# Clinical Study Synopsis for Public Disclosure

This clinical study synopsis is provided in line with **Boehringer Ingelheim's *Policy on Transparency and Publication of Clinical Study Data***.

The synopsis - which is part of the clinical study report - had been prepared in accordance with best practice and applicable legal and regulatory requirements at the time of study completion.

The synopsis may include approved and non-approved uses, doses, formulations, treatment regimens and/or age groups; it has not necessarily been submitted to regulatory authorities.

A synopsis is not intended to provide a comprehensive analysis of all data currently available regarding a particular drug. More current information regarding a drug is available in the approved labeling information which may vary from country to country.

Additional information on this study and the drug concerned may be provided upon request based on **Boehringer Ingelheim's *Policy on Transparency and Publication of Clinical Study Data***.

# 2. SYNOPSIS

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| **Name of company:** Boehringer Ingelheim | | **Tabulated Study Report** | | **(For National Authority Use only)** |
| **Name of finished product:** Lendormin® D tablets | | | | |
| **Name of active ingredient:** Brotizolam (WE 941) | | **Page:** | **Number:** | |
| **Ref. to Documentation:** | **Volume:** | **Page:** to | | **Addendum No.:** |
| **Report date:** 28 November 2002 | **Number:** U03-3269 | **Study period (years):** 9 August 2000 to 13 September 2000 | | |

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| **Title of study:** | The bioequivalence between WE 941 OD tablets (0.25mg as the basis) and brotizolam conventional tablets (Lendormin® tablets, 0.25mg as the basis), both taken with water as a single administration in healthy adult male subjects (open-labelled, 2-way cross-over study) | |
| **Investigator:** | [redacted] | |
| **Study centre:** | [redacted] Japan | |
| **Publication (reference):** | Not yet published | |
| **Clinical phase:** | I | |
| **Objectives:** | The bioequivalence of WE 941 OD tablets prepared in oral disintegrating tablet form and brotizolam conventional tablets (Lendormin® Tablets), both taken with water, was evaluated in healthy adult male subjects | |
| **Methodology:** | Cross-over comparison of two treatment, open-labelled ,PK-measurement | |
| **No. of subjects entered:** | | |
| **total:** | 30 (15 subjects repeated the study and are counted twice) | |
| **each treatment:** | WE 941 OD tablet p.o. - 15; brotizolam conventional tablet p.o. - 15 | |
| **Diagnosis and main criteria for inclusion:** | Healthy male volunteers, age 20 - 35 years, body weight 50 - 80 kg, BMI: ± 20 % | |
| **Test product:** | WE 941 OD tablet | Brotizolam conventional tablet(Lendormin® Tablet) |
| **dose:** | 0.25 mg as the basis | 0.25 mg as the basis |
| **mode of admin.:** | per os | per os |
| **batch no.:** | 00048 | 00046 |
| **Duration of treatment:** | Single dose | |
| **Reference therapy:** | None | |
| **dose:** | Not applicable | |
| **mode of admin.:** | Not applicable | |
| **batch no.:** | Not applicable | |

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|---|---|---|---|
| **Name of company:** Boehringer Ingelheim | | **Tabulated Study Report** | **(For National Authority Use only)** |
| **Name of finished product:** Lendormin® D tablets | | **SUPPLEMENTARY SHEET** | |
| **Name of active ingredient:** Brotizolam (WE 941) | | **Page:** **Number:** | |
| **Ref. to Documentation:** | **Volume:** | **Page:** to | **Addendum No.:** |
| **Report date:** 28 November 2002 | **Number:** U03-3269 | **Study period (years):** 9 August 2000 to 13 September 2000 | |

**Criteria for evaluation:**

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| **Efficacy:** | Not applicable |
| **Pharmacokinetics:** | Bioequivalence |
| **Safety:** | Adverse events, vital signs, laboratory tests |

**Statistical methods:** Based on calculated values of $AUC_{0\text{-}24\,h}$ and $C_{max}$, the bioequivalence between WE 941 OD tablets and brotizolam conventional tablets (Lendormin® Tablets) was evaluated using 90% confidential intervals.
Safety was analysed using descriptive statistics.

**SUMMARY - CONCLUSIONS:**

Efficacy results: Not applicable (In this pharmacokinetic study, there were no measures of efficacy.)

Pharmacokinetic results:
For brotizolam conventional tablets and WE 941 OD tablets, $C_{max}$ was calculated to be 3.30 ± 0.91 ng/mL and 3.35 ± 1.05 ng/mL, respectively; $AUC_{0\text{-}24\,h}$ 27.02 ± 8.13 ng hr/mL and 27.23 ±8.70 ng hr/mL, respectively; $t_{max}$ 1.1 ± 0.7 hours and 1.0 ± 0.6 hours, respectively; and $MRT_{0\text{-}24\,h}$ values 7.2 ± 1.0 hours and 7.2 ± 0.9 hours, respectively.
For $C_{max}$, the ratio of geometric mean for WE 941 OD tablets to that of brotizolam conventional tablets was 100.9%, and the 90% confidence interval for the difference of mean log-transformed values was 92.7 to 109.6%; for $AUC_{0\text{-}24\,h}$, the corresponding values were 100.1% and 94.6 to 105.8%, respectively.

Safety results:
All adverse events were assessed as being causally unrelated to the trial drug. The same applied to the adverse events observed in the post-administration observations conducted following administration period II.

Conclusions:
The 90% confidence intervals for the difference between the two drugs in respective log transformed values of $C_{max}$ and $AUC_{0\text{-}24\,h}$ were within the range of 80 to 125%. The drugs were thus assessed as bioequivalent each other.