Food Considerations for Antiretrovirals

Charts revised May 2015 by www.hiv-druginteractions.org

KEY: With or without food | On an empty stomach | With food

Single Agent Preparations

NRTIs			
Drug		**Usual Adult Dose (UK)**	**Food Considerations**
	Abacavir Ziagen® (ABC)	300 mg twice daily or 600 mg once daily	**Can be taken with OR without food** Food delays absorption and decreases Cmax, but does not affect AUC.
	Didanosine Videx®, VidexEC® (ddI)	Patients ≥60 kg: 400 mg daily, in 1-2 divided doses. Patients <60 kg: 250 mg daily, in 1-2 divided doses.	***EC Capsules:*** **Should be taken on an empty stomach, at least 2 hours before or 2 hours after food** Administration of Videx gastro-resistant capsules with a high fat meal significantly decreased didanosine AUC (19%) and Cmax(46%). Co-administering with, 1 hour before or 2 hours after a light meal, resulted in a significant decrease in AUC (27%, 24% and 10% respectively) and Cmax (22%, 15% and 15% respectively) compared to fasting state. In another study, administration of Videx capsules 1.5, 2 and 3 hours prior to a light meal resulted in equivalent Cmax and AUC values compared to fasting conditions. ***Tablets:*** **Should be taken at least 30 minutes before food** Studies have shown that administration of ddI tablets with a meal significantly decreases ddI AUC and Cmax.
	Emtricitabine Emtriva® (FTC)	One 200 mg capsule once daily	**Can be taken with OR without food** Administration of emtricitabine capsules with a high fat meal or emtricitabine oral solution with a low or high fat meal did not affect the AUC.
	Lamivudine Epivir® (3TC)	300 mg daily, administered as either 150 mg twice daily or 300 mg once daily	**Can be taken with OR without food** Co-administration of lamivudine with food results in a delay of tmax and a lower Cmax (decreased by 47%). However, the extent (based on the AUC) of lamivudine absorbed is not influenced.
	Stavudine Zerit® (d4T)	Patients ≥60 kg: 30 mg twice daily. Patients <60 kg: 40 mg twice daily.	**Ideally taken on an empty stomach, at least 1 hour before food** If this is not possible, it may be taken with a light meal. It may also be administered by opening the capsule and mixing the contents with food. A study in asymptomatic patients receiving 40mg twice daily demonstrated that systemic exposure is similar while Cmax is lower and Tmax is prolonged when stavudine is administered with a standardised, high-fat meal compared with fasting conditions. The clinical significance of this is unknown.
	Tenofovir Disoproxil Fumarate Viread®(TDF)	One 245 mg tablet, taken once daily.	**Should be taken with food** Administration of tenofovir disoproxil fumarate with a high fat meal enhanced the oral bioavailability, with an increase in tenofovir AUC by ~40% and Cmax by ~14%. Administration of tenofovir disoproxil fumarate with a light meal did not have a significant effect on the pharmacokinetics.
	Zidovudine Retrovir® (AZT/ZDV)	Patients ≥30 kg: 500-600 mg daily, in 2-3 divided doses	**Can be taken with OR without food** The extent of zidovudine absorption (AUC) and estimates of half-life following administration of Combivir with food were similar when compared to fasting subjects, although the rates of absorption (Cmax, tmax) were slowed.

NNRTIs			
Drug		**Usual Adult Dose (UK)**	**Food Considerations**
	Efavirenz Sustiva® (EFV)	Patients ≥40 mg: 600 mg once daily	**Should be taken on an empty stomach** The AUC and Cmax of a single dose of efavirenz tablets was increased by 28% and 79% respectively, when given with a high fat meal, relative to fasted conditions. This may lead to an increase in the frequency of adverse reactions
	Etravirine Intelence® (ETV)	200 mg twice daily	**Should be taken with or after a meal** The systemic exposure (AUC) to ETV is decreased by about 50% when administered under fasting conditions, as compared to administration following a meal.
	Nevirapine Viramune® (NVP)	One 200 mg tablet daily for the first 14 days followed by one 200 mg tablet twice daily thereafter	**Can be taken with OR without food** There are no published data concerning pharmacokinetics when nevirapine is given with/without food.
	Nevirapine Viramune Prolonged Release®	One 400 mg prolonged-release tablet once daily. *(Prolonged-release tablets are not suitable for the 14-day lead-in phase for patients starting nevirapine.)*	**Can be taken with OR without food** When Viramune prolonged-release was dosed with a high fat meal, the nevirapine AUC and Cmin were ~94% and 98%, respectively, of the AUC and Cmin when patients were dosed with immediate-release tablets. The difference is not considered clinically relevant.
	Rilpivirine Edurant® (RPV)	25 mg once daily	**Must be taken with a meal** Exposure to RPV was ~40% lower in a fasted state, compared to a normal caloric meal (533 kcal) or high-fat high-caloric meal (928 kcal). RPV must be taken with a meal to obtain optimal absorption. Taking RPV in a fasted state or with only a nutritional drink may result in decreased plasma concentrations

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			and potentially reduced therapeutic effect.

Entry/Integrase inhibitors

Drug	Usual Adult Dose (UK)	Food Considerations
Dolutegravir Tivicay® (DTG)	50 mg once daily or 50 mg twice daily depending on comedications or INSTI-resistance	*In the absence of integrase class resistance:* **Can be taken with OR without food** *In the presence of integrase class resistance:* **DTG should preferably be taken with food to enhance exposure, particularly in patients with Q148 mutations.** Food increased the extent and slowed the rate of absorption of dolutegravir. Bioavailability of dolutegravir depends on meal content: low, moderate, and high fat meals increased dolutegravir AUC by 33%, 41%, and 66%, increased Cmax by 46%, 52%, and 67%, prolonged Tmax to 3, 4, and 5 hours from 2 hours under fasted conditions, respectively. These increases may be clinically relevant in the presence of certain integrase class resistance.
Elvitegravir Vitekta® (EVG)	85 mg or 150 mg once daily depending on coadministered ritonavir-boosted PI	**Must be taken with food** Relative to fasting conditions, administration of elvitegravir as the fixed-dose combination (Stribild®)with food increased EVG Cmax and AUC by 22% and 36% with a light meal (approximately 373 kcal, 20% fat), and by 56% and 91% with a high-fat meal (approximately 800 kcal, 50% fat), respectively.
Maraviroc Celsentri® (MVC)	150 mg, 300 mg or 600 mg twice daily, depending on interactions with co-administered medicinal products	**Can be taken with OR without food** Administration with a high fat breakfast reduced maraviroc Cmax and AUC by 33%. There were no food restrictions in the studies that demonstrated the efficacy and safety of maraviroc, therefore it can be taken with or without food at recommended doses
Raltegravir Isentress® (RAL)	400 mg administered twice daily	**Can be taken with OR without food** Raltegravir was administered without regard to food in pivotal safety and efficacy studies. Administration of multiple doses following a moderate-fat meal did not significantly affect raltegravir AUC, with an increase of 13% relative to fasting. Raltegravir C12 hr was 66% higher and Cmax was 5% higher following a moderate-fat meal compared to fasting. Administration following a high-fat meal increased AUC and Cmax ~2-fold and increased C12 hr 4.1-fold. Administration following a low-fat meal decreased AUC and Cmax by 46% and 52%, respectively. Food appears to increase pharmacokinetic variability relative to fasting.

Protease Inhibitors

Drug	Usual Adult Dose (UK)	Food Considerations
Atazanavir Reyataz® (ATV)	300 mg once daily with RTV 100 mg once daily or Cobi 150 mg once daily	**Should be taken with or after food** When administered with a light meal, a 33% increase in the AUC and a 40% increase in both the Cmax and the 24 hour concentration of atazanavir is observed. Co-administration with a high-fat meal did not affect the AUC of atazanavir relative to fasting conditions. The 24 hour concentration following a high fat meal was increased by ~33% due to delayed absorption.
Darunavir Prezista® (DRV)	*Treatment experienced:* 600 mg twice daily with RTV 100 mg *Treatment naïve (or experienced depending on resistance, viral load and CD4 count):* 800 mg once daily with RTV 100 mg once daily or Cobi 150 mg once daily	**Should be taken with or after food** Darunavir should be taken within 30 minutes after completion of a meal. The type of food does not affect the exposure to darunavir. When administered without food, relative bioavailability of DRV (with ritonavir) is approximately 30% lower, compared to when taken with food.
Fosamprenavir Telzir® (FPV)	700 mg twice daily, with RTV 100 mg	**Can be taken with OR without food** Administration of fosamprenavir tablets in the fed state (standardised high fat meal: 967 kcal, 67 grams fat, 33 grams protein, 58 grams carbohydrate) did not alter plasma amprenavir pharmacokinetics (Cmax, tmax or AUC) compared to the fasted state.
Lopinavir with Ritonavir Kaletra® (LPV/r)	Two 200/50 mg tablets twice daily	**Can be taken with OR without food** Administration of a single 400/100mg dose of Kaletra tablets under fed conditions (high fat, 872 kcal, 56% from fat) compared to fasted state was associated with no significant changes in Cmax and AUCinf.
Ritonavir Norvir® (RTV)	*As a pharmacokinetic enhancer*: 100-200 mg, once or twice daily, depending on co-administered PI	**Should be taken with or after food** Food slightly decreases bioavailability of RTV tablets. Administration with a moderate or high fat meal decreased RTV AUC and Cmax by 20-23%.
Saquinavir Invirase® (SQV)	1000 mg twice daily with RTV 100 mg	**Should be taken with or after food** The AUC, Cmax and Ctrough values of saquinavir under fasting conditions were about 70% lower than with a high-fat meal.
Tipranavir Aptivus® (TPV)	500 mg twice daily with RTV 200 mg	**Should be taken with or after food** Food improves the tolerability of tipranavir/ritonavir

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Pharmacokinetic Enhancers of Antiretrovirals

Drug	Usual Adult Dose (UK)	Food Considerations
Cobicistat Tybost® (Cobi)	150 mg once daily in combination with atazanavir or darunavir.	**Must be taken with food** A food effect study was not conducted for Cobi. In clinical studies, Cobi was coadministered with ATV or DRV under fed conditions as per the SmPCs for these agents. It is recommended that Cobi be administered with food.

Fixed Dose Combinations

Drug	Usual Adult Dose (UK)	Food Considerations
Atripla® (TDF/FTC/EFV)	One tablet once daily	**Take an hour before food, or on an empty stomach** Atripla has not been evaluated in the presence of food. Atripla is recommended for administration on an empty stomach since food may increase efavirenz exposure and may lead to increased frequency of adverse reactions. It is anticipated that tenofovir exposure (AUC) will be ~30% lower following administration of Atripla on an empty stomach as compared to the individual component tenofovir disoproxil fumarate when taken with food.
Combivir® (ZDV/3TC)	One tablet twice daily	**Can be taken with OR without food** The extent of lamivudine and zidovudine absorption (AUC) and estimates of half-life following administration of Combivir with food were similar when compared to fasting subjects, although the rates of absorption (Cmax, tmax) were slowed.
Kivexa® (ABC/3TC)	One tablet once daily	**Can be taken with OR without food** No clinically significant food effect observed between administration of Kivexa in the fasted or fed state.
Trizivir® (ABC/3TC/ZDV)	One tablet twice daily	**Can be taken with OR without food** Food decreased the rate of absorption of Trizivir (slight decrease Cmax (mean 18 - 32 %) and increase tmax (~1 hour), but not the extent of absorption (AUC_0). These changes are not considered clinically relevant
Triumeq® (ABC/3TC/DTG)	One tablet once daily	**Can be taken with OR without food** Plasma Cmax and AUC of dolutegravir following administration of Triumeq with a high fat meal were 37% and 48% higher, respectively, compared to the fasted state). For abacavir there was a decrease in Cmax of 23% and AUC was unchanged. The exposure of lamivudine was similar with and without food. These results indicate that Triumeq can be taken with or without food.
Truvada® (TDF/FTC)	One tablet once daily	**Take with or after food** Administration of Truvada with food resulted in a delay of approximately three quarters of an hour in reaching maximum tenofovir concentrations and increases in tenofovir AUC and Cmax of approximately 35% and 15%, respectively, when administered with a high fat or light meal, compared to the fasted state. In order to optimise the absorption of tenofovir, it is recommended that Truvada should be taken with food.
Eviplera® (TDF/FTC/RPV)	One tablet once daily	**Must be taken with food** Administration of Eviplera with either a light meal (390 kcal) or a standard meal (540 kcal) resulted in increased exposures of rilpivirine and tenofovir relative to fasting conditions. The Cmax and AUC of rilpivirine increased by 34% and 9% (light meal) and 26% and 16% (standard meal), respectively. The Cmax and AUC for tenofovir increased by 12% and 28% (light meal) and 32% and 38% (standard meal), respectively. Emtricitabine exposures were not affected by food.
Stribild® (EVG/Cobi/ TDF/FTC)	One tablet once daily	**Must be taken with food** Relative to fasting conditions, administration of Stribild with food had the following effects on pharmacokinetic parameters: *Light Meal (~373 kcal, 20% fat)* / *High Fat Meal (~800 kcal, 50% fat)* EVG: ↑22% Cmax, ↑36% AUC / ↑56% Cmax, ↑91% AUC TDF: ↑20% Cmax, ↑25% AUC / ↔ Cmax, ↑25% AUC Cobi: ↔ Cmax, ↔ AUC / ↓24% Cmax, ↓18% AUC FTC: ↔ Cmax, ↔ AUC / ↔ Cmax, ↔ AUC
Rezolsta® (DRV/Cobi)	*Treatment naïve and treatment experienced (depending on resistance, viral load and CD4 count):* One 800/150 mg tablet once daily	**Must be taken with food or within 30 minutes of a meal** Patients should be instructed to take Rezolsta within 30 minutes after completion of a meal. When taken with food, DRV exposure was 1.7-fold higher as compared to fasting. The type of food does not affect exposure.
Indinavir	800 mg every eight hours alone	***Alone:* Should preferably be taken one hour before, or two hours after food**

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	Crixivan® (IDV)	or alternatively (based on limited data), 400 mg in combination with RTV 100 mg, both twice daily	For optimal absorption, Indinavir should be administered without food but with water, 1 hour before or 2 hours after a meal. Alternatively, indinavir may be administered with a low–fat, light meal. Administration of indinavir with a meal high in calories, fat, and protein resulted in a blunted and reduced absorption with ~80% reduction in AUC and 86% reduction in Cmax. Administration with light meals (e.g. dry toast with jam or fruit conserve, apple juice, and coffee with skimmed or fat–free milk and sugar or corn flakes, skimmed or fat–free milk and sugar) resulted in plasma concentrations comparable to fasted values. ***With Ritonavir:*** **Can be taken with OR without food** If co-administered with ritonavir, Indinavir may be administered with or without food. No significant difference in exposure was seen when 800mg/100mg indinavir/ritonavir every 12 hours was given with a high-fat meal or a low fat meal.
	Nelfinavir Viracept® (NFV)	1250 mg twice a day, or 750 mg three times a day	**Should be taken with or after food** Cmax and AUC were 2- to 3-fold higher with food compared to fasting. Increased concentrations with food were independent of meal fat content.