

# 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  $f_u=0.3$  and a  $Cl_{ren}=39\text{mL/min}$

$$f_u * GFR = 0.3 * 130\text{mL/min} = 39\text{mL/min}$$

$$Cl_{ren} = f_u * GFR \rightarrow \text{filtered}$$

(2) Drug with  $f_u=0.6$  and a  $Cl_{ren}=30\text{mL/min}$

$$f_u * GFR = 0.6 * 130\text{mL/min} = 78\text{mL/min}$$

$$Cl_{ren} < f_u * GFR \rightarrow \text{reabsorbed}$$

$$f_u * \text{urine flow} = 0.6 * 1.5\text{mL/min} = 0.9\text{mL/min}$$

$$(Cl_{ren} > f_u * \text{urine flow}) \rightarrow \text{not fully reabsorbed}$$

(3) Drug with  $f_u=0.05$  and a  $Cl_{ren}=15\text{mL/min}$

$$f_u * GFR = 0.05 * 130\text{mL/min} = 6.5\text{mL/min}$$

$$Cl_{ren} > f_u * GFR \rightarrow \text{actively secreted}$$

(4) Drug with  $f_u=0.2$  and a  $Cl_{ren}=0.3\text{mL/min}$

$$f_u * GFR = 0.2 * 130\text{mL/min} = 26\text{mL/min}$$

$$Cl_{ren} < f_u * GFR \rightarrow \text{reabsorbed}$$

$$f_u * \text{urine flow} = 0.2 * 1.5\text{mL/min} = 0.3\text{mL/min}$$

$$Cl_{ren} = f_u * \text{urine flow} \rightarrow \text{fully reabsorbed}$$

(5) Drug with  $f_u=0.8$  and a  $Cl_{ren}=0.3\text{mL/min}$

$$f_u * GFR = 0.8 * 130\text{mL/min} = 104\text{mL/min}$$

$$Cl_{ren} < f_u * GFR \rightarrow \text{reabsorbed}$$

$$f_u * \text{urine flow} = 0.8 * 1.5\text{mL/min} = 1.2\text{mL/min}$$

$$(Cl_{ren} < f_u * \text{urine flow}) \rightarrow \text{reabsorbed through transporters}$$

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 glomerular filtration and has 60% plasma protein binding. Please estimate the Clearance of this drug (with Cockcroft-Gault equation)

$$IBW = 50\text{kg} + 2.3\text{kg} * 6 = 63.8\text{kg}$$

$$TBW = 80\text{kg} > 120\%IBW = 76.56 \rightarrow \text{This is an obese patient, so use ABW}$$

$$ABW = IBW + 0.4 * (TBW - IBW) = 63.8 + 0.4 * (80 - 63.8) = 70.28\text{kg}$$

$$GFR \approx CrCl = (140 - \text{age}) * IBW / (72 * \text{serum creatinine}) =$$

$$(140 - 25) * 70.28 / (72 * 1.8) \approx 62.36\text{mL/min} = 3.74\text{L/hr}$$

$$CL = GFR * f_u = 3.74 * (1 - 0.6) = 1.496\text{L/hr}$$

### 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  $GFR \cdot f_u$ .

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