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***.

Name of company: Boehringer Ingelheim		**Tabulated Study Report**		
Name of finished product: APTIVUS®				
Name of active ingredient: Tipranavir		**Page:**	**Number:**	
Ref. to Documentation:	**Volume:**	**Page:**		**Addendum No.:**
Report date: 10 November 2006	**Number:** U06-2081	**Study period (dates):** 16 Nov 05 - 1 Feb 06		

Title of study:	A single-centre, open-label study in healthy adult volunteers to determine the effects of multiple-dose omeprazole (ANTRA® 40 mg qd) on the single-dose pharmacokinetics of tipranavir 500 mg coadministered with ritonavir 200 mg
Investigator:	[redacted]
Study center:	[redacted] Italy
Publication (reference):	
Clinical phase:	I
Objectives:	To determine the effects of multiple-dose omeprazole on the single-dose pharmacokinetics of tipranavir and ritonavir
Methodology:	Open-label, single group TPV/RTV, pharmacokinetic study
No. of subjects:	15 healthy adult
planned:	enrolled: 20
	entered: 15
actual:	enrolled: 17
	entered: 15
	Treatment A: TPV + RTV + Omeprazole entered: 15 treated: 15 analysed (for primary endpoint):15
Diagnosis and main criteria for inclusion:	Healthy male and female volunteers
Test product:	TPV (APTIVUS®), 250 mg, Soft Elastic Capsules (SECs), Self-Emulsifying Drug Delivery System (SEDDS) formulation
dose:	TPV 500 mg qd
mode of admin.:	Oral
batch no.:	PD-2652
Duration of treatment:	2 days

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Test product:	RTV (NORVIR-SEC®) Soft Elastic Capsules (100mg)
dose:	RTV 200 mg qd
mode of admin.:	Oral
batch no.:	28246VA
Duration of treatment:	2 days
Test product:	Omeprazole capsule (ANTRA®) (20 mg)
dose:	40 mg qd
mode of admin.:	Oral
batch no.:	GB5969
Duration of treatment:	7 days
Reference therapy:	None
Criteria for evaluation:	
Efficacy:	There were no efficacy endpoint in this study.
Parmacokinetics:	Primary endpoints: • Tipranavir $AUC_{0\text{-}72h}$, and Cmax Secondary endpoints: • Ritonavir $AUC_{0\text{-}72h}$,and Cmax • Tipranavir and ritonavir $AUC_{0\text{-}\infty}$ MRT, $t_{1/2}$,Tmax, CL/F, Vz/F
Safety:	Subject safety was monitored by assessment of treatment related adverse events at each visit, in addition to laboratory assessment of safety parametry including hematology, chemistry, liver function tests (AST, ALT, alkaline phosphatase, total bilirubin), lipid parameters (triglycerides, cholesterol) at screening and at the final visit.
Statistical methods:	Analysis were based on within subject treatment comparisons. $AUC_{0\text{-}72h}$ and Cmax were estimated from the drug plasma concentrations using the software program WinNonlin®. Cmax was the largest observed concentration and AUC was computed according to the linear trapezoidal rule.
SUMMARY – CONCLUSIONS:	
Efficacy results:	Not applicable

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Pharmacokinetics results:	Tipranavir geometric mean AUC and Cmax were unchanged (increased less than 5%) in the presence of omeprazole. TPV Tmax and $t_{1/2}$ were not affected either. Conversely, ritonavir geometric mean AUC and Cmax decreased approximately 20% in the presence of omeprazole without a change in Tmax or $t_{1/2}$.
Safety results:	AEs were primarily associated with TPV/r treatment (none were reported on OMP alone), with headache affecting 33% of subjects, with other events (nausea, diarrhoea, abdominal pain and fever) affecting fewer subjects. None were serious or severe. Most events were considered drug related. There were no changes in vital signs, and no clinically important findings in laboratory results.
Conclusions:	The bioavailability of single-dose tipranavir 500 mg coadministered with ritonavir 200 mg was not affected by omeprazole 40 mg administered once-daily for 7 days.