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Short communication

Advantages of trend analysis in stability studies for prediction of potential OOS results within estimated shelf-life of medicinal product

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Introduction

Stability studies represent a fundamental requirement in pharmaceutical development, ensuring that medicinal products maintain their quality, safety and efficacy throughout their assigned shelf life. These studies provide essential data that support regulatory submissions and enable continuous monitoring of critical quality attributes (CQAs) over time (U.S. Food and Drug Administration (FDA), 2003).

In addition to routine evaluation of stability data, trend analysis has emerged as a highly valuable tool for deeper interpretation of data. By applying statistical approaches to long-term stability results, it is possible to identify patterns, detect variability and evaluate whether parameters exhibit increasing, decreasing or stable behavior. Such analysis plays an important role in the early identification of potential deviations from expected behavior (Yu et al., 2018). Furthermore, trend analysis enables prediction of future results, including potential out-of-specification (OOS) outcomes within the assigned shelf life. This approach is particularly important from a regulatory perspective, since proactive identification of risks ensures timely implementation of corrective measures and prevents distribution of non-compliant medicinal products (Hahn and Meeker, 1991).

Materials and methods

Trend analysis was performed on long-term stability data of Lisinopril/Amlodipine tablets 20 mg/10 mg obtained from four commercial batches manufactured over consecutive years. Stability studies were conducted in accordance with ICH guidelines under controlled conditions of 25 ± 2 °C and 60 ± 5% relative humidity. Samples were analyzed at predefined time intervals including 0, 3, 6, 9, 12, 18, 24 and 36 months (ICH Q1A (R2), 2003).

Critical quality attributes evaluated in this study included assay of active pharmaceutical ingredients, dissolution rate, related and degradation products, as well as microbiological purity. These parameters were selected based on their relevance as stability-indicating attributes. For quantitative parameters such as assay and impurities, statistical evaluation was performed using the regression control chart method. This approach allows estimation of trends over time, assessment of variability and prediction of expected results at any given time point. For parameters such as dissolution and microbiological purity, which may not always require advanced modeling, descriptive statistics and graphical representation of data trends were applied (ICH Q1A (R2), 2003).

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Results and discussion

The analysis of stability data demonstrated consistent performance of Lisinopril/Amlodipine tablets across all evaluated batches. Regression analysis of assay values for both active components showed no statistically significant time-dependent trend, indicating that the content of active substances remained stable throughout the studied period. All results were within specified acceptance criteria at all time points.

Dissolution profiles and microbiological purity of both active components exhibited stable behavior over time, with no indication of decreased drug release or variability that could impact product performance. These results confirm that the dosage form maintains its functionality during the entire shelf life.

For related and degradation products, the majority of results indicated no significant change and remained close to the initial values. Minor variability was observed for certain impurities in specific batches, showing slight out-of-trend behavior compared to other batches. However, all observed values remained within specification limits and did not indicate increased risk for OOS results.

The application of regression-based trend analysis enabled early detection of such variability and allowed closer monitoring of specific batches. Compared to traditional evaluation methods based solely on tabular data, trending provided a more comprehensive understanding of stability behavior and improved interpretation of long-term data.

Conclusion

Trend analysis represents a powerful and reliable approach for evaluation of stability data in pharmaceutical products. By enabling early identification of variability and detection of potential deviations, it supports prediction and prevention of out-of-specification results within the estimated shelf life.

The use of statistical tools such as regression control charts enhances the robustness of stability data interpretation and allows more accurate assessment of product performance over time. This contributes to improved decision-making processes, better risk management and increased regulatory compliance.

Ultimately, implementation of trend analysis in routine stability evaluation ensures consistent product quality, safety and efficacy, and represents a valuable component of modern pharmaceutical quality systems.

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