In general, FDA’s guidance documents do not establish legally enforceable responsibilities. Instead, guidances describe the Agency’s current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

**Active Ingredient:** Pentoxifylline

**Dosage Form; Route:** Tablet, extended release; Oral

**Recommended Studies:** Two in vivo bioequivalence studies with pharmacokinetic endpoints

1. **Type of study:** Fasting  
   **Design:** Single-dose, two-treatment, two-period crossover in vivo  
   **Strength:** 400 mg  
   **Subjects:** Healthy males and non-pregnant, non-lactating females  
   **Additional comment:** Exclude subjects who have intolerance to methylxanthines such as caffeine, theophylline, and theobromine.

2. **Type of study:** Fed  
   **Design:** Single-dose, two-treatment, two-period crossover in vivo  
   **Strength:** 400 mg  
   **Subjects:** Healthy males and non-pregnant, non-lactating females  
   **Additional comment:** See comment above.

**Analytes to measure:** Pentoxifylline and its active metabolites, Metabolite I (1-[5-hydroxyhexyl]-3,7-dimethylxanthine) and Metabolite V (1-[3-carboxypropyl]-3,7-dimethylxanthine), in plasma

Submit the metabolite data as supportive evidence of comparable therapeutic outcome. For the metabolites, the following data should be submitted: individual and mean concentrations, individual and mean pharmacokinetic parameters, and geometric means and ratios of means for area under the curve and maximum concentration.

Recommended May 2023
**Bioequivalence based on (90% CI):** Pentoxifylline

**Additional Strengths:** Not applicable

**Dissolution test method and sampling times:** For modified release drug products, applicants should develop specific discriminating dissolution methods. Alternatively, applicants may use the dissolution method set forth in any related official United States Pharmacopeia (USP) drug product monograph, or in the FDA’s database, [http://www.accessdata.fda.gov/scripts/cder/dissolution/](http://www.accessdata.fda.gov/scripts/cder/dissolution/), provided that applicants submit adequate dissolution data supporting the discriminating ability of such a method. If a new dissolution method is developed, submit the dissolution method development and validation report with the complete information/data supporting the proposed method. Conduct comparative dissolution testing on 12 dosage units for each of the test and reference products. Specifications will be determined upon review of the abbreviated new drug application.

In addition to the method above, submit dissolution profiles on 12 dosage units for each strength of the test and reference products generated using USP Apparatus 1 at 100 rpm and/or Apparatus 2 at 50 rpm in at least three dissolution media (e.g., pH 1.2, 4.5 and 6.8 buffer). Agitation speeds may be increased if appropriate. It is acceptable to add a small amount of surfactant if necessary. Include early sampling times of 1, 2, and 4 hours and continue every 2 hours until at least 80% of the drug is released to provide assurance against premature release of drug (dose dumping) from the formulation.

**Unique Agency Identifier:** PSG_018631