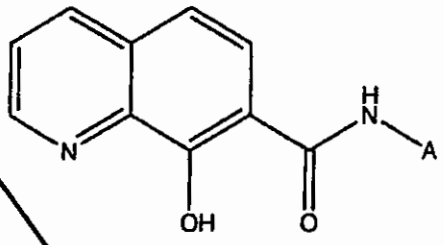
CLAIMS

1. Compound of general formula (I) or a pharmaceutically acceptable salt or derivative thereof



(I)

for use as antifungal agent;

wherein **A** is:

- $-(CH_2)_m-X_1$,
- $-(CH_2)_m-C_3-C_8$ cycloalkyl,
- $-(CH_2)_m-W-X_2$,
- $-(CH_2)_m-W-CH_2-X_1$, or
- $-(CH_2)_m-CHR_9-(CH_2)_m-X_1$;

wherein X_1 is:

- -aryl, optionally substituted by one, two or three R_5,
- -heterocycle, optionally substituted by one or two R_5,
- $-C_1-C_8$ alkyl,
- -CH(OH)-phenyl,
- -S-phenyl,
- $-NHSO_2$-phenyl,
- -CN,
- -OH,
- $-C_3-C_8$ cycloalkyl, or
- -4-cyano-2,3,4,5-tetrafluoro-phenyl;

wherein X_2 is:

- -aryl,
- -heterocycle,
- $-C_1-C_8$ alkyl,

- -CH(OH)-phenyl, or
- -C_3-C_8 cycloalkyl

wherein **W** is:

- -NH-,
- -O-, or
- -S-;

wherein **aryl** is:

- phenyl,
- naphtyl,
- biphenyl,
- tetrahydro-naphthyl, or
- fluorenyl;

wherein **heterocycle** is a 5-,6- or 7-membered saturated or unsaturated ring containing from one to three heteroatoms selected from the group consisting of nitrogen, oxygen and sulphur, and including any bicyclic group in which any of the above heterocyclic rings is fused to a benzene ring or another heterocyclic;

wherein **–cycloalkyl** is a saturated or unsaturated hydrocarbon ring including any bicyclic group in which the above ring is connected to a benzene, heterocyclic or other hydrocarbon ring;

wherein R_9 is:

- -C_1-C_7 alkyl,
- -C_3-C_8 cycloalkyl,
- -$C(O)R_{11}$,
- -$C(O)NHR_{11}$,
- -$C(OH)R_{11}$,
- -CH_2OH,
- -CO_2R_{11}, or
- -aryl;

wherein R_{11} is:

- -H,
- -C_1-C_7 alkyl,
- -$(CH_2)_mX_1$, or

- $-(CH_2)_m-C_3-C_8$ cycloalkyl;

wherein R_4 is:

- -F,
- -Cl,
- -Br,
- -I,
- $-NO_2$,
- $-CF_3$,
- -CN,
- $-CH_2OH$
- $-C_1-C_6$ alkyl,
- $-W-R_{10}$
- $-(CH_2)_m$-aryl,
- $-(CH_2)_m$-heterocycle,
- $-(CH_2)_m-C_3-C_8$ cycloalkyl
- $-SO_2$-NH-heterocycle,
- $-(CH_2)_m-NR_{14}R_{15}$,
- $-(SO_2)-NR_{14}R_{15}$,
- $-(C=O)-NR_{14}R_{15}$, or
- $-(N-C=O)-NR_{14}R_{15}$;

wherein R_5 is:

- -H,
- -F,
- -Cl,
- -Br,
- $-CF_3$,
- $-W-R_{10}$,
- $-C_1-C_6$ alkyl,
- $-(CH_2)_m$-aryl,
- $-(CH_2)_m$-heterocycle, or
- $-(CH_2)_m-C_3-C_8$ cycloalkyl;

wherein R_{10} is:

- -H,
- -C_1-C_6 alkyl,
- -$(CH_2)_m$-aryl,
- -$(CH_2)_m$-heterocycle,
- -$(CH_2)_m$-C_3-C_8 cycloalkyl, or
- -$CH(R_{12})R_{13}$,

wherein R_{12} is:

- -H,
- -$(CH_2)_mCO_2$-C_1-C_6 alkyl,
- -$(CH_2)_m$-phenyl,
- -$(CH_2)_m$-heterocycle,
- -C_1-C_6 alkyl,
- -C_1-C_4 alkyl NH-$COOCH_2$-benzyl, or
- -C_1-C_4 alkyl-S-CH_3;

wherein R_{13} is:

- -NH-$CO_2C(CH_3)_3$,
- -CN,
- -COOH, or
- -CO_2R_{11};

wherein R_{14} and R_{15}, independently from each other, are selected from:

- -H,
- -C_1-C_6 alkyl,
- -$(CH_2)_m$-aryl,
- -$(CH_2)_m$-cycloalkyl,
- -$(CH_2)_m$-heterocycle,
- -$(CH_2)_m$-W-R_{10},
- -$(CH_2)_m$-CN,
- taken together with the nitrogen atom to which they are bound to form an optionally substituted 5- to 8-membered heteromonocycle containing from one to three heteroatoms selected from the group consisting of nitrogen, oxygen and sulphur, or

- taken together with the nitrogen atom to which they are bound to form an optionally substituted 5- to 8-membered heteromonocycle which is fused to one or two optionally substituted saturated or unsaturated rings or to other optionally substituted heterocycles containing from one to three heteroatoms selected from the group consisting of nitrogen, oxygen and sulphur;

wherein **m** is an integer from 0 to 6.

2. Compound for use according to claim 1, wherein **A** is $-(CH_2)_m-X_1$.

3. Compound for use according to claim 1, wherein **m** is an integer from 0 to 1.

4. Compound for use according to claim 1, wherein X_1 is

- -aryl, optionally substituted by one or two R_4,
- -heterocycle, optionally substituted by one or two R_5, or
- $-C_3$-C_8 cycloalkyl.

5. Compound for use according to claim 1, wherein R_4 is

- -Cl,
- -Br,
- $-CF_3$,
- $-W-R_{10}$, or
- $-(CH_2)_m-NR_{14}R_{15}$.

6. Compound for use according to claim 1, wherein **W** is oxygen.

7. Compound for use according to claim 1, wherein R_{10} is

- -H, or
- $-C_1$-C_6 alkyl.

8. Compound for use according to claim 1, wherein R_{14} and R_{15}, independently from each other, are

- $-C_1$-C_6 alkyl, or
- taken together with the nitrogen atom to which they are bound to form an optionally substituted 5- to 8-membered heteromonocycle containing from one to three heteroatoms selected from the group consisting of nitrogen, oxygen and sulphur.

9. Compound for use according to claim 1, wherein **aryl** is phenyl.

10. Compound for use according to claim 1,

wherein **A** is $-(CH_2)_m-X_1$

wherein X_1 is:

- -aryl, optionally substituted by one, two or three R_4,
- -heterocycle, optionally substituted by one or two R_5, or
- -C_3-C_8 cycloalkyl

wherein R_4 is

- -Cl,
- -Br,
- -CF_3,
- -W-R_{10}, or
- -$(CH_2)_m$-$NR_{14}R_{15}$.

wherein R_5 is -C_1-C_6 alkyl

wherein R_{10} is

- -H, or
- -C_1-C_6 alkyl

wherein R_{14} and R_{15} are -C_1-C_6 alkyl,

wherein **W** is oxygen

wherein **m** is an integer from 0 to 1.

11. Compound for use according to claim 1, wherein **heterocycle** is 2,3-dihydrobenzo[b][1,4]dioxine, pyridine, thiophene, triazole, thiazole, isoxazole, benzothiazole, pyrazine, imidazole or furane.

12. Compound for use according to claim 1, selected from the group consisting of:

8-Hydroxy-N-(thiophen-2-ylmethyl)quinoline-7-carboxamide

8-Hydroxy-N-(cyclohexylmethyl)quinoline-7-carboxamide

8-Hydroxy-N-benzyl-quinoline-7-carboxamide

8-Hydroxy-N-(4-chlorobenzyl)quinoline-7-carboxamide

8-Hydroxy-N-(4-methoxyphenyl)quinoline-7-carboxamide

8-Hydroxy-N-(4-(trifluoromethyl)benzyl)quinoline-7-carboxamide

8-Hydroxy-N-phenyl-quinoline-7-carboxamide

8-Hydroxy-N-(2-hydroxybenzyl)quinoline-7-carboxamide

8-Hydroxy-N-(furan-2-ylmethyl)quinoline-7-carboxamide

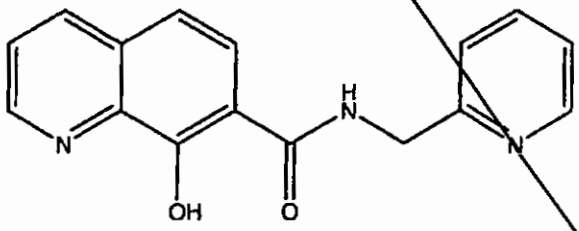
8-Hydroxy-N-(pyridin-3-ylmethyl)quinoline-7-carboxamide

8-Hydroxy-N-(4-methoxybenzyl)quinoline-7-carboxamide

8-Hydroxy-N-(4-bromobenzyl)quinoline-7-carboxamide

8-Hydroxy-N-(1,1-dioxidotetrahydrothien-3-yl)quinoline-7-carboxamide
8-Hyroxy-N-(4-(dimethylamino)benzyl)quinoline-7-carboxamide
8-Hydroxy-N-(tetrahydro-2H-pyran-4-yl)quinoline-7-carboxamide
8-Hydroxy-N-(4-morpholinophenyl)quinoline-7-carboxamide
8-Hydroxy-N-(4-(1H-1,2,4-triazol-1-yl)phenyl)quinoline-7-carboxamide
8-Hydroxy-N-(thiazol-2-yl)quinoline-7-carboxamide
8-Hydroxy-N-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)quinoline-7-carboxamide
8-Hydroxy-N-(4-morpholinobenzyl)quinoline-7-carboxamide
8-Hydroxy-N-((5-methylisoxazol-3-yl)methyl)quinoline-7-carboxamide
8-Hydroxy-N-((4-methylthiazol-2-yl)methyl)quinoline-7-carboxamide
8-Hydroxy-N-(isoxazol-3-yl)quinoline-7-carboxamide
8-Hydroxy-N-(benzo[d]thiazol-2-ylmethyl)quinoline-7-carboxamide
8-Hydroxy-N-((5-methylpyrazin-2-yl)methyl)quinoline-7-carboxamide
8-Hydroxy-N-((1-methyl-1H-imidazol-2-yl)methyl)quinoline-7-carboxamide
8-Hydroxy-N-((4-phenylthiazol-2-yl)methyl)quinoline-7-carboxamide
8-Hydroxy-N-(pyridin-4-ylmethyl)quinoline-7-carboxamide
8-Hydroxy-*N*-(pyridin-2-ylmethyl)quinoline-7-carboxamide.

13. A compound of formula



14. Compound according to any one of the above claims, for use in the treatment and/or prevention of fungal infections.

15. Compound for use according to claim 14, wherein said fungal infection is from Tricophyton Rubrum, Tricophyton Mentagrophytes, Aspergillus Niger, Scopulariopsis Brevicaulis or Candida, such as Candida Albicans or Candida Glabrata.

16. Compound for use according to claim 14, wherein said fungal infection is from dermatophytes and/or molds, preferably from Tricophyton Rubrum, Tricophyton Mentagrophytes, Aspergillus Niger and/or Scopulariopsis Brevicaulis.

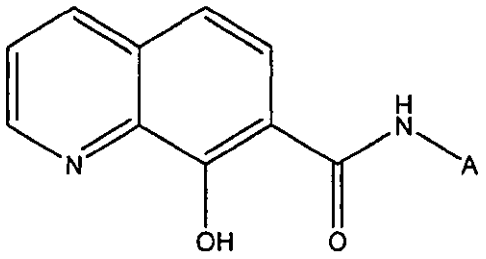
17. Compound for use according to claim 14, wherein said fungal infection is not from yeasts, preferably not from Candida.

18. Compound for use according to any one of claims 15 to 17, wherein the recipient of said treatment and/or prevention is a mammalian.

19. Compound for use according to claim 18, wherein the recipient of said treatment and/or prevention is a human.

THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. Use of a compound of general formula **(I)** or a pharmaceutically acceptable salt or derivative thereof



(I)

for use as antifungal agent;

wherein **A** is:

- $-(CH_2)_m-X_1$,
- $-(CH_2)_m-C_3-C_8$ cycloalkyl,
- $-(CH_2)_m-W-X_2$,
- $-(CH_2)_m-W-CH_2-X_1$, or
- $-(CH_2)_m-CHR_9-(CH_2)_m-X_1$;

wherein $\mathbf{X_1}$ is:

- -aryl, optionally substituted by one, two or three R_4,
- -heterocycle, optionally substituted by one or two R_5,
- $-C_1-C_8$ alkyl,
- -CH(OH)-phenyl,
- -S-phenyl,
- $-NHSO_2$-phenyl,
- -CN,
- -OH,
- $-C_3-C_8$ cycloalkyl, or
- -4-cyano-2,3,4,5-tetrafluoro-phenyl;

wherein $\mathbf{X_2}$ is:

- -aryl,
- -heterocycle,
- $-C_1-C_8$ alkyl,

- -CH(OH)-phenyl, or
- -C_3-C_8 cycloalkyl

wherein **W** is:

- -NH-,
- -O-, or
- -S-;

wherein **aryl** is:

- phenyl,
- naphthyl,
- biphenyl,
- tetrahydro-naphthyl, or
- fluorenyl;

wherein **heterocycle** is a 5-,6- or 7-membered saturated or unsaturated ring containing from one to three heteroatoms selected from the group consisting of nitrogen, oxygen and sulphur, and including any bicyclic group in which any of the above heterocyclic rings is fused to a benzene ring or another heterocyclic;

wherein **–cycloalkyl** is a saturated or unsaturated hydrocarbon ring including any bicyclic group in which the above ring is connected to a benzene, heterocyclic or other hydrocarbon ring;

wherein R_9 is:

- -C_1-C_7 alkyl,
- -C_3-C_8 cycloalkyl,
- -C(O)R_{11},
- -C(O)NHR_{11},
- -C(OH)R_{11},
- -CH_2OH,
- -CO_2R_{11}, or
- -aryl;

wherein R_{11} is:

- -H,
- -C_1-C_7 alkyl,

- $-(CH_2)_mX_1$, or
- $-(CH_2)_m-C_3-C_8$ cycloalkyl;

wherein R_4 is:

- -F,
- -Cl,
- -Br,
- -I,
- $-NO_2$,
- $-CF_3$,
- -CN,
- $-CH_2OH$
- $-C_1-C_6$ alkyl,
- $-W-R_{10}$
- $-(CH_2)_m$-aryl,
- $-(CH_2)_m$-heterocycle,
- $-(CH_2)_m-C_3-C_8$ cycloalkyl
- $-SO_2$-NH-heterocycle,
- $-(CH_2)_m-NR_{14}R_{15}$,
- $-(SO_2)-NR_{14}R_{15}$,
- $-(C=O)-NR_{14}R_{15}$, or
- $-(N-C=O)-NR_{14}R_{15}$;

wherein R_5 is:

- -H,
- -F,
- -Cl,
- -Br,
- $-CF_3$,
- $-W-R_{10}$,
- $-C_1-C_6$ alkyl,
- $-(CH_2)_m$-aryl,
- $-(CH_2)_m$-heterocycle, or

- $-(CH_2)_m-C_3-C_8$ cycloalkyl;

wherein R_{10} is:

- -H,
- $-C_1-C_6$ alkyl,
- $-(CH_2)_m$-aryl,
- $-(CH_2)_m$-heterocycle,
- $-(CH_2)_m-C_3-C_8$ cycloalkyl, or
- $-CH(R_{12})R_{13}$;

wherein R_{12} is:

- -H,
- $-(CH_2)_mCO_2-C_1-C_6$ alkyl,
- $-(CH_2)_m$-phenyl,
- $-(CH_2)_m$-heterocycle,
- $-C_1-C_6$ alkyl,
- $-C_1-C_4$ alkyl NH-$COOCH_2$-benzyl, or
- $-C_1-C_4$ alkyl-S-CH_3;

wherein R_{13} is:

- $-NH-CO_2C(CH_3)_3$,
- -CN,
- -COOH, or
- $-CO_2R_{11}$;

wherein R_{14} and R_{15}, independently from each other, are selected from:

- -H,
- $-C_1-C_6$ alkyl,
- $-(CH_2)_m$-aryl,
- $-(CH_2)_m$-cycloalkyl,
- $-(CH_2)_m$-heterocycle,
- $-(CH_2)_m-W-R_{10}$,
- $-(CH_2)_m-CN$,
- taken together with the nitrogen atom to which they are bound to form an optionally substituted 5- to 8-membered heteromonocycle

containing from one to three heteroatoms selected from the group consisting of nitrogen, oxygen and sulphur, or

- taken together with the nitrogen atom to which they are bound to form an optionally substituted 5- to 8-membered heteromonocycle which is fused to one or two optionally substituted saturated or unsaturated rings or to other optionally substituted heterocycles containing from one to three heteroatoms selected from the group consisting of nitrogen, oxygen and sulphur;

wherein **m** is an integer from 0 to 6 in the manufacture of a medicament for the treatment and/or prevention of fungal infections.

2. Use according to claim 1, wherein **A** is $-(CH_2)_m-X_1$.
3. Use according to claim 1 or 2, wherein **m** is an integer from 0 to 1.
4. Use according to any one of claims 1 to 3, wherein $\mathbf{X_1}$ is
   - -aryl, optionally substituted by one or two R_4,
   - -heterocycle, optionally substituted by one or two R_5, or
   - $-C_3$-C_8 cycloalkyl.
5. Use according to any one of claims 1 to 4, wherein $\mathbf{R_4}$ is
   - -Cl,
   - -Br,
   - $-CF_3$,
   - $-W-R_{10}$, or
   - $-(CH_2)_m-NR_{14}R_{15}$.
6. Use according to any one of claims 1 to 5, wherein **W** is oxygen.
7. Use according to any one of claims 1 to 6, wherein $\mathbf{R_{10}}$ is
   - -H, or
   - $-C_1$-C_6 alkyl.
8. Use according to any one of claims 1 to 7, wherein $\mathbf{R_{14}}$ and $\mathbf{R_{15}}$, independently from each other, are
   - $-C_1$-C_6 alkyl, or
   - taken together with the nitrogen atom to which they are bound to form an optionally substituted 5- to 8-membered heteromonocycle

containing from one to three heteroatoms selected from the group consisting of nitrogen, oxygen and sulphur.

9. Use according to any one of claims 1 to 8, wherein **aryl** is phenyl.

10. Use according to claim 1,

wherein **A** is $-(CH_2)_m-X_1$

wherein X_1 is:

- -aryl, optionally substituted by one, two or three R_4,
- -heterocycle, optionally substituted by one or two R_5, or
- $-C_3-C_8$ cycloalkyl

wherein R_4 is

- -Cl,
- -Br,
- $-CF_3$,
- $-W-R_{10}$, or
- $-(CH_2)_m-NR_{14}R_{15}$.

wherein R_5 is $-C_1-C_6$ alkyl

wherein R_{10} is

- -H, or
- $-C_1-C_6$ alkyl

wherein R_{14} and R_{15} are $-C_1-C_6$ alkyl,

wherein **W** is oxygen

wherein **m** is an integer from 0 to 1.

11. Use according to any one of claims 1 to 10, wherein **heterocycle** is 2,3-dihydrobenzo[b][1,4]dioxine, pyridine, thiophene, triazole, thiazole, isoxazole, benzothiazole, pyrazine, imidazole or furane.

12. Use according to claim 1, wherein the compound is selected from the group consisting of:

8-Hydroxy-N-(thiophen-2-ylmethyl)quinoline-7-carboxamide

8-Hydroxy-N-(cyclohexylmethyl)quinoline-7-carboxamide

8-Hydroxy-N-benzyl-quinoline-7-carboxamide

8-Hydroxy-N-(4-chlorobenzyl)quinoline-7-carboxamide

8-Hydroxy-N-(4-methoxyphenyl)quinoline-7-carboxamide

8-Hydroxy-N-(4-(trifluoromethyl)benzyl)quinoline-7-carboxamide

8-Hydroxy-N-phenyl-quinoline-7-carboxamide

8-Hydroxy-N-(2-hydroxybenzyl)quinoline-7-carboxamide

8-Hydroxy-N-(furan-2-ylmethyl)quinoline-7-carboxamide

8-Hydroxy-N-(pyridin-3-ylmethyl)quinoline-7-carboxamide

8-Hydroxy-N-(4-methoxybenzyl)quinoline-7-carboxamide

8-Hydroxy-N-(4-bromobenzyl)quinoline-7-carboxamide

8-Hydroxy-N-(1,1-dioxidotetrahydrothien-3-yl)quinoline-7-carboxamide

8-Hyroxy-N-(4-(dimethylamino)benzyl)quinoline-7-carboxamide

8-Hydroxy-N-(tetrahydro-2H-pyran-4-yl)quinoline-7-carboxamide

8-Hydroxy-N-(4-morpholinophenyl)quinoline-7-carboxamide

8-Hydroxy-N-(4-(1H-1,2,4-triazol-1-yl)phenyl)quinoline-7-carboxamide

8-Hydroxy-N-(thiazol-2-yl)quinoline-7-carboxamide

8-Hydroxy-N-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)quinoline-7-carboxamide

8-Hydroxy-N-(4-morpholinobenzyl)quinoline-7-carboxamide

8-Hydroxy-N-((5-methylisoxazol-3-yl)methyl)quinoline-7-carboxamide

8-Hydroxy-N-((4-methylthiazol-2-yl)methyl)quinoline-7-carboxamide

8-Hydroxy-N-(isoxazol-3-yl)quinoline-7-carboxamide

8-Hydroxy-N-(benzo[d]thiazol-2-ylmethyl)quinoline-7-carboxamide

8-Hydroxy-N-((5-methylpyrazin-2-yl)methyl)quinoline-7-carboxamide

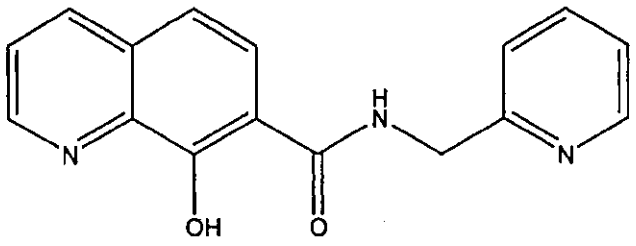
8-Hydroxy-N-((1-methyl-1H-imidazol-2-yl)methyl)quinoline-7-carboxamide

8-Hydroxy-N-((4-phenylthiazol-2-yl)methyl)quinoline-7-carboxamide

8-Hydroxy-N-(pyridin-4-ylmethyl)quinoline-7-carboxamide

8-Hydroxy-*N*-(pyridin-2-ylmethyl)quinoline-7-carboxamide.

13. A compound of formula



14. An antifungal agent comprising a compound of formula (I) as defined in any one of claims 1 to 13.