Table 9: Recommended Dose Adjustments for Use of Selected Fixed-Dose Combination Antiretroviral Medications in Patients With Hepatic or Renal Impairment				
		Renal Impairment Dose Adjustment		
Fixed-Dose Combination	**Hepatic Impairment Dose Adjustment [a]**	**Recommended Dose Adjustment [a]**	**Individual FDC Components and Recommended Dose Adjustment [a]**	**Clinical Comments**
Integrase Strand Transfer Inhibitors				
Abacavir/dolutegravir/ lamivudine (ABC/DTG/3TC; Triumeq)	**Child-Pugh A, B, C:** Do not use.	**CrCl <30 mL/min:** Use of FDC is not recommended.	• **ABC:** No renal dose adjustment is needed. • **DTG:** No renal dose adjustment is needed. • **3TC:** – **CrCl 30 to 49 mL/min:** 150 mg once daily – **CrCl 15 to 29 mL/min:** 150 mg first dose, then 100 mg once daily – **CrCl 5 to 14 mL/min:** 150 mg first dose, then 50 mg once daily – **CrCl <5 mL/min:** 50 mg first dose, then 25 mg once daily	• **CrCl >30 mL/min:** Limited data to support use of FDC; 21 patients with CrCl >30 mL/min received full dose 3TC with minimal increases in AUC. No elevations in lactate or other ADRs reported [Fischetti, et al. 2018]. • **CrCl <30 mL/min, without HD:** Renal adjustment should be based on individual components; 13 patients with CrCl <30 mL/min not on HD received 100 to 150 mg of 3TC with minimal increases in AUC. No elevations in lactate or other ADRs reported [Fischetti, et al. 2018]. • **CrCl <30 mL/min, with HD:** Limited data to support use of FDC. Case series evaluating safety and efficacy of FDC in 9 patients with end-stage renal disease on HD reported viral suppression achieved in all 9 patients. No change in immune function. FDC generally well tolerated; 1 patient complained of nausea, which resolved without drug discontinuation [Michienzi, et al. 2019]. • **Note:** DTG serum concentrations appear to be reduced in uninfected healthy controls with eGFR <30 mL/min/m^2 compared to those with normal kidney function. This may increase the risk of therapeutic failure among patients with HIV drug resistance to INSTIs [FDA(c) 2024].

Table 9: Recommended Dose Adjustments for Use of Selected Fixed-Dose Combination Antiretroviral Medications in Patients With Hepatic or Renal Impairment				
		Renal Impairment Dose Adjustment		
Fixed-Dose Combination	**Hepatic Impairment Dose Adjustment [a]**	**Recommended Dose Adjustment [a]**	**Individual FDC Components and Recommended Dose Adjustment [a]**	**Clinical Comments**
Bictegravir/emtricitabine/ tenofovir alafenamide [b] (BIC/FTC/TAF; Biktarvy)	• **Child-Pugh A, B:** No dose adjustment is needed. • **Child-Pugh C:** Do not use.	**CrCl <30 mL/min:** Use of FDC is not recommended.	• **BIC:** No renal adjustment is needed. • **FTC:** – **CrCl 30 to 49 mL/min:** 200 mg every 48 hours – **CrCl 15 to 29 mL/min:** 200 mg every 72 hours – **CrCl <15 mL/min:** 200 mg every 96 hours • **TAF:** – **CrCl <15 mL/min, without HD:** Use is not recommended. – **CrCl <15 mL/min, with HD:** No renal dose adjustment is needed.	• **CrCl <30 mL/min:** No data to support use of FDC. Renal dose adjustment should be based on individual components. • **CrCl 15 to 29 mL/min:** No BIC dose adjustment is needed. In a study of 10 patients with CrCl 15–29 mL/min compared to 8 patients with normal renal function who received a single dose of BIC 75 mg, severe renal impairment did not produce clinically relevant changes in BIC exposure [Zhang, et al. 2017].
Elvitegravir/cobicistat/ emtricitabine/tenofovir disoproxil fumarate (EVG/COBI/FTC/TDF; Stribild)	• **Child-Pugh A, B:** No dose adjustment is needed. • **Child-Pugh C:** No data; do not use.	• **CrCl <70 mL/min:** Do not initiate therapy. • **Drop in CrCl to <50 mL/min during treatment:** Discontinue therapy.	• **EVG:** No renal dose adjustment is needed. • **EVG/COBI:** No renal dose adjustment is needed. • **FTC:** – **CrCl 30 to 49 mL/min:** 200 mg every 48 hours – **CrCl 15 to 29 mL/min:** 200 mg every 72 hours – **CrCl <15 mL/min:** 200 mg every 96 hours • **TDF:** – **CrCl 30 to 49 mL/min:** 300 mg every 48 hours – **CrCl 10 to 29 mL/min:** 300 mg every 72–96 hours – **CrCl <10 mL/min, without HD:** No data available. – **CrCl <10 mL/min, with HD:** 300 mg every 7 days	• **CrCl <30 mL/min:** No data to support use of FDC. Renal dose adjustment should be based on individual components. • **EVG/COBI:** Dose adjustment not warranted. In 12 patients with eGFR <30 mL/min/m^2 (not on HD) and 12 controls with normal renal function given 7 days of EVG/COBI, lower EVG AUC, C_{max}, and C_{min} values and higher COBI AUC, C_{max}, and C_{min} values were observed in severe renal impairment, but values were not considered clinically relevant [German(b), et al. 2012].

Table 9: Recommended Dose Adjustments for Use of Selected Fixed-Dose Combination Antiretroviral Medications in Patients With Hepatic or Renal Impairment				
		Renal Impairment Dose Adjustment		
Fixed-Dose Combination	**Hepatic Impairment Dose Adjustment [a]**	**Recommended Dose Adjustment [a]**	**Individual FDC Components and Recommended Dose Adjustment [a]**	**Clinical Comments**
Elvitegravir/cobicistat/ emtricitabine/tenofovir alafenamide [b] (EVG/COBI/FTC/TAF; Genvoya)	• **Child-Pugh A, B:** No dose adjustment is needed. • **Child-Pugh C:** Do not use.	**CrCl <30 mL/min:** Use of FDC is not recommended.	• **EVG:** No renal dose adjustment is needed. • **EVG/COBI:** No renal dose adjustment is needed. • **FTC:** – **CrCl 30 to 49 mL/min:** 200 mg every 48 hours – **CrCl 15 to 29 mL/min:** 200 mg every 72 hours – **CrCl <15 mL/min:** 200 mg every 96 hours • **TAF:** – **CrCl <15 mL/min, without HD:** Use is not recommended. – **CrCl <15 mL/min, with HD:** No renal dose adjustment is needed. – **ESRD, with HD:** 1 tablet once daily; administer after HD on HD days.	• **CrCl <30 mL/min, without HD:** No data to support use of FDC. Renal adjustment should be based on individual components. • **CrCl <15 mL/min, with HD:** In a study of 55 patients on FDC for up to 96 weeks, 18 (33%) had grade 3 or higher ADR during treatment, and 3 patients discontinued treatment due to adverse effects. The authors concluded that, at 48 weeks, the FDC regimen was well tolerated in patients on HD [Eron(b), et al. 2018].
Dolutegravir/lamivudine (DTG/3TC; Dovato)	• **Child-Pugh A, B:** No dose adjustment is needed. • **Child-Pugh C:** Do not use.	**CrCl <30 mL/min:** Use of FDC is not recommended.	• **DTG:** No renal dose adjustment is needed. • **3TC:** – **CrCl 30 to 49 mL/min:** 150 mg once daily – **CrCl 15 to 29 mL/min:** 150 mg first dose, then 100 mg once daily – **CrCl 5 to 14 mL/min:** 150 mg first dose, then 50 mg once daily – **CrCl <5 mL/min:** 50 mg first dose, then 25 mg once daily	**CrCl <50mL/min:** No data to support use of FDC. Renal dose adjustment should be based on individual components.
Dolutegravir/rilpivirine (DTG/RPV; Juluca)	• **Child-Pugh A, B:** No dose adjustment is needed. • **Child-Pugh C:** No data; do not use.	**CrCl <30 mL/min or ESRD:** No dose adjustment is needed; increased monitoring is recommended.	—	—

Table 9: Recommended Dose Adjustments for Use of Selected Fixed-Dose Combination Antiretroviral Medications in Patients With Hepatic or Renal Impairment				
		Renal Impairment Dose Adjustment		
Fixed-Dose Combination	**Hepatic Impairment Dose Adjustment [a]**	**Recommended Dose Adjustment [a]**	**Individual FDC Components and Recommended Dose Adjustment [a]**	**Clinical Comments**
Non-Nucleoside Reverse Transcriptase Inhibitor				
Emtricitabine/rilpivirine/ tenofovir alafenamide (FTC/RPV/TAF; Odefsey) [b]	• **Child-Pugh A, B:** No dose adjustment is needed. • **Child-Pugh C:** No data.	**CrCl <30 mL/min:** Use of FDC is not recommended.	• **FTC:** – **CrCl 30 to 49 mL/min:** 200 mg every 48 hours – **CrCl 15 to 29 mL/min:** 200 mg every 72 hours – **CrCl <15 mL/min:** 200 mg every 96 hours • **RPV:** No renal dose adjustment needed. • **TAF:** – **CrCl <15 mL/min, without HD:** Use is not recommended. – **CrCl <15 mL/min, with HD:** No renal dose adjustment is needed.	• **CrCl <30 mL/min, without HD:** No data to support use of FDC. Renal dose adjustment should be based on individual components. • **CrCl <30 mL/min, with HD:** 1 FDC tablet once daily. On HD days, administer after dialysis [DHHS 2024]. • **Note:** Dose recommended based on data using FTC/TAF as part of FDC with EVG/COBI in patients on HD. In a study of 55 patients on EVG/COBI/FTC/TAF for up to 96 weeks, 18 (33%) had grade 3 or higher ADRs during treatment, and 3 patients discontinued treatment due to adverse effects. The authors concluded that, at 48 weeks, the FDC regimen was well tolerated in patients on HD [Eron(b), et al. 2018].
Doravirine/lamivudine/ tenofovir disoproxil fumarate (DOR/3TC/TDF; Delstrigo)	• **Child-Pugh A, B:** No dose adjustment is needed. • **Child-Pugh C:** No data.	**CrCl <50 mL/min:** Use of FDC is not recommended.	• **DOR:** No renal dose adjustment is needed. • **3TC:** – **CrCl 30 to 49 mL/min:** 150 mg once daily – **CrCl 15 to 29 mL/min:** 150 mg first dose, then 100 mg once daily – **CrCl 5 to 14 mL/min:** 150 mg first dose, then 50 mg once daily – **CrCl <5 mL/min:** 50 mg first dose, then 25 mg once daily • **TDF:** – **CrCl 30 to 49 mL/min:** 300 mg every 48 hours – **CrCl 10 to 29 mL/min:** 300 mg every 72–96 hours – **CrCl <10 mL/min, without HD:** No data available. – **CrCl <10 mL/min, with HD:** 300 mg every 7 days	**CrCl <50 mL/min:** No data to support use of FDC. Renal dose adjustment should be based on individual components.

Table 9: Recommended Dose Adjustments for Use of Selected Fixed-Dose Combination Antiretroviral Medications in Patients With Hepatic or Renal Impairment				
		Renal Impairment Dose Adjustment		
Fixed-Dose Combination	**Hepatic Impairment Dose Adjustment [a]**	**Recommended Dose Adjustment [a]**	**Individual FDC Components and Recommended Dose Adjustment [a]**	**Clinical Comments**
Efavirenz/lamivudine/ tenofovir disoproxil fumarate (EFV/3TC/TDF; Symfi Lo)	• **Child-Pugh A:** No dose adjustment is needed. • **Child-Pugh B, C:** No data; do not use.	**CrCl <50 mL/min:** Use of FDC is not recommended.	• **EFV:** No renal dose adjustment is needed. • **3TC:** – **CrCl 30 to 49 mL/min:** 150 mg once daily – **CrCl 15 to 29 mL/min:** 150 mg first dose, then 100 mg once daily – **CrCl 5 to 14 mL/min:** 150 mg first dose, then 50 mg once daily • **TDF:** – **CrCl 30 to 49 mL/min:** 300 mg every 48 hours – **CrCl 10 to 29 mL/min:** 300 mg every 72–96 hours – **CrCl <10 mL/min, without HD:** No data available. – **CrCl <10 mL/min, with HD:** 300 mg every 7 days	**CrCl <50 mL/min:** No data to support use of FDC. Renal dose adjustment should be based on individual components.
Efavirenz/emtricitabine/ tenofovir disoproxil fumarate (EFV/FTC/TDF; Atripla)	• **Child-Pugh A:** No dose adjustment is needed. • **Child-Pugh B, C:** No data; do not use.	**CrCl <50 mL/min:** Use of FDC is not recommended.	• **EFV:** No renal dose adjustment is needed. • **FTC:** – **CrCl 30 to 49 mL/min:** 200 mg every 48 hours – **CrCl 15 to 29 mL/min:** 200 mg every 72 hours – **CrCl <15 mL/min:** 200 mg every 96 hours • **TDF:** – **CrCl 30 to 49 mL/min:** 300 mg every 48 hours – **CrCl 10 to 29 mL/min:** 300 mg every 72–96 hours – **CrCl <10 mL/min, without HD:** No data available. – **CrCl <10 mL/min, with HD:** 300 mg every 7 days	**CrCl <50 mL/min:** No data to support use of FDC. Renal dose adjustment should be based on individual components.

Table 9: Recommended Dose Adjustments for Use of Selected Fixed-Dose Combination Antiretroviral Medications in Patients With Hepatic or Renal Impairment				
		Renal Impairment Dose Adjustment		
Fixed-Dose Combination	**Hepatic Impairment Dose Adjustment [a]**	**Recommended Dose Adjustment [a]**	**Individual FDC Components and Recommended Dose Adjustment [a]**	**Clinical Comments**
Protease Inhibitor				
Darunavir/cobicistat/ emtricitabine/tenofovir alafenamide (DRV/COBI/FTC/TAF; Symtuza) [b]	• **Child-Pugh A, B:** No dose adjustment is needed. • **Child-Pugh C:** Do not use.	**CrCl <30 mL/min:** Use of FDC is not recommended.	• **DRV; DRV/COBI:** No renal dose adjustment required unless when combined with TDF. Renal dose adjustment for CrCl <70 mL/min is recommended when combined with TDF. • **FTC:** – **CrCl 30 to 49 mL/min:** 200 mg every 48 hours – **CrCl 15 to 29 mL/min:** 200 mg every 72 hours – **CrCl <15 mL/min:** 200 mg every 96 hours • **TAF:** – **CrCl <15 mL/min, without HD:** Use is not recommended. – **CrCl <15 mL/min, with HD:** No renal dose adjustment is needed.	• **CrCl <30 mL/min, without HD:** No data to support use of FDC. Renal adjustment should be based on individual components. • **CrCl <30mL/min, with HD:** 1 FDC tablet once daily. On HD days, administer after dialysis [DHHS 2024]. • **Note:** Dose recommended based on data using FTC/TAF as part of FDC with EVG/COBI in patients on HD. In a study of 55 patients on EVG/COBI/FTC/TAF for up to 96 weeks, 18 (33%) had grade 3 or higher ADRs during treatment, and 3 patients discontinued treatment due to adverse effects. The authors concluded that, at 48 weeks, the FDC regimen was well tolerated in patients on HD [Eron(b), et al. 2018].
Nucleoside/Nucleotide Reverse Transcriptase Inhibitors				
Emtricitabine/tenofovir alafenamide (FTC/TAF; Descovy)	• **Child-Pugh A, B:** No dose adjustment is needed. • **Child-Pugh C:** No data.	**CrCl <30 mL/min:** Use of FDC is not recommended.	• **FTC:** – **CrCl 30 to 49 mL/min:** 200 mg every 48 hours – **CrCl 15 to 29 mL/min:** 200 mg every 72 hours – **CrCl <15 mL/min:** 200 mg every 96 hours • **TAF:** – **CrCl <15 mL/min, without HD:** Use is not recommended. – **CrCl <15 mL/min, with HD:** No renal dose adjustment is needed.	• **CrCl <30 mL/min, without HD:** No data to support use of FDC. Renal adjustment should be based on individual components. • **CrCl <30 mL/min, with HD:** 1 FDC once daily. On HD days, administer after HD [DHHS 2024]. • **Note:** Dose recommended based on data using FTC/TAF as part of FDC with EVG/COBI in patients on HD. In a study of 55 patients on EVG/COBI/FTC/TAF for up to 96 weeks, 18 (33%) had grade 3 or higher ADRs during treatment, and 3 patients discontinued treatment due to adverse effects. The authors concluded that, at 48 weeks, the FDC regimen was well tolerated in patients on HD [Eron(b), et al. 2018].

Table 9: Recommended Dose Adjustments for Use of Selected Fixed-Dose Combination Antiretroviral Medications in Patients With Hepatic or Renal Impairment

Fixed-Dose Combination	Hepatic Impairment Dose Adjustment [a]	Renal Impairment Dose Adjustment		
		Recommended Dose Adjustment [a]	Individual FDC Components and Recommended Dose Adjustment [a]	Clinical Comments
Emtricitabine/tenofovir disoproxil fumarate (FTC/TDF; Truvada)	**Child-Pugh A, B, C:** No dose adjustment is needed.	• **CrCl 30 to 49 mL/min:** FTC 200 mg/TDF 300 mg every 48 hours • **CrCl <30 mL/min:** Use of FDC is not recommended.	• **FTC:** – **CrCl 30 to 49 mL/min:** 200 mg every 48 hours – **CrCl 15 to 29 mL/min:** 200 mg every 72 hours – **CrCl <15 mL/min:** 200 mg every 96 hours • **TDF:** – **CrCl 30 to 49 mL/min:** 300 mg every 48 hours – **CrCl 10 to 29 mL/min:** 300 mg every 72 to 96 hours – **CrCl <10 mL/min, without HD:** No data available. – **CrCl <10 mL/min, with HD:** 300 mg every 7 days	**CrCl <30 mL/min:** No data to support use of FDC. Renal dose adjustment should be based on individual components.

Abbreviations: ADR, adverse drug reaction; AUC, area under the curve; C_{max}, maximum plasma concentration; C_{min}, minimum plasma concentration; CrCl, creatinine clearance; FDC, fixed-dose combination; eGFR, estimated glomerular filtration rate; ESRD, end-stage renal disease; HD, hemodialysis; INSTI, integrase strand transfer inhibitor.

Notes:

a. Per prescribing information; see links.
b. Per prescribing information, FTC can be used at standard dose in FDCs that contain FTC/TAF when CrCl is >30 mL/min. FTC as an individual component requires renal dose adjustment when CrCl is <50 mL/min.

Other ARVs, not included above:

- Tenofovir disoproxil fumarate/emtricitabine/rilpivirine (TDF/FTC/RPV; Complera):
  - Renal dose adjustment: CrCl <50 mL/min: Do not use.
  - Hepatic dose adjustment: Child-Pugh A, B—no adjustment; Child-Pugh C—no data.
- Atazanavir (ATV; Reyataz):
  - Renal dose adjustment: No adjustment, but use only 300 mg dose with 100 mg RTV; do not use in treatment-experienced patients on HD.
  - Hepatic dose adjustment: Child-Pugh A, B—no adjustment; Child-Pugh C—no data.
- Atazanavir/cobicistat (ATV/COBI; Evotaz):
  - Renal dose adjustment: Do not use in patients with CrCl <70 mL/min taking a TDF-containing regimen; do not use in treatment-experienced patients on HD.
  - Hepatic dose adjustment: No data; not recommended.
- Raltegravir (RAL; Isentress):
  - Renal dose adjustment: None.
  - Hepatic dose adjustment: 400 mg twice daily: Child-Pugh A, B—no adjustment; Child-Pugh C—no data. 600 mg once daily: No data; use with caution.

References

DHHS. Guidelines for the use of antiretroviral agents in adults and adolescents living with HIV. 2024 Sep 12. https://clinicalinfo.hiv.gov/en/guidelines/adult-and-adolescent-arv/whats-new-guidelines [accessed 2024 Oct 15]

Eron(b) JJ, Lelievre JD, Kalayjian R, et al. Safety of elvitegravir, cobicistat, emtricitabine, and tenofovir alafenamide in HIV-1-infected adults with end-stage renal disease on chronic haemodialysis: an open-label, single-arm, multicentre, phase 3b trial. *Lancet HIV* 2018;6(1):e15–24. [PMID: 30555051] https://pubmed.ncbi.nlm.nih.gov/30555051

FDA(c). Tivicay (dolutegravir) tablets, for oral use. 2024 Apr. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/204790s031,213983s004lbl.pdf [accessed 2024 Oct 15]

Fischetti B, Shah K, Taft DR, et al. Real-world experience with higher-than-recommended doses of lamivudine in patients with varying degrees of renal impairment. *Open Forum Infect Dis* 2018;5(10):ofy225. [PMID: 30302352] https://pubmed.ncbi.nlm.nih.gov/30302352

German(b) P, Wei X, Mizuno V, et al. Pharmacokinetics of elvitegravir and cobicistat in subjects with severe renal impairment. 13 International Workshop on Clinical Pharmacology of HIV Therapy; 2012 Apr 16–18; Barcelona, Spain. https://www.natap.org/2012/pharm/Pharm_29.htm

Michienzi SM, Schriever CA, Badowski ME. Abacavir/lamivudine/dolutegravir single tablet regimen in patients with human immunodeficiency virus and end-stage renal disease on hemodialysis. *Int J STD AIDS* 2019;30(2):181–87. [PMID: 30381029] https://pubmed.ncbi.nlm.nih.gov/30381029

Zhang H, Shao Y, Garner W, et al. The effect of hepatic or renal impairment on bictegravir pharmokinetics. 18th International Workshop on Clinical Pharmacology of Antiviral Therapy; 2017 Jun 14–17; Chicago, IL. https://www.natap.org/2017/Pharm/Pharm_31.htm