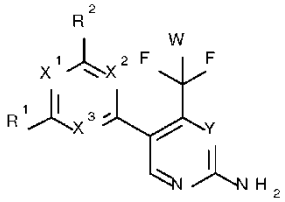
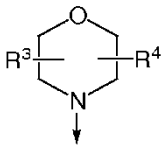
TREATMENT OF SKIN DISORDERS

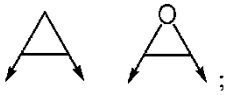
Abstract



(I)



(II)



;

The present invention relates to a compound of formula (I), wherein X^1, X^2 and X^3 are, independently of each other, N or CH; with the proviso that at least two of X^1X^2 and X^3 are N; Y is N or CH; W is H or F; with the proviso that when W is F, then X^1, X^2 and X^3 are N; R^1 and R^2 are independently of each other (i) a morpholinyl of formula (II) wherein the arrow denotes the bond in formula (I); and wherein R^3 and R^4 are independently of each other H, C_1-C_3alkyl optionally substituted with one or two OH, C_1-C_2fluoroalkyl, C_1-C_2alkoxy, C_1-C_2alkoxyC_1-C_3alkyl, CN, or C(0)0-C_1- C_2alkyl; or R^3 and R^4 form together a bivalent residue -R^5R^6- selected from C_1-C_3alkylene optionally substituted with 1 to 4 F, -CH_2-0-CH_2-, -CH_2-NH-CH_2-, or any of the structures wherein the arrows denote the bonds in formula (II); or (ii) a saturated 6-membered heterocyclic ring Z selected from thiomorpholinyl and piperazinyl, optionally substituted by 1 to 3 R^7; wherein R^7 is independently at each occurrence C_1-C_3alkyl optionally substituted with one or two OH, C_1-C_2fluoroalkyl, C_1-C_2alkoxyC_1-C_3alkyl, C_3-C_6cycloalkyl; or two R^7 substituents form together a bivalent residue -R^8R^9- selected from C_1-C_3alkylene optionally substituted with 1 to 4 F, -CH_2-0-CH_2- or -0- CH_2CH_2-0-; with the proviso that at least one of R^1 and R^2 is a morpholinyl of formula II; and prodrugs, metabolites, tautomers, solvates and pharmaceutically acceptable salts thereof, for use in a method of treating a

skin disorder in a subject, wherein said skin disorder is a genodermatosis, a vascular anomaly or a skin disorder selected from scleroderma, sclerodermatous chronic graft-versus-host disease, lichen sclerosus, lichen planus, lichen ruber planus and scars.

[No suitable Figure]