Desipramine

Class: Antidepressant, Tricyclic (Secondary Amine)

Pharmacokinetics

Absorption

i.) Non-genetic
   a. Concomitant medications/substances: p-glycoprotein inhibitors

ii.) Genetic
   a. Genetic variation in p-glycoprotein gene

Distribution

i.) Non-genetic
   a. Altered serum protein (90% protein-bound to alpha 1-acid glycoprotein and albumin): free fraction significantly correlated with alpha 1-acid glycoprotein concentration but not with albumin concentration
   b. Concomitant medications/substances: p-glycoprotein inhibitors or activators

ii.) Genetic
   a. Genetic variation in p-glycoprotein gene

Metabolism

i.) Non-genetic
   a. Age: prolonged elimination half-life in elderly
   b. Concomitant medications/substance: CYP2D6 inducers or inhibitors

ii.) Genetic
   a. Genetic variation in CYP2D6 gene: prolonged elimination half-life in poor metabolizers

Excretion

i.) Non-genetic
   a. Renal impairment: decreased elimination results in accumulation of 2-hydroxy metabolite

ii.) Genetic
   a. No clear genetic factors affecting excretion

Pharmacodynamics

Receptors

i.) Non-genetic
   a. No clear non-genetic factors affecting receptors

ii.) Genetic
   a. Genetic variation in alpha-1 adrenergic receptor gene
   b. Genetic variation in G-protein beta-3 subunit gene
   c. Genetic variation in Gs protein alpha subunit gene

Transporters

i.) Non-genetic
   a. Concomitant medications/substances
      i. Norepinephrine or *serotonin* transporter inhibitors (additive effects)
      ii. P-glycoprotein inhibitors or activators

ii.) Genetic
   a. Genetic variation in p-glycoprotein gene
   b. Genetic variation in norepinephrine transporter gene
   c. *Genetic variation in serotonin transporter gene – may not be clinically significant*