GENERAL DOCUMENTATION

1.1 Identification Code of the Study

Study Number: AZBE052212

Protocol Version: 2.0; Dated: 29-FEB-2024

1.2 Title

An open label, balanced, randomized, two treatments, two sequences, two periods, crossover, single dose, oral bioequivalence study of Etoricoxib 120 mg film coated tablets of Mega labs S.A. and ARCOXIA® (Etoricoxib) 120 mg film coated tablets of MSD in healthy, adult, human subjects under fasting condition.

1.3 Name of Main Researchers

1. **Dr. M. Gowtham., M.B.B.S.,** Principal Investigator
2. **Dr. S. Sathish Kumar., M.B.B.S.,** Sub-Investigator
3. **Dr. N. Sivaranjani., M.B.B.S.,** Sub-Investigator
4. **Mr. T. Nageswara Rao, Ph.D.,** Bioanalytical Investigator
5. **Mr. M. Vishnupravin., M.Sc.,** Statistician

1.4 Name and Address of the Bioequivalence Center Responsible for the Project

Azidus Laboratories Limited,
23, School Road,
Rathinamangalam,
Vandalur, Chennai - 600127,
Tamil Nadu, India.
Phone # 91-44-27405244

1.5 Report Date

18-JUL-2024

1.6 Summary

1.6.1 Title:

An open label, balanced, randomized, two treatments, two sequences, two periods, crossover, single dose, oral bioequivalence study of Etoricoxib 120 mg film coated tablets of Mega labs S.A. and ARCOXIA® (Etoricoxib) 120 mg film coated tablets of MSD in healthy, adult, human subjects under fasting condition.

1.6.2 Sponsor

Mega Labs S.A.

Ruta 101, Km. 23.500, Parque de las Ciencias,

14000 Canelones,

Uruguay.

1.6.3 Objective

To assess the bioequivalence between the test (T) and comparator (R) formulations.

1.6.4 Design

An open label, balanced, randomized, two treatments, two sequences, two periods, crossover, single dose, oral bioequivalence study.

1.6.5 Subjects

A total of 28 healthy, adult, human, male subjects were enrolled, and 26 subjects completed both the periods of the study. Pharmacokinetic blood samples collected from 27 subjects who were exposed to at least one of the study treatments were subjected to analysis. The plasma samples were analyzed for estimation of Etoricoxib concentrations using a validated bio-analytical method involving a LC-MS/MS.

1.6.6 Drug Products

1.6.6.1 Test

Brand Name	:	Davintex 120
Generic Name	:	Etoricoxib 120 mg film coated tablets
Dose Per Unit	:	120 mg
Dosage Form	:	Film coated tablets
Batch Number	:	M09023
Date of Manufacture	:	NOV - 2023
Date of Expiry	:	NOV - 2026
Name of Manufacturer	:	Mega Labs S.A., Uruguay

1.6.6.2 Comparator

Brand Name	:	ARCOXIA®
Generic Name	:	Etoricoxib 120 mg film coated tablets
Dose Per Unit	:	120 mg
Dosage Form	:	Film coated tablets
Batch Number	:	W030763
Date of Manufacture	:	JUN-2022
Date of Expiry	:	JUN-2025
Name of Manufacturer	:	ROVI Pharmaceutical Service, S.A To: Merck sharp & Dohme DE ESPANA S.A,

1.6.7 Results

Summary statistics of log transformed pharmacokinetic parameters of C_{max} and AUC_{0-72} of Etoricoxib was calculated considering pharmacokinetic data obtained from 25 subjects, excluding the data of one S22, as the subject exhibited pre-dose concentrations more than 5% of Cmax. This exclusion of data was based on the pre-defined protocol criterion which states 'If the pre-dose concentration is more than 5% of Cmax of the respective period in a subject, the subject will be excluded from the statistical analysis'.

Table 1: Statistical Results of Test Product-T versus Comparator Product-R for Etoricoxib (N=25)

Product/Statistics	Ln (C_{max})	Ln (AUC_{0-72})
Ratio		
Point Estimate (%)	107.02	94.48
90% confidence interval		
Lower limit: (%)	96.67	90.50
Upper limit: (%)	118.48	98.63
Intra-subject CV (%)	21.06	8.82
Strength of the test	0.9738	1.0000

1.6.8 Discussion and Conclusion

Discussion:

A total of 28 subjects in the age group of 22 to 44 years, who met the study eligibility criteria, participated in the study and 26 subjects completed both the periods of the study.

Two subjects - S08 and S11 were withdrawn from the study for the following reasons:

S08 was withdrawn from the study due to medical event (elevated blood pressure) prior to dosing of period I on 11-JUN-2024 at 07.49 AM.

S11 did not report to the facility due to personal reasons for check-in of period II. Hence, was withdrawn from the study on 20-JUN-2024 at 09.00 PM.

The clinical phase of the study was conducted over a period of 15 days. Blood sampling was done at pre-defined intervals up to 72.00 hours in both the study periods, separated by a washout period of 10 days between subsequent treatments.

Pharmacokinetic blood samples collected from 27 subjects who were exposed to at least one of the study treatments were subjected to analysis. The plasma samples were analyzed for estimation of Etoricoxib concentrations using a validated bio-analytical method involving a LC-MS/MS.

The pharmacokinetic analysis of Etoricoxib was performed using the concentration data obtained from 26 study completers.

Statistical analysis of Etoricoxib was performed using the pharmacokinetic data obtained from 25 subjects, excluding data of one subject - S22 as the subject exhibited pre-dose

concentration more than 5% of Cmax in the respective study period. This exclusion of data was based on the pre-defined protocol criterion.

The primary and secondary pharmacokinetic parameters were estimated for both the Test and comparator treatment.

The 90% confidence interval of C_{max} and AUC_{0-72} was **96.67% - 118.48% and 90.50% - 98.63%** respectively, which were within the acceptable limits of 80.00% to 125.00%. Thus, establishing bioequivalence between the test and comparator drug products.

Conclusion:

Bioequivalence was demonstrated between Etoricoxib 120 mg film coated tablets of Mega labs S.A. and ARCOXIA® (Etoricoxib) 120 mg film coated tablets of MSD in healthy, adult, human subjects under fasting condition.