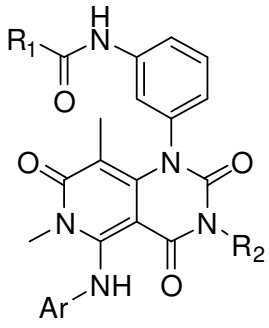
Claims

1. Use of ~~A~~a MEK inhibitor of formula (I),



formula (I),

or a pharmaceutically acceptable salt thereof,

wherein;

R_1 is a C1-C6 alkyl, such as methyl,

R_2 is a C1-C6 alkyl, such as cyclopropyl,

Ar is selected from the group consisting of aryl and heteroaryl;

in the manufacture of a medicament for ~~for use in~~ the prevention or treatment of a stroke in a subject.

~~2. The MEK inhibitor according to claim 1, wherein R_1 is a C1-C3 alkyl.~~

~~3. The MEK inhibitor according to any one of the preceding claims, wherein R_1 is a linear C1-C3 alkyl.~~

4.2. The ~~MEK inhibitor~~use according to any one of the preceding claims, wherein R_1 is methyl or ethyl.

~~5. The MEK inhibitor according to any one of the preceding claims, wherein R_1 is methyl.~~

~~6. The MEK inhibitor according to claim 1, wherein R_2 is C2-C4 alkyl.~~

~~7.~~3. The ~~MEK inhibitor~~use according to any one of the preceding claims, wherein R_2 is C3 or C4 cycloalkyl.

~~8. The MEK inhibitor according to any one of the preceding claims, wherein R_2 is cyclopropyl.~~

~~9.~~4. The ~~MEK inhibitor~~use according to any one of the preceding claims, wherein Ar is phenyl or substituted phenyl.

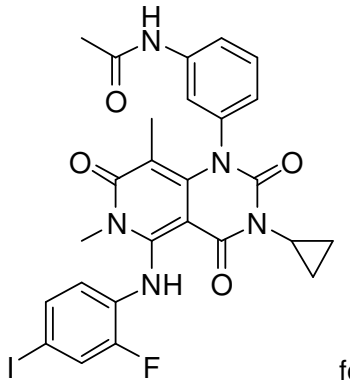
~~10. The MEK inhibitor according to any one of the preceding claims, wherein Ar is substituted phenyl.~~

~~11. The MEK inhibitor according to any one of the preceding claims, wherein Ar is 2-fluoro-4-iodophenyl.~~

~~12. The MEK inhibitor according to any one of the preceding claims, wherein R_1 is a C1-C3 alkyl, R_2 is C2-C4 alkyl, and Ar is substituted phenyl.~~

~~13. The MEK inhibitor according to any one of the preceding claims, wherein R_1 is methyl or ethyl, R_2 is C3 or C4 cycloalkyl, and Ar is substituted phenyl.~~

~~14.~~5. The ~~MEK inhibitor for~~ use according to any one of the preceding claims, wherein the MEK inhibitor is of formula (II),



formula (II),

or a pharmaceutically acceptable salt thereof.

~~15.~~6. The ~~MEK inhibitor for~~ use according to any one of the preceding claims, wherein the stroke is selected from the group consisting of: ischemic stroke, haemorrhagic stroke, and transient ischemic attack.

~~16.~~7. The ~~MEK inhibitor for~~ use according to any one of the preceding claims, wherein the stroke is selected from the group consisting of: global ischemia and focal ischemia.

~~17.~~8. The ~~MEK inhibitor for~~ use according to any one of the preceding claims, wherein the ischemic stroke results from an embolism, thrombosis, systemic hypoperfusion, cerebral venous sinus thrombosis, a sudden drop in blood pressure or heart stop, rupture of a cerebral artery or arteriole, or a combination thereof.

~~18.~~9. The ~~MEK inhibitor for~~ use according to any one of the preceding claims, wherein the haemorrhagic stroke results from intracerebral haemorrhage, subarachnoid haemorrhage, or a combination thereof.

~~19.~~10. The ~~MEK inhibitor for~~ use according to any one of the preceding claims, wherein the intracerebral haemorrhage is intraparenchymal, intraventricular, or a combination thereof.

~~20.~~11. The ~~MEK inhibitor for~~ use according to any one of the preceding claims, wherein the stroke results from subarachnoid haemorrhage (SAH).

~~21.~~12. The ~~MEK inhibitor for~~ use according to any one of the preceding claims, wherein the stroke results from Ischemic Brain Injury (TBI).

~~22.~~13. The ~~MEK inhibitor for~~ use according to any one of the preceding claims, wherein the stroke is a delayed cerebral ischemia (DCI).

~~23.~~14. The ~~MEK inhibitor for~~ use according to any one of the preceding claims, wherein the DCI presents with inflammation, oedema, delayed cerebral vasospasm (CVS), blood-brain barrier disruption and/or increase in contractile receptor expression, such as those for endothelin, angiotensin, serotonin and thromboxane or prostaglandins.

~~24. The MEK inhibitor for use according to any one of the preceding claims, wherein the MEK inhibitor is administered to the subject without surgery prior to, concurrent with, or subsequent to the administration.~~

~~25.~~15. The ~~MEK inhibitor for~~ use according to any one of the preceding claims, wherein the MEK inhibitor is to be administered to the subject prior to, concurrent with, or subsequent to thrombectomy.

~~26.~~16. The ~~MEK inhibitor for~~ use according to any one of the preceding claims, wherein the MEK inhibitor is to be administered to the subject prior to, concurrent with, or subsequent to thrombolysis.

~~27.~~17. The ~~MEK inhibitor for~~ use according to any one of the preceding claims, wherein the MEK inhibitor is to be administered to the subject prior to, concurrent with, or subsequent to a surgical procedure selected from the group consisting of: coiling and clipping.

~~28.~~18. The ~~MEK inhibitor for~~ use according to any one of the preceding claims, wherein the MEK inhibitor is to be administered to the subject prior to, concurrent with, or subsequent to a neuroradiological procedure, and wherein the MEK inhibitor reduces or prevents reperfusion damage resulting from the neuroradiological procedure.

~~29. The MEK inhibitor for use according to any one of the preceding claims, wherein the MEK inhibitor reduces or prevents reperfusion damage resulting from the neuroradiological procedure.~~

~~30. The MEK inhibitor for use according to any one of the preceding claims, wherein the MEK inhibitor is administered to the subject before it has been determined if the subject suffers from an acute ischemic stroke or a haemorrhagic stroke.~~

~~31. The MEK inhibitor for use according to any one of the preceding claims, wherein the MEK inhibitor is administered orally, intrathecally, intraperitoneally, intraocularly, intranasally, or intravenously.~~

~~32. The MEK inhibitor for use according to any one of the preceding claims, wherein the MEK inhibitor is administered intravenously.~~

~~33.~~19. ~~MEK inhibitor for use~~ The use according to any one of the preceding claims, wherein the MEK inhibitor is to be administered to the subject up to 6 hours subsequent to the onset of the stroke, such as up to 1 hour, such as up to 2 hours, such as up to 3 hours, such as up to 4 hours, such as up to 5 hours subsequent to the onset of the stroke, or wherein the MEK inhibitor is to be administered one or more times daily for up to 3 days subsequent to the onset of the stroke .

~~34. The MEK inhibitor for use according to any one of the preceding claims, wherein the MEK inhibitor is administered one or more times daily for up to 3 days subsequent to the onset of the stroke.~~

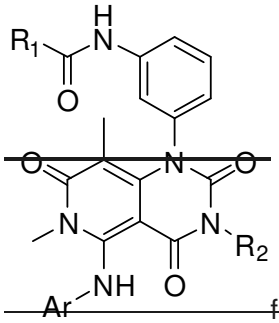
~~35. The MEK inhibitor for use according to any one of the preceding claims, wherein the subject is a human subject.~~

~~36. Use of a MEK inhibitor of formula (I) as defined in any one of the preceding claims, for:~~

~~a. reducing endothelin-1 induced contractility;~~
~~b. increasing endothelin B receptor function; and/or~~

~~c. improving neurological score, which may be evaluated by a subject's ability to traverse a rotating pole, after induced subarachnoid haemorrhage.~~

~~37. A method of treating or reducing the risk of developing a stroke in a subject, wherein the method comprises the steps of administering a MEK inhibitor of formula (I),~~



~~formula (I),~~

~~or a pharmaceutically acceptable salt thereof, wherein;~~

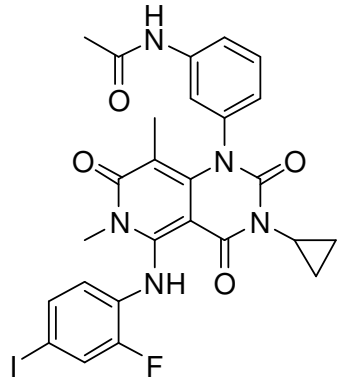
~~R_1 is a C1-C6 alkyl, such as methyl,~~

~~R_2 is a C1-C6 alkyl, such as cyclopropyl,~~

~~Ar is selected from the group consisting of aryl, phenyl, and heteroaryl;~~

~~to a subject in need thereof, thereby treating or reducing the risk of developing a stroke.~~

~~38.~~20. A composition comprising, separately or together, the MEK inhibitor of formula (II),



formula (II),

or a pharmaceutically acceptable salt thereof, and a further medicament selected

from the group consisting of: a calcium channel blocker, such as Nimodipine, and an endothelin receptor (ET) receptor blocker, such as clazosentan.

~~39. The composition according to any one of the preceding claims, wherein the further medicament is selected from the group consisting of: a calcium channel blocker, such as Nimodipine, and an endothelin receptor (ET) receptor blocker, such as clazosentan.~~

~~40. A kit of parts comprising; a MEK inhibitor as defined in any one of the preceding claims; and a further medicament as defined in any one of the preceding claims; wherein the MEK inhibitor and the further medicament are formulated for simultaneous or sequential use; and optionally instructions for use.~~