

OXYTOCIN INJECTION

Clarification of stability data and storage statement requirements

Oxytocin, indicated for prevention and treatment of postpartum haemorrhage, is a lifesaving medicine. Recent and past surveys undertaken by WHO and others have revealed that a significant number of samples of oxytocin injection collected from the market contain unacceptable levels of the active ingredient and related substances^{1,2}. These non-compliant products, usually found in high ambient temperature countries, are of particular concern given the high risk of treatment failure.

Based on the survey results, PQT Medicines (PQT-m) experts are of the opinion, that the main reason for the non-compliant assay and related substance levels observed in samples collected from the field appears to be inappropriate storage of the products out of refrigeration. This happens either due to failure to observe the labelled storage conditions or inappropriate labelling of the products with statements allowing long term storage or short term excursions out of refrigeration.

PQTm understands that the product is used at primary health care facilities or higher health institutions where facilities to store the product at the required storage condition of 2-8°C throughout the product shelf life should be available. PQT-m also recognises that statements on short term excursions may be confusing and may therefore contribute to unregulated excursions. For these reasons, PQT-m has not been accepting oxytocin injection applications that propose long term storage out of 2-8°C or those that propose short term excursions out of the long term storage condition of 2-8°C.

This notice is issued to clarify the required stability data and storage statement for prequalification of oxytocin injection products.

Stability data requirement

The required long term stability study condition for prequalification of oxytocin injection is 5°C ± 3°C. Consequently, the accelerated stability studies should be conducted at 25°C or higher. At the time of submission, at least six months accelerated and six months long term data should be included in the submitted dossier.

In addition, to account for potential water loss, for products packaged in plastic ampoules (semipermeable containers), the accelerated stability study should be conducted at low relative humidity conditions (i.e., at 40%RH or lower). Alternatively, as described in the WHO and ICH stability guidelines, the applicant can perform the stability studies under higher RH and calculate the water loss at the low RH.

¹ Survey of the Quality of Medicines Identified by the UN Commission Life-Saving Commodities for Women and Children. Geneva: World Health Organization, 2015.

² Torloni M, Gomes Freitas C, Kartoglu U, Metin Gülmezoglu A, Widmer M. Quality of oxytocin available in low- and middle-income countries: A systematic review of the literature. BJOG: An International Journal of Obstetrics and Gynaecology 2016

Storage statement requirement

The acceptable storage statement for prequalification is “Store in a refrigerator (2 °C to 8 °C). Do not freeze.” In some cases, “Store in the provided carton to protect the product from light” may also need to be added depending on the nature of the proposed primary container closure system and the photostability of the FPP. Omission of “Do not freeze” will only be considered with provision of supportive freeze-thaw data.