

Losartan

Class: Angiotensin II Receptor Antagonist (ARB), Antihypertensive Agent

Pharmacokinetics

Absorption

- i.) Non-genetic
 - a. Food: decreased absorption rate, slight decrease in area under the curve
 - b. Hepatic insufficiency: ~2-fold higher oral bioavailability
 - c. Gender: plasma concentration twice as high in female vs male hypertensives (metabolite concentrations are similar)
- ii.) Genetic
 - a. No clear genetic factors affecting absorption

Distribution

- i.) Non-genetic
 - a. Altered serum protein (98.7% protein bound, primarily to albumin)
- ii.) Genetic
 - a. No clear genetic factors affecting distribution

Metabolism

- i.) Non-genetic
 - a. Concomitant medications/substances: CYP2C9, CYP3A4 inducers or inhibitors
 - b. Hepatic impairment: reduced clearance
- ii.) Genetic
 - a. Genetic variation in drug metabolizing enzyme gene(s): CYP2C9, CYP3A4, *aldosterone synthase*

Excretion

- i.) Non-genetic
 - a. Renal function: reduced clearance in patients with acute CrCl < 30 mL/min + dialysis
 - b. Congestive heart failure: slightly longer half-life
- ii.) Genetic
 - a. No clear genetic factors affecting excretion

Pharmacodynamics

Receptors

- i.) Non-genetic
 - a. Concomitant medication: angiotensin receptor agonists or antagonists (may block or enhance effects of losartan)
- ii.) Genetic
 - a. Genetic variation in angiotensin II type I receptor gene

Transporters

- i.) Non-genetic
 - a. No clear non-genetic factors affecting transporters
- ii.) Genetic
 - a. No clear genetic factors affecting transporters