

## **PHA 5128 Dose Optimization II, Spring 2012, Case Study V Solution**

If you have any questions regarding this case study, do not hesitate to contact Benjamin Weber ([benjaminweber@ufl.edu](mailto:benjaminweber@ufl.edu)). Please remember that attendance is mandatory. 10 points will be deducted from your final score if you do not attend a case study without being officially excused by Dr. Derendorf (GNV students) or your respective course facilitator (non-GNV students).

### **Problem 1 (Digoxin)**

A.P., a 75-year-old, 65-kg man (non-obese), was admitted with complaints of increased shortness of breath and yellow sputum production. He has a medical history of congestive heart failure. During his hospital stay, he developed atrial fibrillation and was given digoxin to slow his ventricular rate. He received 3 doses 0.25-mg digoxin IV every 3 hours (starting at 9pm on day 1) and was given a maintenance dose of 0.25-mg tablets each morning (starting at 9am on day 2). His serum creatinine is stable at 1.3 mg/dL.

Calculate his expected digoxin plasma concentration at 9am on day 4. (Hint: A graph of the expected concentration time profile might be helpful to answer this problem)

A digoxin level obtained at 9am on the morning of day 4 was 1.5  $\mu\text{g/L}$ . Do you observe any discrepancy between expected and observed digoxin plasma concentration level? If yes, explain the discrepancy between expected and observed dose.

### **Problem 2 (Methotrexate)**

V.A., a 53-year-old, 65-kg woman (non-obese,  $\text{SCr} = 1.2 \text{ mg/dL}$ ) is to receive a course of methotrexate (MTX) therapy for acute lymphoblastic leukemia. Her regimen will consist of 400-mg MTX loading dose to be administered over 15 minutes followed by an IV infusion of 50 mg/h for the next 36 hours. Calculate her anticipated MTX plasma levels (in  $\mu\text{M}$ ) for the following scheduled sampling times: 24h, 48h, and 60h, after the beginning of the 50 mg/h infusion. You may assume that steady state has been achieved after 24h. A sketch of the expected plasma-concentration-time profile may be helpful to answer this problem.

### **Problem 3 (Theophylline)**

S.R., a 66-kg (non-obese), 40-year-old woman, has been receiving an IV aminophylline infusion at a rate of 35 mg/h. Her steady state theophylline concentration is 15 mg/L and her therapeutic response is considered optimal at this concentration. Calculate an appropriate oral dosing regimen (for theophylline tablets and  $\tau = 6\text{h}$ ) and ESTIMATE the peak and trough concentrations that would be produced by the regimen. Assume that theophylline tablets are available in doses of 100-mg, 150-mg, and 200-mg. (Hint: Textbook (Fifth Edition): p.423 – p.426)

**Problem 4 (Cyclosporine)**

R.I., a 39-year-old, 102-kg woman, 5'6" tall, who received a liver transplant, is to be started on oral treatment with cyclosporine. Recommend a dosing regimen that would achieve free steady state concentrations of 40 and 15 ng/mL. Cyclosporine is available in oral doses of 25-mg and 100-mg. Calculate the anticipated total cyclosporine plasma concentrations (in ng/mL) based on dosing regimen that you suggest. You may assume a rapid absorption process and, thus, use the equations for IV bolus administration.

**Problem 5 (Lidocaine)**

P.M., a 45-year-old, 65-kg man, was admitted to the coronary care unit with a diagnosis of heart failure, probable myocardial infarction. Calculate a bolus dose that achieves lidocaine plasma level of 3mg/L which should achieve an immediate response. (Note: Lidocaine is available as lidocaine hydrochloride).

Calculate a maintenance infusion rate of that will achieve a steady-state lidocaine concentration of 3 mg/L. (Note: Lidocaine is available as lidocaine hydrochloride).