

SANOFI-SYNTHELABO

SL80.0750-23 (Zolpidem)

**Relative bioavailability study comparing a new tablet formulation (MRbis) of zolpidem and the reference tablet formulation (MR) at 12.5 mg, after single oral administration, in healthy male and female subjects.
Open, randomized, crossover and single center study.**

BDR5478

First subject enrolled: **29 September 2003**

Study completion date: **04 December 2003**

Phase: **I**

Design: **Single center, open-label, randomized 2-treatment (A and B), 2-period (1 and 2), 2-sequence crossover study.**

Principal Investigator or person in charge of the study and affiliation:

**Gérard PAUX, MD
CéMAX
3, rue Dufay
76100 Rouen - France**

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This study was performed in compliance with Good Clinical Practices, including the archiving of essential documents. This report has been prepared in accordance with the ICH Harmonized Tripartite Guideline on the Structure and Content of Clinical Study Reports, dated July 1996, using SOP WDSR-CL00115-EN-E03.

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11.4 Pharmacokinetic results

11.4.1 Analysis of pharmacokinetics

11.4.1.1 Plasma concentrations

All predose plasma samples received and analyzed were below the limit of quantification (LOQ). The number of subjects with zolpidem plasma concentrations above the LOQ in the 10-16 hour postdose interval is presented in Table (15.2) 1.

Individual and mean zolpidem plasma concentrations, as well as the sampling times, are listed in Appendices 16.2.5.2.2 and 16.2.5.4.1. Individual zolpidem plasma concentrations versus time profiles are presented in Appendix 16.2.5.2.3 and by treatment in Figure (15.2) 1. Subject No. 44 experienced vomiting 1.33 hours after study drug intake in Period 1 Day 1. This subject was thus excluded from the pharmacokinetic analysis for Period 1. The zolpidem plasma concentrations observed for this subject in Period 1 are listed in Appendix 16.2.5.2.2.

Plots of the mean (SD) zolpidem plasma concentrations for each treatment group are shown in Figure (11.4.1.1) 1.

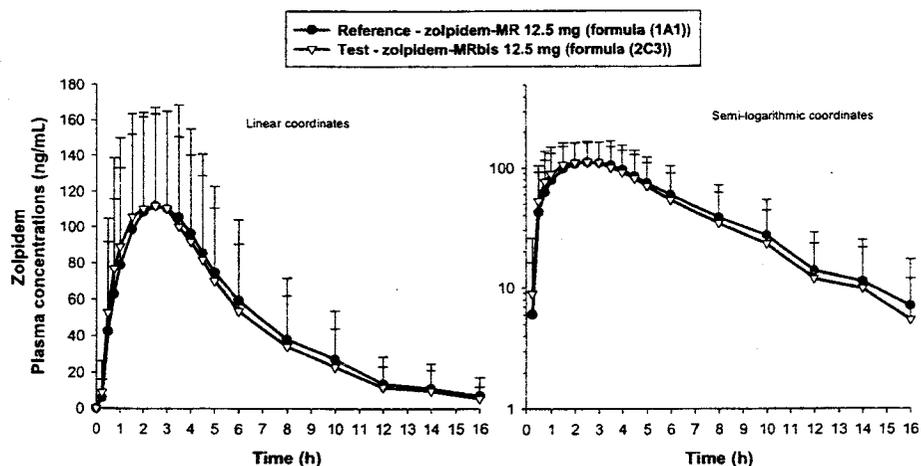


Figure (11.4.1.1) 1 - Mean (SD) zolpidem plasma concentrations vs. time profile after a 12.5 mg single dose of zolpidem-MR (reference) or zolpidem-MRbis (test)

11.4.1.2 Pharmacokinetic parameters

The mean (SD) zolpidem pharmacokinetic parameters are presented in Table (11.4.1.2) 1. Individual and mean parameters are listed in Appendices 16.2.5.3 and 16.2.5.4.1, respectively and summarized by treatment in Table (15.2) 2 and Table (15.2) 3. The descriptive statistics by gender are provided in Appendix 16.2.5.4.1 and Table (15.2) 4. The descriptive statistics for the secondary parameters, MRT and HVD, are provided in Appendix 16.2.5.4.1.

Results of the statistical analysis are presented in Appendix 16.2.5.4.2 and summarized in Table (15.2) 5.

Table (11.4.1.2) 1 - Mean (SD) zolpidem PK parameters for each treatment group

Zolpidem Parameters		12.5 mg Zolpidem-MRbis (Test)	12.5 mg Zolpidem-MR (Reference)
N		71	72
C _{max} (ng/mL)	Mean (SD)	136 (58.6)	136 (63.3)
	CV%	43.0	46.5
	Geometric mean	122	121
t _{max} (h)	Median [range]	2.00 [0.50 – 5.00]	2.29 [0.50 – 8.00]
t _{lag} (h)	Median [range]	0.00 [0.00-0.75]	0.00 [0.00-1.00]
AUC _{last} (ng.h/mL)	Mean (SD)	721 (403)	749 (445)
	CV%	55.9	59.4
	Geometric mean	599	615
AUC (ng.h/mL)	Mean (SD)	748 (434)	787 (501)
	CV%	58.0	63.7
	Geometric mean	615	636
t _{1/2z} (h)	Mean (SD)	2.67 (0.76)	2.70 (0.86)
	CV%	28.5	31.9

Ref.: Appendix 16.2.5.4.1