

Impact of Food/Meal on Antiretroviral Drug Absorption

Drug	Dose	Type of Meal	AUC	CV	Cmax	CV	Recommendation	Reference
PROTEASE INHIBITORS								
Atazanavir	400 mg	Light meal (357 kCal, 8.2 g fat, 10.6 g protein)	↑ 70%	~ ↓ 50%	↑ 57%	~ ↓ 50%	Administration of REYATAZ with food enhances bioavailability and reduces pharmacokinetic variability. REYATAZ capsules must be taken with food.	US Product Monograph, March 2007
	“	High fat meal (721 kcal, 37.3 g fat, 29.4 g protein)	↑ 35%	~ ↓ 50%	N/c	~ ↓ 50%		
	300/100 mg	High Fat (721 kCal, 37.3 g fat, 29.4 g protein)	↑ 35%	~ ↓ 50%	N/c	~ ↓ 50%	ATV C24 ↓ 53% fasting vs. fed. RTV AUC ↓ 26%, Cmax ↑ 4%, C24 ↓ 53%. Take with food. Atazanavir AUC with ritonavir is increased with a light meal, and C24 is ↑ with both a light or high fat meal, with lower variability under both fed conditions relative to fasting. Take with food.	US Product Monograph, March 2007 Giguere et al. 11 th IWCPHT 2010, #30.
	300/100 mg (15 day study in HIV-infected subjects)	Standardized meal (440 kCal, 10 g fat, 24 g protein) vs. fasting	↓ 41%		↓ 32%			
	300/100 mg	fasting	-	45%	-	49%		
“	High fat (951 kcal, 52% fat)	No change	35%	↓ 11%	35%	Cmin ↑ 40% vs. fasting Cmin ↑ 33% vs. fasting.	Child et al. 8 th IWCPHT 2007, #25.	
“	Light meal (336 kcal, 14% fat)	↑ 33%	37%	↑ 40%	37%			
Darunavir	600/100 mg BID	Exposure to darunavir unaffected by type of meal (standard, high-fat, nutritional protein rich drink, or croissant with coffee).	↑ 35%				Darunavir tablets, co-administered with ritonavir, should be taken with food, which could be a light snack.	Sekar et al. J Clin Pharmacol 2007;47:479-84.
	800/150 mg cobicistat QD (fixed-dose combination tablet)	High fat breakfast (1160 kcal, 70.3g fat)	↑ 63%		↑ 127%		Take darunavir/cobicistat fixed-dose combination tablet with food.	Kakuda et al. 14 th IWCPHT 2013, #P_10.
Fosamprenavir tablets	1400 mg	high-fat meal: 967kcal, 67g fat, 33g protein, 58g carbohydrate)	N/c		N/c		TELZIR™ tablets may be taken with or without food.	Canadian Product Monograph, December 2004.
Fosamprenavir calcium oral		high fat meal	↓ 25%		↓ 40%		The TELZIR™ oral suspension should be taken without food and on an	Canadian Product Monograph, December

Drug	Dose	Type of Meal	AUC	CV	Cmax	CV	Recommendation	Reference
suspension							empty stomach at the same dose as the tablets.	2004.
Lopinavir capsules	400/100 mg	Moderate fat meal (500-682 kcal, 23 to 25% calories from fat)	↑ 48%		↑ 23%		To enhance bioavailability and minimize pharmacokinetic variability KALETRA should be taken with food.	US Product Monograph, April 2005.
"	"	high fat meal (872 kcal, 56% from fat)	↑ 97%		↑ 43%			"
Lopinavir oral solution	400/100 mg	Moderate fat meal (500-682 kcal, 23 to 25% calories from fat)	↑ 80%		↑ 54%		To enhance bioavailability and minimize pharmacokinetic variability KALETRA oral solution should be taken with food.	"
"	"	high fat meal (872 kcal, 56% from fat)	↑ 130%		↑ 56%			"
Lopinavir tablets	400/100 mg	moderate fat meal (500 – 682 Kcal, 23 to 25% calories from fat)	↑ 26.9%	↓	↑ 17.6%	↓	Kaletra tablets may be taken with or without food.	US Product monograph, October 2005
"	"	high fat meal (872 Kcal, 56% from fat)	↑ 18.9%		N/c			"
Nelfinavir 250 mg tablets	1250 mg	125 Kcal, 20% calories from fat	2.2-fold ↑		2.0-fold ↑		VIRACEPT should be taken with a meal.	US Product Monograph, April 2004.
"	"	500 Kcal, 20% calories from fat 1000 Kcal, 50% calories from fat	3.1-fold ↑ 5.2-fold ↑		2.3-fold ↑ 3.3-fold ↑			"
Nelfinavir 625 mg tablets	1250 mg	Standard breakfast: 820 kcal (protein 110 kcal, fat 400 kcal, carbohydrates 310 kcal)	↑ 509%	15% ↓ (66.1 → 56.1%)	↑ 431%	44% ↓ (64.5 → 36.1%)	Decreased variability when administered with food.	Kaaser et al. Int J Clin Pharmacol Ther 2005;43:154-62.
		Standard breakfast: 820 kcal (protein 110 kcal, fat 400 kcal, carbohydrates 310 kcal)	↑ 733%	20% ↓ (85.4 → 67.9%)	↑ 413%	38% ↓ (65.5 → 40.6%)	VIRACEPT should be taken with a meal. Decreased variability when administered with food.	"
Ritonavir 100 mg tablets	100 mg single dose	high fat meal (907 kcal; 52% fat, 15% protein, 33% carbohydrates) vs. fasting	23% ↓		23% ↓		The type of meal administered did not change ritonavir tablet bioavailability when high fat was compared to moderate fat meals. Take ritonavir tablets with meals.	US Product Monograph, February 2010.
		moderate fat meal vs fasting	21% ↓		22% ↓			
Saquinavir 200 mg hard gel capsules	600 mg	high-fat breakfast (48 g protein, 60 g carbohydrate, 57 g fat; 1006 kcal).	↑ 571%	N/c (35%)			The effect of food has been shown to persist for up to 2 hours. INVIRASE and ritonavir should be	US Product Monograph December 2004

Drug	Dose	Type of Meal	AUC	CV	Cmax	CV	Recommendation	Reference
		Saquinavir 24-hour AUC and C _{max} (n=6) following the administration of a higher calorie meal (943 kcal, 54 g fat) were on average 2 times higher than after a lower calorie, lower fat meal (355 kcal, 8 g fat).					taken within 2 hours after a meal.	
Saquinavir soft-gel capsules	1200 mg TID	Normal breakfast (600 kcal, 22 g or 33%, 16% protein, 51% carbohydrates)	1.25 mg/L*h		0.49 mg/L		Approximately 2-fold ↑ in saquinavir exposure with high-fat vs. normal meal.	Hugen et al. Pharmacy World Sci 2002;24:83-6.
		High fat breakfast (1040 kcal, 62 g or 54% fat, 15% protein, 31% carbohydrates)	3.8		0.88 mg/L			
Saquinavir soft-gel capsules	1000/100 mg BID	Normal breakfast + 250 mL single-strength grapefruit juice Saquinavir exposure was similar when FORTOVASE plus ritonavir (1000-mg/100-mg bid) were administered following a high-fat (45 g fat) or moderate-fat (20 g fat) breakfast.	5.2				Saquinavir AUC ↑ 5-fold when taken with normal meal plus grapefruit juice compared to normal meal alone.	"
Saquinavir 500 mg tablets	1000/100 mg BID	Breakfast: 1091 kcal, 46 g fat; Dinner: 1080 kcal, 66 g fat	238% ↑		245% ↑		INVIRASE and ritonavir should be taken within 2 hours after a meal. Saquinavir levels were mildly decreased with a standard meal vs. a high fat meal. All patients had C _{trough} > cut off of 100ng/ml. The authors conclude that SQV should be given with food, but the fat content of the meal is not critical.	Boffito et al. 7 th IWCPHT 2006, #66. Boffito et al. 47 th ICAAC 2007, #A-1423.
	"	Standard meal: 651 kcal, 15g fat High fat meal: 1291 kcal, 55g fat	31% ↓		26% ↓			
Tipranavir	500/200 mg BID (old capsule formulation) 500/200 mg BID	High-fat meal (868 kcal, 53% derived from fat, 31% derived from carbohydrates)	31% ↑		16% ↑		APTIVUS capsules co-administered with ritonavir should be taken with food.	US Product monograph, November 2005.
			No change		No change		Tipranavir/ritonavir may be taken with	La Porte et al. 8 th

Drug	Dose	Type of Meal	AUC	CV	Cmax	CV	Recommendation	Reference
	capsules 500/200 mg BID oral solution		23% ↑		14% ↑		or without food. Tipranavir/ritonavir may be taken with or without food.	IWCPHT 2007, #59. La Porte et al. 8 th IWCPHT 2007, #59.
INTEGRASE INHIBITORS								
Dolutegravir	50 mg single dose in healthy subjects	Fasted stated compared to: <ul style="list-style-type: none"> low-fat (300 kcal, 7% fat) moderate fat (600 kcal, 30% fat) high fat (870 kcal, 53% fat) meal 	↑ 33% ↑ 41% ↑ 66%		↑ 46% ↑ 52% ↑ 67%		Dolutegravir may be administered with or without food and without regard to fat content.	Song et al. 12 th IWCPHT 2011, #P12.
	Administered as a fixed dose combination tablet (50 mg dolutegravir, 600 mg abacavir, 300 mg lamivudine) in healthy volunteers	High fat meal compared to fasted.	48% ↑		37% ↑		The fixed-dose combination tablet may be taken with without regard to meals.	Weller et al. JAIDS 2014; 66:393–8.
Elvitegravir	Administered as a fixed dose combination tablet (elvitegravir, emtricitabine, tenofovir, cobicistat) in healthy volunteers	Light meal (373 kcal, 20% fat) compared to fasted. High-fat meal (800 kcal, 50% fat) compared to fasted.	34% ↑ 87% ↑		22% ↑ 56% ↑		Take fixed-dose tablet with food.	German et al. ICAAC 2009, #A1-1300.
	Administered as a fixed dose combination tablet (elvitegravir, emtricitabine, tenofovir, cobicistat) in healthy Japanese volunteers	Fasting vs. standard breakfast (413 kcal, 9.6 g fat) Protein rich nutritional drink (250 mL Ensure, 250 kcal, 8.8 g fat) vs standard breakfast	↓ 50%		↓ 55%		No difference in elvitegravir exposures with standard vs. nutritional shake. Take with food.	Shiomi et al. J Clin Pharmacol 2014;54:640-8.
	Raltegravir	400 mg single dose	standard moderate-fat meal (600 Kcal, 21 g fat) or in the fasted state	13% ↑		5% ↑	Raltegravir C12 hr was 66% higher and Cmax was 5% higher following a moderate-fat meal	Canadian Product Monograph, September 2010.

Drug	Dose	Type of Meal	AUC	CV	Cmax	CV	Recommendation	Reference
							<p>compared to fasting and AUC was not affected in a clinically significant manner.</p> <p>Take raltegravir with or without food.</p>	
	400 mg BID x 10/7 in healthy subjects	<p>Fasting versus:</p> <ul style="list-style-type: none"> Low-fat meal: 2 slices bread, 2 packets jelly, 8 oz skim milk; ~300 kcal, 7% fat (2.5 g) Moderate-fat meal: 4 slices bread, 2 slices American cheese, 2 slices low-fat ham, 8 oz skim milk; ~600 kcal, 31% fat (21 g) High-fat meal: 2 eggs, 2 strips bacon, 4 oz hash browns, 2 slices bread, 2 teaspoons butter, 8 oz whole milk; ~825 kcal, 57% fat (52 g) 	<p>↓ 46%</p> <p>↑ 13%</p> <p>↑ 111%</p>		<p>↓ 52%</p> <p>↑ 5%</p> <p>↑ 96%</p>		<p>Impact on C12 vs fasting: ↓ 14% (low fat), ↑ 66% (moderate fat), ↑ 313% (high fat).</p> <p>In the current study, when raltegravir was given with food, considerable variability was seen, particularly with respect to C12h, which had coefficients of variation of 201%, 123%, and 221% for low-, moderate-, and high-fat meals, respectively, compared with only 47% for the fasted state.</p> <p>In summary, a low-fat meal appearing to modestly decrease absorption with little effect on trough concentrations (C12h), a moderate-fat meal having little to no effect, and a high-fat meal appearing to modestly increase absorption, although none of these effects appear clinically meaningful.</p>	Brainard et al. J Clin Pharmacol 2011;51(3):422-7.
		Administration of the chewable tablet with a high fat meal vs fasting.	6% ↓		62% ↓		<p>Impact on C12 vs fasting: 188% ↑</p> <p>Administration of the chewable tablet with a high fat meal does not affect raltegravir pharmacokinetics to a clinically meaningful degree and the chewable tablet can be administered without regard to food.</p>	US Product Monograph, December 2011.
	Raltegravir 1200 mg QD in healthy subjects	<p>Standard raltegravir tablets (3 x 400 mg)</p> <ul style="list-style-type: none"> With low fat meal vs fasting With high fat meal vs fasting 	<p>↓ 71%</p> <p>↑ 26%</p>		<p>↓ 75%</p> <p>↓ 24%</p>			Krishna et al. EACS 2013, #PE10/17.

Drug	Dose	Type of Meal	AUC	CV	Cmax	CV	Recommendation	Reference
		Reformulated raltegravir tablets (2 x 600 mg): <ul style="list-style-type: none"> With low fat meal vs fasting With high fat meal vs fasting 	↓ 40% ↑ 3%		↓ 52% ↓ 28%			
NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS								
Etravirine	100 mg single dose tablet in healthy subjects	Fasted state compared to a standard breakfast (561 kCal, 15.3 g fat). Light Breakfast - croissant (345 kCal, 17.4 g fat) compared to a standard breakfast. Enhanced Fiber Breakfast (685 kCal, 3.1 g fat) compared to a standard breakfast. High Fat Breakfast (1160 kCal, 70.3 g fat) compared to a standard breakfast.	51% ↓ 20% ↓ 25% ↓ 9% ↑		44% ↓ 3% ↓ 38% ↓ 5% ↓		Give with food. Type of meal not important.	Scholler-Gyure et al. Pharmacotherapy 2008;28(10):1215-22.
Nevirapine	200 mg single dose administered to 24 healthy subjects (12 male, 12 female)	High fat breakfast (857 kcal, 50 g fat, 53% of calories from fat) or antacid (Maalox® 30 mL) compared to fasting.	No change				Nevirapine may be administered with or without food or antacid.	Canadian Product Monograph, July 2009.
Ralpivirine	75 mg tablet single dose in healthy subjects	<ul style="list-style-type: none"> Fasting vs. standard breakfast (21 g fat, 533 kcal). Protein rich nutritional drink (8 g fat, 300 kcal) vs standard breakfast High Fat Breakfast (56 g fat, 928 kcal) compared to standard breakfast 	43% ↓ 50% ↓ 8% ↓		46% ↓ 50% ↓ 8% ↓		Give rilpivirine with food (standard or high fat meal). Do not give rilpivirine on an empty stomach or with a protein rich nutritional drink.	Crauwels et al. 9 th IWCPHT 2008, #P32.
	As part of the single tablet regimen	<ul style="list-style-type: none"> Standard meal (540 kcal, 21 g fat) vs. fasting 	16% ↑		21% ↓		When administered as a single-tablet regimen (Complera®), food has a modest effect on rilpivirine	Custodio et al. J Clin Pharmacol 2014;54:378-85.

Drug	Dose	Type of Meal	AUC	CV	Cmax	CV	Recommendation	Reference
	Complera® (emtricitabine/rilpivirine/tenofovir) in healthy subjects (n=24); 3-period, six-sequence crossover single dose study	<ul style="list-style-type: none"> Light meal (390 kcal, 12 g fat) vs. fasting 	9% ↑				pharmacokinetics, with no relevant differences between a light meal versus a standard meal. Complera® may be administered with a light or standard meal.	Previously presented at: Ramanathan et al. 11 th Congress on Drug Therapy in HIV Infection (Glasgow) 2012, abstract P68.
REVERSE TRANSCRIPTASE INHIBITORS								
Didanosine, enteric-coated (Videx EC®)	Open-label, single dose studies in healthy volunteers.	With a high-fat meal compared to fasted.	19% ↓		46% ↓		VIDEX EC should be taken on an empty stomach, at least 1.5 hours before or 2 hours after a meal.	Damle B et al. J Clin Pharmacol 2002; 42:419-427.
		With a light meal compared to fasted.	27% ↓		22% ↓			
		Videx EC given 1.5 hours before a light meal.	24% ↓		15% ↓			
		Videx EC given 2 hours after a light meal.	10% ↓		15% ↓			
		Videx EC beadlets with yogurt or apple sauce compared to fasting.	20% ↓ 18% ↓		30% ↓ 24% ↓			
		Administration of VIDEX EC capsules 1.5, 2 or 3 hours before a light meal resulted in equivalent C _{max} and AUC values compared to those obtained under fasting conditions.						
	Randomized, open-label study of 28 days ddl monotherapy in HIV-infected, treatment-naïve subjects (n=21).	Didanosine-EC administered 1 hour before or 2 hours after breakfast, vs. administered with a fat-rich breakfast (350 kcal).					Mean ddl trough plasma levels at day 28 were 0.0234 mg/L for patients taking ddl on an empty stomach and 0.0227 mg/L for those taking it after a fat-rich breakfast, showing no statistically significant difference (P=0.96). There was no difference in the rate of decrease of HIV-1 RNA between the two groups.	Hernandez-Novoa et al. HIV Med 2008;9: 187-191.
OTHER								

Drug	Dose	Type of Meal	AUC	CV	Cmax	CV	Recommendation	Reference
Cobicistat	Administered as a fixed dose combination tablet (elvitegravir, emtricitabine, tenofovir, cobicistat) in healthy volunteers	Light meal (373 kcal, 20% fat) compared to fasted. High-fat meal (800 kcal, 50% fat) compared to fasted.	2% ↑ 17% ↓		4% ↑ 24% ↓		Take fixed-dose tablet with food.	German et al. ICAAC 2009, #A1-1300.
HCV PROTEASE INHIBITORS								
Boceprevir	800 mg TID	<ul style="list-style-type: none"> Administered with a meal vs. fasting state No difference between high-fat vs. low-fat 	↑ 60%				<p>The bioavailability of boceprevir was similar regardless of meal type (e.g., high-fat vs. low-fat) or whether taken 5 minutes prior to eating, during a meal, or immediately following completion of the meal.</p> <p>Boceprevir should be taken with a meal or light snack.</p>	Victrelis Product Monograph, Canada, July 2011.
Telaprevir	750 mg single dose in healthy volunteers	<ul style="list-style-type: none"> Standard breakfast (533 kcal, 21 g fat) versus: Fasting Low-calorie/low-fat breakfast (249 kcal, 3.6g fat) Low-calorie/high protein breakfast (260 kcal, 9g fat) High-fat breakfast (928 kcal, 56g fat) 	↓ 73% ↓ 39% ↓ 26% ↑ 20%		↓ 83% ↓ 38% ↓ 25% ↓ 1%		<p>Take telaprevir with food or a snack that contains some fat (~20 g).</p> <p>The systemic exposure (AUC) to telaprevir was increased by 237% when telaprevir was administered with a standard fat meal (containing 533 kcal and 21 g fat) compared to when telaprevir was administered under fasting conditions. In addition, the type of meal significantly affects exposure to telaprevir. Relative to fasting, when telaprevir was administered with a low-fat meal (249 kcal, 3.6 g fat) and a high-fat meal (928 kcal, 56 g fat), the systemic exposure (AUC) to telaprevir was increased by approximately 117% and 330%, respectively. Doses of INCIVEK were administered within 30 minutes of completing a meal or snack</p>	<p>Van Heeswijk et al. 6th Int Workshop on Clin Pharmacol of Hepatitis Therapy 2011, #PK_19.</p> <p>Incivek Product Monograph, USA, May 2011.</p>

Drug	Dose	Type of Meal	AUC	CV	Cmax	CV	Recommendation	Reference
							containing approximately 20 grams of fat in the Phase 3 trials. Therefore, INCIVEK should always be taken with food (not low fat).	