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***.

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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.

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2. SYNOPSIS

Name of company: Boehringer Ingelheim		**Tabulated Study Report**		**(For National Authority Use only)**
Name of finished product: Tipranavir				
Name of active ingredient: Tipranavir		**Page:**	**Number:**	
Ref. to Documentation:	**Volume:**	**Page:** xxx **to** xxxx		**Addendum No.:** N/A
Report date: 18 October 2001	**Number:** U01-3295	**Study period (years):** 2 October 2000 to 23 December 2000		

Title of study:	An Open-label, Parallel Group, Multiple-dose Investigation of the Pharmacokinetics of Tipranavir Soft Elastic Capsules SEDDS and Ritonavir Soft Gel Capsules and Their Effects on Cytochrome P-450 (3A4) Activity in Normal Healthy Volunteers
Investigator:	[redacted]
Study center(s):	[redacted]
Publication (reference):	N/A
Clinical phase:	I
Objectives:	The objective of this study was to establish the tipranavir-ritonavir steady-state dose-exposure relationships when administered on a twice a day (bid) dosing regimen; to determine the effects of tipranavir (TPV) and ritonavir (RTV) on cytochrome P-450 (CYP3A4) activity; to establish the dependency of the TPV M1 metabolite on RTV co-administration. Additionally, the short-term safety and tolerance of this drug combination was evaluated.
Methodology:	Open-label, parallel group, multiple-dose, treatment design
No. of subjects entered: **total:** **each treatment:**	113 subjects entered 95 subjects completed 12 per arm
Diagnosis and main criteria for inclusion:	Male or female of any race, in good health and between the ages of 18 and 75 years, inclusive. Negative HIV, Hepatitis B and Hepatitis C serology
Test product: **dose:** **mode of admin.:** **batch no.:** **Test product:** **dose:** **mode of admin.:**	Tipranavir Soft Elastic Capsules SEDDS formulation (250 mg) 250, 500, 750, 1000 and 1250 mg bid Oral PD-2005 Ritonavir Soft Gel Capsules, NORVIR® (100 mg) 100, 200 mg bid Oral
Duration of treatment:	32 consecutive days
Reference therapy:	Not applicable

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Name of company: Boehringer Ingelheim		**Tabulated Study Report**		**(For National Authority Use only)**
Name of finished product: Tipranavir		**SUPPLEMENTARY SHEET**		
Name of active ingredient: Tipranavir		**Page:**	**Number:**	
Ref. to Documentation:	**Volume:**	**Page:** xxx **to** xxxx		**Addendum No.:**
Report date: 18 October 2001	**Number:** U01-3295	**Study period (years):** 02 October 2000 to 23 December 2000		

Criteria for evaluation:	Safety: Adverse events and laboratory assessments
Statistical methods:	Regression analysis of steady state pharmacokinetic parameters and descriptive statistical analyses of safety parameters.

SUMMARY - CONCLUSIONS:

Efficacy results: N/A

Safety results: Of 113 subjects 109 (96.5%) experienced at least one adverse event. Ninety-six percent of adverse events were of mild intensity and 5% of moderate intensity. No serious adverse events were reported.

Adverse events occurring with >5% in individual subjects included gastrointestinal adverse (GI) events (91%), headache (30%), and dizziness (17%). GI adverse events were reported as diarrhea (75%), nausea (53%), vomiting (41%), abdominal pain (20%) and anorexia (9%).

Prothrombin Time (PT) prolongation and elevations in Gamma Glutamyl Transferase (GGT) occurred in <15% subjects and was clinically not significant.

No dose-limiting toxicity occurred and the adverse events were associated with minimal risk.

Conclusions: Median plasma TPV T_{max} and steady state mean plasma TPV C_{min}, C_{max}, Area Under the Curve (AUC) and TPV clearance were determined. Mean TPV C_{min} plasma levels consistent with that reported for anti-viral activity was seen at all TPV dose levels and RTV co-administered doses (100 mg and 200 mg). TPV half-lives ranged from 3.6 hours-3.9 hours for 100 mg RTV subjects and 4.5-5.2 hours for the 200 mg subjects.

Measurements of the TPV M1 metabolite and results of the erythromycin breath test (ERMBT) demonstrated increased, stable TPV plasma levels with co-administration of 100 mg or 200 mg RTV at all TPV doses used in this trial.

Sustained TPV plasma levels of reported therapeutic efficacy could be achieved with co-administered RTV (100 mg/200 mg). The TPV/RTV dosage combinations tested demonstrated acceptable safety and toxicity results.