

Table 1S: Demographics of subpopulations A-F, derived from the total data pool G. Weight and age given as mean (SD), gender as (female:male), lamotrigine dose as range in mg/day, number of patients receiving co-medication with an anti-epileptic drug (AED) given with (dosing range); only shown here are the AEDs given to at least 10 individuals in the total dataset (carbamazepine, clobazam, clonazepam, gabapentin, levetiracetam, oxcarbazepine, phenobarbital, phenytoin, topiramate and valproic acid).

Demographic	Populations						Total (G)
	A	B	C	D	E	F	
Weight (kg)	70.1 (21.3)	67.8 (18.9)	69.2 (20)	76.3 (17.5)	35.7 (15.7)	9.6 (2.4)	52.1 (36.6)
Age (years)	33.2 (14.1)	33.9 (14.4)	35:3 (12.8)	72.5 (5.5)	7.8 (2.7)	1.2 (0.5)	32.8 (28.1)
Gender (M:F)	41:39	14:18	51:45	58:58	18:6	64:80	246:246
# of patients	80	32	96	116	24	144	492
Formulations	IR and XR	IR and XR	XR	XR	XR	IR	IR and XR
LMT dose	12.5-1200	12.5-800	12.5-600	12.5-500	5-634	2-87	2-1200
Comedication frequency (dose range in mg/day)							
CBZ	20 (300-1200)	4 (600-1200)	24 (400-1200)	12 (300-1200)	0	2 (300-300)	62 (300-1200)
CLBZ (mcg)	4 (10-40)	2 (10-20)	3 (15-20)	0	0	2 (2.5-5)	11 (2.5-40)
CLNZ (mcg)	7 (0.5-175)	2 (1-2)	3 (0.5-3)	1 (0.5-0.5)	0	9 (0.25-2)	22 (0.25-175)
GBP	1 (400-400)	0	1 (2400-2400)	11 (100-3600)	0	0	13 (100-3600)
LVT	6 (1000-4250)	3 (500-3000)	10 (1000-4000)	46 (125-3500)	0	2 (125-500)	67 (125-4250)
OXC	3 (450-1200)	2 (600-1200)	9 (600-1500)	7 (150-1500)	0	4 (270-420)	25 (150-1500)
PHB	3 (60-400)	1 (120-120)	2 (120-120)	3 (60-120)	0	24 (24-120)	33 (24-400)
PHT	20 (200-780)	10 (200-400)	12 (200-400)	36 (200-400)	0	3 (40-40)	81 (40-780)
TPM	9 (25-400)	1 (100-100)	13 (100-700)	5 (25-200)	0	9 (12.5-400)	37 (12.5-700)
VPA	30 (250-3000)	12 (600-2100)	19 (600-3000)	11 (250-2000)	0	3 (250-600)	75 (250-3000)

Table 2S: Overview of the steps in model development and corresponding objective function value (OFV), starting from the base model (including population pharmacokinetic (PK) parameters accounting for the extended- (Ka XR) and immediate absorption rates (Ka IR), clearance (CL) and volume of distribution (V)), used to create the final lamotrigine model.

Model	Population(s)	Used model	OFV	p(dOFV)
A1	Pop. A	Base	9089.129	-
A2	“	A1 + η_{CL}	3284.756	<0.05
A3	“	A2 + η_V	3050.895	<0.05
A4	“	A3 + $\eta_{Ka\ XR}$	2809.051	<0.05
A5	“	A4 + $\eta_{Ka\ IR}$	2785.005	<0.05
A6	“	A5 + Allometry V and CL	2798.125	>0.05
A7	“	A6 + CBZ on CL	2787.155	<0.05
A8	“	A7 + PHT on CL	2749.179	<0.05
A	“	A8 + VPA on CL	2710.545	<0.05
B	Pop. B	Model A	1097.47	-
B*	“	Model B	982.732	<0.05
B**	Pop. A+B	Model B*	3657.37	-
C	Pop. C	Model B**	1289.906	-
C*	“	Model C	1041.63	<0.05
C**	Pop. A-C	Model C*	4890.933	-
D	Pop. D	Model C**	1507.48	-
D*	“	Model D	1235.55	<0.05
D**	Pop. A-D	Model D*	6236.311	-
E	Pop. E	Model D**	111.707	-
E*	“	Model E	86.707	<0.05
E**	Pop. A-E	Model E*	6347.644	-
F	Pop. F	Model E**	85.641	-
F*	“	Model F	-595.285	<0.05
F1*	“	Model F* + Maturation	-598.044	>0.05
F**	Pop. A-F	Model F*	6361.691	-
Final	“	Model F** + Maturation	6301.631	<0.05