Changes in pharmacokinetic parameters in patients with chronic kidney disease

Pharmacokinetic parameter	Definition	Influenced by	Examples of changes in chronic kidney disease	Impact of those changes
Absorption	A determinant of drug bioavailability, representing the amount of administered dose reaching systemic circulation	• Gastric pH • Gastrointestinal motility • First-pass metabolism	• Increased gastric pH (conversion of high salivary urea concentrations into ammonia by gastric urease) • Delayed gastric emptying in patients with concomitant diabetic gastroparesis • Gastrointestinal edema occurring in patients with concomitant cirrhosis or congestive heart failure	• Impacts the time required to reach maximal plasma concentration • Decreases maximum plasma concentration
Volume of distribution	The extent of drug distribution throughout the body; especially the amount of drug distributed into extravascular tissues	• Plasma protein binding • Tissue binding • Total body water	• Hypoalbuminemia • Increased concentrations of alpha-1-acid glycoprotein • Fluid retention, increasing total body water	• Impacts concentration of free drug available to bind to receptors • Increased volume of distribution for hydrophilic drugs
Elimination	The extent of drug clearance either renally or nonrenally	• Renal: number of functioning nephrons, renal blood flow, glomerular filtration rate, and tubular secretion • Nonrenal: hepatic and extrahepatic metabolism (cytochrome P450, UGT, and NAT enzymes), and transport pathways	Renal • Decreased amount of functioning nephrons • Reduced renal blood flow • Reduced glomerular filtration rate • Reduced tubular secretion Nonrenal • Decreased activity of cytochrome P450, UGT, and NAT • Cytochrome P450 3A4 downregulation via direct inhibition by uremic toxins	• Diminished overall elimination leading to overall drug accumulation

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Data compiled from:

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