NONMEM Simulation Dataset

Article Title: Population Pharmacokinetics of deferiprone in healthy subjects

Analyte(s): Deferiprone

Matrix: Plasma

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# NONMEM Dataset Variables and Descriptions

| **Data Item ID** | **Data Item Description** | **Format** | **Sig Digit Display** | **Input Decimal  Places** | **Units** | **Data Item Notes** |
| --- | --- | --- | --- | --- | --- | --- |
| C | Comment Data Item | C or .  (Text) | N/A | N/A | N/A | * Top row of dataset should contain ‘C’ with variable names in each column * Any observation or dosing records to be excluded should be commented out (Insert ‘C’), otherwise the field should be set to missing (ie, “.”) |
| ID | NONMEM Specific  Subject / Patient Identification Number | (Numerical Integer) | 4 | 0 | N/A | * Each subject has a unique ID value * ID should be sequential starting from 1 to 9,999 subjects throughout the dataset |
| TRT | Treatment Group | Numerical (Integer) | 1 | 0 | N/A | * Each subject is assigned a treatment group. * If all treatments are the same, each subject will have the same treatment group |
| NTIM | Nominal Time from First Dose | XX.XXX | 5 | 3 | hr | * Nominal time * Time record if there was no deviation from sampling time * Recorded on each record * TIME should be set to missing “.” for any records prior to the first dosing record |
| NTAD | Nominal Time After Most Recent Dose | XX.XXX | 5 | 3 | hr | * Nominal Time * Time record if there was no deviation from sampling 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 | 3 | hr | * Actual time * Recorded on each record * TIME should be set to missing “.” for any records prior to the first dosing record |
| TAD | Time After Most Recent Dose | XX.XXX | 5 | 3 | hr | * Actual Time * Recorded on each record * Resets back to 0 for each additional dose after the first dose |
| DOSE | Total Oral Dosage Administered | XX | 2 to 7 | 0 | 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); for pre-dose values, DOSE should be carried backward. |
| AMT | Total Oral Dosage Amount Data Item | XX | 2 to 7 | 0 | mg | * If a value is entered into the AMT variable, the DV variables for that record should be set to missing “.” * Values should be positive and only located on the “dosing” records * For observation records, set to missing ‘.’ * Dose is assumed to be administered by subcutaneous route |
| SS | Steady State | 0 = No  1 = Yes | 1 | 0 | N/A | * Used to identify if the records following are for a drug at steady state or not |
| II | Dosing Interval | Numerical (Integer) or “.” | 2 | 0 | hr | * Denotes the time in-between multiple doses * If a single dose is given, the record should be “.” for all observations |
| DV | Dependent Variable Data Items | XX.XX | 3 or 4 | N/A | mg/L | * If a value is entered into the DV variable, the AMT variable for that record should be set to missing “.” * Each time point at which DV variables are measured should be entered as a new record * Simulated deferiprone level including inter-individual and residual variability |
| MDV | Missing Dependent Variable Data Item | 0 = Value in DV  1 = Missing DV | 1 | 0 | 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. |
| EVID | Event Identification Data Item | 0 = Value in DV  1 = Dosing Event | 1 | 0 | N/A | * If EVID = 0, AMT, RATE, SS, and II must = “.” * If EVID = 1, DV must = “.” |
| CMT | Compartment Number | Numerical  (Integer) | 1 | 0 | N/A | * If CMT = 1, it must be a dosing record * If CMT = 2, it must be an observation record |
| SEX | Gender of Subject | 0 = Female  1 = Male | 3 | 1 | years | * Individual subject gender * Should be recorded on all records * Categorical Covariate * Categorical Probability: 0.5 |
| Post Execution Table | | | | | | |
| IPRE | Individual Prediction | XX.XX | 3 or 4 | N/A | mg/L | * If a value is entered into the IPRE variable, the AMT variable for that record should be set to missing “.” * Deferiprone plasma levels for a typical patient, including inter-individual variability |
| PRED | Population Prediction | XX.XX | 3 or 4 | N/A | mg/L | * Population level observation * Propagated forward on all records for each respective ID |
| IWRE | Individual Weighted Residual | X.XX | 3 | N/A | N/A | * Difference between that individual’s observation and the population level observation, including residual variability and weighted by the value of the observation |
| IRES | Individual Residual | X.XX | 3 | N/A | mg/L | * Difference between that individual’s observation and the average observation of the population, including residual variability |
| WRES | Weighted Residual | X.XX | 3 | N/A | N/A | * Difference between that individual’s observation and the population level observation, weighted by the value of the observation |
| RES | Residual | X.XX | 3 | N/A | mg/L | * Difference between that individual’s observation and the population level observation |
| KA | Absorption Rate Constant | XXX | 3 | N/A | 1/hr | * THETA1 * Empirical Bayesian Estimate of the individual’s deferiprone absorption rate constant * Value should be positive and the same for all records for a particular individual * Propagated forward on all records for each respective ID |
| CL | Apparent Central Compartment Clearance | XXX | 3 | N/A | L/hr | * THETA2 * Empirical Bayesian Estimate of the individual’s deferiprone central compartment clearance * Value should be positive and the same for all records for a particular individual * Propagated forward on all records for each respective ID * Doesn’t take bioavailability into account |
| V | Apparent Central Compartment Volume | XXX | 3 | N/A | L | * THETA3 for SEX = 0 & THETA4 for SEX = 1 * Empirical Bayesian Estimate of the individual’s deferiprone central compartment volume * Value should be positive and the same for all records for a particular individual * Propagated forward on all records for each respective ID * Doesn’t take bioavailability into account |
| ALAG1 | Lag Time into Absorption Compartment | XXX | 3 | N/A | hr | * THETA5 * Empirical Bayesian Estimate of the individual’s deferiprone lag time * Value should be positive and the same for all records for a particular individual * Propagated forward on all records for each respective ID |
| Vss | Volume Distribution at Steady State | XX.XX | 3 or 4 | N/A | L | * Vss = V * Propagated forward on all records for each respective ID * Doesn’t take bioavailability into account |
| T12 | Terminal Half-life | XX.XX | 3 or 4 | N/A | hr | * Calculated as 0.693 / (K10) * Propagated forward on all records for each respective ID |
| MRT | Mean Residence Time | XX.XX | 3 or 4 | N/A | hr | * Calculated as 1 / (K10) * Propagated forward on all records for each respective ID |
| AREA | Area Under the Curve | XXX.XX | 4 or 5 | N/A | mg\*hr/L | * Calculated as DOSE / CL * Propagated forward on all records for each respective ID * Doesn’t take bioavailability into account |
| AUMC | Area Under the First Moment Curve | XXX.XX | 4 or 5 | N/A | mg\*hr2/L | * Calculated as AREA \* MRT * Propagated forward on all records for each respective ID * Doesn’t take bioavailability into account |
| ETA1 | Between Subject Variability | X.XXX | 4 | N/A | N/A | * Exponential relationship of individual variability for CL/F |
| ETA2 | Between Subject Variability | X.XXX | 4 | N/A | N/A | * Exponential relationship of individual variability for V/F |
| ETA3 | Between Subject Variability | X.XXX | 4 | N/A | N/A | * Exponential relationship of individual variability for KA |