Summary of Evidence-based Guideline for **CLINICIANS**

# ANTIEPILEPTIC DRUG SELECTION FOR PEOPLE WITH HIV/AIDS

This is a summary of the American Academy of Neurology (AAN) and International League Against Epilepsy (ILAE) guideline regarding antiepileptic drug (AED) selection for people with HIV/AIDS.

***Please refer to the full guideline at AAN.com for more information, including definitions of the classifications of evidence.***

## What is the evidence that AED-antiretroviral (ARV) interactions are clinically meaningful?

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| **Weak evidence** | It may be important to avoid enzyme-inducing AEDs (EI-AEDs) in people on ARV regimens that include protease inhibitors (PIs) or nonnucleotide reverse transcriptase inhibitors (NNRTIs), as pharmacokinetic interactions may result in virologic failure, which has clinical implications for disease progression and development of ARV resistance. If such regimens are required for seizure control, patients may be monitored through pharmacokinetic assessments to ensure efficacy of the ARV regimen (**Level C**). |

## What is the evidence for an interaction between AEDs and PI ARVs?

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| **Phenytoin: impact on lopinavir/ritonavir** | |
| **Weak evidence** | Patients receiving phenytoin may require a lopinavir/ritonavir dosage increase of about 50% to maintain unchanged serum concentrations (**Level C**†). |
| **Atazanavir and atazanavir/ritonavir: impact on lamotrigine** | |
| **Weak evidence** | Coadministration of atazanavir and lamotrigine may not require lamotrigine dosage adjustment (**Level C**). |
| | Patients receiving ritonavir/atazanavir may require a lamotrigine dosage increase of about 50% to maintain unchanged lamotrigine serum concentrations (**Level C**). |

## What is the evidence for interaction between AEDs and integrase inhibitors?

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| **Raltegravir: impact on lamotrigine** | |
| **Weak evidence** | Coadministration of raltegravir and lamotrigine may not require lamotrigine dosage adjustment (**Level C**). |
| **Raltegravir: impact on midazolam** | |
| **Weak evidence** | Coadministration of raltegravir and midazolam may not require midazolam dosage adjustment (**Level C**). |

## What is the evidence for an interaction between AEDs and nucleoside reverse transcriptase inhibitor and NNRTI ARVs?

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| **Valproic acid: impact on efavirenz / Efavirenz: impact on valproic acid** | |
| **Weak evidence** | Coadministration of valproic acid and efavirenz may not require efavirenz dosage adjustment (**Level C**). |
| **Valproic acid: impact on zidovudine** | |
| **Weak evidence** | Patients receiving valproic acid may require a zidovudine dosage reduction to maintain unchanged serum zidovudine concentrations (**Level C**). |

## Effects of combining other AEDs and ARVs

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| **Insufficient evidence** | Patients may be counseled that it is unclear whether dosage adjustment is necessary when other AEDs and ARVs are combined (**Level U**). |

## Clinical context

A retrospective cohort study and numerous pharmacokinetic studies indicate that EI-AEDs interact with ARVs. The optimal choice of epilepsy treatment in patients with HIV should reflect an accounting for the metabolic and inhibitory/inducing profiles of coadministered drugs. Clinicians who prescribe ARVs and AEDs are encouraged to refer to the US Department of Health and Human Services treatment guidelines for HIV/AIDS, which provide specific recommendations for the management of possible drug–drug interactions with AED-ARV combinations (available at *aidsinfo.nih.gov/contentfiles/AdultandAdolescentGL.pdf*). For newer ARV agents, minimal data exist on drug interactions with AEDs.



†**Classification of Recommendations: A** = Established as effective, ineffective or harmful (or established as useful/predictive or not useful/predictive) for the given condition in the specified population. (Level A rating requires at least two consistent Class I studies.)* **B** = Probably effective, ineffective or harmful (or probably useful/predictive or not useful/predictive) for the given condition in the specified population. (Level B rating requires at least one Class I study or two consistent Class II studies.) **C** = Possibly effective, ineffective or harmful (or possibly useful/predictive or not useful/predictive) for the given condition in the specified population. (Level C rating requires at least one Class II study or two consistent Class III studies.) **U** = Data inadequate or conflicting; given current knowledge, treatment (test, predictor) is unproven.

*In exceptional cases, one convincing Class I study may suffice for an "A" recommendation if 1) all criteria are met, 2) the magnitude of effect is large (relative rate improved outcome >5 and the lower limit of the confidence interval is >2).

INTERNATIONAL LEAGUE AGAINST EPILEPSY ILAE

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Copies of this summary and additional companion tools are available at *AAN.com* or through AAN Member Services at (800) 879-1960.