

## Oral and LAI Comparison\*

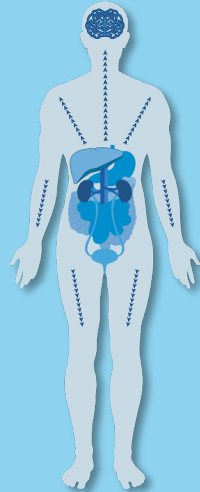
Click on each term to learn more

### A > Absorption

Absorption differs in rate, impacting time to maximum plasma concentration ( $T_{max}$ )<sup>1</sup>

### D > Distribution

Distribution is relatively similar once drug is absorbed<sup>1</sup>



### M > Metabolism

Oral drugs undergo first-pass metabolism, while LAIs do not<sup>1</sup>

### E > Elimination

Elimination of LAIs is similar to orals once absorbed<sup>1</sup>

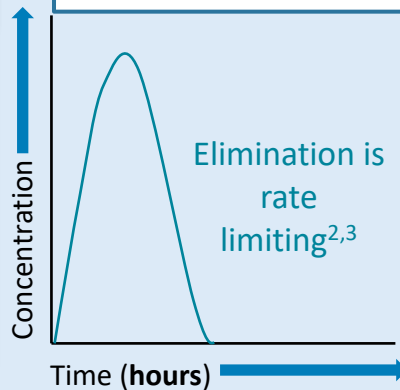
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## LAI Formulations Exhibit Flip-Flop Kinetics

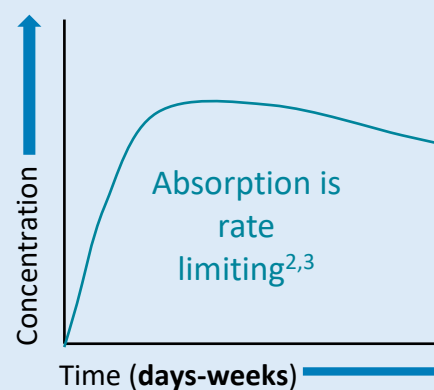
When the absorption process is much slower than the elimination process, the apparent half-life significantly increases due to the slow absorption step, resulting in flip-flop kinetics<sup>1,2</sup>

Click on each graph title to reveal the limiting step

### Typical Pharmacokinetics: Immediate-Release Oral Formulations<sup>†</sup>



### Flip-Flop Kinetics: LAI Formulations<sup>†</sup>



## LAI Formulations Slow Absorption Kinetics

### Initiation strategy<sup>‡,1,4</sup>:

|                      |                      |
|----------------------|----------------------|
| Initiation injection | Oral supplementation |
| Loading dose         | None                 |

### LAI formulation<sup>5,6</sup>:

|                      |                        |
|----------------------|------------------------|
| IM depot particle    | SQ bioresorbable depot |
| IM depot microsphere |                        |

## ABSORPTION

Click on each number below to learn more

Click here to learn more about LAI formulations



1

Slower absorption rate of LAIs compared with oral medications in some cases leads to...

2

...reduced peak ( $C_{max}$ )-to-trough ( $C_{min}$ ) plasma concentration differences...

3

...which are hypothesized to contribute to tolerability<sup>1,7,8</sup>

\*Illustrations were compiled from Adobe stock images and used under free use purposes. Free use allows the copying of copyrighted material in educational settings without permissions. <sup>†</sup>Graphs are illustrative. <sup>‡</sup>More than 1 initiation strategy may be utilized for 1 LAI formulation. IM, intramuscular; LAI, long-acting injectable; SQ, subcutaneous. 1. Correll CU, et al. *CNS Drugs*. 2021;35(1):39-59. 2. Zou H, et al. *Front Pharmacol*. 2020;11:997. 3. Fan J, et al. *Biochem Pharmacol*. 2014;87(1):93-120. 4. Jain R, et al. *CNS Spectr*. 2020;25(3):323-330. 5. Shi Y, et al. *Acta Pharm Sin B*. 2021;11(8):2396-2415. 6. Roberge C, et al. *J Control Release*. 2020;319:416-427. 7. Sheehan JJ, et al. *Innov Clin Neurosci*. 2012;9(7-8):17-23. 8. Kenakin TP. In: Kenakin TP, ed. *Pharmacology in Drug Discovery*. Academic Press. 2012:155-183.

