



## 1.12 Valproic Acid

### Pharmacokinetic Parameters

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**Table 1.12-1. Clearance by Age in the Absence of Clearance-Altering Factors**

Age Group	Clearance at Steady State <sup>a</sup> (Mean ± SD or Range)
Neonates (<4 weeks) <sup>1</sup>	0.011 to 0.018 L/hr/kg
Infants (4 weeks –<1 year) <sup>1-3</sup>	0.019 ± 0.008 L/hr/kg
Children (3–16 years) <sup>2,4,5</sup>	0.018 ± 0.006 L/hr/kg
Adults (18 –<60 years) <sup>6,7</sup>	0.009 ± 0.005 L/hr/kg
Geriatrics (≥60 years) <sup>8,9</sup>	0.007 ± 0.005 L/hr/kg

<sup>a</sup>Use ideal body weight (IBW) in obese patients.

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**Table 1.12-2. Bioavailability of Dosage Forms**

Dosage Form	Bioavailability
Intravenous	100% (F = 1)
Intramuscular	IM injection is not recommended
Oral capsules and syrups	95%; range 90%–100% (F ~ 0.95)
Enteric-coated tablets (Depakote)	95%; range 90%–100% (F ~ 0.95)
Extended-release tablets (Depakote ER)	87% (F = 0.87)

## References

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## Self-Assessment Problems

1. Design a dosing regimen to produce predicted average steady state concentrations ( $C_{ss_{avg}}$ ) of around 60 to 70 mg/L, using Depakote tablets, for the following patients. Available doses are 125-, 250-, and 500-mg tablets, and intervals are generally every 8 or 12 hours. What would be the  $C_{ss_{avg}}$  on the dose and schedule you choose?
  - A. A 12-year-old who weighs 105 lb
  - B. A 45-year-old male who weighs 205 lb and is 5'8" tall
  - C. A 75-year-old who weighs 60 kg (ABW = IBW)
2. A 22-year-old, 78-kg, female patient has been receiving 500-mg valproic acid capsules every 8 hours for seizure activity. A steady state valproic acid concentration is measured midway through the interval ( $C_{ss_{avg}}$ ) and reported as 44 mg/L.
  - A. What is the patient's clearance relative to weight (L/hr/kg)? How does this relate to the population clearance?
  - B. What factors should be considered in determining whether the dose should be adjusted to reach the therapeutic range of 50–100 mg/L?
  - C. Assuming a change is desired, use 75 mg/L as the target  $C_{ss_{avg}}$  and then pick a reasonable dose for an every 8-hour interval.