Notes on the design of bioequivalence study: Pyridoxine

Notes on the design of bioequivalence studies with products invited for submission to the WHO Prequalification Unit – Medicines Assessment Team (PQT/MED) are issued to aid manufacturers with the development of their product dossier. Deviations from the approach suggested below can be considered acceptable if justified by sound scientific evidence.

The current notes should be read and followed in line with the general guidelines of submission of documentation for WHO prequalification. For guidance on issues related to bioequivalence (BE) studies for immediate-release, solid oral dosage forms, see the ICH Harmonised Guideline M13A Bioequivalence for Immediate-Release Solid Oral Dosage Forms (2024). For BE issues outside the scope of the ICH M13A guideline, e.g., for additional strength biowaivers, please consult the "Multisource (generic) pharmaceutical products: guidelines on registration requirements to establish interchangeability" in: *Fifty-seventh report of the WHO Expert Committee on Specifications for Pharmaceutical Preparations,* Geneva, World Health Organization, 2024. WHO Technical Report Series, No. 1052, Annex 8.

Below, additional specific guidance is provided on the invited immediate release products containing pyridoxine.

Pharmacokinetics of Pyridoxine

Pyridoxine peak absorption is observed after 1.3 h and its half-life is very short (0.75 h), which may be responsible for a large intra-subject variability.

Pyridoxine is considered a highly soluble and highly permeable drug substance.

Guidance for the demonstration of *in vitro* bioequivalence

Taking into account the pharmacokinetic properties of pyridoxine, a biowaiver approach (akin to a BCS-based biowaiver) is recommended.

The following requirements should be met:

a) The formulation should contain standard excipients in usual amounts. Novel excipients should not be employed. As PQT/MED has not identified a comparator product for pyridoxine tablets, qualitative and quantitative comparison to a comparator product is not required, however, the use of excipients that are known to affect in vivo absorption, e.g., surfactants, should be avoided.

b) Dissolution data should be submitted at pH 1.2, 4.5 and 6.8 at 50 rpm in the paddle apparatus or 100 rpm in the basket apparatus showing very rapid or rapid dissolution of the proposed 10 and 50 mg tablets. Please refer to Section 5.2 of WHO guideline on Biopharmaceutics Classification System-based biowaiver (2024) - TRS1052, Annex 7 and the Section 5.2 annotations in PQT/MED-specific Annotations for the WHO guideline on Biopharmaceutics Classification System-based biowaivers (2024) for more information on the dissolution conditions that should be employed for this biowaiver.