



Interactions between antiepileptic drugs, and between antiepileptic drugs and other drugs

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Received May 15, 2014; Accepted August 6, 2014

Main Mechanisms of Interactions Involving AEDs

- ❖ Alterations in drug absorption, e.g. impairment in phenytoin absorption by some nasogastric tube feedings
- ❖ Plasma protein binding interactions (e.g. displacement of protein-bound phenytoin by valproic acid) → usually clinically not important, except for changed relationship between total serum concentration and effect
- ❖ Inhibition of drug metabolism, e.g. increase in serum lamotrigine levels by valproic acid

Main Mechanisms of Interactions Involving AEDs

- ❖ Induction of drug metabolism, e.g. increased clearance of steroid oral contraceptives by carbamazepine
- ❖ Pharmacodynamic interactions, e.g. increased risk of neurotoxic side effects when combining sodium channel blocking AEDs

Table 2. Pharmacokinetic interactions between AEDs¹. The vertical column refers to the AED which is added. The boxes on each line illustrate the expected changes in serum concentrations of the pre-existing drug. The magnitude of each interactions and its clinical relevance reflects the authors' judgment and need to be interpreted flexibly because intersubject variability in magnitude and consequences can be considerable.

	Pre-existing AED	First generation AEDs								Second-generation AEDs															
		CBZ	CLB	CNP	ETS	PB	PHT	PRM	VPA	ESL	FBM	GBP	LEV	LTG	LCM	PER	PGB	OXC	RTG	RFN	STP	TGB	TPM	VGB	ZNS
AED added																									
CBZ			2	3			4						5		6				7						
CLB ^{III}				9																					
CNP ^x			11																						
ETS ^{III}							13		14																
PB			15	16			17	18					19		20										
PHT			21					22					23		24				25						
PRM			26				27	28					29												
VPA			30				31											34							35
ESL																		36							
FBM			37	38																					
GBP																									
LEV																									
LTG				39					40																
LCM																									
PER ^{III}																									
PGB												43													
OXC			44							45															
RTG ^{III}														47											
RFN																									
STP ^{III}																									
TGB																									
TPM																									
VGB																									
ZNS																									

	Marked increase in serum concentration
	Slight to moderate increase in serum concentration
	No change
	No change anticipated
	Mild to moderate decrease in serum concentration
	Marked decrease in serum concentration
	Not known
	Complex or variable interaction (see note)