



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

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Committee for Medicinal Products for Human Use (CHMP)

## Miglustat hard capsules 100 mg product-specific bioequivalence guidance\*

Draft agreed by Pharmacokinetics Working Party (PKWP)	October 2013
Adoption by CHMP for release for consultation	24 October 2013
Start of public consultation	15 November 2013
End of consultation (deadline for comments)	15 February 2014
Agreed by Pharmacokinetics Working Party	22 October 2014
Adopted by CHMP	20 November 2014
Date for coming into effect	1 June 2015

\*This guideline was previously published as part of a "compilation of individual product-specific guidance on demonstration of bioequivalence Rev.3 EMA/CHMP/736403/2014"

<b>Keywords</b>	<b><i>Bioequivalence, generics, miglustat</i></b>
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## Miglustat hard capsules 100 mg product-specific bioequivalence guidance

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)\*

<p><b>BCS Classification**</b></p>	<p><b>BCS Class:</b> <input type="checkbox"/> I <input type="checkbox"/> III <input type="checkbox"/> Neither of the two</p> <p><b>Background:</b> the available data on solubility does not allow the BCS classification of miglustat. If the Applicant generates the solubility data and classifies the drug according to the BCS criteria as highly soluble, a BCS biowaiver could be applicable.</p>
<p><b>Bioequivalence study design</b></p> <p><i>in case a BCS biowaiver is not feasible or applied</i></p>	<p><b>single dose</b></p> <p><b>cross-over</b></p>
	<p><b>healthy volunteers</b></p>
	<p><input checked="" type="checkbox"/> <b>fasting</b> <input type="checkbox"/> <b>fed</b> <input type="checkbox"/> <b>both</b> <input type="checkbox"/> <b>either fasting or fed</b></p>
	<p><b>Strength:</b> 100 mg</p> <p><b>Background:</b> 100 mg is the only strength</p>
	<p><b>Number of studies:</b> one single dose study</p>

<b>Analyte</b>	<input checked="" type="checkbox"/> parent <input type="checkbox"/> metabolite <input type="checkbox"/> both
	<input checked="" type="checkbox"/> plasma/serum <input type="checkbox"/> blood <input type="checkbox"/> urine
	<b>Enantioselective analytical method:</b> <input type="checkbox"/> yes <input checked="" type="checkbox"/> no
<b>Bioequivalence assessment</b>	<b>Main pharmacokinetic variables:</b> AUC <sub>0-t</sub> and C <sub>max</sub>
	<b>90% confidence interval:</b> 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<sub>max</sub>. If high intra-individual variability (CV<sub>intra</sub> > 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 seems 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).