Method Development and Validation for the Determination of Related Substances of Ezetimibe in Tablet Dosage Form

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ABSTRACT

The aim of present work was to develop and validate a accurate, precise and sensitive method for the determination of related substances of Ezetimibe in tablet dosage form. The RP-HPLC method has shown adequate separation for Ezetimibe and its Impurities from its degradation products. The separation was achieved on Fortis C18 (50 X 4.6mm), 2.5µ, with a gradient mixture of pottasium dihydrogen orthophosphate buffer : mobile phase B (55:45, v/v) as a Mobile phase A, and acetonitrile : methanol (78:22, v/v) as a Mobile phase B. Apparent pH of buffer was adjusted to 3.5 ± 0.05 with ortho phosphoric acid (88%). The mobile phase at a flow rate of 1.2 ml/min, Injection volume 5µl and wavelength of detection was kept at 210nm. The retention time of Ezetimibe, Desflouro Ezetimibe, Benzylated Ezetimine and Diol of Ezetimibe were about 4.919±0.1 min, 4.274±0.1 min, 15.497±0.1 min, 2.645±0.1 min respectively. The described method was linear over a range of 0.2-4.2

μg/ml. The correlation coefficient for Ezetimibe, Desflouro Ezetimibe, Benzylated Ezetimibe and Diol of Ezetimibe were 0.99993, 0.99998, 0.99983, 0.99996. respectively. The limit of detection for Ezetimibe, Desflouro Ezetimibe, Benzylated Ezetimine and Diol of Ezetimibe was 0.070, μg/ml and the limit of quantification were 0.210, 0.211, 0.209, 0.209 μg/ml respectively. Force degradation study was carried out on dosage form as per ICH guideline and it was exposed to hydrolytic (water, acid and base hydrolysis), oxidative and thermal conditions to apply stress. Proposed methods were validated as per ICH guidelines for linearity, accuracy, precision, specificity and robustness for estimation of Ezetimibe in commercially available tablet dosage form and results were found to be satisfactory. Thus the developed and validated stability indicating method can be used successfully for marketed formulations.

Key words: Ezetimibe, Desflouro Ezetimibe, Benzylated Ezetimine and Diol of Ezetimibe, stability indicating RP-HPLC method, Force degradation