# PHA 5127 Dose Optimization I

## Case Study IV

1. For the following situations, indicate whether the drug is: filtered, reabsorbed (if fully or if reabsorbed through transporters), or actively secreted (Assume GFR is 130mL/min, urine flow is 1.5mL/min)

(1) Drug with fu= 0.3 and a $Cl_{ren}$=39mL/min
fu*GFR=0.3*130mL/min=39mL/min
$Cl_{ren}$= fu*GFR → filtered

(2) Drug with fu=0.6 and a $Cl_{ren}$=30mL/min
fu*GFR=0.6*130mL/min=78mL/min
$Cl_{ren}$ < fu* GFR → reabsorbed
fu*urine flow=0.6*1.5mL/min=0.9mL/min
($Cl_{ren}$>fu*urine flow) → not fully reabsorbed

(3) Drug with fu=0.05 and a $Cl_{ren}$=15mL/min
fu*GFR=0.05*130mL/min=6.5mL/min
$Cl_{ren}$>fu* GFR → actively secreted

(4) Drug with fu=0.2 and a $Cl_{ren}$=0.3mL/min
fu*GFR=0.2*130mL/min=26mL/min
$Cl_{ren}$<fu* GFR → reabsorbed
fu*urine flow=0.2*1.5mL/min=0.3mL/min
$Cl_{ren}$=fu*urine flow → fully reabsorbed

(5) Drug with fu=0.8 and a $Cl_{ren}$=0.3mL/min
fu*GFR=0.8*130mL/min=104mL/min
$Cl_{ren}$<fu* GFR → reabsorbed
fu*urine flow=0.8*1.5mL/min=1.2mL/min
($Cl_{ren}$<fu*urine flow) → reabsorbed through transporters

2. A 25 year old, 5'6'', 80kg male patient with a serum creatinine concentration of 1.8mg/dL was given a drug treatment. Knowing this drug is mainly eliminated by glomerula filtration and has 60% plasma protein binding. Please estimate the Clearance of this drug (with Cockcroft-Gault equation)

IBW=50kg + 2.3kg * 6=63.8kg
TBW=80kg > 120%IBW=76.56 → This is an obese patient, so use ABW
ABW= IBW+0.4*(TBW-IBW)=63.8 + 0.4*(80-63.8)=70.28kg
GFR≈ CrCl = (140-age)*IBW/(72*serum creatinine)=
(140-25)*70.28/(72*1.8)≈62.36mL/min=3.74L/hr
CL=GFR*fu=3.74*(1-0.6)=1.496L/hr

3. **TRUE (T) or FALSE (F)**

For a high extraction drug, liver blood flow is important to both hepatic clearance and oral bioavailability.

T F

For low extraction drug, $f_u$ (fraction of unbound drug in plasma) is important to both hepatic clearance and oral bioavailability.

T F

Basic drugs that are polar in their unionized form, the extent of re-absorption depends on the degree of its ionization.

T F

Secretion is indicated when renal clearance is larger than GFR*fu.

T F

It is possible for renal clearance to be close to the kidney blood flow.

T F

Assuming no plasma protein binding, the renal clearance equals the urine flow when full reabsorption occurs.

T F