Antiretroviral Dosing in Adults with Renal Impairment

Revised November 2022

Protease Inhibitors (PIs)

Antiretroviral	Usual adult dose	Considerations for renal impairment	Considerations for haemodialysis
Atazanavir alone (ATV)	400 mg once daily	No dosage adjustment is needed for atazanavir in renal impairment	Atazanavir use in haemodialysis patients is not recommended in the European label. Atazanavir pharmacokinetic parameters decreased by 25-43% in patients undergoing haemodialysis compared to patients with normal renal function.
Atazanavir/cobicistat (ATV/c)	300/150 mg once daily	No special precautions or dose adjustments of ATV/c are required for patients with renal impairment. ATV/c should not be initiated in patients with CrCl <70 ml/min if any co-administered agent requires dose adjustment based on creatinine clearance. Cobicistat decreases estimated creatinine clearance due to inhibition of tubular secretion of creatinine. This should be taken into consideration when the estimated creatinine clearance is used to guide aspects of clinical management, including adjusting doses of co-administered medicinal products.	ATV/c is not recommended for haemodialysis patients.
Atazanavir/ritonavir (ATV/r)	300/100 mg once daily	No dosage adjustment is needed for atazanavir in renal impairment	ATV/r is not recommended in haemodialysis patients in the European label. The US label states that ATV/r is not recommended in HIV-treatment-experienced haemodialysis patients but can be used in HIV-treatment-naive haemodialysis patients.
Darunavir/cobicistat (DRV/c)	800/150 mg once daily	Based on the very limited renal elimination of cobicistat and darunavir, no special precautions or dose adjustments of DRV/c are required for patients with renal impairment DRV/c should not be initiated in patients with CrCl <70 ml/min if any co-administered agent requires dose adjustment based on creatinine clearance. Cobicistat decreases estimated creatinine clearance due to inhibition of tubular secretion of creatinine. This should be taken into consideration when the estimated creatinine clearance is used to guide aspects of clinical management, including adjusting doses of co-administered medicinal products.	Darunavir, cobicistat, or the combination of both have not been studied in patients receiving dialysis, and therefore no recommendation can be made for these patients.
Darunavir/ritonavir (DRV/r)	*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	No dose adjustment is required for darunavir/ritonavir in patients with renal impairment. The pharmacokinetics of darunavir were not significantly affected in HIV-infected subjects with CrCl 30-60 m/min (n=20). No pharmacokinetic data are available in HIV-1-infected patients with severe renal impairment or end stage renal disease. However, because the renal clearance of darunavir is limited, a decrease in total body clearance is not expected in patients with renal impairment.	As darunavir and ritonavir are highly bound to plasma proteins, it is unlikely that they will be significantly removed by haemodialysis or peritoneal dialysis. No special precautions or dose adjustments are required.
Lopinavir/ritonavir (LPV/r)	400/100 mg twice daily 800/100 mg once daily	Since the renal clearance of lopinavir and ritonavir is negligible, increased plasma concentrations are not expected in patients with renal impairment.	As lopinavir and ritonavir are highly protein bound, they are unlikely to be significantly removed by haemodialysis.
Ritonavir	(Dose depends on coadministered PI)	Since the renal clearance of ritonavir is negligible, no changes in the total body clearance are expected in patients with renal impairment. As ritonavir is primarily metabolised by the liver, ritonavir may be appropriate for use with caution as a pharmacokinetic enhancer in patients with renal insufficiency depending on the specific protease inhibitor with which it is co-administered.	As ritonavir is highly protein bound it is unlikely that it will be significantly removed by haemodialysis.

Key: *No dose alteration required* | *Alteration in dose or dosing interval; or monitoring recommended for some levels of renal impairment/dialysis* | *Not recommended for any level of renal impairment/dialysis*

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Antiretroviral Dosing in Adults with Renal Impairment

Revised November 2022

Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs)

Antiretroviral	Usual adult dose	Considerations for renal impairment	Considerations for haemodialysis
Doravirine	100 mg once daily	No dose adjustment is required in patients with mild, moderate, or severe renal impairment. Doravirine has not been studied in patients with end-stage renal disease.	Data from 8 patients on intermittent haemodialysis (4 hour) showed doravirine was moderately removed by haemodialysis but doravirine concentrations at the end of the haemodialysis session (785 (101-1851) ng/ml) remained far above the protein binding adjusted EC50 (5 ng/ml) (*Molto et al, 2022*).
Efavirenz	600 mg once daily	The pharmacokinetics of efavirenz have not been studied in patients with renal insufficiency. <1% of a dose is excreted unchanged in the urine, so the impact of renal impairment on efavirenz elimination should be minimal. There is no experience in patients with severe renal failure and close safety monitoring is recommended in this population.	Since efavirenz is highly protein bound, dialysis is unlikely to significantly remove the drug from blood.
Etravirine	200 mg twice daily	No dose adjustment is required in patients with renal impairment. The pharmacokinetics of etravirine have not been studied in patients with renal insufficiency. <1.2% of the administered dose of etravirine is excreted in the urine. The impact of renal impairment on etravirine elimination is expected to be minimal.	As etravirine is highly bound to plasma proteins, it is unlikely that it will be significantly removed by haemodialysis or peritoneal dialysis
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)	Patients with CrCl ≥20 ml/min do not require a dose adjustment. Renal impairment (mild, moderate and severe) resulted in no significant change in the pharmacokinetics of nevirapine. The pharmacokinetics of nevirapine have not been evaluated in patients with CrCl <20 ml/min.	Patients with ESRD requiring dialysis exhibited a 43.5% reduction in nevirapine AUC over a one-week exposure period, and accumulation of nevirapine hydroxy-metabolites in plasma. An additional 200 mg dose of nevirapine (immediate release) following each dialysis treatment is recommended for patients requiring dialysis. Nevirapine metabolites may accumulate in patients receiving dialysis; however, the clinical significance of this is not known.
Rilpivirine	25 mg once daily	No dose adjustment is required in patients with mild or moderate renal impairment. In patients with severe renal impairment or end-stage renal disease, rilpivirine should be used with caution and with increased monitoring for adverse effects. In patients with severe renal impairment or end-stage renal disease, the combination of rilpivirine with a strong CYP3A inhibitor (e.g. ritonavir-boosted HIV protease inhibitor) should only be used if the benefit outweighs the risk (European label). Treatment with rilpivirine may result in an early small increase of mean serum creatinine levels which is not considered clinically relevant	As rilpivirine is highly bound to plasma proteins, it is unlikely that it will be significantly removed by haemodialysis or peritoneal dialysis

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Antiretroviral Dosing in Adults with Renal Impairment

Revised November 2022

Nucleoside/tide Reverse Transcriptase Inhibitors (1/2)

<table>
<tr><th>Antiretroviral</th><th>Usual adult dose</th><th>Considerations for renal impairment</th><th>Considerations for haemodialysis</th></tr>
<tr><td>Abacavir</td><td>300 mg twice daily
or
600 mg once daily</td><td>No dosage adjustment of abacavir is necessary in patients with renal impairment.
Abacavir is not recommended for patients with ESRD.</td><td>It is not known whether abacavir can be removed by haemodialysis.</td></tr>
<tr><td>Emtricitabine</td><td>Hard Capsules:
200 mg once daily

10 mg/ml Oral Solution:
240 mg (24 ml) once daily</td><td>Emtricitabine is eliminated by renal excretion and exposure was significantly increased in patients with renal insufficiency. Dose OR dose interval adjustment is required in all patients with CrCl <30 ml/min (European label) or <50 ml/min (US label). Clinical response to treatment and renal function should be closely monitored.
<table>
<tr><th>Creatinine clearance (ml/min)</th><th>Hard capsules</th><th>Oral solution</th></tr>
<tr><td>≥30 (European label)</td><td>200 mg every 24 h</td><td>240 mg (24 ml) every 24 h</td></tr>
<tr><td>30-49 (US label)</td><td>200 mg every 48 h</td><td>120 mg (12 ml) every 24 h</td></tr>
<tr><td>15-29</td><td>200 mg every 72 h</td><td>80 mg (8 ml) every 24 h</td></tr>
<tr><td><15 (and/or intermittent haemodialysis*)</td><td>200 mg every 96 h</td><td>60 mg (6 ml) every 24 h</td></tr>
</table>
*Dosing for intermittent dialysis assumes a 3h haemodialysis session three times weekly; at least 12h after administration of the last dose of emtricitabine.</td><td>If dosing on day of dialysis, give dose after dialysis.
In patients with ESRD on haemodialysis, ~30% of the emtricitabine dose was recovered in dialysate over a 3 hour dialysis period, started within1.5 hours of emtricitabine dosing (blood flow rate 400 ml/min; dialysate flow rate ~600 ml/min).
Patients with ESRD managed with other forms of dialysis such as ambulatory peritoneal dialysis have not been studied and dose recommendations cannot be made.</td></tr>
<tr><td>Lamivudine</td><td>300 mg once daily
or
150 mg twice daily</td><td>Lamivudine concentrations are increased in patients with moderate-severe renal impairment due to decreased clearance. Dosing is adjusted according to renal function.
<table>
<tr><th>Creatinine clearance (ml/min)</th><th>First dose</th><th>Maintenance dose</th></tr>
<tr><td>30-<50</td><td>150 mg</td><td>150 mg once daily</td></tr>
<tr><td>15 to <30</td><td>150 mg</td><td>100 mg once daily*</td></tr>
<tr><td>5 to <15</td><td>150 mg</td><td>50 mg once daily*</td></tr>
<tr><td><5</td><td>50 mg*</td><td>25 mg once daily*</td></tr>
</table>
* Use oral solution for doses <150 mg</td><td>No additional dosing of lamivudine is required after routine (4 hour) haemodialysis or peritoneal dialysis.</td></tr>
</table>

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Antiretroviral Dosing in Adults with Renal Impairment

Revised November 2022

Nucleoside/tide Reverse Transcriptase Inhibitors (2/2)

<table>
<tr><th>Antiretroviral</th><th>Usual adult dose</th><th>Considerations for renal impairment</th><th>Considerations for haemodialysis</th></tr>
<tr><td>Tenofovir-DF
(TDF)</td><td>245 mg once daily</td><td>Tenofovir should only be used in patients with renal impairment if the potential benefits of treatment outweigh potential risks. The European label recommends dose adjustment using tenofovir granules rather than tablets where possible.
<table>
<tr><th rowspan="2">Creatinine clearance (ml/min)</th><th colspan="2">Tenofovir-DF Dose</th></tr>
<tr><th>Granules</th><th>Tablet (if unable to take granules)</th></tr>
<tr><td>30-49</td><td>132 mg (4 scoops) once daily</td><td>245 mg every 48 h</td></tr>
<tr><td>20-29</td><td>65 mg (2 scoops) once daily</td><td>245 mg twice a week</td></tr>
<tr><td>10-19</td><td>33 mg (1 scoop) once daily</td><td>245 mg twice a week</td></tr>
<tr><td><10 (no haemodialysis)</td><td colspan="2">No dosing recommendations can be given</td></tr>
<tr><td>Haemodialysis</td><td>16.5 mg (0.5 scoop) once daily</td><td>245 mg every 7 days</td></tr>
</table>
Renal failure, renal impairment, elevated creatinine, hypophosphataemia and proximal tubulopathy (including Fanconi syndrome) have been reported with the use of tenofovir-DF in clinical practice. Monitoring of renal function is recommended.</td><td>Once daily dosing of tenofovir granules (16.5 mg) may be given following completion of a 4 hour haemodialysis session.
Once weekly dosing of tenofovir tablets (245 mg) assumes three haemodialysis sessions per week, each of ~4 h duration, or after 12 cumulative hours of haemodialysis. Tenofovir should be administered following completion of a dialysis session.
Tenofovir is efficiently removed by haemodialysis with an extraction coefficient of ~ 54%.</td></tr>
<tr><td>Tenofovir alafenamide (TAF)</td><td>(Dose depends on coadministered ARV)</td><td>For dose modifications of fixed-dose combinations containing tenofovir alafenamide, please see listings for the combination.</td><td></td></tr>
<tr><td>Zidovudine
(ZDV)</td><td>250 mg twice daily
or
300 mg twice daily</td><td>No dose adjustment required for mild or moderate renal impairment.
<table>
<tr><th>Creatinine clearance (ml/min)</th><th>Zidovudine Dose</th></tr>
<tr><td><10 (European label)
<15 (US label)</td><td>100 mg every 6-8 h (300-400 mg daily)</td></tr>
<tr><td>Haemodialysis or peritoneal dialysis</td><td>100 mg every 6-8 h (300-400 mg daily)</td></tr>
</table>
Haematological parameters and clinical response may influence the need for subsequent dosage adjustment</td><td>Haemodialysis and peritoneal dialysis have no significant effect on zidovudine elimination whereas elimination of the inactive glucuronide metabolite is increased.</td></tr>
</table>

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Antiretroviral Dosing in Adults with Renal Impairment

Revised November 2022

Integrase Inhibitors

Antiretroviral	Usual adult dose	Considerations for renal impairment	Considerations for haemodialysis
Bictegravir	50 mg once daily (as fixed dose combination with emtricitabine and tenofovir alafenamide)	*For dose modifications of the fixed-dose combination containing bictegravir, please see listings for the combination.*	
Cabotegravir	30 mg orally once daily (with rilpivirine) or 400 mg IM injection monthly (with rilpivirine IM) or 600 mg IM injection every 2 months (with rilpivirine IM) *PrEP* 600 mg IM injection every 2 months	The European product label advises no dosage adjustment is required in patients with mild to severe renal impairment (CrCl <30 mL/min) and not on dialysis. The American product label advises no dosage adjustment in patients with mild or moderate renal impairment, but recommends increased monitoring for adverse effects in individuals with severe renal impairment (CrCl 15 to <30 mL/min) or end-stage renal disease (CrCl <15 mL/min).	Cabotegravir has not been studied in patients with end-stage renal disease on renal replacement therapy. As cabotegravir is greater than 99% protein bound, dialysis is not expected to alter exposures of cabotegravir. If administered in a patient on renal replacement therapy, cabotegravir should be used with caution.
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.	Exposure to dolutegravir decreased by ~40% in subjects with severe renal impairment. The mechanism is unknown. No dosage adjustment is recommended in the European label for patients with any degree of renal impairment. The US label advises caution is warranted for patients with severe renal impairment if INSTI resistance is documented or suspected, as the decrease in dolutegravir concentrations may result in loss of therapeutic effect and development of resistance.	Data from 10 subjects on dolutegravir while receiving haemodialysis for at least 6 months suggest dolutegravir was generally safe and effective for use at standard dosages (*Kreft et al, 2019*).
Elvitegravir	150 mg once daily (as fixed dosed combination with cobicistat, emtricitabine, and tenofovir-DF or tenofovir alafenamide)	*For dose modifications of fixed-dose combinations containing elvitegravir, please see listings for the combination.*	
Raltegravir	400 mg twice daily or 1200 mg once daily (if treatment naïve or virally suppressed on 400 mg twice daily)	No dosage adjustment is required for patients with renal impairment. In adults, there were no clinically important pharmacokinetic differences between patients with severe renal insufficiency and healthy subjects.	Avoid dosing before a dialysis session. Case reports (both of 2 patients) suggest minimal removal of raltegravir by haemodialysis (*Molto et al, 2010*) and that raltegravir twice daily is safe in patients on haemodialysis with long-term viral suppression (*Yanagisawa K et al, 2016*).

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Antiretroviral Dosing in Adults with Renal Impairment

Revised November 2022

Entry, Attachment and Capsid Inhibitors

Antiretroviral	Usual adult dose	Considerations for renal impairment	Considerations for haemodialysis
Albuvirtide	320 mg by IV infusion once a week	The pharmacokinetics of albuvirtide have not been assessed in patients with renal impairment.	No specific recommendations.
Enfuvirtide	90 mg SC twice daily	No dose adjustment is required for patients with renal impairment including those receiving dialysis. Analysis of plasma concentration data from patients in clinical trials indicated that the clearance of enfuvirtide is not affected to any clinically relevant extent in patients with mild to moderate renal impairment. Data are limited in patients with moderate to severe renal impairment, and in patients maintained on dialysis. Enfuvirtide should be used with caution in these populations. In a renal impairment study AUC of enfuvirtide was increased on average by 43-62% in patients with severe or end stage renal disease compared to patients with normal renal function.	Haemodialysis did not significantly alter enfuvirtide clearance. Less than 13% of the dose was removed during haemodialysis. No dose adjustment is required for patients receiving dialysis.
Fostemsavir	600 mg twice daily	No dosage adjustment is required for patients with renal impairment or those on haemodialysis. A clinical study showed there was no clinically relevant effect of renal impairment on pharmacokinetic exposure parameters (Cmax and AUCs) of temsavir in subjects with mild, moderate or severe renal impairment or in patients with end stage renal disease on haemodialysis.	Temsavir was not readily cleared by haemodialysis; ~12.3% of the dose was removed during a 4-hour haemodialysis session. Haemodialysis initiated 4 hours after temsavir dosing increased temsavir Cmax by 46% and decreased AUC by 11%, when compared to PK off haemodialysis.
Ibalizumab	Loading dose: 2000 mg IV Maintenance dose: 800 mg IV every 2 weeks	No formal studies were conducted to examine the effects of renal impairment on the pharmacokinetics of ibalizumab. Renal impairment is not anticipated to impact the pharmacokinetics of ibalizumab.	No specific recommendations.
Lenacapavir	*Oral loading doses prior to SC injections every 6 months:* 600 mg/day orally on days 1 & 2 300 mg/day orally on day 8	No dose adjustment is required in patients with mild, moderate, or severe renal impairment. Lenacapavir AUC and Cmax increased by 84% and 162% in subjects with severe renal impairment compared with those with normal renal function; however, this was not considered clinically relevant. Lenacapavir has not been studied in patients with end stage renal disease (CrCl <15 mL/min or on renal replacement therapy) and should be used with caution in these patients.	As lenacapavir is approximately 99.8% protein bound, dialysis is not expected to alter exposures of lenacapavir.
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	Exposures in subjects with severe renal impairment and end stage renal disease were within the range observed in single maraviroc 300 mg dose studies with normal renal function. Dose adjustment in renal impairment depends on coadministered drugs. **Creatinine clearance (ml/min)** / **Maraviroc dose** <80 (without a potent CYP3A4 inhibitor) — No dose adjustment 30-79 (with a potent CYP3A4 inhibitor) — 150 mg once daily <30 (with a potent CYP3A4 inhibitor) — 150 mg once daily with caution (European label) Contraindicated (US label) An increased risk of postural hypotension may occur in patients with severe renal insufficiency who are treated with potent CYP3A inhibitors and maraviroc.	Dialysis had a minimal effect on exposure in subjects with end stage renal disease.

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Antiretroviral Dosing in Adults with Renal Impairment

Revised November 2022

Fixed Dose Combinations - PIs + NRTIs

Name	ARVs	Considerations for renal impairment	Considerations for haemodialysis
Symtuza	Darunavir/cobicistat + Emtricitabine Tenofovir alafenamide	No dose adjustment of Symtuza is required in patients with CrCl ≥30 ml/min. Symtuza is not recommended in patients with CrCl <30 ml/min, as there are no data available regarding the use of Symtuza in this population. Symtuza should be discontinued in patients if CrCl declines below 30 ml/min during treatment. Cobicistat decreases estimated creatinine clearance due to inhibition of tubular secretion of creatinine. This should be taken into consideration when the estimated creatinine clearance is used to guide aspects of clinical management, including adjusting doses of co-administered medicinal products.	No specific recommendation.

Fixed Dose Combinations - NNRTIs + NRTIs

Name	ARVs	Considerations for renal impairment	Considerations for haemodialysis
Atripla	Efavirenz + Emtricitabine Tenofovir-DF	Atripla is not recommended for patients with moderate or severe renal impairment (CrCl <50 ml/min). Such patients require dose interval adjustment of emtricitabine and tenofovir-DF that cannot be achieved with a fixed dose combination tablet. As Atripla may cause renal damage, monitoring of renal function is recommended (European label).	No specific recommendation.
Delstrigo	Doravirine + Lamivudine Tenofovir-DF	No dose adjustment of Delstrigo is required in adults with CrCl ≥50 ml/min. Delstrigo should not be initiated in patients with CrCl <50 ml/min and should be discontinued if CrCl declines below 50 ml/min, as patients with moderate or severe renal impairment require a dose interval adjustment of lamivudine and tenofovir-DF that cannot be achieved with a fixed dose combination tablet.	No specific recommendation.
Eviplera (Europe) **Complera (US)**	Rilpivirine + Emtricitabine Tenofovir-DF	Limited data from clinical studies support use of Complera/Eviplera in patients with mild renal impairment (CrCl 50-80 ml/min) if potential benefits outweigh risks. Complera/Eviplera is not recommended in patients with moderate or severe renal impairment or end stage renal disease (CrCl <50 ml/min). Such patients require a dose interval adjustment of emtricitabine and tenofovir-DF that cannot be achieved with a fixed dose combination tablet.	Complera is not recommended in patients that require dialysis (US label).
Odefsey	Rilpivirine + Emtricitabine Tenofovir alafenamide	No dose adjustment is required in patients with CrCl) ≥30 ml/min. Odefsey should be discontinued in patients with estimated CrCl that declines below 30 ml/min during treatment. No dose adjustment is required in adults with end stage renal disease (CrCl <15 ml/min) on chronic haemodialysis. However, Odefsey should, generally, be avoided but may be used with caution in these patients if the potential benefits are considered to outweigh the potential risks. Odefsey is not recommended in patients with CrCl 15-29 ml/min, or in patients with CrCl <15 ml/min who are not on chronic haemodialysis, as the safety of Odefsey has not been established in these populations.	On days of haemodialysis, Odefsey should be administered after completion of haemodialysis treatment.

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Antiretroviral Dosing in Adults with Renal Impairment

Revised November 2022

Fixed Dose Combinations – multiple NRTIs

Name	ARVs	Considerations for renal impairment	Considerations for haemodialysis
Combivir	Lamivudine Zidovudine	Lamivudine and zidovudine concentrations increase in patients with renal impairment due to decreased clearance. Combivir is not recommended for patients with CrCl <30 ml/min (European label, 2022) or <50 ml/min (US label, 2019) as dosage adjustment of lamivudine and zidovudine may be necessary and cannot be achieved with a fixed dose combination tablet. If a dose reduction of lamivudine or zidovudine is required for patients with renal impairment, individual components should be used.	No specific recommendation.
Descovy	Emtricitabine Tenofovir alafenamide	No dose adjustment of Descovy is required in patients with CrCl ≥30 ml/min. Descovy should be discontinued in patients with estimated CrCl that declines <30 ml/min during treatment. No dose adjustment of Descovy is required in patients with ESRD (CrCl <15 ml/min) on chronic haemodialysis. However; Descovy should only be used (and with caution) in these patients if the benefits outweigh the risks as emtricitabine exposure was significantly higher in these patients. Descovy should be avoided in patients with CrCl 15-29 ml/min, or in patients with CrCl<15 ml/min who are not on chronic haemodialysis, as the safety of Descovy has not been established in these populations.	On days of haemodialysis, Descovy should be administered after completion of haemodialysis treatment.
Kivexa (Europe) **Epzicom (US)**	Abacavir Lamivudine	No dose adjustment is required in patients with mild or moderate renal impairment. However, the lamivudine exposure is significantly increased in patients with a creatinine clearance <50 ml/min. Patients with CrCl 30 -49 ml/min should be monitored for lamivudine-related adverse events, notably haematologic toxicities. Kivexa/Epzicom is not recommended for patients with CrCl <30 ml/min as dosage adjustment of lamivudine may be necessary and cannot be achieved with a fixed dose combination tablet. If a dose reduction of lamivudine is required then the individual components should be used.	No specific recommendation.
Trizivir	Abacavir Lamivudine Zidovudine	Trizivir is not recommended for patients with CrCl <30 ml/min (European label) or CrCl <50 ml/min (US label) as dosage adjustment of lamivudine and zidovudine may be necessary and cannot be achieved with a fixed dose combination tablet. If a dose reduction of lamivudine and zidovudine is required, separate preparations of abacavir, lamivudine and zidovudine be used. Trizivir should not be administered to patients with ESRD (European label).	No specific recommendation.
Truvada	Emtricitabine Tenofovir-DF	Emtricitabine and tenofovir exposure increases in patients with renal dysfunction. Truvada should only be used in patients with CrCl <80 ml/min if the potential benefits outweigh the risks.	Use of Truvada for the treatment of HIV or for PrEP is not recommended in patients requiring haemodialysis.

Creatinine clearance (ml/min)	HIV Treatment	PrEP
60-80	No adjustment required. Limited clinical study data support once daily dosing	Limited clinical study data support once daily dosing
50-59		Not recommended
30-49	Administration every 48 h is recommended	Not recommended
<30	Not recommended. Appropriate dose reductions cannot be achieved with the combination tablet.	Not recommended

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Antiretroviral Dosing in Adults with Renal Impairment

Revised November 2022

Fixed Dose Combinations - Integrase Inhibitors + NRTIs

Name	ARVs	Considerations for renal impairment	Considerations for haemodialysis
Biktarvy	Bictegravir + Emtricitabine Tenofovir alafenamide	No dose adjustment of Biktarvy is required in patients with CrCl ≥30 ml/min. No dose adjustment of Biktarvy is required in adult patients with end stage renal disease (ESRD; CrCl <15 ml/min) who are receiving chronic haemodialysis. However, Biktarvy should generally be avoided and only be used in these patients if the potential benefits are considered to outweigh the potential risks Biktarvy is not recommended in patients with CrCl 15-29 ml/min, or in patients with CrCl <15 mL/min who are not receiving chronic haemodialysis, as the safety of Biktarvy has not been established in these populations. Biktarvy is not recommended in patients with no antiretroviral treatment history and ESRD who are receiving chronic haemodialysis (US label).	On days of haemodialysis, administer the daily dose of Biktarvy after completion of haemodialysis treatment. Biktarvy was well tolerated in 10 patients with ESRD on haemodialysis and all patients maintained virological suppression (*Eron et al, 2020*).
Dovato	Dolutegravir + Lamivudine	No dose adjustment is required in patients with mild renal impairment. Dovato is not recommended for patients with CrCl <50 ml/min (European label) or CrCl <30 ml/min (US label) because Dovato is a fixed-dose combination and the dosage of the individual components cannot be adjusted. If a dose reduction of lamivudine, a component of Dovato, is required then the individual components should be used.	No specific recommendation.
Genvoya	Elvitegravir/cobicistat + Emtricitabine Tenofovir alafenamide	No dose adjustment is required in patients with CrCl ≥30 ml/min. Genvoya should be discontinued in patients with CrCl that declines below 30 ml/min during treatment. No dose adjustment of Genvoya is required in adults with ESRD (estimated CrCl <15 ml/min) on chronic haemodialysis; however, Genvoya should only be used in these patients if the benefits outweigh the risks as emtricitabine exposure was significantly higher in these patients. Genvoya is not recommended in patients with estimated CrCl 15-29 ml/min, or in patients with CrCl <15 ml/min who are not on chronic haemodialysis, as the safety of Genvoya has not been established in these populations.	On days of haemodialysis, Genvoya should be administered after completion of haemodialysis treatment. Genvoya was well tolerated in 55 patients with CrCl <15 ml/min on haemodialysis (*Eron et al, 2019*).
Juluca	Dolutegravir + Rilpivirine	No dosage adjustment is required in patients with mild or moderate renal impairment (CrCl ≥30 ml/min). In patients with severe renal impairment (CrCl <30 ml/min) or ESRD, increased monitoring for adverse effects is recommended. The combination of Juluca with a strong CYP3A inhibitor in patients with CrCl <30 ml/min should only be used if the benefit outweighs the risk (European label).	No data are available in subjects receiving dialysis although differences in pharmacokinetics are not expected in this population.
Stribild	Elvitegravir/cobicistat + Emtricitabine Tenofovir-DF	It is recommended that Stribild is not initiated in patients with CrCl <90 ml/min unless, after review of the available treatment options, Stribild is considered the preferred treatment for the individual patient (European label). Stribild should not be initiated in patients with CrCl <70 ml/min. Stribild should be discontinued if CrCl declines <50 ml/min during treatment as dose interval adjustment is required for emtricitabine and tenofovir-DF and this cannot be achieved with the fixed-dose combination tablet.	No specific recommendation
Triumeq	Dolutegravir + Abacavir Lamivudine	Triumeq is not recommended for patients with CrCl <30 ml/min because Triumeq is a fixed-dose combination and the dosage of the individual components cannot be adjusted. No dose adjustment is required in patients with mild or moderate renal impairment. However, the lamivudine exposure is significantly increased in patients with a creatinine clearance <50 ml/min. Patients with CrCl 30 -49 ml/min should be monitored for lamivudine-related adverse events, notably hematologic toxicities. If a dose reduction of lamivudine, a component of Triumeq, is required for patients with CrCl <50 ml/min, then the individual components should be used.	A case series of 9 patients with ESRD receiving haemodialysis suggests that Triumeq may be safe and effective based on viral response, but this should be confirmed in a larger trial with PK analysis (*Michienzi et al, 2019*).

Key: *No dose alteration required* | *Alteration in dose or dosing interval; or monitoring recommended for some levels of renal impairment/dialysis* | *Not recommended for any level of renal impairment/dialysis*

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