Food Considerations for Oral Antiretrovirals

Revised October 2022

Protease Inhibitors (PIs)

Antiretroviral	Usual adult dose	Food requirements	Comments
Atazanavir alone	400 mg once daily	Should be taken with food	Administration of atazanavir (400 mg single dose) with a light meal (357 kcal, 8.2g fat, 10.6 g protein) or a high-fat meal (721 kcal, 37.3 g fat, 29.4 g protein) had the following effects on pharmacokinetic parameters (relative to fasting): *Light Meal* / *High Fat Meal* AUC ↑70% / ↑35% Cmax ↑57% / ↔ Administration of atazanavir with either a light meal or high-fat meal decreased the coefficient of variation of AUC and Cmax by approximately one-half compared to the fasting state.
Atazanavir/cobicistat	300/150 mg once daily	Should be taken with food	Administration of a single dose of atazanavir/cobicistat with either a light meal (336 kcal, 5.1 g fat, 9.3 g protein) or a high fat meal (1038 kcal, 59 g fat, 37 g protein) had the following effects on pharmacokinetic parameters (relative to fasting): *Light Meal* (*Atazanavir* / *Cobicistat*) / *High Fat Meal* (*Atazanavir* / *Cobicistat*) AUC ↑28% / ↑24% / ↓4% / ↑12% Cmax ↑42% / ↑31% / ↓14% / ↔ C24 ↑35% / ND / ↑23% / ND Atazanavir Cmax and AUC after a high fat meal decreased 36% and 25% in comparison to a light meal, respectively, however, C24 was similar.
Atazanavir/ritonavir	300/100 mg once daily	Should be taken with food	Administration of atazanavir/ritonavir (300/100 mg single dose) with a light meal or a high fat meal had the following effects on atazanavir pharmacokinetic paramaters (relative to fasting): *Light Meal* / *High Fat Meal* AUC ↑33% / ↔ Cmax ↑40% / 11% C24 ↑40% / ↑33% Administration with food decreased the coefficient of variation of AUC and Cmax by ~25% compared to the fasting state.
Darunavir/cobicistat	800/150 mg once daily	Should be taken with food	Administration of darunavir/cobicistat to healthy adult subjects with a high-fat meal (965 total kcal: 129 kcal from protein, 236 kcal from carbohydrates and 600 kcal from fat) increased darunavir AUC and Cmax by 70% and 127%, when compared to fasted conditions. Cobicistat exposures were not affected by food. The type of food does not affect darunavir exposure.
Darunavir/ritonavir	*ARV-naïve patients and ARV-experienced patients (with no darunavir resistance, with plasma HIV-1 RNA <100,000 copies/ml & CD4 cell count ≥100)*: 800/100 mg once daily *Other ARV-experienced patients*: 600/100 mg twice daily	Should be taken with food	Administration of darunavir/ritonavir with food increased darunavir Cmax and AUC by ~40% relative to the fasting state (total calorie content of the various meals evaluated ranged from 240 Kcal and 12 g fat to 928 Kcal and 56 g fat). The type of food does not affect darunavir exposure.
Lopinavir/ritonavir	400/100 mg twice daily 800/100 mg once daily	*Tablets:* Can be taken with or without food	Administration of a single 400/100 mg dose of Kaletra tablets with a high fat meal (872 kcal, 56% fat) was associated with no significant changes in Cmax and AUC when compared to fasted state.
		Oral solution: Should be taken with food	Administration of a single 400/100 mg dose of Kaletra oral solution with a moderate fat meal (500-682 kcal, ~25% from fat) increased lopinavir AUC and Cmax by 80% and 54%, relative to fasting. Administration with a high fat meal (872 kcal, 56% fat) increased lopinavir AUC and Cmax by 130% and 56%, relative to fasting conditions.
Ritonavir	(Dose depends on coadministered PI)	Should be taken with food	Administration ritonavir (100 mg single dose) with a moderate or high fat meal decreased ritonavir AUC and Cmax by 20-23% (tablets) or 23-49% (oral solution), relative to fasting conditions.

Key: *Can be taken with or without food* | *Specific requirements for dosing relative to food intake* | *↑ Increase; ↓decrease; ↔ no change; ND not determined*

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Food Considerations for Oral Antiretrovirals

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Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)

Antiretroviral	Usual adult dose	Food requirements	Comments
Doravirine	100 mg once daily	Can be taken with or without food	Administration of a single doravirine tablet with a high-fat meal (1000 kcal, 50% fat) to healthy subjects increased doravirine AUC, Cmax and C24 by 16%, 3% and 36%, relative to fasting conditions.
Efavirenz	600 mg once daily	Should be taken on an empty stomach	Administration of a single 600 mg efavirenz tablet with a high fat meal (~1000 kcal, ~50% fat) increased efavirenz AUC and Cmax 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. Administration of a single 600 mg dose of efavirenz capsules with a high-fat and calorie meal (894 kcal, 54 g fat, 54% calories from fat) increased efavirenz AUX and Cmax by 22% and 39%, whereas a reduced-fat and normal calorie meal (440 kcal, 2 g fat, 4% calories from fat) increased efavirenz AUC and Cmax by 17% and 51% (all relative to the exposures under fasted conditions).
Etravirine	200 mg twice daily	Should be taken following a meal	Etravirine AUC decreased by ~50% when administered under fasting conditions, as compared to administration following a meal. The total caloric content of the various meals evaluated ranged from 345 kcal (17 grams fat) to 1160 kcal (70 grams fat).
Nevirapine	*[Lead in dose - 200 mg once daily for the first 14 days]* 200 mg twice daily (immediate release) 400 mg once daily (prolonged release)	Can be taken with or without food	Administration of nevirapine immediate release (200 mg) to 24 healthy adults (12 female, 12 male), with a high-fat breakfast (857 kcal, 50 g fat, 53% of calories from fat) had no effect on nevirapine AUC relative to that observed under fasting conditions. Administration of nevirapine prolonged-release with a high fat meal, decreased nevirapine AUC and Cmin by ~6% and 2% relative to when patients were dosed with immediate-release tablets. The difference is not considered clinically relevant. The difference in nevirapine pharmacokinetics observed when nevirapine prolonged-release tablets are dosed under fasted or fed conditions is not considered clinically relevant.
Rilpivirine	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). When rilpivirine was taken with only a protein-rich nutritional drink, exposures were 50% lower than when taken with a meal. 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.

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Food Considerations for Oral Antiretrovirals

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Nucleoside/tide Reverse Transcriptase Inhibitors

Antiretroviral	Usual adult dose	Food requirements	Comments
Abacavir	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.
Emtricitabine	*Hard Capsules:* 200 mg once daily *10 mg/ml Oral Solution:* 240 mg (24 ml) once daily	Can be taken with or without food	Administration of emtricitabine capsules with a high fat meal (~1000 kcal) had no effect on emtricitabine AUC and decreased Cmax by 29%. Emtricitabine AUC and Cmax were unaffected when emtricitabine oral solution was administered with either a high-fat or low-fat meal.
Lamivudine	300 mg once daily or 150 mg twice 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 was not affected.
Tenofovir-DF	245 mg once daily	*European SmPC:* Should be taken with food *US Prescribing Information:* Can be taken with or without food	Administration of tenofovir-DF with a high fat meal (~700-1000 kcal, 40-50% fat) increased tenofovir AUC and Cmax by ~40% and ~14%. Administration of tenofovir-DF with a light meal had no significant effect on tenofovir pharmacokinetics.
Zidovudine	250 mg twice daily or 300 mg twice daily	Can be taken with or without food	Zidovudine AUCs were similar when a single dose of zidovudine was administered with or without food.

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Food Considerations for Oral Antiretrovirals

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Integrase Inhibitors

Antiretroviral	Usual adult dose	Food requirements	Comments
Bictegravir	50 mg once daily (as fixed dose combination with emtricitabine and tenofovir alafenamide)	Can be taken with or without food	Administration of bictegravir/emtricitabine/tenofovir alafenamide with a moderate fat (~600 kcal, 27% fat) or high fat meal (~800 kcal, 50% fat) increased in bictegravir AUC and Cmax by 24% and 13%, relative to fasting conditions. This modest change is not considered clinically meaningful.
Cabotegravir	30 mg once daily (with rilpivirine)	Cabotegravir tablets may be taken with or without food. When taken at the same time as rilpivirine tablets, cabotegravir tablets should be taken with a meal.	Food increased the extent of absorption of cabotegravir. Bioavailability of cabotegravir is independent of meal content: high fat meals increased cabotegravir AUC by 14% and increased Cmax by 14% relative to fasted conditions. These increases are not clinically significant.
Dolutegravir	*Patients without documented or suspected INSTI resistance:* 50 mg once daily (twice daily when taken with some medicines). *Patients with INSTI resistance (documented or suspected):* 50 mg twice daily.	*In the absence of integrase class resistance:* Can be taken with or without food *In the presence of integrase class resistance (European SmPC):* Preferably taken with food to enhance exposure, particularly in patients with Q148 mutations.	Administration of dolutegravir with 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 relative to fasting conditions. The European product label suggests that these increases may be clinically relevant in the presence of certain integrase class resistance and recommends dolutegravir to be taken with food by patients infected with HIV with integrase class resistance. The US product label states that dolutegravir can be taken with or without food in all patients.
Elvitegravir	150 mg once daily (as fixed dosed combination with cobicistat, emtricitabine, and tenofovir-DF or tenofovir alafenamide)	Should be taken with food	Administration of elvitegravir as a fixed-dose combination with food increased elvitegravir Cmax and AUC, relative to fasting conditions (see the FDC listing for full details).
Raltegravir	400 mg twice daily or 1200 mg once daily (if treatment naïve or virally suppressed on 400 mg twice daily)	Can be taken with or without food	Administration of raltegravir film-coated tablets with food had the following effects on raltegravir pharmacokinetics (relative to fasting): *400 mg twice daily*: Low fat: AUC ↓46%, Cmax ↓52%, Cmin ↓14%; Moderate fat: AUC ↑13%, Cmax ↑5%, Cmin ↑66%; High fat: AUC ↑111%, Cmax ↑96%, Cmin ↑313% *1200 mg once daily*: Low fat: AUC ↓42%, Cmax ↓52%, Cmin ↓16%; High fat: AUC ↑2%, Cmax ↓28%, Cmin ↓12% Administration of raltegravir chewable tablets with a high fat meal decreased AUC and Cmax by 6% and 62%, and increased Cmin by 188%. The effect of food on oral suspension was not studied. Food appears to increase pharmacokinetic variability relative to fasting.

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Food Considerations for Oral Antiretrovirals

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Entry/Attachment/Capsid Inhibitors

Antiretroviral	Usual adult dose	Food requirements	Comments
Fostemsavir	600 mg twice daily	Can be taken with or without food	Fostemsavir is a prodrug that is metabolised to temsavir. Temsavir AUC was not impacted by a standard meal (approximately 423 kcal, 36% fat) but increased 81% with a high-fat meal (approximately 985 kcal, 60% fat) and is not considered clinically significant. Regardless of calorie and fat content, food had no impact on plasma temsavir Cmax.
Lenacapavir	*Oral loading doses prior to SC injections:* 600 mg/day orally on days 1 &2 300 mg/day orally on day 8	Can be taken with or without food	Initiation of treatment with lenacapavir requires lenacapavir film-coated tablets to be taken as oral loading prior to administration of lenacapavir injection. Lenacapavir AUC, Cmax and Tmax were comparable following administration of a low fat (~400 kcal, 25% fat) or high fat (~1000 kcal, 50% fat) meal relative to fasted conditions.
Maraviroc	*With potent CYP3A inhibitors ± potent CYP3A inducers:* 150 mg twice daily *Without potent CYP3A inhibitors or inducers:* 300 mg twice daily *With potent CYP3A inducer but no potent CYP3A inhibitor:* 600 mg twice daily	Can be taken with or without food	Administration of a maraviroc tablet (300 mg) with a high fat breakfast decreased maraviroc Cmax and AUC by 33%. Administration of maraviroc oral solution (75 mg) with a high fat breakfast decreased maraviroc AUC by 73%. Studies with the tablets demonstrated a reduced food-effect at higher doses. There were no food restrictions in adult studies (using tablet formulations) or in a paediatric study (using both tablet and oral solution formulations) and results did not indicate any relevant efficacy or safety concern related to either fed or fasted dosing conditions. Therefore, maraviroc tablets and oral solution can be taken with or without food.

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Food Considerations for Oral Antiretrovirals

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Fixed Dose Combinations - PIs + NRTIs

Name	ARVs	Food requirements	Comments
Symtuza	Darunavir/cobicistat + Emtricitabine Tenofovir alafenamide	Should be taken with food	Administration with a high fat meal (928 kcal; 504 kcal fat (56 g), 260 kcal carbohydrates, 164 kcal protein) had the following effects on the components of Symtuza (relative to fasting): *Darunavir* / *Cobicistat* / *Emtricitabine* / *Tenofovir alafenamide* AUC: ↑52% / ↑41% / ↔ / ↑12% Cmax: ↑82% / ↑30% / ↓21% / ↓45% The type of food does not affect exposure to Symtuza.

Fixed Dose Combinations - NNRTIs + NRTIs

Name	ARVs	Food requirements	Comments
Atripla	Efavirenz + Emtricitabine Tenofovir-DF	Take 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. Administration of efavirenz tablets with a high fat meal increased efavirenz AUC and Cmax by 28% and 79%, relative to fasting. It is anticipated that tenofovir AUC will be ~30% lower following administration of Atripla on an empty stomach as compared to the individual component when taken with food. Administration of emtricitabine/tenofovir-DF with either a high fat or light meal had no effect on emtricitabine but increased tenofovir AUC and Cmax by 35% and 15%, relative to fasting.
Delstrigo	Doravirine + Lamivudine Tenofovir-DF	Can be taken with or without food	Administration of a single Delstrigo tablet with a high fat meal (~1000 kcal, 50% fat) had the following effects on the components of Delstrigo (relative to fasting): *Doravirine* / *Lamivudine* / *Tenofovir-DF* AUC: ↑10% / ↓7% / ↑27% Cmax: ↓5% / ↓19% / ↓12% C24: ↑26% / ND / ND
Eviplera (Europe) **Complera (US)**	Rilpivirine + Emtricitabine Tenofovir-DF	Must be taken with food	Administration with either a light meal (390 kcal. 12 g fat) or a standard meal (540 kcal, 21 g fat) increased exposures of rilpivirine and tenofovir relative to fasting conditions. Emtricitabine exposures were not affected by food. *Light Meal*: *Rilpivirine* / *Tenofovir-DF* *Standard Meal*: *Rilpivirine* / *Tenofovir-DF* AUC: ↑9% / ↑28% / ↑16% / ↑38% Cmax: ↑34% / ↑12% / ↑26% / ↑32%
Odefsey	Rilpivirine + Emtricitabine Tenofovir alafenamide	Must be taken with food	Administration of a single Odefsey tablet with either a moderate fat meal (~600 kcal. 27% fat) or a high fat meal (~800 kcal, 50% fat) had the following effects on the components of Odefsey (relative to fasting): *Moderate Fat Meal*: *Rilpivirine* / *Emtricitabine* / *Tenofovir alafenamide* *High Fat Meal*: *Rilpivirine* / *Emtricitabine* / *Tenofovir alafenamide* AUC: ↑13% / ↓9% / ↑45% / ↑72% / ↓12% / ↑39%

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Food Considerations for Oral Antiretrovirals

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Fixed Dose Combinations – multiple NRTIs

Name	ARVs	Food requirements	Comments
Combivir	Lamivudine Zidovudine	Can be taken with or without food	Lamivudine and zidovudine AUCs were similar when Combivir was administered with food and compared to fasting subjects, although the rates of absorption (Cmax, Tmax) were slowed.
Descovy	Emtricitabine Tenofovir alafenamide	Can be taken with or without food	Administration with a high fat meal (~800 kcal, 50% fat) had the following effects on the components of Descovy (relative to fasting): *Emtricitabine* *Tenofovir alfenamide* AUC ↓9% ↑75% Cmax ↓26% ↓15%
Kivexa (Europe) **Epzicom (US)**	Abacavir Lamivudine	Can be taken with or without food	No clinically significant food effect was observed. Administration of a single tablet of abacavir/lamivudine with a high-fat meal had no effect on abacavir AUC but decreased Cmax by ~24% relative to fasting conditions. There was no change in lamivudine AUC or Cmax.
Temixys	Lamivudine Tenofovir-DF	Can be taken with or without food	*(No details of the effect of food on the fixed dosed combination are given in the product label.)*
Trizivir	Abacavir Lamivudine Zidovudine	Can be taken with or without food	Administration of a single Trizivir tablet with a high fat meal decreased Cmax of abacavir, lamivudine and zidovudine by 32%, 18% and 28%, relative to fasting conditions. There was no effect on the AUCs of abacavir, lamivudine and zidovudine.
Truvada	Emtricitabine Tenofovir-DF	*European SmPC:* It is preferable that Truvada is taken with food. *US Prescribing Information:* Can be taken with or without food	Administration of Truvada with either a light meal (373 kcal. 8 g fat) or a high fat meal (784 kcal, 49 g fat) increased tenofovir AUC and Cmax by ~35% and 15%, relative to fasting conditions. Emtricitabine AUC and Cmax were not affected by either a light meal or a high fat meal, relative to fasting conditions.

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Fixed Dose Combinations - Integrase Inhibitors + NRTIs

Name	ARVs	Food requirements	Comments
Biktarvy	Bictegravir + Emtricitabine Tenofovir alafenamide	Can be taken with or without food	Administration of Biktarvy with a high fat meal (800 kcal, 50% fat) had the following effects on pharmacokinetic parameters (relative to fasting): *Bictegravir* / *Emtricitabine* / *Tenofovir alafenamide* AUC ↑24% / ↓4% / ↑63% Cmax ↑13% / ↓14% / ↓8%
Dovato	Dolutegravir + Lamivudine	Can be taken with or without food	Administration with a high fat meal (~900 kcal, 56% fat) had no clinically significant effect on the pharmacokinetics of either component of Dovato. When compared to fasting conditions, administration with food increased dolutegravir AUC by 33% and decreased lamivudine AUC by 9%.
Genvoya	Elvitegravir/cobicistat + Emtricitabine Tenofovir alafenamide	Should be taken with food	Administration of Genvoya with a light meal (~373 or 400 kcal, 20% fat) or a high fat meal (~800 kcal, 50% fat) had the following effects on pharmacokinetic parameters (relative to fasting): *Light Meal* (*AUC* / *Cmax*) / *High Fat Meal* (*AUC* / *Cmax*) Elvitegravir ↑34% / ↑22% / ↑87% / ↑56% Cobicistat ↑3% / ↔ / ↓17% / ↓24% Emtricitabine ↓5% / ↔ / ↓4% / ↔ Tenofovir alafenamide ↑15% / ↔ / ↑18% / ↔
Juluca	Dolutegravir + Rilpivirine	Must be taken with food to obtain optimal absorption of rilpivirine	Administration of Juluca with a moderate fat meal (~625 kcal, 32% fat) or a high fat meal (~900 kcal, 56% fat) had the following effects on pharmacokinetic parameters (relative to fasting): *Moderate Fat Meal* (*AUC* / *Cmax*) / *High Fat Meal* (*AUC* / *Cmax*) Dolutegravir ↑87% / ↑75% / ↑87% / ↑75% Rilpivirine ↑57% / ↑89% / ↑72% / ↑117% Rilpivirine exposures were 50% lower when taken with only a protein-rich nutritional drink than with a meal. Taking Juluca in a fasted condition or with only a protein-rich nutritional drink may decrease rilpivirine concentrations, which could potentially reduce the therapeutic effect of Juluca.
Stribild	Elvitegravir/cobicistat + Emtricitabine Tenofovir-DF	Should be taken with food	Administration of Stribild with a light meal (~373 kcal, 20% fat) or a high fat meal (~800 kcal, 50% fat) had the following effects on pharmacokinetic parameters (relative to fasting): *Light Meal* (*AUC* / *Cmax*) / *High Fat Meal* (*AUC* / *Cmax*) Elvitegravir ↑34% / ↑22% / ↑87% / ↑56% Cobicistat ↑3% / ↔ / ↓17% / ↓24% Emtricitabine ↓5% / ↔ / ↓4% / ↔ Tenofovir-DF ↑24% / ↑20% / ↑23% / ↔
Triumeq	Dolutegravir + Abacavir Lamivudine	Can be taken with or without food	Administration of Triumeq with a high fat meal (869 kcal, 53% fat) had the following effects on pharmacokinetic parameters (relative to fasting): *Dolutegravir* / *Abacavir* / *Lamivudine* AUC ↑48% / ↔ / ↔ Cmax ↑37% / ↓23% / ↔

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