New topical pharmaceutical compositions have been developed comprising, based on the total weight of the composition:

a) from 1.5 wt. % to 5 wt. % of terbinafine or any pharmaceutically acceptable salt thereof;

b) from 15 wt. % to 35 wt. % of urea; and

c) more than 25 wt. % of water.

The ~~invention~~ present disclosure further relates to a composition as defined above for use in the treatment or prevention of topical fungal infections, preferably onychomycosis.

In a first aspect of the present disclosure, there is provided a topical pharmaceutical composition comprising, based on the total weight of the composition:

a) from 1.5 wt. % to 5 wt. % of terbinafine or any pharmaceutically acceptable salt thereof;

b) from 15 wt. % to 35 wt. % of urea; and

c) more than 25 wt. % of water.

In a second aspect of the present disclosure, there is provided a composition according to the first aspect for use in the treatment of topical fungal infections, preferably onychomycosis.

In a third aspect of the present disclosure, there is provided a use of a composition as defined in the first aspect in the manufacture of a medicament for the topical treatment of fungal infection, preferably onychomycosis.

In a fourth aspect of the present disclosure, there is provided a kit of parts comprising a composition according to the first aspect, a nail file and plasters, together with instructions for use.

In a fifth aspect of the present disclosure, there is provided a use of urea for solubilizing antifungal agents in topical formulations comprising more than 25% of water, based on the total weight of the composition.

DETAILED DESCRIPTION OF THE INVENTION

Terbinafine is an allylamine antifungal drug that inhibits the growth of fungi by blocking the enzyme squalene epoxidase, a key enzyme in fungal ergosterol biosynthesis. Examples of other allylamines antifungal agents include amorolfine, naftifine and butenafine.

In one embodiment of the present invention, the amount of terbinafine or a pharmaceutically acceptable salt thereof is in the range of 2 wt. % to 4 wt. %. In a preferred embodiment, the amount of terbinafine is in the range of 2 wt. % to 3 wt. %.

Preferably, terbinafine is in the form of terbinafine hydrochloride.

In one embodiment of the present invention, the amount of urea is in the range of 15 wt. % to 30 wt. %. In a preferred embodiment, the amount of urea is in the range of 15 wt. % to 25 wt. %.

Typically, the amount of water is more than 35 wt. %, preferably more than 40 wt. % and more preferably more than 45 wt. %.

In one embodiment of the present invention, the amount of water is in the range of 25 wt.% to 65 wt.%. In a preferred embodiment, the amount of water is in the range of 35 wt.% to 55 wt.%. In a more preferred embodiment, the amount of water is in the range of 40 wt.% to 50 wt.%.

In a particular embodiment, the topical semi-solid pharmaceutical composition comprises, based on the total weight of the composition:

9. A composition according to any preceding claim, wherein the composition further comprises e) a gelling agent.

10. A composition according to claim 9, wherein the gelling agent is selected from the group consisting of calcium carboxymethylcellulose, sodium carboxymethylcellulose, hyaluronic acid or any pharmaceutically acceptable salt thereof, sodium starch glycolate (sodium carboxymethyl starch), xanthan gum, polyethylene glycol (having a nominal average molecular weight ranging from 200 to 10,000,000; preferably ranging from 5,000 to 8,000,000; more preferably ranging from 1,000,000 to 5,000,000) carbomer, poloxamer, povidone (polyvinylpyrrolidone) and a polyquaternium polymer.

11. A composition according to claim 9 or claim 10, wherein the gelling agent is selected from the group consisting of hyaluronic acid or any pharmaceutically acceptable salt thereof and a polyquaternium polymer.

12. A composition according to claim anyone of claims 9 to 11, wherein the amount of gelling agent is in the range of 0.5 wt. % to 4 wt. %, preferably from 1 wt. % to 3 wt. %.

13. A composition according to any preceding claim, further comprising f) a buffering agent.

14. A composition according to any one of claims 1 to 13 for use in the treatment of topical fungal infections, preferably onychomycosis.

15. Use of a composition as defined in any one of claims 1 to 13 in the manufacture of a medicament for the topical treatment of fungal infection, preferably onychomycosis.

~~16. A method for treating a subject afflicted with a topical fungal infection, preferably onychomycosis, which comprises applying to said subject an effective amount of a composition as defined in any one of claims 1 to 13.~~

~~17.~~ 16. A kit of parts comprising a composition according to claim 1, a nail file and plasters, together with instructions for use.

~~18.~~17. Use of urea for solubilizing antifungal agents in topical formulations comprising more than 25% of water, based on the total weight of the composition.

~~19.~~18. Use according to claim ~~18~~ 17 wherein the antifungal agent is selected from terbinafine, amorolfine and ciclopirox, or any pharmaceutically acceptable salt thereof.