solid solutions of active ingredients in an auxiliary agent matrix. The matrix contains a homopolymer or a copolymer of N-vinyl pyrrolidone and a liquid or semi-solid surfactant.

WO 00/57854 discloses mechanically stable pharmaceutical dosage forms for peroral administration which contain at least one active compound, at least one thermo-plastically mouldable, matrix-forming auxiliary and more than 10% and up to 40% by weight of a surface-active substance that has an HLB of between 2 and 18, is liquid at 20°C, or has a drop point at between 20 °C and 50°C.

US 2005/0208082 discloses a solubilizing composition comprising a mixture of vitamin E TPGS and linoleic acid. The solubilizing composition is used to disperse a lipophile in an aqueous phase. The lipophile may be a therapeutically effective lipophile such as lipophilic vitamins, coenzyme Q10, carotenoids, alpha-lipoic acid or essential fatty acids.

US 2005/0236236 discloses pharmaceutical compositions for administration of hydrophobic drugs, particularly steroids. The pharmaceutical compositions include a hydrophobic drug, a vitamin E substance and a surfactant. The reference claims a synergistic effect between the hydrophobic drug and the vitamin E substance.

SUMMARY

Due to the presence of a sulfanyl group in its molecular structure, ABT-263 is prone to oxidation to sulfoxides which do not retain the therapeutic effect of ABT-263. For this reasons, oral liquid solutions of ABT-263 have been prepared immediately prior to use.

We now have found that a solid dispersion of ABT-263 and at least one pharmaceutically acceptable polymer not only shows adequate bioavailability after oral administration but also results in a storage-stable, ready-to-use dosage form. Quite surprisingly, in the solid dispersions the ABT-263 molecule, despite its essentially non-crystalline amorphous state, is largely resistant against oxidation even in presence of only a minor amount of antioxidant or the absence of an antioxidant. "Essentially non-crystalline amorphous state" means no more than 5%, preferably no more than 2% crystallinity, determined by X-ray diffraction analysis, and most preferably no detectable crystallinity, determined by polarization microscopy.

In a first aspect, t~~T~~he ~~invention~~disclosure relates to a pharmaceutical dosage form which comprises a solid dispersion product comprising a pharmaceutically active ingredient, at least one pharmaceutically acceptable polymer, and at least one pharmaceutically acceptable

solubilizer, said pharmaceutically active ingredient being N-(4-(4-((2-(4-chlorophenyl)-5,5-dimethyl-1-cyclohex-1-en-1-yl)methyl)piperazin-1-yl)benzoyl)-4-(((1R)-3-(morpholin-4-yl)-1-((phenylsulfanyl)methyl)propyl)amino)-3-((trifluoromethyl)sulfonyl)benzenesulfonamide, a salt, hydrate or solvate thereof.

In a second aspect, there is provided the use of the dosage form as defined herein in the manufacture of a medicament for treating a proliferative disorder.

In a third aspect, there is provided a process for preparing a solid dosage form as defined herein, comprising:

(a) preparing a homogeneous melt of the pharmaceutically active ingredient or a salt, hydrate or solvate thereof, the at least one pharmaceutically acceptable polymer and the at least one solubilizer, and

(b) allowing the melt to solidify to obtain a solid dispersion product.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 shows at different time points the plasma concentration of ABT-263 administered as dihydrochloride salt in a formulation containing Span 20 as solubilizer, wherein the formulation orally has been administered in doses of 50, 100 or 200 mg to fasted or fed dogs.

Fig. 2 shows at different time points the plasma concentration of ABT-263 administered as dihydrochloride salt in a formulation containing Vitamin E-TPGS as solubilizer, wherein the formulation orally has been administered in doses of 50, 100 or 200 mg to fasted or fed dogs.

Fig. 3 shows at different time points the plasma concentration of ABT-263 administered as free base in a formulation containing Vitamin E-TPGS only (Formulation 13), or as dihydrochloride salt in a formulation containing Vitamin E-TPGS plus propylene glycol as plasticizer (Formulation 10), wherein the formulation orally has been administered at a dose of 50 mg to fed dogs.

Fig. 4 and Fig. 5 show the results of an accelerated stability study using open dishes, wherein the sulfoxide content of different ABT-263 formulations was determined a different time points.

Fig. 6 and Fig. 7 show the results of an accelerated stability study using closed bottles, wherein the sulfoxide content of different ABT-263 formulations was determined at different time points.

Fig. 8 shows the release of ABT-263 from tablets containing different ABT-263 formulations.

DETAILED DESCRIPTION

In the dosage forms of the invention, the active ingredient is present as a solid dispersion or as a solid solution. The term "solid dispersion" defines a system in a solid state (as opposed to a liquid or gaseous state) comprising at least two components, wherein one component is dispersed evenly throughout the other component or components. For example, the active ingredient or combination of active ingredients is dispersed in a matrix comprised

19. Use of~~A method for treating a proliferative disorder, comprising administering~~ the dosage form of Claim 1 in the manufacture of a medicament for treating a proliferative disorder~~to a subject in need thereof~~.

20. The use~~method~~ of claim 19, wherein the proliferative disorder is selected from tumors and cancers.

21. The use~~method~~ of claim 20, wherein the proliferative disorder is selected from the group consisting of mesothelioma, bladder cancer, pancreatic cancer, skin cancer, cancer of the head or neck, cutaneous or intraocular melanoma, ovarian cancer, breast cancer, uterine cancer, carcinoma of the fallopian tubes, carcinoma of the endometrium, carcinoma of the cervix, carcinoma of the vagina, carcinoma of the vulva, bone cancer, cervical cancer, colon cancer, rectal cancer, cancer of the anal region, stomach cancer, gastrointestinal (gastric, colorectal and duodenal) cancer, chronic lymphocytic leukemia, acute lymphocytic leukemia, esophageal cancer, cancer of the small intestine, cancer of the endocrine system, cancer of the thyroid gland, cancer of the parathyroid gland, cancer of the adrenal gland, sarcoma of soft tissue, cancer of the urethra, cancer of the penis, testicular cancer, hepatocellular cancer (hepatic and biliary duct), primary or secondary central nervous system tumor, primary or secondary brain tumor, Hodgkin's disease, chronic or acute leukemia, chronic myeloid leukemia, lymphocytic lymphoma, lymphoblastic leukemia, follicular lymphoma, lymphoid malignancies of T-cell or B-cell origin, melanoma, multiple myeloma, oral cancer, ovarian cancer, non-small-cell lung cancer, prostate cancer, small-cell lung cancer, cancer of the kidney and ureter, renal cell carcinoma, carcinoma of the renal pelvis, neoplasms of the central nervous system, primary central nervous system lymphoma, non-Hodgkin's lymphoma, spinal axis tumors, brains stem glioma, pituitary adenoma, adrenocortical cancer, gall bladder cancer, cancer of the spleen, cholangiocarcinoma, fibrosarcoma, neuroblastoma, retinoblastoma, and combinations thereof.

22. A process for preparing a solid dosage form of Claim 1, comprising:
    (a) preparing a homogeneous melt of the pharmaceutically active ingredient or a salt, hydrate or solvate thereof, the at least one pharmaceutically acceptable polymer and the at least one solubilizer, and
    (b) allowing the melt to solidify to obtain a solid dispersion product.

23. The process of Claim 22, further comprising grinding said solid dispersion product and