NONMEM Simulation Dataset

Article Title: Population Pharmacokinetic Modelling and Estimation of Dosing Strategy for NXY-059, a Nitrone Being Developed for Stroke

Analyte(s): NXY-059

Model: 2 CMT IV Infusion Linear Elimination

Citation: Clin Pharmacokinet. 2005;44(8):863-78.

# NONMEM Dataset Variables and Descriptions

| **Data Item ID** | **Data Item Description** | **Format** | **Sig Digit Display** | **Units** | **Data Item Notes** |
| --- | --- | --- | --- | --- | --- |
| ID | Patient Identification Number | (Numerical Integer) | 4 | N/A | * Each subject has a unique ID value * ID should be sequential starting from 1 to n subjects throughout the dataset |
| NTIM | Nominal Time from First Dose | XXX | 1 to 3 | hr | * Nominal time * Recorded on each record |
| NTAD | Time After Most Recent Dose | XX.XXX | 5 | hr | * Nominal time * Recorded on each record * Resets back to 0 for each additional dose after the first dose |
| TIME | Numerical Time from First Dose | XX.XXX | 5 | hr | * Actual time * Recorded on each record |
| TAD | Time After Most Recent Dose | XX.XXX | 5 | hr | * Actual time * Recorded on each record * Resets back to 0 for each additional dose after the first dose |
| DOSE | Total IV Dosage Administered | XXXXXXX | 2 to 7 | mg | * This variable is identical to AMT, but should be propagated forward for each record from the most recent dosing record (for each treatment/PK Visit). |
| AMT | Total IV Dosage Amount Data Item | XXXXXXX | 2 to 7 | mg | * If a value is entered into the AMT variable, the DV variables for that record should be set to 0 * Values should be positive and only located on the “dosing” records * For observation records, set to 0 |
| DUR | Infusion Duration | X.XX | 1 to 3 | hr | * Total duration of infusion * For observation records, set to 0 |
| EVID | Event Identification Data Item | 0 = Value in DV  1 = Dosing Event | 1 | N/A | * If EVID = 1, DV must = 0. |
| MDV | Missing Dependent Variable Data Item | 0 = Value in DV  1 = Missing DV | 1 | N/A | * If there is an observation value defined in the DV data item, the MDV variable should be set to 0 * If there is NOT an observation in the DV data item, the MDV variable should be set to 1 |
| CMT | Compartment | X | 1 | N/A | * For dosing records, model compartment that dose was administered * For observation records, model compartment that observation was taken |
| CRCL | Creatinine Clearance | XXX.XX | 4 to 5 | mL/min | * Subject creatinine clearance at time of initial dose * Continuous covariate * Simulated from a normal distribution with mean: 71 and SD: 10 |
| WTKG | Body Weight | XXX.XX | 4 to 5 | kg | * Subject body weight at time of initial dose * Continuous covariate * Simulated from a normal distribution with mean: 77 and SD: 14.8 |
| CL | Clearance | X.XXXX | 5 | L/hr | * Empirical Bayesian Estimate of the individual’s clearance * Value should be positive and the same for all records for a particular individual |
| Q | Inter-compartmental Clearance | X.XXXX | 5 | L/hr | * Empirical Bayesian Estimate of the individual’s inter-compartmental clearance * Value should be positive and the same for all records for a particular individual |
| V1 | Central Compartment Volume | XX.XXX | 5 | L | * Empirical Bayesian Estimate of the individual’s central volume * Value should be positive and the same for all records for a particular individual |
| V2 | Peripheral Compartment Volume | XX.XXX | 5 | L | * Empirical Bayesian Estimate of the individual’s peripheral volume * Value should be positive and the same for all records for a particular individual |
| ETA1 | Between Subject Variability | X.XXX | 5 | N/A | * Measurement of BSV for CL |
| ETA2 | Between Subject Variability | X.XXX | 5 | N/A | * Measurement of BSV for V1 |
| THALF | Terminal Half-life | XX.XX | 3 or 4 | hr | * Calculated as log(2) / beta |
| MRT | Mean Residence Time | XX.XX | 3 or 4 | hr | * Calculated as 1 / beta |
| AREA | Area Under the Curve | XXX.XX | 4 or 5 | mg\*hr/L | * Calculated as DOSE / CL |
| AUMC | Area Under the First Moment Curve | XXX.XX | 4 or 5 | mg\*hr2/L | * Calculated as AREA \* MRT * Propagated forward on all records for each respective ID |
| VSS | Volume Distribution at Steady State | XX.XX | 3 or 4 | L | * Calculated as V1 + V2 for a 2 CMT model |
| IRES | Individual Residual | XXX.XX | 4 or 5 | mg/L | * Difference between that individual’s observation and the average observation of the population, including residual variability |
| IPRE | Individual Prediction | XXX.XX | 4 or 5 | mg/L | * If a value is entered into the IPRE variable, the AMT variable for that record should be set to 0 * Simulated plasma level for a patient including inter-individual variability |
| DV | Dependent Variable Data Items | XXX.XX | 4 or 5 | mg/L | * Simulated plasma level for a patient, including inter- and intra-individual variability * If a value is entered into the DV variable, the AMT variable for that record should be set to 0 * Each time point at which DV variables are measured should be entered as a new record |
| PRED | Population Prediction | XXX.XX | 4 or 5 | mg/L | * Simulated population plasma level |
| RES | Residual | XXX.XX | 4 or 5 | mg/L | * Difference between that individual’s observation and the population level observation |