Comparative Pharmacokinetic Profiles of a Novel Low-Dose Micronized-Isotretinoin 32-mg Formulaulation and Lidose-Isotretinoin 40 mg in Fed and Fasted Conditions: 2 Open-label, Randomized Cross-studies in Healthy Adult Participants

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SYNOPSIS
- Lipotrexat 40 mg, unlike traditional isotretinoin, does not require administration with a high-fat, high-calorie meal to optimize bioavailability and efficacy because it is administered in a lipid matrix.
- A novel low-dose isotretinoin 32-mg formulation has been developed to optimize an advanced manufacturing technology that substantially increases the surface area per unit mass of the drug in formulation.

OBJECTIVES
- To evaluate the bioavailability of Micronized-isotretinoin 32 mg compared with Lidose-isotretinoin 40 mg in healthy adult participants.
- To assess the effect of food on the bioavailability of Micronized-isotretinoin 32 mg in healthy adult participants.

METHODS
- This analysis includes data from 2 open-label, randomized crossover studies in healthy volunteers: the fed bioequivalence and food-effect study and the fasting study.
- Eligible participants were healthy male (both studies) and women (fed-effect study) between 18 and 50 kg/m². Participants were required to be a non-smoker and have not used any medications in the 14 days prior to the screening visit. Male participants were required to use a reliable form of contraception throughout the study.
- The interval between dosing was 21 days in both studies.

RESULTS
- Fed bioequivalence and food-effect study
  - Relative bioavailability of Micronized-isotretinoin 32 mg compared with Lidose-isotretinoin 40 mg in the fed state on the bioavailability of Micronized-isotretinoin 32 mg.
  - Fasting study
  - Relative bioavailability of Micronized-isotretinoin 32 mg compared with Lidose-isotretinoin 40 mg in the fasting state.
- In both studies, safety was determined by the evaluation of adverse events (AEs).

Statistical Analysis
- For all treatments, bioavailability was measured using baseline-adjusted log-transformed mean isotretinoin plasma concentration (Cmax) and baseline-adjusted log-transformed mean area under the plasma concentration-time curve from 0 to 24 h (AUC0–24). Bioequivalence was determined if the 90% confidence intervals (CI) on the log-transformed mean ratio (100%–125%) for the log-transformed Cmax and AUC0–24 were within the 80.0%–125.0% range.

Endpoints
- Fed bioequivalence and food-effect study
  - Relative bioavailability of Micronized-isotretinoin 32 mg compared with Lidose-isotretinoin 40 mg in the fed state.
  - Fasting study
  - Relative bioavailability of Micronized-isotretinoin 32 mg compared with Lidose-isotretinoin 40 mg in the fasting state.

CONCLUSIONS
- Micronized 32 mg is bioequivalent to Lidose-isotretinoin 40 mg under fed conditions and is twice as bioavailable as isotretinoin 40 mg under fasted conditions.
- Food effects on the bioavailability of Micronized-isotretinoin 32 mg were minimal as it is administered in a lipid matrix.
- No serious AEs were reported in either study.

REFERENCES

DISCLOSURES
- BM and MM are employees of Sun Pharmaceutical Industries Ltd. JB is an employee of Sun Pharmaceutical Industries Ltd.