Clinical Study Program for 505 (b) (2) NDA Application – The Fast Path to Approval
Juan He*, Masood Bhatti, and Lorelei Lutter, BioPharma Services Inc. Toronto, ONT, Canada

Abstract

The MRA product is similar to Patent 1, with only minor changes in the chemical structure. The drug product is not eligible for filing in an ANDA but is available for filing in a 505(b)(2) application.

The response of patients to the modified release product should be assessed if the compound is known to produce different systemic and peak exposures at morning or evening dosing. The study will be single dose and the fasted control MRA01 should be tested and each of the groups compared to the control.

Multiple-Dose Study

An MRA drug can be intrinsically marketed using a CIP strategy. A critical question is whether the drug is intrinsically marketed. A drug is considered intrinsically marketed if the drug is marketed in a manner that the compound is known to produce different systemic and peak exposures at morning or evening dosing. The trials will be multiple dosing, 1, 2, 3, 4, 6, 7, 8, 8.5, 9, 9.5, 10, 10.5, 11, 12, 14, 16, 18, 20, 24, 36, and 48 hours.

PK/PD Correlation

Steady State comparative Bioavailability study after the fasted and food effect studies showed favorable results. The expected outcome will be: Comparable overall bioavailability of the compound from both products at the steady state.

72.03% Cmax
0.03785% - 114%
93.87% AUC
P90% CI
(MRA01/A01)
Relative Bioavailability

505 B2 Route

The MR investigational product.
In vivo correlation) study will be useful to set up the product specification.

Correlation
Estimate in vivo time course using deconvolution

Clinical Studies for Compound MRA01

The study will be multiple dosing, 1, 2, 3, 4, 6, 7, 8, 8.5, 9, 9.5, 10, 10.5, 11, 12, 14, 16, 18, 20, 24, 36, and 48 hours.

Food Effect Study

The PK parameters will be Cmax and AUC from a single dose study.

Special Populations (Renal/Hepatic)

The correlation between the Cmax/AUC and the blood pressure will be carried out for both treatments.

Conclusion

Steady State comparative Bioavailability study after the fasted and food effect studies showed favorable results. The study will be multiple dosing, 1, 2, 3, 4, 6, 7, 8, 8.5, 9, 9.5, 10, 10.5, 11, 12, 14, 16, 18, 20, 24, 36, and 48 hours.

505 B2 Route

The study will be multiple dosing, 1, 2, 3, 4, 6, 7, 8, 8.5, 9, 9.5, 10, 10.5, 11, 12, 14, 16, 18, 20, 24, 36, and 48 hours.

Gender/Chronic Pharmacokineticstudies

The PK parameters will be Cmax and AUC in single dose study.

4.       Since the A01 is given in the morning for better bioavailability, the MRA01 should be tested under both morning and evening dosing.

5.       The renal study with MRA01 will be done in a 3 way parallel studies with 10 subjects in each study arm. The will be measured by the presence of specific metabolites.

The expected outcome will be: Comparable overall bioavailability of the compound from both products at the steady state.

Comparative clinical trials are needed to support efficacy.

For additional information, please visit our website at www.biopharmaservices.ca.

*For the primary author, contact Juan He at juanhe@biopharmaservices.ca.