Food Considerations for Antiretrovirals

Updated March 2016

NRTIs - Single Agent Preparations

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 h before or 2 h 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 decreased 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 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** Coadministration of lamivudine with food delayed Tmax and decreased Cmax 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 40 mg twice daily demonstrated systemic exposure was 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 oral bioavailability (tenofovir AUC and Cmax increased by ~40% and ~14%). Administration of tenofovir disoproxil fumarate with a light meal had no significant effect on tenofovir 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.

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Efavirenz Sustiva® (EFV)	Patients ≥40 mg: 600 mg once daily	**Should be taken on an empty stomach** AUC and Cmax of a single dose of efavirenz tablets 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** Systemic exposure (AUC) of etravirine decreased by ~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 or 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, nevirapine AUC and Cmin decreased by ~6% and 2% relative to 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** Rilpivirine exposure was ~40% lower in a fasted state, compared to a normal meal (533 kcal) or high-fat high-calorie meal (928 kcal). Rilpivirine must be taken with a meal to obtain optimal absorption. Taking rilpivirine in a fasted state or with only a nutritional drink may result in decreased plasma concentrations and potentially reduced therapeutic effect.

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

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Entry/Integrase Inhibitors - Single Agent Preparations

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:* **Preferably 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 h (from 2 h 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 elvitegravir 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 decreased 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 C12h 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 by ~2-fold and increased C12h by 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 - Single Agent Preparations

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** Administration with a light meal increased atazanavir AUC by 33%, Cmax by 40% and C24h by 40%. Co-administration with a high-fat meal did not affect the atazanavir AUC relative to fasting conditions. Atazanavir C24h 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 darunavir (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 g fat, 33 g protein, 58 g 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 400/100 mg 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 AUC.
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 decreased bioavailability of ritonavir tablets. Administration with a moderate or high fat meal decreased ritonavir AUC and Cmax by 20-23%.
Saquinavir Invirase® (SQV)	1000 mg twice daily with RTV 100 mg	**Should be taken with or after food** Saquinavir AUC, Cmax and Ctrough decreased by ~70% under fasting conditions compared 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.

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 cobicistat. In clinical studies, cobicistat was coadministered with atazanavir or darunavir under fed conditions as per the product labels for these agents. It is recommended that cobicistat be administered with food.

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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 was observed when Kivexa was administered 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 (Cmax decreased by 18-32% and Tmax increased by ~1 h), but not the extent of absorption (AUC). These changes are not considered clinically relevant.
Triumeq® (ABC/3TC/DTG)	One tablet once daily	**Can be taken with or without food** Dolutegravir Cmax and AUC were 37% and 48% higher following administration of Triumeq with a high fat meal compared to the fasted state. Abacavir Cmax decreased by 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® (FTC/TDF)	One tablet once daily	**Take with or after food** Administration of Truvada with a high fat or light meal delayed tenofovir Tmax by ~0.75 h and increased tenofovir AUC and Cmax by ~35% and ~15%, respectively, compared to the fasted state. In order to optimise the absorption of tenofovir, it is recommended that Truvada should be taken with food.
Eviplera® (FTC/TDF/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) increased exposures of rilpivirine and tenofovir relative to fasting conditions. Rilpivirine Cmax and AUC increased by 34% and 9% (light meal) and 26% and 16% (standard meal), respectively. Tenofovir Cmax and AUC increased by 12% and 28% (light meal) and 32% and 38% (standard meal), respectively. Emtricitabine exposures were not affected by food.
Stribild® (EVG/Cobi/ FTC/TDF)	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
Genvoya® (EVG/Cobi/ FTC/TAF)	One tablet once daily	**Must be taken with food** Relative to fasting conditions, administration of Genvoya 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 Cobi: ↔ Cmax, ↔ AUC / ↓24% Cmax, ↓18% AUC FTC: ↔ Cmax, ↔ AUC / ↔ Cmax, ↔ AUC *Light Meal (~400 kcal, 20% fat)* / *High Fat Meal (~800 kcal, 50% fat)* TAF: ↔ Cmax, ↑15% AUC / ↔ Cmax, ↑18% 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 of completion of a meal. When taken with food, darunavir exposure was 1.7-fold higher as compared to fasting. The type of food does not affect exposure.

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

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