1 April 2015
EMA/CHMP/116356/2014
Committee for Medicinal Products for Human Use (CHMP)

Overview of comments received on 'Draft carglumic acid product-specific bioequivalence guidance' (CHMP/PKWP/EMA/422457/2013)

Interested parties (organisations or individuals) that commented on the draft document as released for consultation.

Stakeholder no.	Name of organisation or individual
1	MEB, The Netherlands
2	Apothecon Pharmaceuticals PVT LTD, India

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

1. General comments – overview

Stakeholder no.	General comment (if any)	Outcome (if applicable)
1	Why a specific BE guidance for carglumic acid (dispersible tablets) as the general BE guidance can be followed without problems. 1. Some APIs are stated as BCS Class I or III (e.g. sunitinib, Emtricitabine/tenofovir disoproxil, etc.), and also requirements for BE study are stated. It is unclear if the meaning is this API is not qualify for BCS-biowaiver. 2. Maybe add one row of "remarks for biowaiver"? information for additional strengths, BCS-biowaiver, and solution with sorbitol (e.g. Oseltamivir) can put here. 3. Background is written differently for the same statement in BCS and strength. 4. With regards to API with unknown BCS, should we give recommendations for biowaiver? We have seen "The available data on solubility does not allow the BCS classification of oseltamivir. 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." This recommendation never appears with other APIs under the same conditions.	1. Accepted. 2. The comment has been acknowledged; however, this is addressed in the guideline, therefore no further action is needed. 3. Accepted. 4. As it is neither BCS Class I nor BCS Class III, a BCS biowaiver is not possible.
2	As per Daily dose of Carglumic acid Dispersible tablets, 200mg, tablets required 100mg/kg , if we consider 75 kg weight of average subject then we required atleast 37 tablets per subjects and if we can plan minimum 18 subjects BE study then applicant required Innovator products at least 666 Tablets (Carbaglu) from Europe markets.	For the design of BE studies with healthy volunteers the strength is applicable and not the dose. BE studies should be performed with 200mg of Carglumic acid (its strength) and not following the dose as the question suggests.

Stakeholder no.	General comment (if any)	Outcome (if applicable)
	Carbaglu registered in Europe as Orphan drug and 666 tablets of single lot of Carbaglu is not available in Europe Market. In such circumstances, Can generic company use multiple different lots of Carbaglu for as a reference drugs in single BE study? Pl. guide	