Macedonian Pharmaceutical Bulletin, 72 (Suppl 1) 289 - 290 (2026)
Online ISSN: 1857-8969
DOI: 10.33320/maced.pharm.bull.2026.72.03.139
Short communication

Stability study to support transport and distribution of an oral suspension

Matilda Petrova*, Katerina Veljanovska Prisagjanec, Cveta Dolikjoska-Trajkova, Marija Mojsovska, Natasa Anevska Stojanovska

Alkaloid AD, Boulevard Aleksandar Makedonski 12, 1000 Skopje, Republic of North Macedonia

Introduction

The term drug stability refers to the extent to which a drug substance or product retains, within specified limits and throughout its period of storage and use, the same properties and characteristics that it possessed at the time of its manufacture (Wong & Datla, 2005).

There are several stages that a product must pass through before it is administered to patients. The storage conditions established during the formal stability study are generally maintained during the manufacturing stage. However, the stage where storage condition excursions most frequently occur is transportation. For this reason, transportation study is conducted to complement the formal stability data and to define appropriate handling conditions for the product (Arana et al., 2023).

Temperature excursion is a deviation from given instructions. It is defined in the WHO Model Guidance as "an excursion event in which a Time Temperature Sensitive Pharmaceutical Product (TTSPP) is exposed to temperatures outside the range(s) prescribed for storage and/or transport. Temperature ranges for storage and transport may be the same or different; they are determined by the product manufacturer, based on stability data" (World Health Organization, 2011).

To understand the impact of temperature excursions on product quality, especially during shipments involving multiple legs and stress events, thermal-cycling studies can be conducted. In these studies, the product is intentionally exposed to different temperature conditions, ranging from low to high, for durations corresponding to the longest anticipated transport periods. The study is performed in three cycles to simulate cumulative exposure during international distribution. After each cycle, critical quality parameters are analyzed to detect any changes in the finished drug product. Such studies help determine how repeated temperature stress may affect product quality during actual distribution. The purpose of this study is to support the excursions that may occur during storage, transportation and distribution of the finished drug product (FDP) (Arana et al., 2023).

Materials and methods

Materials

The batch of oral suspension 100 mg/5mL, manufactured and packaged by Alkaloid AD Skopje, was subjected to a thermal-cycling study. The primary packaging consisted of a brown neutral glass bottle supplied with a PP 28 screw cap, child-resistant tamper-evident ring with embossing and liner.

Methods

For performing the study, the product is placed in the chosen transport container during a period corresponding to the longest anticipated transport duration. Data from critical stability-indicating

*mpetrova@Alkaloid.com.mk

parameters were collected after being stored at each temperature to evaluate any changes that may occur within the finished product. Two types of studies were done: Thermal and Freeze-Thaw studies by exposing the drug product to a few temperature cycles.

Performed thermal-cycling study consisted of 3 cycles, each cycle containing 3 different conditions for storage of this product and it was kept at the prescribed condition for 2 and/or 3 days. First condition was chosen to be -20±5 °C; second condition was +5±3 °C and the third condition was set at 50±2 °C.

After prescribed number of days at each temperature, at the end of each cycle, the samples and placebo were evaluated for selected critical quality parameters (CQPs). The parameters considered critical for the respective drug product are: appearance, color, pH value, viscosity, relative density, dissolution, assay of the active pharmaceutical ingredient (API) and preservative, related and degradation products, and microbiological quality. Validated stability-indicating methods were used for API and preservative assay determination, as well as related and degradation products.

Results and discussion

The results of the stability study conducted to support transport and distribution conditions on one batch of oral suspension with concentration of 100 mg/5mL, subjected to multiple brief exposures to low, medium and high temperature stress conditions, demonstrate that all tested parameters, whether physical or chemical, remained stable throughout the duration of the thermal-cycling study.

The appearance and color of the samples, pH value, relative density and viscosity remained stable over the thermal-cycling study period. No crystallization occurred in the drug product.

The assay values for the active compound, as well as for the preservative, remained within the shelf-life specification during the studies. Results obtained from the dissolution and related and degradation products meet the acceptance criteria. There was no increase observed in any individual impurity as well as the total impurities.

Microbiological quality was maintained during all cycles.

Conclusion

All CQPs for this drug product remained within the shelf-life specification during the thermal-cycling study and no physical and chemical changes were detected. Nevertheless, to avoid any kind of damage of the primary packaging at extremely low temperatures (-20 °C), storage and transport under ambient conditions with tolerated temperature excursions between +5°C and +50°C are recommended. Additionally, a storage advice “Do not freeze” may be considered.

References

Arana, C. et al., 2023. Industry perspective on temperature cycling studies to meet regulatory temperature excursion support requirements: Survey outcome and recommendations. Journal of Pharmaceutical Sciences 112(12), 2981–2990. https://doi.org/10.1016/j.xphs.2023.09.014

World Health Organization, 2011. Annex 9: Model guidance for the storage and transport of time and temperature sensitive pharmaceutical products. In WHO technical report series (No. 961). World Health Organization. https://www.who.int/publications/i/item/9789241209618

Wong, A. W. & Datla, A., 2005. Assay and stability testing, in: S. Ahuja & M. W. Dong (Eds.), Handbook of modern pharmaceutical analysis 6, 335–358. https://doi.org/10.1016/S0149-6395(05)80057-1