Table 35: Anticonvulsants [a] (also see prescribing information)		
→ Including phenytoin, phenobarbital, carbamazepine, oxcarbazepine, lamotrigine, valproic acid, gabapentin, topiramate, zonisamide		
Class or Drug	**Mechanism of Action**	**Clinical Comments**
Tenofovir disoproxil fumarate (TDF)	• **Zonisamide:** TDF may increase concentration of zonisamide. • **Topiramate:** No significant interactions reported.	• **Zonisamide:** When using with TDF, monitor for adverse effects. • **Topiramate:** When using with TDF, monitor renal function (topiramate may cause kidney stones; TDF is associated with renal toxicity).
Tenofovir alafenamide (TAF)	Coadministration with strong CYP3A inducers (phenytoin, phenobarbital, etc.) may decrease TAF concentrations.	Coadministration with strong CYP3A inducers is not recommended because it may reduce TAF concentrations.
Other NRTIs	No interactions reported.	No dose adjustments are necessary.
Cabotegravir (CAB)	• **Carbamazepine, oxcarbazepine, phenobarbital, phenytoin:** Coadministration may significantly reduce CAB concentrations through induction of CYP450, UGT1A, and/or P-gP system. • **Gabapentin, topiramate, zonisamide:** No significant interactions are expected.	• **Carbamazepine, oxcarbazepine, phenobarbital, phenytoin:** Concomitant use is contraindicated. • **Gabapentin, topiramate, zonisamide:** No dose adjustments are necessary.
• Dolutegravir (DTG) • Bictegravir (BIC)	Coadministration with strong CYP3A inducers (phenytoin, phenobarbital, etc.) may decrease DTG or BIC concentrations.	No dose adjustments necessary.
Raltegravir (RAL)	Coadministration with strong UGT1A1 inducers (phenytoin, phenobarbital, etc.) may decrease RAL concentrations.	Coadministration with strong UGT1A1 inducers is not recommended.
Elvitegravir (EVG), boosted	**Carbamazepine, oxcarbazepine, phenobarbital, and phenytoin:** Coadministration may significantly reduce concentrations of ARVs through induction of CYP450 system.	**Carbamazepine, oxcarbazepine, phenobarbital, phenytoin:** • Coadministration is not recommended; use alternative anticonvulsant. • If benefit of use outweighs risk, monitor carefully for efficacy and toxicity. • Perform TDM.
Ritonavir (RTV)	• **Phenytoin:** Concurrent use may reduce RTV and phenytoin concentrations, resulting in loss of viral suppression and seizure control. • **Lamotrigine:** RTV-boosted ARVs may reduce lamotrigine efficacy. • **Valproic acid:** RTV may reduce valproic acid concentrations.	• **Phenytoin:** – Coadministration is not recommended; use alternative anticonvulsant. – If benefit of use outweighs risk, monitor carefully for efficacy and toxicity. – Perform TDM. • **Lamotrigine:** Titrate slowly to achieve clinical effect; monitor for efficacy. • **Valproic acid:** Consider using COBI when ARV boosting is required.

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→ Including phenytoin, phenobarbital, carbamazepine, oxcarbazepine, lamotrigine, valproic acid, gabapentin, topiramate, zonisamide		
Class or Drug	**Mechanism of Action**	**Clinical Comments**
Boosted PIs	• **Carbamazepine, oxcarbazepine, phenobarbital, phenytoin:** Coadministration may significantly reduce concentrations of ARVs through induction of CYP450 system. • **Zonisamide:** CYP3A4 inhibition may increase zonisamide concentrations.	• **Carbamazepine, oxcarbazepine, phenobarbital, phenytoin:** – Coadministration is not recommended; use alternative anticonvulsant. – If benefit of use outweighs risk, monitor carefully for efficacy and toxicity. – Perform TDM. • **Zonisamide:** Monitor for efficacy and adverse effects; adjust dose as needed.
NNRTIs	**Carbamazepine, oxcarbazepine, phenobarbital, and phenytoin:** Coadministration may significantly reduce ARV concentrations through induction of CYP450 system.	**Carbamazepine, oxcarbazepine, phenobarbital, phenytoin:** • Coadministration is not recommended; use alternative anticonvulsant. • If benefit of use outweighs risk, monitor carefully for efficacy and toxicity. • Perform TDM if use cannot be avoided.
Rilpivirine (RPV)	• **Carbamazepine, oxcarbazepine, phenobarbital, phenytoin:** Coadministration may significantly reduce RPV concentrations through induction of CYP450, UGT1A, and/or P-gP system. • **Gabapentin, topiramate, zonisamide:** No significant interactions are expected.	• **Carbamazepine, oxcarbazepine, phenobarbital, phenytoin:** Concomitant use is contraindicated with oral and injectable RPV (see prescribing information for Cabenuva and Edurant). • **Gabapentin, topiramate, zonisamide:** No dose adjustments are necessary.
• Efavirenz (EFV) • Etravirine (ETR)	• **Lamotrigine, zonisamide:** EFV and ETR may reduce lamotrigine and zonisamide efficacy. • **Gabapentin, topiramate:** No significant interactions reported.	• **Lamotrigine, zonisamide:** Titrate slowly to achieve clinical effect; monitor for efficacy. • **Gabapentin, topiramate:** No dose adjustments are necessary.
Fostemsavir (FTR)	**Carbamazepine, oxcarbazepine, phenobarbital, phenytoin:** Significantly reduced FTR levels are expected.	Avoid coadministration due to potential loss of FTR efficacy.
Lenacapavir (LEN) for HIV treatment	**Carbamazepine, eslicarbazepine, oxcarbazepine, phenobarbital, phenytoin, primidone:** CYP3A4 and P-gP induction potentially decreases LEN levels.	• **Carbamazepine, eslicarbazepine, phenytoin:** Do not coadminister. • **Oxcarbazepine, phenobarbital, primidone:** Coadministration is not recommended. • Consider alternative anticonvulsants such as levetiracetam.
Lenacapavir (LEN) for HIV prevention [b]	**Carbamazepine, eslicarbazepine, oxcarbazepine, phenobarbital, phenytoin, primidone:** CYP3A4 and P-gP induction potentially decreases LEN levels.	**Carbamazepine, oxcarbazepine, phenytoin (strong CYP3A4 inducers):** • Consider alternative anticonvulsants such as levetiracetam. • At initiation of strong CYP3A4 inducer in patients already using LEN PrEP, see Table 4 of the Yeztugo prescribing information

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→ Including phenytoin, phenobarbital, carbamazepine, oxcarbazepine, lamotrigine, valproic acid, gabapentin, topiramate, zonisamide		
Class or Drug	**Mechanism of Action**	**Clinical Comments**
		(page 6) for instructions on administering a supplemental dose of LEN PrEP. • After stopping use of strong CYP3A4 inducer, continue to administer LEN PrEP every 6 months as scheduled without supplemental subcutaneous or oral dosing. Supplemental dosing only continues until the patient has stopped the inducer. **Eslicarbazepine, phenobarbital, primidone (moderate CYP3A4 inducers):** • Consider alternative anticonvulsants such as levetiracetam. • At initiation of moderate CYP3A4 inducer in patients already using LEN PrEP, see Table 5 of the Yeztugo prescribing information (page 6) for instructions on administering a supplemental dose of LEN PrEP. • After stopping use of moderate CYP3A4 inducer, continue to administer LEN PrEP every 6 months as scheduled without supplemental subcutaneous dosing. Supplemental dosing only continues until the patient has stopped the inducer.

Abbreviations: ARV, antiretroviral; COBI, cobicistat; CYP, cytochrome P450; NNRTI, non-nucleoside reverse transcriptase inhibitor; NRTI, nucleoside reverse transcriptase inhibitor; P-gP, P-glycoprotein; PI, protease inhibitor; TDM, therapeutic drug monitoring; UGT, uridine diphosphate glucuronosyltransferase.

Notes:

a. Levetiracetam is safe with all ARVs, with no significant interactions expected and no dose adjustments required.
b. For individuals using subcutaneous LEN every 6 months for HIV prevention. No guidance is currently available for (1) individuals using weekly oral LEN for HIV prevention or (2) initiating subcutaneous LEN in individuals already using strong or moderate CYP3A4 inducers.