

A Greener Process for the DLK Inhibitor GDC-0134

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GDC-0134 is a Dual Leucine Zipper Kinase (DLK) inhibitor considered as a potential treatment of amyotrophic lateral sclerosis [1,2]. The development of a sustainable second generation process for the manufacturing of GDC-0134 will be presented. Development was conducted with particular focus on safety and greenness while complying with tight specifications to supply pivotal clinical studies. The solvents classified as substances of very high concern by the REACH regulation were banned from the process. Conditions for a faster and safer oxidation process of a methyl sulfide to the corresponding sulfone were identified. A solvent and time consuming azeotropic distillation was avoided and the change of the solvent for final crystallization allowed for operation at higher concentration and delivery of an API of very high purity. The new improved process with a process mass intensity reduced by approx. 40% has been used successfully to produce > 150 kg GDC-0134.

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