

Project 105c-030
(Data as of: November 27, 1996)

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Table 29
Individual and Combined Center Summary of Reasons for Treatment Escape
Per Protocol Analysis for Patients with Secondarily Generalized Seizures

Region/ Study- Center	LAMICTAL										VPA			
	Reasons for Escape										Reasons for Escape			
	No. Pts.	No. Pts.	No. Pts.	No. Pts.	No. Pts.	No. Pts.	No. Pts.	No. Pts.	No. Pts.	No. Pts.	Double Monthly Seizure Frequency	Double Highest Two Day and Worst Seizure Type	Emergence of New Seizure Type	Significant Prolongation of Seizure
Combined	23	12 (52%)	3 (25%)	6 (50%)	0 (0%)	5 (42%)	22	15 (68%)	3 (20%)	9 (60%)	0 (0%)	3 (20%)	0 (0%)	0 (0%)
Northeast	6	4 (67%)	1 (25%)	2 (50%)	0 (0%)	0 (0%)	6	4 (67%)	0 (0%)	4 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
030-0001	2	1 (50%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
030-0015	3	2 (67%)	1 (50%)	1 (100%)	0 (0%)	0 (0%)	3	1 (33%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
031-0015	1	1 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1	1 (100%)	0 (0%)	1 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
031-0017	0	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Southeast	5	2 (40%)	0 (0%)	1 (50%)	0 (0%)	2 (100%)	4	3 (75%)	1 (33%)	1 (33%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
030-0002	0	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
030-0003	2	1 (50%)	0 (0%)	1 (100%)	0 (0%)	1 (100%)	1	1 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
030-0008	1	1 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1	1 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
031-0014	1	1 (100%)	0 (0%)	0 (0%)	0 (0%)	1 (100%)	1	1 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
031-0018	1	1 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Midwest	8	5 (63%)	2 (40%)	2 (40%)	0 (0%)	3 (60%)	8	5 (63%)	2 (40%)	2 (40%)	0 (0%)	1 (20%)	0 (0%)	0 (0%)
030-0004	1	1 (100%)	0 (0%)	0 (0%)	0 (0%)	1 (100%)	1	1 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
030-0005	1	1 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
030-0014	1	1 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
030-0024	0	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
031-0004	1	1 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1	1 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
031-0009	2	1 (50%)	0 (0%)	1 (100%)	0 (0%)	0 (0%)	2	2 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
031-0011	1	1 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
031-0016	1	1 (100%)	0 (0%)	0 (0%)	0 (0%)	1 (100%)	1	1 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
031-0024	0	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
West	4	1 (25%)	0 (0%)	1 (100%)	0 (0%)	0 (0%)	4	3 (75%)	0 (0%)	2 (67%)	0 (0%)	1 (33%)	0 (0%)	0 (0%)
030-0006	0	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
031-0023	4	1 (25%)	0 (0%)	1 (100%)	0 (0%)	0 (0%)	3	1 (33%)	0 (0%)	2 (100%)	0 (0%)	1 (33%)	0 (0%)	0 (0%)

Multiple reasons for escape are possible per patient.
Centers with no patients in this analysis: 030-0007, 030-0010, 031-0013, 031-0019, 031-0020, 031-0021, 031-0022, and 031-0026.

030-0010, 030-0012, 030-0013, 030-0020, 030-0021, 030-0025, 031-0006,

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Table 30
Individual and Combined Center Summary of Reasons for Treatment Failure
Intent-to-Treat Analysis for Patients with Secondarily Generalized Seizures

LAMICTAL

Region/ Study- Center	Reasons for Failure					Reasons for Failure						
	No. of Pts.	No. of Failures	Escape	Adverse Experi- ence	Inade- quate Response	Other	No. of Pts.	No. of Failures	Escape	Adverse Experi- ence	Inade- quate Response	Other
Combined	38	27 (71%)	12 (44%)	7 (26%)	4 (15%)	4 (15%)	27	20 (74%)	15 (75%)	2 (10%)	0 (0%)	3 (15%)
Northeast	13	11 (85%)	4 (36%)	5 (45%)	1 (9%)	1 (9%)	9	7 (78%)	4 (57%)	2 (29%)	0 (0%)	1 (14%)
030-0001	2	1 (50%)	1 (100%)	0 (0%)	0 (0%)	0 (0%)	0	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
030-0015	6	5 (83%)	2 (40%)	3 (60%)	0 (0%)	0 (0%)	4	2 (50%)	1 (50%)	1 (100%)	0 (0%)	0 (0%)
031-0006	1	1 (100%)	0 (0%)	1 (100%)	0 (0%)	0 (0%)	1	1 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
031-0015	2	2 (100%)	1 (50%)	0 (0%)	1 (50%)	0 (0%)	1	1 (100%)	1 (100%)	0 (0%)	0 (0%)	0 (0%)
031-0017	2	2 (100%)	0 (0%)	1 (50%)	1 (50%)	1 (50%)	3	3 (100%)	2 (67%)	0 (0%)	0 (0%)	1 (33%)
Southeast	10	7 (70%)	2 (29%)	1 (14%)	3 (43%)	1 (14%)	6	5 (83%)	3 (60%)	0 (0%)	0 (0%)	2 (40%)
030-0002	1	1 (100%)	0 (0%)	0 (0%)	1 (100%)	0 (0%)	1	1 (100%)	1 (100%)	0 (0%)	0 (0%)	0 (0%)
030-0003	2	1 (50%)	1 (100%)	0 (0%)	0 (0%)	0 (0%)	1	1 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
030-0008	1	1 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2	2 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
030-0025	1	1 (100%)	0 (0%)	0 (0%)	1 (100%)	0 (0%)	0	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
031-0014	4	4 (100%)	1 (25%)	1 (25%)	2 (50%)	1 (25%)	2	2 (100%)	1 (50%)	0 (0%)	0 (0%)	1 (50%)
031-0018	1	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Midwest	10	7 (70%)	5 (71%)	1 (14%)	1 (14%)	1 (14%)	8	5 (63%)	5 (100%)	0 (0%)	0 (0%)	3 (38%)
030-0004	1	1 (100%)	1 (100%)	0 (0%)	0 (0%)	0 (0%)	1	1 (100%)	1 (100%)	0 (0%)	0 (0%)	0 (0%)
030-0005	1	1 (100%)	1 (100%)	0 (0%)	0 (0%)	0 (0%)	0	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
030-0014	1	1 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1	1 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
030-0024	1	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
031-0004	0	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
031-0009	3	2 (67%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1	1 (100%)	1 (100%)	0 (0%)	0 (0%)	0 (0%)
031-0011	2	2 (100%)	1 (50%)	1 (50%)	0 (0%)	0 (0%)	0	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
031-0016	1	1 (100%)	1 (100%)	0 (0%)	0 (0%)	0 (0%)	0	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
031-0024	1	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1	1 (100%)	1 (100%)	0 (0%)	0 (0%)	0 (0%)
West	5	2 (40%)	1 (50%)	0 (0%)	1 (50%)	1 (50%)	4	3 (75%)	3 (100%)	0 (0%)	0 (0%)	1 (25%)
030-0006	0	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1	1 (100%)	1 (100%)	0 (0%)	0 (0%)	0 (0%)
031-0023	5	2 (40%)	1 (50%)	0 (0%)	1 (50%)	1 (50%)	3	2 (67%)	2 (100%)	0 (0%)	0 (0%)	1 (33%)

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NOTES: In the intent-to-treat analysis, failure is defined as any patient who escaped or dropped out of the study.
Centers with no patients in this analysis: 030-0007, 030-0010, 030-0012, 030-0013, 030-0020, 030-0021, 031-0007, 031-0010, 031-0013, 031-0019, 031-0020, 031-0021, 031-0022, and 031-0026.

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Table 37
Summary of Seizure Description Data
Intent-to-Treat Population

Week Parameter	Category/ Statistic	LAMICTAL	VPA
8 No. of Patients		75	78
One/More than One Type of Seizure			
Major/Minor Seizures	Generally More than One Type Generally One Type	43 (57.3%) 32 (42.7%)	42 (53.8%) 36 (46.2%)
No. Major Seizures	Both Major and Minor Seizures Typically Only Major Seizures Typically Only Minor Seizures	40 (53.3%) 8 (10.7%) 26 (34.7%)	41 (52.6%) 8 (10.3%) 29 (37.2%)
	N	51	49
	Mean	6.4	9.8
	Std. Deviation	8.8	14.7
	Median	3	6
	Minimum		
	Maximum		
Length of Major Seizures (min)	N	33	33
	Mean	8.8	8.9
	Std. Deviation	12.8	14.3
	Median	3	3
	Minimum		
	Maximum		
No. Minor Seizures	N	57	53
	Mean	15.6	16.5
	Std. Deviation	15.7	14.9
	Median	10	12
	Minimum		
	Maximum		
Length of Minor Seizures (min)	N	39	41
	Mean	5.9	3.0
	Std. Deviation	11.4	3.8
	Median	2	2
	Minimum		
	Maximum		
No. Past AEDs	N	74	77
	Mean	4.4	4.7
	Std. Deviation	2.6	2.8
	Median	4	4
	Minimum		
	Maximum		
Type of Seizures ¹	Simple Partial	31 (41.3%)	33 (42.3%)

¹ Multiple seizure types are possible within patient.

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Table 37
Summary of Seizure Description Data
Intent-to-Treat Population

Week Parameter	Category/ Statistic	LAMICTAL	VPA
8 Type of Seizures ¹			
	Complex Partial	36 (48.0%)	51 (65.4%)
	Generalized Tonic-Clonic	11 (14.7%)	20 (25.6%)
	Absence	6 (8.0%)	9 (11.5%)
	Myoclonic	1 (1.3%)	1 (1.3%)
	Does Not Know	18 (24.0%)	22 (28.2%)
	Other	7 (9.3%)	3 (3.8%)
16 No. of Patients		51	63
One/More than One Type of Seizure	Generally More than One Type	24 (47.1%)	38 (60.3%)
	Generally One Type	25 (49.0%)	25 (39.7%)
Major/Minor Seizures	Both Major and Minor Seizures	24 (47.1%)	33 (52.4%)
	Typically Only Major Seizures	4 (7.8%)	4 (6.3%)
	Typically Only Minor Seizures	21 (41.2%)	26 (41.3%)
No. Major Seizures	N	31	32
	Mean	5.2	7.3
	Std. Deviation	6.2	9.7
	Median	3	3
	Minimum		
	Maximum		
Length of Major Seizures (min)	N	23	23
	Mean	7.3	8.3
	Std. Deviation	9.0	14.4
	Median	3	3
	Minimum		
	Maximum		
No. Minor Seizures	N	34	50
	Mean	13.5	17.3
	Std. Deviation	15.6	19.2
	Median	8	11
	Minimum		
	Maximum		
Length of Minor Seizures (min)	N	25	32
	Mean	16.1	1.9
	Std. Deviation	12.2	1.3
	Median	2	1
	Minimum		
	Maximum		
No. Past AEDs	N	50	62

¹ Multiple seizure types are possible within patient.

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Table 37
Summary of Seizure Description Data
Intent-to-Treat Population

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Week Parameter	Category/ Statistic	LAMICTAL	VPA
16 No. Past AEDs	Mean Std. Deviation Median Minimum Maximum	4.3 2.5 4 1 11	4.5 2.8 4 1 14
Type of Seizures ¹	Simple Partial Complex Partial Generalized Tonic-Clonic Absence Myoclonic Does Not Know Other	18 (35.3%) 26 (51.0%) 11 (21.6%) 2 (3.9%) 1 (2.0%) 13 (25.5%) 1 (2.0%)	35 (55.6%) 39 (61.9%) 14 (22.2%) 10 (15.9%) 3 (4.8%) 15 (23.8%) 1 (1.6%)
20 No. of Patients		40	30
One/More than One Type of Seizure	Generally More than One Type Generally One Type	21 (52.5%) 19 (47.5%)	14 (46.7%) 15 (50.0%)
Major/Minor Seizures	Both Major and Minor Seizures Typically Only Major Seizures Typically Only Minor Seizures	16 (40.0%) 2 (5.0%) 22 (55.0%)	13 (43.3%) 2 (6.7%) 14 (46.7%)
No. Major Seizures	N Mean Std. Deviation Median Minimum Maximum	19 2.8 2.3 2	13 5.4 5.8 3
Length of Major Seizures (min)	N Mean Std. Deviation Median Minimum Maximum	14 6.6 8.4 4	9 6.3 6.7 5
No. Minor Seizures	N Mean Std. Deviation Median Minimum Maximum	33 11.5 14.5 5	22 11.4 8.7 10
Length of Minor Seizures (min)	N	25	15

¹ Multiple seizure types are possible within patient.

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Table 37
Summary of Seizure Description Data
Intent-to-Treat Population

Week Parameter	Category/ Statistic	LAMICTAL	VPA
20 Length of Minor Seizures (min)	Mean Std. Deviation Median Minimum Maximum N	2.1 1.5 1 39 3.9 2.3 3	3.2 4.9 1 30 3.6 2.0 3
No. Past AEDs	Mean Std. Deviation Median Minimum Maximum N	14 (35.0%) 22 (55.0%) 7 (17.5%) 1 (2.5%) 0 (0.0%) 10 (25.0%) 1 (2.5%) 31	12 (40.0%) 21 (70.0%) 8 (26.7%) 0 (0.0%) 1 (3.3%) 6 (20.0%) 1 (3.3%) 15
Type of Seizures ¹	Simple Partial Complex Partial Generalized Tonic-Clonic Absence Myoclonic Does Not Know Other	13 (41.9%) 17 (54.8%) 8 (25.8%) 2 (6.5%) 21 (67.7%) 13 8.8 22.7 1 11 3.6 2.9 3 24	9 (53.3%) 7 (46.7%) 5 (33.3%) 1 (6.7%) 9 (60.0%) 7 4.7 6.6 3 6 3.3 2.3 4 12
28 No. of Patients	Generally More than One Type Generally One Type Both Major and Minor Seizures Typically Only Major Seizures Typically Only Minor Seizures N	Mean Std. Deviation Median Minimum Maximum N	Mean Std. Deviation Median Minimum Maximum N
One/More than One Type of Seizure	Mean Std. Deviation Median Minimum Maximum N	Mean Std. Deviation Median Minimum Maximum N	Mean Std. Deviation Median Minimum Maximum N
Major/Minor Seizures	Mean Std. Deviation Median Minimum Maximum N	Mean Std. Deviation Median Minimum Maximum N	Mean Std. Deviation Median Minimum Maximum N
No. Major Seizures	Mean Std. Deviation Median Minimum Maximum N	Mean Std. Deviation Median Minimum Maximum N	Mean Std. Deviation Median Minimum Maximum N
Length of Major Seizures (min)	Mean Std. Deviation Median Minimum Maximum N	Mean Std. Deviation Median Minimum Maximum N	Mean Std. Deviation Median Minimum Maximum N
No. Minor Seizures	Mean Std. Deviation Median Minimum Maximum N	Mean Std. Deviation Median Minimum Maximum N	Mean Std. Deviation Median Minimum Maximum N

¹ Multiple seizure types are possible within patient.

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Table 37
Summary of Seizure Description Data
Intent-to-Treat Population

Week Parameter	Category/ Statistic	LAMICTAL	VPA
28 No. Minor Seizures	Mean Deviation Std. Median Minimum Maximum	9.9 17.3 4	5.3 3.0 5
Length of Minor Seizures (min)	N Mean Std. Median Minimum Maximum	16 2.4 2.1 1	8 1.8 1.6 1
No. Past AEDs	N Mean Std. Median Minimum Maximum	30 3.6 2.3 3	15 3.4 1.9 3
Type of Seizures ¹	Simple Partial Complex Partial Generalized Tonic-Clonic Absence Does Not Know	9 (29.0%) 14 (45.2%) 2 (6.5%) 1 (3.2%) 12 (38.7%)	8 (53.3%) 10 (66.7%) 5 (33.3%) 2 (13.3%) 1 (6.7%)

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¹ Multiple seizure types are possible within patient.

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Table 44
Summary of Days Missed From Work and Leisure
Intent-to-Treat Population

Scale	Week	LAMICTAL (N=76)						VPA (N=80)					
		N	Mean	SD	Median	Min.	Max.	N	Mean	SD	Median	Min.	Max.
Days from Work	8	19	1.7	4.1	0.0	0.0	18.0	18	3.4	7.4	0.0	0.0	30.0
	16	17	0.4	1.0	0.0	0.0	3.0	11	1.0	1.9	0.0	0.0	6.0
	20	13	0.0	0.0	0.0	0.0	0.0	5	0.0	0.0	0.0	0.0	0.0
	28	8	0.1	0.4	0.0	0.0	1.0	1	0.0	0.0	0.0	0.0	0.0
Days of Leisure	8	21	0.6	1.3	0.0	0.0	5.0	28	2.0	4.2	0.0	0.0	20.0
	16	22	0.9	1.1	0.0	0.0	3.0	18	2.5	4.2	0.0	0.0	15.0
	20	18	0.4	1.2	0.0	0.0	5.0	8	0.1	0.4	0.0	0.0	1.0
	28	14	2.4	8.2	0.0	0.0	31.0	2	0.0	0.0	0.0	0.0	0.0

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Table 47
Summary of Patients Reporting Epilepsy Related Emergency Room Visits and Hospitalization
Intent-to-Treat Population

Patients Requiring...	Week	LAMICTAL		VPA	
		N	No. (%) of Patients	N	No. (%) of Patients
ER Visit	8	56	3 (5%)	65	6 (9%)
	16	46	3 (7%)	54	5 (9%)
	20	36	0 (0%)	28	2 (7%)
	28	26	1 (4%)	14	0 (0%)
Hospitalization	8	56	0 (0%)	65	3 (5%)
	16	46	1 (2%)	54	3 (6%)
	20	36	1 (3%)	28	0 (0%)
	28	26	0 (0%)	14	0 (0%)

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Table 54
Summary of Study Drug Plasma Concentrations by Strata Analysis
Per Protocol Population

Phase	Study Week	Efficacy	Baseline AED	LAMICTAL						VPA							
				Plasma Concentration (ug/mL)			N	Mean	SD	Median	Min.	Max.	Plasma Concentration (ug/mL)			N	Mean
B/Wk8	8	Completer	All CBZ PHT	42 25 17	0.0 0.0 0.0	0.0 0.0 0.0							0.0 0.0 0.0	47 29 18	0.4 0.0 1.1		
T/Wk2	10	Completer	All CBZ PHT	40 23 17	2.5 2.7 2.3	1.4 1.4 1.4	2.1 2.7 1.7	49 33 16	47.1 49.7 41.8	23.0 24.7 18.5	45.2 45.5 38.6						
T/Wk4	12	Completer	All CBZ PHT	38 24 14	3.9 4.4 3.0	2.2 2.3 1.8	3.5 4.4 2.6	51 34 17	49.6 51.1 46.5	20.3 19.5 22.0	46.2 46.0 52.9						
		Escaper	All CBZ PHT	6 2 4	4.9 3.7 5.6	3.3 0.0 4.0	3.7 3.7 3.9	7 3 4	28.3 28.5 28.2	6.5 6.6 7.5	29.6 26.0 30.7						
T/Wk6	14	Completer	All CBZ PHT	34 23 11	4.6 5.3 3.1	2.7 3.0 1.1	4.0 4.6 3.0	32 22 10	43.2 46.7 35.5	21.6 22.3 18.5	42.5 47.5 32.6						
		Escaper	All CBZ PHT	8 3 5	4.4 7.1 2.7	2.4 0.2 1.2	3.7 7.0 3.1	15 9 6	42.3 43.9 40.0	14.9 16.3 13.6	36.2 35.6 40.3						
T/Wk8	16	Completer	All CBZ PHT	25 18 7	5.6 6.4 3.5	2.9 2.8 1.9	4.9 6.1 3.3	21 15 6	49.1 54.2 36.1	15.8 15.8 12.2	49.1 52.4 35.9						
		Escaper	All CBZ PHT	2 1 1	4.3 2.3 5.6	1.9	4.3 2.9 5.6	11 6 5	40.9 38.4 44.0	19.8 26.5 9.1	42.4 37.8 42.4						
M/Wk4	20	Completer	All CBZ PHT	28 21 7	7.8 8.1 7.0	3.0 3.1 2.9	7.2 7.3 7.2	10 6 4	70.6 72.9 67.1	20.9 20.8 23.7	75.1 75.1 64.6						

PHASE: B=Baseline, T=Transition, M=Monotherapy, F=Follow-Up. Post '/' indicates specific timepoint within phase.

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(Data as of: November 27, 1996)

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Table 54
Summary of Study Drug Plasma Concentrations by Strata Analysis
Per Protocol Population

Phase	Study Week	Efficacy	Baseline AED	LAMICTAL						VPA							
				Plasma Concentration (ug/mL)						Plasma Concentration (ug/mL)							
				N	Mean	SD	Median	Min.	Max.	N	Mean	SD	Median	Min.	Max.		
M/Wk4	20	Escaper	All CBZ	0 0													
M/Wk8	24	Completer	All CBZ PHT	26 20 6	9.5 10.3 6.8	4.6 4.8 3.0	8.5 9.5 6.5										
		Escaper	All CBZ	1 1	10.1 10.1		10.1 10.1										
M/Wk12	28	Completer	All CBZ PHT	15 11 4	8.8 9.8 6.1	3.9 3.7 3.2	7.9 9.8 6.0										
		Escaper	All CBZ	1 1	6.5 6.5		6.5 6.5										

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PHASE: B-Baseline, T-Transition, M-Monotherapy, F-Follow-Up. Post '/' indicates specific timepoint within phase.

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(Data as of: November 27, 1996)

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q6b5(0301ds08) 19DEC96 11:51

Table 55
Summary of AED Plasma Concentrations by Visit and Efficacy Response
Per Protocol Population

AED Phase	Study Week	Efficacy	LAMICTAL			VPA		
			N	Mean	SD	Median	Min.	Max.
CBZ	B/Wk0	ALL	30	9.1	2.8	8.6		
		Completer	30	9.1	2.8	8.6		
	B/Wk4	ALL	23	9.6	2.6	9.0		
		Completer	23	9.6	2.6	9.0		
	B/Wk8	ALL	29	8.9	3.0	7.9		
		Completer	29	8.9	3.0	7.9		
	T/Wk2	ALL	29	8.2	3.3	8.0		
		Completer	29	8.2	3.3	8.0		
	T/Wk4	ALL	28	7.9	3.0	7.4		
		Completer	26	7.7	2.8	7.4		
	T/Wk6	ALL	27	5.7	1.9	5.9		
		Completer	23	5.8	1.8	6.0		
PHT	B/Wk0	ALL	20	17.4	7.0	17.0		
		Completer	20	17.4	7.0	17.0		
	B/Wk4	ALL	17	19.4	9.4	19.0		
		Completer	17	19.4	9.4	19.0		
	B/Wk8	ALL	19	19.3	7.2	18.0		
		Completer	19	19.3	7.2	18.0		
	T/Wk2	ALL	19	21.2	8.7	20.0		
		Completer	19	21.2	8.7	20.0		
	T/Wk4	ALL	19	18.5	7.2	18.0		
		Completer	15	18.3	6.4	18.0		
		Escaper	4	19.0	10.7	20.0		

PHASE: B-Baseline, T-Transition. Post "/" indicates specific timepoint within phase.

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Table 55
Summary of AED Plasma Concentrations by Visit and Efficacy Response
Per Protocol Population

AED Phase	Study Week	Efficacy	LAMICTAL						VPA					
			AED Plasma Concentration (ug/mL)						AED Plasma Concentration (ug/mL)					
			N	Mean	SD	Median	Min.	Max.	N	Mean	SD	Median	Min.	Max.
PHT T/Wk6	14	ALL	16	8.8	5.2	8.5			19	6.4	4.8	5.0		
		Completer	11	8.4	6.0	8.0			12	6.4	5.4	4.0		
		Escaper	5	9.6	3.2	10.0			7	6.4	3.9	5.0		
T/Wk8	16	ALL	8	2.5	2.0	1.5			11	1.8	0.6	1.5		
		Completer	7	2.6	2.1	1.5			6	1.8	0.6	1.5		
		Escaper	1	1.5		1.5			5	1.8	0.7	1.5		

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PHASE: B-Baseline, T-Transition. Post '/' indicates specific timepoint within phase.

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(Data as of: November 27, 1996)

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Table 61
Summary of Average and Modal Total Daily Dose of LANICTAL Monotherapy

Weeks on Monotherapy	Average Dose (mg)			Modal Dose (mg)		
	N	Mean	Std. Dev.	Median	Minimum	Maximum
0-2	4	468.8	62.5	500.0		
>2-4	1	500.0		500.0		
>4-6	3	500.0	0.0	500.0		
>6-8	1	475.0		475.0		
>8-10	3	474.3	44.5	500.0		
>10-12	18	489.4	36.1	500.0		
>12-14	13	492.3	21.7	500.0		
					Mean	Std. Dev.
					Median	Minimum Maximum
					500.0	0.0
					500.0	0.0
					500.0	0.0
					500.0	0.0
					466.7	57.7
					488.9	47.1
					500.0	0.0

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Summary of Most Common Treatment Emergent Adverse Experiences
Table 66
Total Population

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Preferred Adverse Experience Term	LAMICTAL (N-76)				VPA (N-80)				
	No. (%) of Pts.		No. of Pts. with Maximum Intensity		No. (%) of Pts.		No. of Pts. with Maximum Intensity		
			Mild	Mod	Sev		Mild	Mod	Sev
DIZZINESS	18	(24%)				21	(26%)		
NAUSEA	14	(18%)				16	(20%)		
HEADACHE	13	(17%)				16	(20%)		
COORDINAT ABNORM	13	(17%)				0	(0%)		
VOMIT	12	(16%)				10	(13%)		
ASTHENIA	11	(14%)				6	(8%)		
ALL RASH	11	(14%)				13	(16%)		
TREMOR	10	(13%)				13	(16%)		
SOMNOLENCE	8	(11%)				10	(13%)		
INJURY ACCID	7	(9%)				13	(16%)		
INSOMNIA	7	(9%)				10	(13%)		
DIPLOPIA	7	(9%)				9	(11%)		
AMBLYOPIA	7	(9%)				5	(6%)		
NYSTAGMUS	7	(9%)				4	(5%)		
ATAXIA	7	(9%)				0	(0%)		
PAIN	6	(8%)				4	(5%)		
DIARRHEA	6	(8%)				4	(5%)		
INFECT	5	(7%)				3	(4%)		
NERVOUSNESS	5	(7%)				11	(14%)		
RHINITIS	4	(5%)				4	(5%)		
PAIN ABDO	4	(5%)				6	(8%)		
PAIN CHEST	4	(5%)				6	(8%)		
ALOPECIA	4	(5%)				4	(5%)		
IRRITABILITY	4	(5%)				3	(4%)		
SWEAT	4	(5%)				2	(3%)		
LYMPHADENO	4	(5%)				2	(3%)		
PRURITUS	4	(5%)				2	(3%)		
SINUSITIS	4	(5%)				0	(0%)		
DYSPEPSIA	4	(5%)				0	(0%)		
FLU SYND	3	(4%)				0	(0%)		
ECCHYMOSIS	1	(1%)				12	(15%)		
						6	(8%)		
						4	(5%)		

All adverse experiences occurring in >= 5% of patients in either treatment group.
ALL RASH is any of the following AEs: RASH, RASH MAC PAP, URTICARIA, ERYTHEMA, RASH PETECH,
STEVENS JOHNSON SYND, RASH PUST, OR RASH VESIC BULL.

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Summary of Most Common Treatment	Table 67 Emergent Adverse Experiences Total Population	Experiences Occurring During Monotherapy	Experiences Occurring During Monotherapy

Preferred Adverse Experience Term	LAMICTAL (N=43)				VPA (N=44)			
	No. (%) Of Pts.	No. Of Pts. with Maximum Intensity			No. (%) Of Pts.	No. Of Pts. with Maximum Intensity		
		Mild	Mod	Sev		Mild	Mod	Sev
VOMIT	4	{	9%		0	{	0%	
HEADACHE	3	{	7%	1	0	{	14%	0
DYSPEPSIA	3	{	7%	1	0	{	2%	1
NAUSEA	3	{	7%	2	0	{	2%	0
RHINITIS	3	{	7%	0	0	{	2%	0
COORDINAT	3	{	7%	1	1	{	2%	0
DIZZINESS	3	{	7%	1	1	{	0%	0
TREMOR	2	{	5%	1	0	{	0%	0
DIARRHEA	0	{	0%	0	3	{	7%	1
		{	0%		4	{	9%	0

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All adverse experiences occurring in >= 5% of patients in either treatment group. ALL RASH is any of the following AEs: RASH, RASH MAC PAP, URTICARIA, ERYTHEMA, RASH PETECH, STEVENS JOHNSON SYND, RASH PUST, OR RASH VESIC BULL.

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Table 76
Summary of Serious Adverse Experiences

Body System/ Preferred AE Term	LAMICTAL (N=76)				VPA (N=80)				Between Treatment Comparison	
	No. (%) of Pts	No. of Pts. with Maximum Intensity			No. (%) of Pts.	No. of Pts. with Maximum Intensity			Diff in Prop.	95% CI
		Mild	Mod	Sev		Mild	Mod	Sev		
No. of Patients with AEs	4 (5%)	1			4 (5%)					
GENERAL										
FEVER	1 (1%)				0 (0%)				0.01	(-0.01,0.04)
HEADACHE	1 (1%)	0			0 (0%)	0			0.01	(-0.01,0.04)
PAIN	1 (1%)	1			0 (0%)	0			0.01	(-0.01,0.04)
CHEST	1 (1%)	1			0 (0%)	0			0.01	(-0.01,0.04)
REACT AGGRAV	0 (0%)	1			0 (0%)	0			0.01	(-0.01,0.04)
DIGESTIVE					2 (3%)				-0.03	(-0.06,0.01)
NAUSEA	1 (1%)	1			0 (0%)	0			0.01	(-0.01,0.04)
NERVOUS SYSTEM										
DIZZINESS	1 (1%)	1			0 (0%)				0.01	(-0.01,0.04)
SUICIDAL IDEATION	1 (1%)	0			0 (0%)	0			0.01	(-0.01,0.04)
CONVULS GRAND MAL	0 (0%)	0			1 (1%)	0			0.01	(-0.01,0.04)
PARANOID REACT	0 (0%)	0			1 (1%)	0			-0.01	(-0.04,0.01)
RESPIRATORY									-0.01	(-0.04,0.01)
DYSPNEA	1 (1%)	1			0 (0%)	0			0.01	(-0.01,0.04)
SKIN										
RASH	1 (1%)	1			0 (0%)				0.01	(-0.01,0.04)
STEVENS JOHNSON SYND	1 (1%)	0			0 (0%)	0			0.01	(-0.01,0.04)

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1 Male specific AEs will use the following denominators: LTG-33 and VPA-32.
2 Female specific AEs will use the following denominators: LTG-43 and VPA-48.

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Table 78
Summary of Serious Adverse Experiences
Occurring During Transition Period

Body System/ Preferred AE Term	LAMICTAL (N-76)			VPA (N-80)			Between Treatment Comparison	
	No. of Pts. (%)	No. of Pts. with Maximum Intensity		No. of Pts. (%)	No. of Pts. with Maximum Intensity		Diff in Prop.	95% CI
		Mild	Mod Sev		Mild	Mod Sev		
No. of Patients with AEs	2 (3%)	0		4 (5%)				
GENERAL								
FEVER	1 (1%)	0		0 (0%)			0.01	(-0.01, 0.04)
REACT AGGRAV	0 (0%)	0		2 (3%)			-0.03	(-0.06, 0.01)
NERVOUS SYSTEM								
CONVULS GRAND MAL	0 (0%)	0		1 (1%)			-0.01	(-0.04, 0.01)
PARANOID REACT	0 (0%)	0		1 (1%)			-0.01	(-0.04, 0.01)
SKIN								
RASH	1 (1%)	1		0 (0%)			0.01	(-0.01, 0.04)
STEVENS JOHNSON SYND	1 (1%)	0		0 (0%)			0.01	(-0.01, 0.04)

APPEARS THIS WAY
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1 Male specific AEs will use the following denominators: LTG-33 and VPA-32.
2 Female specific AEs will use the following denominators: LTG-43 and VPA-48.

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Table 79
Summary of Serious Adverse Experiences
Occurring During Monotherapy Period

Body System/ Preferred AE Term	LAMICTAL (N=43)		VPA (N=44)				Between Treatment Comparison	
	No. (%) of Pts.	No. of Pts. with Maximum Intensity	No. of Pts. with Maximum Intensity		No. (%) of Pts.	No. of Pts. with Maximum Intensity	Diff	95% CI
			Mild	Mod		Mild		
No. of Patients with AEs	2 (5%)	1			0 (0%)	0		
GENERAL								
HEADACHE	1 (2%)	1			0 (0%)	0	0.02	(-0.02, 0.07)
PAIN CHEST	1 (2%)	1			0 (0%)	0	0.02	(-0.02, 0.07)
DIGESTIVE NAUSEA	1 (2%)	1			0 (0%)	0	0.02	(-0.02, 0.07)
NERVOUS SYSTEM DIZZINESS	1 (2%)	1			0 (0%)	0	0.02	(-0.02, 0.07)
SUICIDAL IDEATION	1 (2%)	0			0 (0%)	0	0.02	(-0.02, 0.07)
RESPIRATORY DYSPNEA	1 (2%)	1			0 (0%)	0	0.02	(-0.02, 0.07)

APPEARS THIS WAY
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1 Male specific AEs will use the following denominators: LTG-22 and VPA-16.
2 Female specific AEs will use the following denominators: LTG-21 and VPA-28.

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Table 80
Summary of Adverse Experiences Leading to Discontinuation

Body System/ Preferred AE Term	LAMICTAL (N-76)			VPA (N-80)			Treatment Comparison	
	No. (%) Of Pts.	No. of Pts. with Maximum Intensity		No. (%) Of Pts.	No. of Pts. with Maximum Intensity		Diff In Prop.	95% CI
		Mild	Mod Sev		Mild	Mod Sev		
No. of Patients with AEs	15 (20%)	5		6 (8%)	2			
GENERAL								
FEVER	2 (3%)	0		0 (0%)	0		0.03	{-0.01, 0.06}
ASTHENIA	1 (1%)	0		0 (0%)	0		0.01	{-0.01, 0.04}
HEADACHE	1 (1%)	1		1 (1%)	1		0.00	{-0.03, 0.04}
PAIN CHEST	1 (1%)	1		0 (0%)	0		0.01	{-0.01, 0.04}
PAIN NECK	1 (1%)	1		0 (0%)	0		0.01	{-0.01, 0.04}
DIGESTIVE								
DIARRHEA	1 (1%)	0		0 (0%)	0		0.01	{-0.01, 0.04}
NAUSEA	1 (1%)	1		0 (0%)	0		0.01	{-0.01, 0.04}
VOMIT	1 (1%)	1		0 (0%)	0		0.01	{-0.01, 0.04}
DYSPEPSIA	0 (0%)	0		1 (1%)	0		-0.01	{-0.04, 0.01}
HEPATITIS	0 (0%)	0		1 (1%)	0		-0.01	{-0.04, 0.01}
HEMIC & LYMPHATIC								
LYMPHADENO	2 (3%)	2		0 (0%)	0		0.03	{-0.01, 0.06}
METABOLIC & NUTRITIONAL								
WEIGHT INC	1 (1%)	0		0 (0%)	0		0.01	{-0.01, 0.04}
MUSCULOSKELETAL								
CRAMPS LEG	1 (1%)	0		0 (0%)	0		0.01	{-0.01, 0.04}
MYALGIA	1 (1%)	0		0 (0%)	0		0.01	{-0.01, 0.04}
NERVOUS SYSTEM								
DIZZINESS	3 (4%)	2		1 (1%)	1		0.03	{-0.02, 0.08}
ANXIETY	2 (3%)	0		1 (1%)	0		0.01	{-0.03, 0.06}
ATAXIA	1 (1%)	0		0 (0%)	0		0.01	{-0.01, 0.04}
PERSON DISORDER	1 (1%)	1		0 (0%)	0		0.01	{-0.01, 0.04}
TREMOR	1 (1%)	0		0 (0%)	0		0.01	{-0.01, 0.04}
PARANOID REACT	0 (0%)	0		1 (1%)	0		-0.01	{-0.04, 0.01}
RESPIRATORY								
DYSPNEA	1 (1%)	1		0 (0%)	0		0.01	{-0.01, 0.04}
SKIN								

1 Male specific AEs will use the following denominators: LTC-33 and VPA-32.
2 Female specific AEs will use the following denominators: LTC-43 and VPA-48.

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Project 105c-030
(Data as of: November 27, 1996)

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Table 80
Summary of Adverse Experiences Leading to Discontinuation

Body System/ Preferred AE Term	LAMICTAL (N=76)				VPA (N=80)				Between Treatment Comparison	
	No. (%) Of Pts.	No. Of Pts. with Maximum Intensity			No. (%) Of Pts.	No. Of Pts. with Maximum Intensity			Diff in Prop.	95% CI
		Mild	Mod	Sev		Mild	Mod	Sev		
RASH	3 (4%)		2		1 (1%)		0		0.03	(-0.02, 0.08)
PRURITUS	2 (3%)		1		0 (0%)		0		0.03	(-0.01, 0.06)
RASH MAC PAP	2 (3%)		1		0 (0%)		0		0.03	(-0.01, 0.06)
ALOPECIA	1 (1%)		0		0 (0%)		0		0.01	(-0.01, 0.04)
STEVENS JOHNSON SYND	1 (1%)		0		0 (0%)		0		0.01	(-0.01, 0.04)
SPECIAL SENSES										
DIPLOPIA	2 (3%)		0		0 (0%)		0		0.03	(-0.01, 0.06)

APPEARS THIS WAY
ON ORIGINAL

1 Male specific AEs will use the following denominators: LTG-33 and VPA-32.
2 Female specific AEs will use the following denominators: LTG-43 and VPA-48.

APPEARS THIS WAY
ON ORIGINAL

Attachment I

DIVISION OF NEUROPHARMACOLOGICAL DRUG PRODUCTS
CLINICAL REVIEW OF NDA

NDA Number	20,241 Supplement
Generic (Brand) Name	Lamictal (lamotrigine)
Sponsor	Glaxo Wellcome, Inc.
Indication	Monotherapy of Partial Seizures in Adults
Correspondence Date	24 February 1997
Original Receipt Date	25 February 1997
Medical officer review completed	15 December 1997
New patient review	3 February 1998

Following are patients from monotherapy trial US30/31 who have been reclassified as escapers for the purposes of statistical reassessment:

- 30-1-01038 (LTG) - met criteria for doubling the highest 2-day seizure frequency (3/16-17/95).
- 31-6-06046 (LTG) - met criteria for doubling the highest 4-week seizure frequency (4/30-5/30/95).
- 31-17-17041 (LTG) - inadequate documentation of seizures diaries (missing data, 1/6-25/95).
- 31-17-17032 (LTG) - consent withdrawal: per available medical documentation, the patient was "still having seizures, wants to try something else."
- 31-14-14055 (LTG) - protocol violation: per available medical documentation, the patient "verbally" reported a seizure count but did not keep a diary.
- 31-21-21177 (VPA) - protocol violation, but also met the highest 2-day seizure rate multiple times. (To meet escape criteria, this patient needed to have 2 seizures over a 2-day period. From 3/10-18/96, the patient had 1 seizure per day and also had 2 seizures over the 2-day periods of 3/31-4/1/96 and 4/12-4/13/96).

NOTE: This list, compiled in association with Dr. Sue-Jane Wang (Biometrics), is based on new data from the 2/2/98 telecon with the sponsor. It therefore supercedes information presented in the medical review of the supplemental NDA.

/S/

Richard M. Tresley MD
Medical Reviewer

NDA 20,241 Supplement (Monotherapy) div file/Katz R/Ware J/Tresley R/3 February 1998