

S36-4 Process Development of a PDE 5 inhibitor KF31327

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An efficient process suitable for a large-scale preparation of KF31327 (**1**), a potent and selective inhibitor of cyclic nucleotide phosphodiesterase 5, has been developed. The key strategic improvements from the original route are as follows: (i) 7-chloro-2,4(1*H*,3*H*)-quinazolin-2(1*H*)-one (**2**) was selected as a starting material to give the desired 6-nitro compound with good selectivity, (ii) the chlorination conditions in the preparation of a 2,4-dichloroquinazoline compound **3** were optimized to minimize the amount of phosphorus oxychloride, and (iii) the construction of the imidazothione ring of compound **1** was achieved by using phenyl isocyanate instead of extremely flammable carbon disulfide. Multikilograms of KF31327 have been successfully prepared by these procedures.

