ester,
cis-8-Chloro-5-methyl-1-(4-phenoxy-cyclohexyl)-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzoazulene,

trans-8-Chloro-5-ethyl-1-[4-(5-fluoro-pyridin-2-yloxy)-cyclohexyl]-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene,
trans-8-Chloro-5-ethyl-1-[4-(6-methyl-pyridin-2-yloxy)-cyclohexyl]-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene, and
trans-8-Chloro-5-methyl-1-[4-(6-methyl-pyridin-2-yloxy)-cyclohexyl]-5,6-dihydro-4H-2,3,5,10b-tetraaza-benzo[e]azulene.

~~21.~~ 7. A selective V1a antagonist for use in the treatment and/or prevention of phase shift sleep disorders, wherein the V1a antagonist is



example 1.