EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

30 March 2023
EMA/CHMP/901584/2022
Committee for Medicinal Products for Human Use (CHMP)

Pirfenidone film-coated tablets 267, 537 and 801 mg, and hard capsules 267 mg product-specific bioequivalence guidance

Draft agreed by Pharmacokinetics Working Party (PKWP) / Methodology Working Party (MWP)	February 2023
Adopted by CHMP for release for consultation	30 March 2023
Start of public consultation	June 2023
End of consultation (deadline for comments)	30 September 2023
Agreed by Methodology Working Party (MWP)	
Adopted by CHMP	
Date for coming into effect	

Comments should be provided using this template. The completed comments form should be sent to GenericsDG@ema.europa.eu

Keywords	***Bioequivalence, generics, pirfenidone***

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Disclaimer:

This guidance should not be understood as being legally enforceable and is without prejudice to the need to ensure that the data submitted in support of a marketing authorisation application complies with the appropriate scientific, regulatory and legal requirements.

Requirements for bioequivalence demonstration (PKWP)*

BCS Classification**	**BCS Class:** ☒ **I** ☐ **III** ☐ **Neither of the two** **Background:** Pirfenidone is considered a high solubility compound with complete absorption
Bioequivalence study design *in case a BCS biowaiver is not feasible or applied*	**single dose** **cross-over**
	healthy volunteers
	☐ **fasting** ☐ **fed** ☐ **both** ☒ **either fasting or fed** The SmPC recommends intake in fed state to minimise the risk of risk of nausea and dizziness. A fed study is, therefore, acceptable. However, a fasted study is also acceptable.
	Strength: film-coated tablets: 801 mg, capsules 267 mg. **Background:** Linear pharmacokinetics has been demonstrated following single-dose oral administration of 200–600 mg pirfenidone. No deviation from dose-proportional pharmacokinetics has been observed over the dose range 801–4005 mg/day under steady-state conditions. Highest strength recommended. However, it is also possible to use the lower strengths for a drug with linear pharmacokinetics and high solubility. The

	study could be performed using either the originator tablet formulation or the originator capsule (using multiple capsules if applicable) as comparator. For the capsules, 267 mg is the only strength.
	Number of studies: one single dose study.
	Other design aspects:
Analyte	☒ **parent** ☐ **metabolite** ☐ **both**
	☒ **plasma/serum** ☐ **blood** ☐ **urine**
	Enantioselective analytical method: ☐ **yes** ☒ **no**
Bioequivalence assessment	**Main pharmacokinetic variables:** C_{max} and AUC_{0-t}
	90% confidence interval: 80.00–125.00%

* As intra-subject variability of the reference product has not been reviewed to elaborate this product-specific bioequivalence guideline, it is not possible to recommend at this stage the use of a replicate design to demonstrate high intra-subject variability and widen the acceptance range of C_{max}. If high intra-individual variability (CV_{intra} > 30%) is expected, the applicants might follow respective guideline recommendations.

** This tentative BCS classification of the drug substance serves to define whether in vivo studies seem to be mandatory (BCS class II and IV) or, on the contrary (BCS Class I and III), the Applicant may choose between two options: in vivo approach or in vitro approach based on a BCS biowaiver. In this latter case, the BCS classification of the drug substance should be confirmed by the Applicant at the time of submission based on available data (solubility experiments, literature, etc.). However, a BCS-based biowaiver might not be feasible due to product specific characteristics despite the drug substance being BCS class I or III (e.g. in vitro dissolution being less than 85% within 15 min (BCS class III) or 30 min (BCS class I) either for test or reference, or unacceptable differences in the excipient composition).