The Primary Care Companion
FOR CNS DISORDERS

Supplementary Material

Article Title: Effect of Lemborexant on Daytime Functioning in Adults With Insomnia: Patient-Reported Outcomes From a Phase 3 Clinical Trial

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LIST OF SUPPLEMENTARY MATERIAL FOR THE ARTICLE

DISCLAIMER

	Study 303		
	Placebo N=318	**LEM5 N=316**	**LEM10 N=315**
Age			
Mean age, years (SD)	54.5 (14.0)	54.2 (13.7)	54.8 (13.7)
Median age, years (range)	56.0 (18–83)	55.0 (20–85)	55.0 (18–88)
Sex, n (%)			
Male	102 (32.1)	107 (33.9)	93 (29.5)
Female	216 (67.9)	209 (66.1)	222 (70.5)
Race, n (%)			
White	232 (73.0)	222 (70.3)	225 (71.4)
Black or African American	23 (7.2)	27 (8.5)	26 (8.3)
Japanese	54 (17.0)	53 (16.8)	54 (17.1)
Other Asian	5 (1.6)	8 (2.5)	4 (1.3)
Other	4 (1.3)	6 (1.9)	6 (1.9)
BMI, kg/m^2, mean (SD)	27.2 (5.5)	27.3 (6.3)	27.2 (5.6)
ISI-TS, mean (SD)	19.0 (3.1)	19.6 (3.3)	19.1 (3.4)
ISI-DFS, mean (SD)	11.0 (2.1)	11.4 (2.0)	11.1 (2.2)
ISI "interference with daily functioning" item score, mean (SD)	2.6 (0.8)	2.7 (0.7)	2.6 (0.8)
FSS, mean (SD)	35.1 (13.6)	37.4 (12.7)	36.0 (13.0)

Supplementary Table 1. Baseline demographics and subject characteristics in Study 303. BMI, body mass index; FSS, Fatigue Severity Scale; ISI, Insomnia Severity Index; ISI-DFS, Insomnia Severity Index Daytime Functioning Score; ISI-TS, Insomnia Severity Index Total Score; LEM5, lemborexant 5 mg; LEM10, lemborexant 10 mg; SD, standard deviation.

	Placebo					LEM5					LEM10				
	ISI-TS at 1 month														
BL	**No clinically significant insomnia**	**Sub-threshold insomnia**	**Moderate insomnia**	**Severe insomnia**	**Total**	**No clinically significant insomnia**	**Sub-threshold insomnia**	**Moderate insomnia**	**Severe insomnia**	**Total**	**No clinically significant insomnia**	**Sub-threshold insomnia**	**Moderate insomnia**	**Severe insomnia**	**Total**
No clinically significant insomnia	1 (100%)	0	0	0	1	0	0	0	0	0	1 (100%)	0	0	0	1
Sub-threshold insomnia	1 (9.1%)	8 (72.7%)	1 (9.1%)	1 (9.1%)	11	1 (11.1%)	6 (66.7%)	2 (22.2%)	0	9	1 (14.3%)	5 (71.4%)	1 (14.3%)	0	7
Moderate insomnia	28 (12.5%)	103 (46.0%)	91 (40.6%)	2 (0.9%)	224	48 (22.7%)	100 (47.4%)	58 (27.5%)	5 (2.4%)	211	46 (21.9%)	87 (41.4%)	70 (33.3%)	7 (3.3%)	210
Severe insomnia	6 (10.0%)	13 (21.7%)	27 (45.0%)	14 (23.3%)	60	20 (24.7%)	17 (21.0%)	29 (35.8%)	15 (18.5%)	81	22 (31.9%)	23 (33.3%)	15 (21.7%)	9 (13.0%)	69
Total	36	124	119	17	296	69	123	89	20	301	70	115	86	16	287
***P*-value vs placebo**									<0.0001					<0.0001	
	ISI-DFS at 1 month														
BL	**No-to-mild problem**	**Mild-to-moderate problem**	**Moderate-to-severe problem**	**Severe-to-very severe problem**	**Total**	**No-to-mild problem**	**Mild-to-moderate problem**	**Moderate-to-severe problem**	**Severe-to-very severe problem**	**Total**	**No-to-mild problem**	**Mild-to-moderate problem**	**Moderate-to-severe problem**	**Severe-to-very severe problem**	**Total**
No-to-mild problem	1 (100%)	0	0	0	1	0	0	0	0	0	0	1 (100%)	0	0	1
Mild-to-moderate problem	7 (23.3%)	19 (63.3%)	3 (10.0%)	1 (3.3%)	30	7 (31.8%)	14 (63.6%)	1 (4.6%)	0	22	8 (29.6%)	13 (48.2%)	5 (18.5%)	1 (3.7%)	27
Moderate-to-severe problem	32 (15.8%)	84 (41.6%)	78 (38.6%)	8 (4.0%)	202	52 (26.1%)	81 (40.7%)	60 (30.2%)	6 (3.0%)	199	53 (27.8%)	73 (38.2%)	59 (30.9%)	6 (3.1%)	191
Severe-to-very severe problem	11 (17.5%)	12 (19.1%)	28 (44.4%)	12 (19.1%)	63	18 (22.5%)	16 (20.0%)	26 (32.5%)	20 (25.0%)	80	18 (26.5%)	25 (36.8%)	16 (23.5%)	9 (13.2%)	68
Total	51	115	109	21	296	77	111	87	26	301	79	112	80	16	287
***P*-value vs placebo**									<0.0001					<0.0001	

Supplementary Table 2. Overall shifts in ISI-TS and ISI-DFS categories from baseline to 1 month. *P*-values represent Cochran–Mantel–Haenszel test of general association vs placebo. ISI-DFS, Insomnia Severity Index Daytime Functioning Score; ISI-TS, Insomnia Severity Index Total Score; LEM5, lemborexant 5 mg; LEM10, lemborexant 10 mg.

	Study 303		
	Placebo	**LEM5**	**LEM10**
1-month visit shift in score, n (%)			
3/4→0/1	47 (29.0%)	71 (37.4%)	63 (41.7%)
3/4→2	62 (38.3%)	50 (26.3%)	47 (31.1%)
3/4→3/4	53 (32.7%)	69 (36.3%)	41 (27.2%)
P-value vs placebo		0.1839	0.1604
6-month visit shift in score, n (%)			
3/4→0/1	58 (40.6%)	95 (57.6%)	74 (60.7%)
3/4→2	54 (37.8%)	43 (26.1%)	33 (27.0%)
3/4→3/4	31 (21.7%)	27 (16.4%)	15 (12.3%)
P-value vs placebo		0.0306	0.0035

Supplementary Table 3. **Shift in the ISI "interference with daily functioning" item score at 1 and 6 months in subjects reporting a score of 3 or 4 at baseline.** *P*-values represent Cochran–Mantel–Haenszel test of general association vs placebo for overall "interfering with daily functioning" individual item score shifts from 3 or 4 at baseline to 0, 1, 2, 3, or 4 at Months 1 and 6. ISI, Insomnia Severity Index; LEM5, lemborexant 5 mg; LEM10, lemborexant 10 mg.

	Study 303		
n (%)	**Placebo N=319**	**LEM5 N=314**	**LEM10 N=314**
Any TEAE	200 (62.7)	192 (61.1)	187 (59.6)
Severe TEAEs	10 (3.1)	13 (4.1)	8 (2.5)
Serious TEAEs	5 (1.6)	7 (2.2)	9 (2.9)
Most frequent TEAEs (>5%)			
Headache	21 (6.6)	28 (8.9)	21 (6.7)
Somnolence	5 (1.6)	27 (8.6)	41 (13.1)
Influenza	15 (4.7)	15 (4.8)	16 (5.1)
Treatment-related TEAEs	44 (13.8)	78 (24.8)	91 (29.0)
TEAEs leading to study discontinuation	12 (3.8)	13 (4.1)	26 (8.3)
Discontinuations due to TEAEs of somnolence	2 (0.6)	3 (1.0)	9 (2.9)

Supplementary Table 4. Safety data. LEM5, lemborexant 5mg; LEM10, lemborexant 10 mg; TEAE, treatment-emergent adverse event.