

DEVELOPING POWDER X-RAY DIFFRACTION (XRD) QUANTITATIVE METHOD FOR OROS[®] RWJ-333369 POLYMORPHS

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Abstract

An ALZA OROS drug delivery system was evaluated for potential development for RWJ-333369 (S-2-O-carbamoyl-1-o-chlorophenyl-ethanol, a novel neuromodulatory agent initially developed by SK Bio-Pharmaceuticals and licensed by Johnson & Johnson) to increase drug load and reduce side affects. RWJ-333369 was found to have two crystalline forms. The two crystalline forms (form A and form B) are enantiotropically related. Form A used in the AP-66 formulation is the thermodynamically stable form at room temperature. A partial polymorphic conversion in the solid state is observed at an elevated temperature of 60° C during two weeks stability test.

During the OROS RWJ-333369 manufacturing process, milling, granulation, compression, sub-coating, membrane coating, drilling and drying are used to produce capsule-shaped OROS tablet. It is possible that polymorphic conversion could take place during the manufacturing process and stability test. FTIR, Raman and XRD methods were evaluated for detecting polymorphic impurities. XRD was found to be a preferred method to monitoring polymorphic impurities.

Pure polymorph A and polymorph B reference materials were used for method development. Mixtures with different ratios of polymorph A and polymorph B were made to generate a calibration curve. The XRD scan peak height and peak area were calculated for the calibration curve. OROS RWJ-333369 formulations were spiked with polymorph B reference. It was found that the detection limit for polymorph B in the formulations is about 2% by using the 22 ° 2θ diffraction angle relative peak area. Samples from different OROS manufacturing process and stability tests were analyzed. The results indicate that polymorph A is not converted to polymorph B during manufacturing process.