1. If the MTC is 100 ng/mL and the MEC is 0.12 ng/mL, which of the following dosing regimen(s) are in the therapeutic window?

A. 5 mg/kg glabridin (iv.)
B. 5 mg/kg glabridin (p.o.)
C. 20 mg/kg glabridin (p.o.)
D. B and C.
E. All of them are in the therapeutic window.

2. Which of the above dosing regimen(s) has the greatest AUC?

A. 5 mg/kg glabridin (iv.)
B. 5 mg/kg glabridin (p.o.)
C. 20 mg/kg glabridin (p.o.)
D. Not information to determine.

3. What is the $C_{max}$ and $T_{max}$ for the oral dose of 20 mg/kg glabridin?

A. 50 ng/mL and 4 hr
B. 50 ng/mL and 4 hr
C. 50 ng/mL and 4 hr
D. 50 ng/mL and 0 hr
E. None of the above
4. Which of the following is true?
   
   A. P-glycoprotein does not affect the bioavailability of drugs that are substrates of P-glycoprotein.  
   B. Drug interactions like grapefruit juice (CYP3A4 inhibitor) can decrease the AUC of drugs that are substrates of CYP3A4.  
   C. Poorly perfused tissues and organs are located in the tissue compartment of a 2-compartment model.  
   D. The one-compartment model has slow distribution throughout the entire body.  
   E. The two-compartment model has instantaneous distribution to most body tissues and fluids.

5. Which of the following is correct?
   
   A. The elimination rate constants, \( k_e \), and \( k_r \), for both zero- and 1st-order elimination kinetics remain the same.  
   B. For 1st-order elimination, the fraction of drug removed per unit time, remains the same.  
   C. For 1st-order elimination, a natural log of plasma concentration (\( \ln C_p \)) versus time (t) plot produces a straight line.  
   D. Only A and B are correct.  
   E. A, B and C are correct.

6. Which of the following is true?
   
   A. One- and two-compartment PK models exhibit first-order elimination kinetics.  
   B. A one-compartment model can exhibit both zero-order and first-order elimination kinetics.  
   C. The elimination rate constant for zero-order elimination, \( k_e \), is in units of inverse time.  
   D. The elimination half-life, \( t_{1/2} \), is constant for both zero- and 1st-order elimination kinetics.  
   E. For zero-order elimination, the fraction of drug removed per unit time, remains the same.

7. Which of the following is correct?
   
   A. The equation \( C_p = C_p^0 - k_t t \) is for first-order elimination.  
   B. The equation \( \ln C_p = \ln C_p^0 - k_t t \) is for zero-order elimination.  
   C. The equation \( C_p = Ae^{-kt} + Be^{-kt} \) is for a one-compartment model.  
   D. The equation for the elimination half-life of a one-compartment model is \( t_{1/2} = \frac{0.693}{k} \).  
   E. All of the above are correct.
8. Which of the following is false concerning non-linear elimination kinetics (Michaelis Menten Kinetics)?

A. The elimination half-life, $t_{1/2}$, decreases with increase dose. ✓
B. The elimination rate constant, $k$, decreases with increase dose. ✓
C. The AUC is directly proportional to the dose administered with increasing dose. NO ✓
D. Volume of distribution ($V_d$) and total plasma clearance ($Cl_p$) remains the same with increases in dose. NO - $Cl_p$ may or may not change.
E. All of the above are false.

9. Which of the following is false concerning first-order elimination kinetics?

A. If a drug has a volume of distribution ($V_d$) of 3 L, this indicates that the drug is primarily located in the plasma. YES. $V_d/Cl_p$
B. If a drug has a volume of distribution ($V_d$) of 440 L, the plasma concentrations of the drug will be low compared to the concentrations in the tissues. YES. $V_d/Cl_p$
C. Volume of distribution ($V_d$) indicates the efficiency of an organ to remove drug from the blood. NO, $Cl_p$ does.
D. Volume of distribution ($V_d$) and total plasma clearance ($Cl_p$) remains the same with increases in dose. TRUE.
E. None of the above.

10. The elimination half-life for quinidine sulfate ($F = 0.8$) is approximately 6 hours. What percent of this drug would be still remaining in the body 12 hours after 100 mg IV bolus dose? Assume first-order kinetics.

\[ t_{1/2} = 6 \text{ hr} \]
\[ t = 0.1155/\text{hr} \]

\[ \frac{25}{e^{-t} = e^{-0.1155(12 \text{ hrs})}} \]
\[ = 0.25 = 25\% \]

11. What percent of this drug will have been eliminated after 18 hours after a 150 mg ORAL dose of quinidine sulfate (in question #10 above)?

\[ 18\text{ hr} = 3t_{1/2} \]
\[ \frac{Fraction \, eliminated}{1 - e^{-t\%}} \]
\[ 0.1155(18\text{ hr}) \]
\[ = 1 - e^{-0.1155(18\text{ hr})} \]
\[ = 1 - 0.125 \]
\[ = 0.875 = 87.5\% \]
Questions 12 - 15: Below is a table of the results following an i.v. bolus dose of 50 mg of beaverolol which has a $t_{1/2}$ of 2.7 hr.

\[ F = 1 \]

\[ \frac{f_e}{0.693/2.7 hr} = 0.2567/hr = k \]

<table>
<thead>
<tr>
<th>TIME</th>
<th>CONCENTRATION (mg/L)</th>
<th>AUC WITHIN TIME INTERVAL (mg.hr/L)</th>
<th>AMOUNT EXCRETED IN TIME INTERVAL (mg)</th>
<th>CUMULATIVE AMOUNT EXCRETED (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2.0</td>
<td>4.00</td>
<td>16.0</td>
<td>16.0</td>
</tr>
<tr>
<td>3</td>
<td>1.13</td>
<td>2.26</td>
<td>9.0</td>
<td>25.0</td>
</tr>
<tr>
<td>5</td>
<td>0.70</td>
<td>1.40</td>
<td>5.6</td>
<td>30.6</td>
</tr>
<tr>
<td>7</td>
<td>0.43</td>
<td>0.86</td>
<td>3.4</td>
<td>34.0</td>
</tr>
<tr>
<td>10</td>
<td>0.20</td>
<td>0.80</td>
<td>3.2</td>
<td>37.2</td>
</tr>
<tr>
<td>18</td>
<td>0.025</td>
<td>0.43</td>
<td>1.9</td>
<td>39.1</td>
</tr>
</tbody>
</table>

Total $\xi = 9.75 \text{ mg.hr/L}$

12. What is the fraction excreted unchanged, $f_e$, for beaverolol?
   - A. 1
   - B. 0.78
   - C. 0.32
   - D. 0.04
   - E. None of the above

\[ f_e = \frac{A_{ceo}}{D.F.S.} = \frac{39.1 \text{ mg}}{50 \text{ mg}} = 0.782 \]

13. What is the non-renal clearance, $C_l_{nr}$, for beaverolol?
   - A. 5.1 L/hr
   - B. 4.0 L/hr
   - C. 1.1 L/hr
   - D. 0.3 L/hr
   - E. None of the above

\[ C_l_{nr} = C_l_p - C_l_r \]
\[ C_l_p = \frac{Dose}{AUC} \]
\[ C_l_p = \frac{50 \text{ mg}}{9.75 \text{ mg.hr/L}} \]
\[ C_l_p = 5.13 \text{ L/hr} \]
\[ C_l_r = \frac{4.01 \text{ L/hr}}{0.782} \]
\[ C_l_{nr} = 5.13 \text{ L/hr} - 4.01 \text{ L/hr} = 1.12 \text{ L/hr} \]

14. What is the volume of distribution, $V_d$, for beaverolol?
   - A. 1.7 L
   - B. 4.3 L
   - C. 15.6 L
   - D. 19.9 L
   - E. None of the above

\[ V_d = \frac{C_l_p}{k} = \frac{5.13 \text{ L/hr}}{0.2567 \text{ hr}} = 19.98 \text{ L} = V_d \]

15. What is the $C_p$ 60 minutes after a 150 mg i.v bolus dose?
   - A. 1.5 mg/L
   - B. 3.08 mg/L
   - C. 5.83 mg/L
   - D. 116 mg/L
   - E. None of the above

\[ C_p = \frac{150 \text{ mg}}{19.98 \text{ L}} e^{-0.2567 \times 1 \text{ hr}} \]

\[ C_p = 5.81 \text{ mg/L} \]
For questions 16 and 17, use the information below:

Leuprolide is a LHRH agonist used for the treatment of prostatic cancer. It is a nonapeptide that is poorly absorbed upon oral administration. It is therefore marketed as a parenteral dosage form. A bioavailability study was conducted to evaluate inhalations as an alternate route of administration. Each of the following treatments was administered to 23 normal adult males.

Treatment 1: Inhalation of 2 sprays of leuprolide acetate Formulation A.
Treatment 2: Inhalation of 2 sprays of leuprolide acetate Formulation B.
Treatment 3: Inhalation of 2 sprays of leuprolide acetate Formulation C.
Treatment 4: Intravenous injection of leuprolide acetate 1 mg.

Pharmacokinetic parameters of Leuprolide Acetate Aerosols following inhalation delivery to Humans.

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Dose</th>
<th>( T_{max} ) (hr)</th>
<th>( C_{max} ) (ng/ml)</th>
<th>AUC (ng - hr/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Form A</td>
<td>1 mg</td>
<td>2.3 (2.2)</td>
<td>0.97 (0.43)</td>
<td>7.80 (3.94)</td>
</tr>
<tr>
<td>Form B</td>
<td>1 mg</td>
<td>1.6 (0.8)</td>
<td>4.38 (1.74)</td>
<td>33.14 (10.10)</td>
</tr>
<tr>
<td>Form C</td>
<td>2 mg</td>
<td>1.1 (0.8)</td>
<td>11.37 (16.65)</td>
<td>51.90 (20.90)</td>
</tr>
<tr>
<td>IV control</td>
<td>1 mg</td>
<td>—</td>
<td>133.22 (7.33)</td>
<td>181.15 (26.92)</td>
</tr>
</tbody>
</table>

* Data presented are mean and (standard deviation) for 23 patients.

16. What is the absolute bioavailability of Formulation C?

A. 0.043  
B. 0.085  
C. 0.143  
D. 0.287  
E. None of the above

\[ \frac{F_C}{F_{IV}} = \frac{\text{Dose}_C}{\text{AUC}_C} \cdot \frac{\text{AUC}_{IV}}{\text{Dose}_{IV}} = \frac{1\text{mg}}{181.15\text{ng.hr/ml}} \cdot \frac{51.90\text{ng.hr/ml}}{2\text{mg}} = 0.143 \]

17. What are the relative bioavailability of Formulation B to Formulation C, \((F_B/F_C)\)?

A. 1.57  
B. 1.28  
C. 0.78  
D. 0.64  
E. None of the above

\[ \frac{F_B}{F_C} = \frac{\text{Dose}_B}{\text{AUC}_B} \cdot \frac{\text{AUC}_C}{\text{Dose}_C} = \frac{2\text{mg}}{51.90\text{mg.hr/ml}} \cdot \frac{181.15\text{mg.hr/ml}}{1\text{mg}} = 1.28 \]
For questions 18 and 20, use the information below:

The population pharmacokinetics of the oral antiarrhythmic drug, mexiletine hydrochloride, for a 70-kg person are:

\[
F = 0.87 \\
S = 0.83 \\
V_d = 343 \text{ L} \\
Cl_p = 26.46 \text{ L/hr}
\]

\[
\frac{C_p}{V_d} \cdot k = \frac{F}{S} = \frac{26.46 \text{ L/hr}}{343 \text{ L}} = 0.077/\text{hr}
\]

18. Calculate the elimination half-life, \( t_{1/2} \), of mexiletine.
   A. 0.053 hr
   B. 0.077 hr
   C. 9 hr
   D. 13 hr
   E. None of the above

   \[
   t_{1/2} = \frac{0.693}{k} \Rightarrow k = 0.077/\text{hr} \\
   t_{1/2} = \frac{0.693}{0.077/\text{hr}} = 9 \text{ hr}
   \]

19. Calculate the accumulation ratio/accumulation index of mexiletine hydrochloride (250 mg given orally daily in the morning).
   A. 0.16
   B. 0.84
   C. 1.04
   D. 1.19
   E. None of the above

   \[
   \frac{C(t)}{C(0)} = 1 - \frac{1}{1 - e^{-kT}} = 1 - \frac{1}{1 - e^{-0.077 \times 24 \text{hr}}} = 1.19
   \]

20. What is the minimum plasma concentration at steady state, \( C_{p_{\text{min}}} \), of mexiletine hydrochloride (250 mg given orally twice daily)? Assume first-order elimination kinetics and that absorption is instantaneous relative to elimination.
   A. 0.345 mg/L
   B. 0.87 mg/L
   C. 1.21 mg/L
   D. 99.1 mg/L
   E. None of the above

   \[
   \frac{C_{p_{\text{min}}}}{C_{p_{\text{max}}}} = e^{- \frac{D \cdot F \cdot S}{V_d(1-e^{-kT})}} \Rightarrow \frac{(250 \text{mg})(0.87)(0.83)}{343 \text{L}(1-e^{-0.077 \times 12 \text{hr}})} e^{- \frac{D \cdot F \cdot S}{V_d(1-e^{-0.077 \times 12 \text{hr}})}}
   \]

   \[
   \frac{0.345 \text{mg}}{\text{L}} = \frac{180 \text{mg}}{343 \text{L}(0.60307)} \approx 0.39693
   \]
For questions 21 and 24, use the information below:

Sumycin® (tetracycline) is primarily used as a broad spectrum antibiotic for infections. Sumycin® is available in 250 mg and 500 mg capsules and is usually administered every 12 hrs. Tetracycline has the following pharmacokinetic parameters:

\[ F = 0.77, \text{fe} = 0.58, V_1 = 105 \text{L}, \text{and} \ k = 0.0654/\text{hr}. \]

Assume one-compartment elimination kinetics and that absorption is instantaneous relative to its elimination.

\[ \text{Cp} = 6.8674/\text{hr} \]

21. How long will it take for tetracycline to reach steady state concentrations?
A. 0.327 hr
B. 10.6 hrs
C. 53 hrs
D. Not enough information is given.
E. None of the above

\[ 10.6 \text{hr} \times 5 = 52.98 \text{hr} = 53 \text{hrs} \]

22. What will the AUC be for tetracycline following a 500 mg ORAL dose?
A. 72.8 mg*hr/L
B. 56.1 mg*hr/L
C. 32.5 mg*hr/L
D. 3.7 mg*hr/L
E. None of the above

\[ \text{AUC} = \frac{D \cdot F \cdot S}{\text{Cp}} \]

\[ 56.1 \text{mg/hr/L} \]

23. What is the "average concentration of tetracycline in the body, \( C_{pave} \)" in the above patient who has been receiving 200 mg tetracycline intravenously twice daily for 3 days?
A. 29.12 mg/L
B. 2.43 mg/L
C. 1.87 mg/L
D. 1.47 mg/L
E. None of the above

\[ C_{pave} = \frac{D \cdot F \cdot S}{\text{Cp}} \]

\[ \frac{(200 \text{mg})(1)}{(0.8674/\text{hr})(12 \text{hr})} = 2.43 \text{mg/L} \]

24. What will the patient's "minimum amount, \( A_{min} \)" in question #23 be at 24 hrs following a 200-mg i.v. dose of tetracycline given every 12 hours.
A. 102 mg
B. 133 mg
C. 291 mg
D. 368 mg
E. None of the above

\[ A_{Nmin} = A_{Nmax} \cdot e^{-\frac{N \cdot t}{12}} \]

\[ A_{Nmax} = A_{Nmax} \cdot e^{-\frac{N \cdot t}{12}} \]

\[ A_{min} = \frac{200 \text{mg}(1-e^{-\frac{2}{12}})}{1-e^{-\frac{2}{12}}} \]

\[ A_{min} = 32.9 \text{mg} \cdot \frac{200 \text{mg}(0.79187)}{0.45621} \]

\[ (0.45621) \]