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Short communication

Improvement of the analytical method for content determination of Rosuvastatin film coated tablets during lifecycle

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Introduction

The lifecycle monitoring of the analytical procedures includes risk assessment and systematic experimental evaluation to gain enhanced understanding of the procedure parameters critical to the consistent delivery of reportable results. As stated in ICH Q12, the analytical method Lifecycle Management (LCM) is encompassing all activities, from method development to validation, routine use, change control and retirement of the method. This enhanced approach improves the method understanding and performance, facilitates method transfer and leads to fewer out-of-specifications results (OOS).

The in-house method for content determination of Rosuvastatin film coated tablets is adopted from an in-license partner. The European Pharmacopoeia (Ph.Eur.) Commission has adopted a new monograph on Rosuvastatin tablets (3008) at its 163rd session (March 2019). The monograph was published in the first supplement to the 10th Edition (available in October 2019) and gained effectiveness on 1st April 2020.

Rosuvastatin tablets is the first monograph on a multi-source medicinal product to have been adopted and the product itself is one of the most widely used and prescribed medicines. This monograph is the result of a close cooperation between manufacturers, experts and the EDQM. This short paper reflects how the analytical method for content determination of Rosuvastatin film coated tablets was improved during the lifecycle.

Materials and methods

Method Origin / Comparison with current Pharmacopoeia Monographs

Method 1 – Chromatographic conditions – In-house method

The chromatographic separation was performed on Symmetry C18 250 x 4.6mm, 5µm at temperature of 35 °C. The Phenomenex Luna C18 column was found suitable too. Autosampler temperature was set at 4°C and the injection volume was 10 µL. The mobile phase A consisted of Buffer 0.01M pH 3.5 (65% v/v), acetonitrile (30% v/v) and tetrahydrofuran (THF) (5% v/v). Acetonitrile was used as mobile phase B. The flow rate was set to 1.0 mL/min. Gradient program was incorporated with chromatography run time of 42 minutes with ultraviolet (UV) detection at 280 nm.

Method 2 – Chromatographic conditions – Ph Eur 10.1 04/2020:3008 Monograph

XTerra MS C18 column, 150 mm length, 3.0 mm internl diameter and 3,5 µm particle size was used and termostated at 40 °C. Autosampler temperature was set as room temperature and injection volume of 10 µL. Mobile phase A consisted of 1 per cent (v/v) solution of trifluoroacetic acid R, acetonitrile for chromatography R, water for chromatography R (1:31:68 v/v/v), whereas the mobile phase B consisted of 1 per cent (v/v) solution of trifluoroacetic acid R, acetonitrile for chromatography R in ration 1:100 (v/v). The flow rate was set to 0.7 mL/min. Gradient program was incorporated with chromatography run time of 20 minutes with UV detection at 242 nm.

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Results and discussion

Analytical method transfer with the in - license partner was successfully performed and the method is applied in the routine analysis. Continuously key method performance characteristics are reviewed to verify that the measurement system and the analytical operations associated with the analytical procedure are adequate during the intended time period of analysis and enable the detection of potential failures. As main characteristics that are followed during the LCM of the current method are the System suitability test (SST) parameters: similarity between standard solution1 and standard solution 2 (98,0-102,0 %), recovery (98,0-102,0 %), relative standard deviation of the areas of Rosuvastatin peak in the standard solution (≤ 2.0 %), peak asymmetry (not more than 2.0) and theoretical plates (≥ 2000). During the lifecycle of the method in the laboratories for finished products and long-term stability, issues with non-fulfillment of the criteria for SST (lack of similarity between two preparations of standard solution) with increased frequency of occurrence regardless of the sensitivity of the HPLC instrument used (UV/Vis or DAD), were detected.

Theoretically, the method described in the Ph.Eur. monograph is easier for performing, there is no use of THF in the mobile phase, the chromatography run time is much shorter (20 minutes instead of 42 minutes). Considering the above mentioned, it was decided to adapt the existing pharmacopoeial method to our product Rosuvastatin film coated tablets 5 mg, 10 mg, 20 mg and 40 mg.

After defining the analytical target profile in the development phase, several analyzes were performed in order to check the appropriateness of the pharmacopoeial method. From the obtained results it was observed that with the newly optimized method the problems with achieving SST criteria have been overcome, a better chromatography has been obtained and the duration time of one analysis has been significantly shortened. For comparison, the time needed for analysis of one batch with the in-house method was 630 minutes (about 10.5 h), while with the Ph.Eur. method the total analysis time of one batch was found to be 300 minutes (about 5 h).

After the successful optimization of the pharmacopoeial method, validation of the analytical method for content determination of Rosuvastatin film coated tablets 5mg, 10mg, 20mg, 40mg has been performed. The validation parameters include specificity, linearity and range, accuracy, precision, robustness, stability and filtration of solutions, as per internal validation guideline.

Consequently, change request was initiated for all markets where the product has a marketing authorization license.

Conclusion

Recent developments in the progression and initiation of ICH quality guidelines (ICH Q12, Q2 revision, and ICH Q14) show that the regulatory aspects of the development and lifecycle management of analytical procedures is likely to be of continuing interest in the coming years.

References

Ermer, J. and Nethercote, P., 2015. Method Validation in Pharmaceutical Analysis. A Guide to Best Practice. WILEY-VCH Verlag GmbH&Co.KGaA.

ICH Guideline Q2(R1): "Validation of Analytical procedures: Text and Methodology", November 2005.

ICH Guideline Q12: "Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management", November 2019.

Ph. Eur. 10.1, 3008 (04/2020), Rosuvastatin tablets monograph, EDQM Council of Europe, 7 allée Kastner, CS 30026, F-67081 Strasbourg, France