Reviewer’s report

Title: Pharmacokinetic Study of Single- and Multiple-dosing with Metolazone Tablets in Healthy Chinese Population

Version: 1 Date: 28 Nov 2016

Reviewer: Melanie Felmlee

Reviewer’s report:

The revised manuscript by Li et al addresses some of the concerns raised in the initial review; however, some comments were not addressed.

1) While the authors made some revisions to the English grammar and flow of the paper, further revision is required. The manuscript should be edited by a native English speaker, if possible, to improve the readability.

2) The figures need further revision. The authors have removed figure 7 based on the earlier review, but the other figures are still difficult to interpret. I would like to suggest two possible options for revising the PK figures:

   a) Present the individual data points with a single line illustrating the mean data profile

   b) Present mean ± SD with a connecting line.

Either of these options should be available in the graphical section of Phoenix WinNonLin. It would be beneficial to combine figures 4 and 5 to observe a direct comparison between the fed and fasted state PK data.

3) Comment 4 Reviewer 2 from earlier review: The additional information added helped with clarification, but lead to overlap between the study design and drug administration sections. It would be helpful to combine these sections to reduce the repetition.

4) Discussion: Validation of LC/MS/MS assay to quantify metolazone was not discussed in the results section. The validation results should be included in the results section with the validation measures listed in the discussion.

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.
Yes

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

Yes

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

**Quality of written English**
Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

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