Peer Review File

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Comment 1: The author should point out the new meaning of this study, explain the clinical significance and the basis of SNP site selection.
Reply 1: We are very grateful to your comments. At present, there are few reports in the literature, so we select the sites related to the indication diseases and the common sites of the drug metabolizing enzymes.

Comment 2: The author should indicate whether the sample processing and preservation process remains stable.
Reply 2: Thank you for your valuable comments. The treatment and preservation of blood samples are stable and have been verified by existing methods.

Comment 3: The author should explain why blood samples were collected at 4th and 96th hours and what is the standard of dosage selection.
Reply 3: Thank you for your careful reading and valuable question. To monitor the safety of the subjects after taking the medicine, the peak time and the time of basic elimination were selected.

Comment 4: The author did not point out whether the length of the cleaning period meets the half-life requirement.
Reply 4: Thanks a lot for your careful comments. According to the PK results of this test, the wash out period meets the requirements of 7 times half-life.

Comment 5: The author should indicate whether this document complies with the standard biosafety and institutional safety procedures.
Reply 5: Thank you for your valuable comments. We strictly follow the standard biosafety and institutional safety procedures.

Comment 6: Are the statistical methods sufficiently documented to allow replication studies?
Reply 6: Thank you for your careful reading and valuable question. Since it is a bioequivalence test, the test results are correlated with different tests and different subject states. Repeatability is not just about statistical methods.

Comment 7: Why does no SNP site have a significant effect on PK under fed condition? Does it indicate that the differences between individuals are more due to fasting than to differences in SNP sites?
Reply 7: Thank you for your valuable comments. Such a possibility exists, and the instructions for cinacalcet suggest that the drug should be taken with or immediately after meals. Therefore, the differences between individuals under fasting may be caused by the combined effect of food and subject genetic polymorphisms.

Comment 8: Whether the PD of cinacalcet detected after single administration is representative?
Reply 8: Thank you for your valuable comments. In this study, the PD of cinacalcet was more used as a safety indicator in the bioequivalence test, rather than reflecting drug efficacy.

Comment 9: Is there any comparability between the PD indexes of healthy subjects after single administration and those of other literatures after multiple administration?
Reply 9: Thank you for your valuable comments. This study is a single dose, PD index is more to reflect the safety of the test, considering the difference between patients and healthy subjects, as well as the steady state of blood concentration after single dose and long-term administration, there are also differences between the two, so the representative of PD index in this study is weak, which is one of the possible reasons for not finding statistically significant results in SNP sites such as CASR.

Comment 10: The author should explain whether there are other drug transporters that may be involved in the in vivo process of cinacalcet and contribute to individual differences in subjects.
Reply 10: Thank you for your valuable comments. There is no such data and literature report, therefore no investigation has been conducted.

Comment 11: The author should emphasize the limitations and advantages of this article.
Reply 11: Thank you for your valuable comments. Limitations: It is a bioequivalence test, single administration only, and subjects were all healthy people;
Advantages: Potential sites related to metabolism of cinacalcet have been found, which can provide reference for guiding individualized and rational use of cinacalcet.

Comment 12: Dose the references list cover the relevant literature adequately?
Reply 12: Thank you for your careful reading and valuable question. Yes, the list of references fully covers the relevant literature.

Comment 13: Apart from PTH, the levels of serum calcium, phosphorus and calcium-phosphorus products in SHPT patients can be effectively reduced by cinacalcet too.
Reply 13: Apart from PTH, administrating cinacalcet also reduces the level of serum calcium, phosphorus, and calcium-phosphorus in SHPT patients.
Changes in the text: Thanks, we have modified our text as advised (see Page 4, Line 11-12).

Comment 14: In addition, we investigated whether the SNPs of CASR and VDR which had been reported to have effects on PD of cinacalcet, had any effects on response of healthy Chinese subjects to cinacalcet after receiving a single dose of administration under fasting condition.
Reply 14: Besides, we investigated whether the SNPs of CASR and VDR had any

impact on the response of healthy Chinese subjects to cinacalcet after receiving a single dose administration under fasting conditions, though those SNPs have been reported affecting PD of cinacalcet.
Changes in the text: Thanks, we have modified our text as advised (see Page 6, Line 4-7).

We sincerely and earnestly appreciate for Editors/Reviewers' warm work. In addition, the whole manuscript has been polished.

Once again, thank you very much for your comments and suggestions.