CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-562

STATISTICAL REVIEW(S)

STATISTICS FILING CHECKLIST FOR A NEW NDA/BLA

NDA/BLA Number: 22562 **Applicant: Orphan Europe, SARL** **Stamp Date: 6/18/2009**

Drug Name: Carbaglu (carglumic acid) Tablets **NDA/BLA Type: Orig. Application 505(b)(1) NME Priority Review** **Indication: hyperammonemia in NAGS deficiency**

On **initial** overview of the NDA/BLA application for RTF:

	Content Parameter for RTF	Yes	No	NA	Comments
1A	Paper Submission: Index is sufficient to locate necessary reports, tables, data, etc.	X			
1B	Electronic Submission: Indexing and reference links within the electronic submission are sufficient to permit navigation through the submission, including access to reports, tables, data, etc.			X	
2	ISS, ISE, and complete study reports are available (including original protocols, subsequent amendments, etc.)			X	
3	Safety and efficacy were investigated for gender, racial, and geriatric subgroups investigated.			X	
4	Data sets in EDR are accessible and conform to applicable guidances (e.g., existence of define.pdf file for data sets).			X	

IS THE STATISTICAL SECTION OF THE APPLICATION FILEABLE? NA

Content Parameter (possible review concerns for 74-day letter)	Yes	No	NA	Comment
Designs utilized are appropriate for the indications requested.			X	
Endpoints and methods of analysis are specified in the protocols/statistical analysis plans.			X	
Interim analyses (if present) were pre-specified in the protocol and appropriate adjustments in significance level made. DSMB meeting minutes and data are available.			X	
Appropriate references for novel statistical methodology (if present) are included.			X	
Safety data organized to permit analyses across clinical trials in the NDA/BLA.			X	
Investigation of effect of dropouts on statistical analyses as described by applicant appears adequate.			X	

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Reviewer Comments:

This product was originally submitted to DGP under NDA (b) (4) (July 2008) and was subsequently withdrawn due to fileability issues. A pre-NDA meeting was held Sept. 26, 2008 to discuss format and content of the revised NDA.

Hyperammonemia in NAGS (N-acetylglutamate synthase) deficiency is an orphan designation. Prevalence of this disease is extremely low and clinical trials are not deemed possible. This submission consists of a retrospective compilation of the case histories of 24 NAGS deficiency patients treated with carglumic acid during the period 1991 to 2007.

A main review concern will be quality and consistency of data among patient narratives, CRFs, and electronic data files, all derived from multiple kinds of source documentation. Efficacy data presented are descriptive only, and review conclusions will largely be based on clinical judgment. No statistical or inferential conclusions are possible since the data were not collected and analyzed within the framework of an experimental design.

No formal statistical review of this submission is warranted. However, the statistical team should be available to advise the medical reviewers as needed with regard to data presentation or computational issues.

Requests to the Applicant for the 74-day letter:

None

M. Welch July 28, 2009

Reviewing Statistician Date

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

MICHAEL E WELCH
07/28/2009