Drug Delivery 1 – First Pass Effect Active Learning Module

Fill in the data on the chart on the next page. Then use the data to explain the following.

A. Two different patients are taking 400 mcg of Actiq Transmucosal lozenges for breakthrough pain. Patient A places that lozenge in the mouth between their cheek and gum and actively sucks on the lozenge until they feel pain relief. Patient B places the lozenge in their mouth and after a few minutes chews up the lozenge and swallows the dosage form but never really feels a significant reduction in pain.

i. Why are they seeing differences in pain relief?

B. Is a 400 mcg dose for one of these dosage forms equivalent to a 400 mcg dose of the other three? In other words, can you substitute a 400mcg Actiq for a 400 mcg Subsys, or 400 mcg Fentora, or 400 mcg Onsolis and expect the same amount of drug to reach the systemic circulation?

i. If Yes, why?

ii. If No, why not?

C. Why are there so many different doses available for these dosage forms?
Transmucosal Fentanyl - To treat break through pain (BTP)

<table>
<thead>
<tr>
<th>Route of Administration</th>
<th>Subsys</th>
<th>Actiq</th>
<th>Fentora</th>
<th>Onsolis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of Dosage Form</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Method of Administration</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Can Dosage Form be Cut in Half?</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dose</td>
<td>400 mcg</td>
<td>400 mcg</td>
<td>400 mcg</td>
<td>400 mcg</td>
</tr>
</tbody>
</table>

| Absolute Availability   |        |       |         |         |
| Amount of Drug Reaching the Systemic Circulation | | | | |
| Amount of Drug Absorbed Transmucosal | | | | |
| Amount of Drug Swallowed | | | | |
| Amount of Swallowed Drug that Reaches the Systemic Circulation | | | | |
| Frequency of Administration | | | | |
| $C_{\text{max}}$ | | | | |
| $t_{\text{max}}$ | | | | |
| AUC | | | | |
| Onset time | | | | |
| Factors that reduce Bioavailability | | | | |
| Proper Disposal | | | | |

Extra thought: A doctor calls and asks you how much fentanyl is absorbed from a transdermal patch if it is ingested. What should you ask and where should you look for information
2. Draw an IV bolus vs. time curve on the graphs below.

- Label the axis
- Identify $C_{\text{max}}$, $t_{\text{max}}$ and AUC on the graph
- List the routes of administration that have this plasma curve
- Draw a line that represents a minimum effective concentration of 5 mg/L
- Draw a line that represents a minimum toxic concentration of 9 mg/L
- What is the duration of action?
- What is the onset time?
- What is the therapeutic window?
- Label the elimination phase and the absorption phase
3. Draw an extravascular vs. time curve on the graphs below.

- Label the axis
- Identify $C_{\text{max}}$, $t_{\text{max}}$ and AUC on the graph
- List the routes of administration that have this plasma curve
- Draw a line that represents a minimum effective concentration of 5 mg/L
- Draw a line that represents a minimum toxic concentration of 9 mg/L
- What is the duration of action?
- What is the onset time?
- What is the therapeutic window?
- Label the elimination phase and the absorption phase
4. When the oral dose of a medication is doubled what happens to each of the following?

A. Amount of drug reaching the systemic circulation __________________________
B. The maximum plasma concentration ______________________________
C. Area under the curve ______________________________

5. What is AUC directly related to?

6. \( F = 1 \) for the solution in the graph below. Assuming the dose administered was the same for all three dosage forms. What is the most likely reason that Tablet 1 and Tablet 2 have and \( F \) less than 1? Why is the AUC for Tablet 2 less than Tablet 1?

![Extravascular graph](image)

7. What is the first pass effect?

8. Where does the first pass effect occur?
9. What routes of administration expose some or the entire absorbed to the first pass effect prior to the drug reaching the systemic circulation?

10. Where is the primary site of drug absorption following oral administration?

11. What factors might delay drug reaching the small intestine following oral administration? How might delaying the time to reach the primary site of absorption affect the onset time of the drug?

12. A patient in the hospital has been receiving 100 mg of Drug A for pain, IV bolus, every 8 hours. At discharge a prescription for 100 mg Drug A, PO tid, is written. The patient calls the pharmacy to complain that the medication is not working. What issues might be causing this drug to not work?

13. A patient is admitted to the hospital and the chart states NPO. They have been taking 80 mg of propranolol once daily at bedtime for hypertension. What IV dose is appropriate for this patient and why?

14. Motrin (brand name ibuprofen) has an F = 0.9, if a generic ibuprofen tablet has an F = 0.9.
   a. If 200 mg of each is administered to a patient how much drug from each will be absorbed?

   Motrin ________________________   Generic Ibuprofen ________________________
   F for Motrin  _________________  F for Generic Ibuprofen __________________

   b. If 400 mg of each is administered to a patient how much drug from each will be absorbed?

   Motrin ________________________   Generic Ibuprofen ________________________
   F for Motrin  _________________  F for Generic Ibuprofen __________________

   c. If 100 mg of each is administered to a patient how much drug from each will be absorbed?

   Motrin ________________________   Generic Ibuprofen ________________________
   F for Motrin  _________________  F for Generic Ibuprofen __________________
15. Tylenol (brand name acetaminophen) has an $F = 0.98$, if a generic acetaminophen tablet has an $F = 0.85$.

a. If 350 mg of each is administered to a patient how much drug from each will be absorbed?

Tylenol ________________________   Generic Acetaminophen ____________________
F for Tylenol ________________  F for Generic Acetaminophen _____________

b. If 500 mg of each is administered to a patient how much drug from each will be absorbed?

Tylenol ________________________   Generic Acetaminophen ____________________
F for Tylenol ________________  F for Generic Acetaminophen _____________

c. If 250 mg of each is administered to a patient how much drug from each will be absorbed?

Tylenol ________________________   Generic Acetaminophen ____________________
F for Tylenol ________________  F for Generic Acetaminophen _____________

16. Imitrex Case: Imitrex is a drug used to treat migraine. It is available in three dosage forms: oral, SC, and nasal. Fill in the table below.

<table>
<thead>
<tr>
<th></th>
<th>Oral</th>
<th>Nasal</th>
<th>SC</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dose</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Frequency of Administration</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$C_{\text{max}}$</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$t_{\text{max}}$</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>AUC</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Onset time</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Absolute Availability</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Bioavailability relative to the SC</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Bioavailability relative to the Nasal</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td><strong>Factors that reduce Bioavailability</strong></td>
<td></td>
<td></td>
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<tr>
<td><strong>First Pass Effect % Metabolized</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
a. When a patient uses the nasal dosage form and needs a second dose, does it make a
difference in bioavailability if the patient uses the same nostril of give the second
dose in the opposite nostril?

b. What physiological issues might cause the onset of the oral dosage form to be longer
than expected?

17. Draw plasma vs. time curves for a 600 mg dose and a 300 mg dose for both routes of
administration.

What happens to $C_{max}$, $t_{max}$, and AUC?

**IV Bolus**

**Extravascular**