Table 1 IV Bolus Dosing

|  |  |  |
| --- | --- | --- |
| **Structure** | **Kinetics** | **Citation** |
| 1 Compartment Model | Linear |  |
| Non Linear |  |
| 2 Compartment Model | Linear | Rosario BJCP 1998 |
| Non Linear | Hope AAC 2012 |
| 3 Compartment Model | Linear | Lee JPKPD 2016 |
| Non Linear | Kuan PAGE 2012 |

Table 2 IV Infusion Dosing

|  |  |  |
| --- | --- | --- |
| **Structure** | **Kinetics** | **Citation** |
| 1 Compartment Model | Linear | Di Paolo IJAA 2013 |
| Non Linear | Wu JCP 2012 |
| 2 Compartment Model | Linear | Jonsson ClinPK 2005, Samara AAC 2012 |
| Non Linear | Friberg AAC 2012 |
| 3 Compartment Model | Linear |  |
| Non Linear | Chen JCP 2014 |

Table 3 Extravascular Dosing No Lag Time

|  |  |  |
| --- | --- | --- |
| **Structure** | **Kinetics** | **Citation** |
| 1 Compartment Model | Linear | Sidhu BJCP 1998, Rubino AAC 2007 |
| Non Linear | Odani BPB 1996, Valodia TDM 2000, Ding Clin PK 2015 |
| 2 Compartment Model | Linear |  |
| Non Linear | Endres JCP 2014 |
| 3 Compartment Model | Linear | Lindemalm BMCP 2005, Li AAPS 2010 |
| Non Linear |  |

Table 4 Extravascular Dosing With Lag Time

|  |  |  |
| --- | --- | --- |
| **Structure** | **Kinetics** | **Citation** |
| 1 Compartment Model | Linear | Bellanti BJCP 2014 |
| Non Linear |  |
| 2 Compartment Model | Linear | Jin CCP 2016 |
| Non Linear | Hope AAC 2012 |
| 3 Compartment Model | Linear | Zhou MJ 2014 (3cmt no lag & 2cmt w/ lag) |
| Non Linear |  |

We could further breakdown the tables/literature into small v large sample size studies, small v large residual variability/error in the models.

Other potential options to explore:

* Different extravascular routes i.e. SC, inhaled
* Oral formulations: ER, DR, potential for double peaks
* Inclusion of urine analysis to coincide with urine NCA to calculate renal clearance