

BLA Filing Letter - GLASSIA

Our STN: BL 125325/0

Kamada Ltd.

Attention: -----(b)(4)-----

Dear ----(b)(4)----:

This letter is in regard to your biologics license application (BLA) submitted under section 351 of the Public Health Service Act.

We have completed an initial review of your application dated May 29, 2009, for Alpha-1-Proteinase Inhibitor (Human) to determine its acceptability for filing. Under 21 CFR 601.2(a) we have filed your application today. The review goal date is April 1, 2010. This acknowledgment of filing does not mean that we have issued a license nor does it represent any evaluation of the adequacy of the data submitted.

We will contact you regarding your proposed labeling no later than March 2, 2010. If postmarketing study commitments (506B) are required, we will contact you no later than March 2, 2010.

While conducting our filing review, we identified the following potential review issues:

1. Please submit an analysis of the subjects in each treatment group who had the onset of their adverse event (AE) during or within 24 hours of the end of an infusion of study product. For cases in which the time of onset of the AE was not captured, assume that all AEs that began on either the day of an infusion or the day following an infusion occurred within 24 hours of the end of an infusion. Present these data (a) only for the initial 12 weeks parallel portion of the study, by treatment group and (b) for the entire duration of study, by actual treatment.
2. Your study report for this study states on page 7 "two subjects were withdrawn due to AEs, one subject (ID No. -----(b)(6)-----) for pulmonary emboli (Prolastin®) and one subject with urticaria (Kamada-API)." The raw dataset for serious adverse events (SAEs) in study -(b)(4)- API 002 ("SERIOU18") lists 6 SAEs (4 unique AE terms) reported for 4 subjects, all in "GROUP" "API." GROUP is defined as "Static value of API for every subject." Please provide the field name in this dataset that indicates to which randomization treatment group each subject belongs.
3. Why were 2 subjects with AAT phenotype MZ enrolled in study -(b)(4)- API 002, given that this phenotype normally is not associated with serum A1-PI levels < ~ 17 microM?
4. Please provide the elapsed time (the time blood samples were taken to measure plasma concentrations) after drug administration for PK study under the PKTP column within the PKLABDAT data set.

We are providing the above comments to give you preliminary notice of potential review issues. Our filing review is only a preliminary evaluation of the application and is not indicative of deficiencies that may be identified during our complete review. Issues may be added, deleted, expanded upon, or modified as we review the application. If you

respond to these issues during this review cycle, we may not consider your response before we take an action on your application. Following a review of the application, we shall advise you in writing of any action we have taken and request additional information if needed.

If you have any questions, please contact the Regulatory Project Manager, Cherie Ward-Peralta, at (301) 827-9170.

Sincerely yours,

Basil Golding, M.D.

Director

Division of Hematology

Office of Blood Research and Review

Center for Biologics Evaluation and Research

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