

Pharmacogenomics for General Practitioners



Drug Class	Relevance	Major Finding (approx. %)^	Outcome	CPIC Guidelines*	Dutch Pharmacogenetics Working Group Guidelines**
Tricyclic Antidepressants	TCA's are initially converted to an active metabolite by CYP2C19 and then deactivated by CYP2D6; genetic variation in these enzymes can affect blood levels and the likelihood of toxicity or therapy failure	60%	Dose alterations or alternative antidepressants recommended	✓	✓
SSRIs	Most SSRIs are deactivated by CYP2C19 and/or CYP2D6; genetic variation in these enzymes can affect blood levels and the likelihood of toxicity	20-55%	Dose alterations or alternative antidepressants recommended	✓	✓
Duloxetine; Venlafaxine; Mirtazapine	These antidepressants are deactivated by CYP2D6; genetic variation in CYP2D6 may affect blood levels and the likelihood of toxicity	20%	Dose alterations or alternative antidepressants recommended	✗	✓
Proton-pump inhibitors	PPIs are metabolised by CYP2C19; ultrarapid metabolisers may experience sub-therapeutic blood levels at standard doses	30%	Possible explanation for therapy failure and dose alteration suggestions	✗	✓
Codeine, Tramadol	Codeine and tramadol achieve their analgesic effect by endogenous conversion to an active metabolite via CYP2D6; poor metabolisers are unlikely to achieve pain relief; ultrarapid metabolisers may experience toxicity	20%	Possible explanation for therapy failure and alternative analgesics recommended	✓ (Codeine)	✓
NSAIDs	Most NSAIDs are metabolised by CYP2C9; poor metabolism has been associated with elevated blood levels and increased risk of GI bleeding	15%	Lower starting dose recommended for at-risk patients; possible co-administration of PPI	#	#

* The Clinical Pharmacogenetics Implementation Consortium; guidelines are peer-reviewed and published in a leading journal

** Established by the Royal Dutch Pharmacist's Association; guidelines based on systematic literature reviews

^ Major Finding: A genetic result that is predictive of significantly altered drug metabolism; based on an analysis of 4,500 patients tested by My DNA Life; allele frequencies are significantly different in various ethnic groups

Whilst no formal guidelines exist, the FDA has issued a warning regarding the use of celecoxib in CYP2C9 poor metabolisers

For further enquiries contact **1300 436 373** or visit **www.mydna.life**