

bound) differences in CYP1B from placebo after baseline concentration were 10.7 (15.1) and 23.3 (28.4) milligrams, respectively. Baseline steady-state rifampin 75 mg once daily and 200 mg once daily resulted in mean steady-state C₁₂ exposures that were 15% and 30% above the mean C₁₂ observed with the recommended 25 mg once daily dose of rifampine (see Warnings and Precautions (5.6)).

12.3 Pharmacokinetics

Pharmacokinetics in Adults

The pharmacokinetic properties of rifampine have been evaluated in adult healthy subjects and in adult antiretroviral treatment-naïve HIV-1-infected subjects. Rifampine was generally lower in HIV-1-infected subjects than in healthy subjects.

Table 1: Pharmacokinetic Estimates of Rifampine 25 mg Once Daily in Antiretroviral Treatment-Naïve HIV-1-Infected Adult Subjects (Pooled Data from Two Phase 3 Trials)

Parameter	Rifampine 25 mg once daily N=979
AUC ₀₋₂₄ (ng·h/mL)	2,255(61)
Mean(Standard Deviation)	2,098 (198 to 2,307)
C ₁₂ (mg/mL)	79(35)
Mean(Standard Deviation)	73 (2 to 288)
Absorption and Bioavailability	
After oral administration, the maximum plasma concentration of rifampine is generally achieved within 4 to 5 hours. The absolute bioavailability of rifampine is unknown.	
Effects of Food on Absorption	
Rifampine is approximately 89% lower when rifampine was taken in a fasted condition as compared to a normal caloric meal (533 kcal) or high-fat caloric meal (828 kcal). When rifampine was taken with only a protein-rich normal caloric meal, exposures were 95% lower than when taken with a meal.	
Distribution	
Rifampine is approximately 99.7% bound to plasma proteins in vitro, primarily to albumin. The distribution of rifampine into compartments other than plasma (e.g., cerebrospinal fluid, genital secretions) has not been evaluated in humans.	
Metabolism	
Metabolism	
Metabolism	

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Metabolism

Table 12: Drug Interactions: Pharmacokinetic Parameters for Coadministered Drugs in the Presence of Rifampine

Coadministered Drug	Coadministered Drug	Pharmacokinetic Parameters
Danavone/rifampine	800/100 mg q.d.	150 mg q.d. ^a
Lopinavir/rifampine	400/100 mg b.i.d. (soft gel capsules)	150 mg q.d. ^a
Tenofovir disoproxil fumarate	300 mg q.d.	150 mg q.d. ^a
Cabotegravir	30 mg q.d.	25 mg q.d. ^a
Raltegravir	400 mg b.i.d.	25 mg q.d. ^a
Simeprevir	150 mg q.d.	25 mg q.d. ^a
Acetaminophen	500 mg single dose	150 mg q.d. ^a
Atazanavir	40 mg q.d.	150 mg q.d. ^a
2-ethoxy-2-phenylpropanoic acid	150 mg q.d.	150 mg q.d. ^a
4-hydroxy-2-ethoxy-2-phenylpropanoic acid	150 mg q.d.	150 mg q.d. ^a
Chlorzoxazone	500 mg single dose taken 2 hours after rifampine	150 mg q.d. ^a
Diphenhydramine	0.5 mg single dose	25 mg q.d. ^a
Ethinylloestradiol	0.05 mg q.d.	25 mg q.d. ^a
Norethindrone	1 mg q.d.	25 mg q.d. ^a
Ketconazole	400 mg q.d.	150 mg q.d. ^a
R(-)-methadone	50 to 100 mg q.d., individualized dose	25 mg q.d. ^a
S(-)-methadone	50 to 100 mg q.d., individualized dose	25 mg q.d. ^a
Mefenamic acid	500 mg single dose	25 mg q.d. ^a
Omeprazole	20 mg q.d.	150 mg q.d. ^a
Rifampin	600 mg q.d.	150 mg q.d. ^a
25-deoxythymine	150 mg q.d.	150 mg q.d. ^a
Sildenafil	50 mg single dose	75 mg q.d. ^a
N-methyl-D-erythritol	150 mg q.d.	150 mg q.d. ^a

Coadministered With HIV Nucleoside or Nucleotide Reverse Transcriptase Inhibitors (NRTI/NRTIs)

Coadministered With HIV Integrase Strand Transfer Inhibitors

Coadministered With Other Antivirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

Coadministered With Drugs other than Antiretrovirals

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively

respectively