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Development of Titanium Dioxide-Free Drotaverine 80 mg Film-Coated Tablets and Validation of HPLC Methods for Assay and Impurity Determination

ABSTRACT

Titanium dioxide (TiO_2, E171) has long been widely used in pharmaceutical film coatings due to its ability to provide opacity and protection against ultraviolet radiation. Following growing concerns regarding its safety and the ban on its use as a food additive within the European Union, increasing attention has been directed toward the development of alternative formulation approaches for medicinal products. The aim of this study was to formulate titanium dioxide-free 80 mg drotaverine hydrochloride film-coated tablets and to validate HPLC analytical methods for the determination of active pharmaceutical ingredient assay and impurities in accordance with current regulatory requirements. Drotaverine, a phosphodiesterase type 4 (PDE4) inhibitor, is a widely used antispasmodic agent indicated for the treatment of disorders associated with smooth muscle spasms. In the formulation developed by F1 Pharma, titanium dioxide was replaced with iron oxides, while maintaining the required functional properties of the film coating. In parallel, high-performance liquid chromatography (HPLC) methods for assay and impurity determination were developed and validated in accordance with ICH Q2(R2) guidelines. The final product was subjected to stability studies under accelerated (40°C/75% RH), intermediate (30°C/65% RH), and long-term (25°C/60% RH) storage conditions. The obtained results demonstrated that the titanium dioxide-free coating had no adverse effect on the quality or stability of the medicinal product. The validated HPLC methods enabled reliable monitoring of both active substance content and impurity profiles, providing a robust tool for routine quality control and stability assessment. The findings confirm that TiO_2 can be successfully replaced in drotaverine hydrochloride film-coated tablets while maintaining the required quality attributes and ensuring compliance with anticipated future regulatory requirements.

Keywords: Titanium-free formulation, Drotaverine, HPLC, method validation

BIOGRAPHY

Dr. Magdalena Strzebońska is an Assistant Professor at the Department of Environmental Protection, Faculty of Geology, Geophysics and Environmental Protection, AGH University of Krakow, Poland. She specializes in analytical chemistry, with particular emphasis on liquid chromatography (HPLC) and instrumental analysis. She has extensive experience in laboratory research, with expertise in the development and validation of analytical methods compliant with GMP, GLP, and European Union regulations. Her scientific activity also includes the development and implementation of analytical methods in environmental studies, with a focus on the analysis of water, wastewater, and sediments. From 2001 to 2009, she worked as a Quality Control Specialist at Pliva Kraków, where she was responsible for analytical method validation, documentation, and ensuring compliance and quality of medicinal products within the pharmaceutical industry.