IMPROVEMENT OF THE ANALYTICAL METHOD FOR CONTENT DETERMINATION OF ROSUVASTATIN FILM COATED TABLETS DURING LIFECYCLE

Aleksandra Damjanoska[1*], Cveta Dolikjoska Trajkova[1], Matilda Petrova[1], Milena Nikolovska[1], Mena Ivanoska Zdravkovska[1], Hristina Babunovska[1]

[1]ALKALOID AD Skopje, Pharmaceutical, Chemical and Cosmetics Company, Aleksandar Makedonski 12, 1000 Skopje, Republic of North Macedonia

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).

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	
Column	*Symmetry C18, Phenomenex Luna C18 250x4.6mm, 5µm or equivalent*
Detection	*UV - 280 nm*
Injection volume	*10 µl*
Flow rate	*1.0 mL/min*
Autosampler temperature	*4 °C*
Column temperature	*35 °C*
Mobile phase A	*Buffer 0.01M pH 3.5 (65% v/v): acetonitrile (30% v/v): tetrahydrofuran (THF) (5% v/v)*
Mobile phase B	*Acetonitrile*
Run time	*34 minutes*
Equilibration time	*7 minutes (incorporated into gradient program as below)*

Chromatographic conditions – in-house method

Time (min)	*Mobile phase A (% V/V)*	*Mobile phase B (% V/V)*
0	*100*	***0***
24	*100*	***0***
34	*80*	***20***
35	*100*	***0***
42	***100***	***0***

Gradient program – in house method

Method 2 – Chromatographic conditions – Ph Eur 10.1 04/2020:3008 Monograph	
Column	*XTerra MS C18 3.0 x 150mm; 3.5 µm or equivalent*
Detection	*UV - 242 nm*
Injection volume	*10 µL*
Flow rate	*1.0 mL/min*
Autosampler temperature	*Room temperature*
Column temperature	*40 °C*
Mobile phase A	*1 % V/V solution of trifluoroacetic acid R, acetonitrile for chromatography, Purified Water (1:31:68 V/V/V)*
Mobile phase B	*1 % V/V solution of trifluoroacetic acid R, acetonitrile for chromatography (1:100 V/V)*
Run time	*15 minutes*
Equilibration time	*5 minutes (incorporated into gradient program as below)*

Chromatographic conditions -Ph Eur method

Time (min)	*Mobile phase A (% V/V)*	*Mobile phase B (% V/V)*
0	*100*	***0***
14	*100*	***0***
15	*10*	***90***
16	*100*	***0***
20	***100***	***0***

Gradient program – Ph Eur method

RESULTS AND DISCUSSION

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.

Main characteristics that are followed during the LCM	
Similarity	*between standard solution 1 and standard solution 2 (98.0-102.0 %)*
Recovery	*98.0-102.0 %*
RSD of the areas of Rosuvastatin peak in the standard solution	*≤ 2.0 %*
Peak asymmetry	*not more than 2.0*
Theoretical plates	*≥ 2000*

Key method performance characteristics

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).

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

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.

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