

PXRD INVESTIGATION OF CHANGES IN DEHYDRATION BEHAVIOR OF 7-METHOXY-1-METHYL-5-(4-(TRIFLUOROMETHYL)PHENYL)-[1,2,4]TRIAZOLO[4,3-A]QUINOLIN-4-AMINE HYDRATE AFTER MICRONIZATION

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Micronization is a commonly used technique in pharmaceutical product development to achieve enhancement in bioavailability. However, mechanical stress during micronization may also introduce unwanted changes in physical properties such as polymorphic transformation and physical instability. A thorough understanding of the solid-state of materials post micronization is therefore required to mitigate potential risks in product development.

Herein, we report results from an investigation of the dehydration behavior of the title compound before and after micronization. Distinct dehydration processes were found for the non-micronized and micronized samples. The non-micronized material showed a two-step dehydration process whereas the micronized one followed a one-step process. The dehydration of the non-micronized sample was best fit by a two-step consecutive reaction. The first step is a diffusion limited reaction and the second step is a 2nd order reaction. For the micronized material, the best-fit model is a simple one-step nth order reaction.

Crystalline lattice changes for both non-micronized and micronized samples were studied by powder indexing and Rietveld analysis. The results are consistent with the observed rates of water departure upon heating the non-micronized versus the micronized material. In addition, a general trend was observed in associated diffraction peaks with preferred orientation effects observed in non-micronized vs micronized reflection data. A significant decrease in intensity post micronization was observed in peaks due to the (001), (010), (0-11), (011), (002), (0-21), and (003) planes. All of these planes are parallel to *a*-axis, which is the axis long which the water channels sit.