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(54) Title: PROCESS OF PREPARING REMIBRUTINIB SUBSTANTIALLY FREE OF NITROSAMINE IMPURITY

(57) Abstract: This invention relates to a new process for preparing *N*-(3-(6-Amino-5-(2-(N- methylacrylamido)ethoxy)pyrimidin-4-yl)-5-fluoro-2-methylphenyl)-4-cyclopropyl-2- fluorobenzamide (LOU064) drug substance substantially free of nitrosamine impurities as well as new crystalline forms of salt and solvate of LOU064 used in the process. The invention further relates to pharmaceutical composition comprising *N*-(3-(6-Amino-5-(2-(N- methylacrylamido)ethoxy)pyrimidin-4-yl)-5-fluoro-2-methylphenyl)-4-cyclopropyl-2- fluorobenzamide, wherein the composition is substantially free of a nitrosamine impurity, e.g. the nitrosamine impurity *N*-(3-(6-amino-5-(2(methyl)(nitroso)amino)ethoxy)pyrimidin-4-yl)-5-fluoro-2- methylphenyl)-4-cyclopropyl-2-fluorobenzamide. Pharmaceutical products containing said drug substance and compositions are also disclosed, as well as methods for preparing said drug substance, pharmaceutical compositions and products.

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