Appendix Table 1: Benefits and harms of pregabalin in the management of neuropathic pain

Outcome	Overall analysis	Subgroup analyses		Test for subgroup differences
		Central neuropathic pain	*Peripheral neuropathic pain*	
Mean change in pain scores - NRS	(n = 5093): SMD -0.49 (-0.66 to -0.32, P < 0.00001, I^2=88%	(n = 785): SMD -0.38 (-0.80 to 0.04), P = 0.08, I^2=89%	(n = 4308): SMD -0.52 (-0.71 to -0.33), P < 0.00001, I^2=88%	P = 0.56, I^2=0%
Mean change in sleep interference scores - NRS	(n = 1641): SMD -0.38 (-0.50 to -0.26, P < 0.00001, I^2=32%	(n = 357): SMD -0.49 (-0.70 to -0.28), P < 0.00001, I^2=0%	(n = 1284): SMD -0.35 (-0.50 to -0.19), P < 0.0001, I^2=45%	P = 0.30, I^2=8%
Mean change in HADS-anxiety scores	(n = 1041): SMD -0.12 (-0.29 to 0.04, P = 0.14, I^2=44%	(n = 418): SMD -0.27 (-0.46 to -0.08, P = 0.006, I^2=0%	(n = 623): SMD -0.00 (-0.16 to 0.15, P = 0.97, I^2=0%	P = 0.04, I^2=77.2%
Mean change in HADS-depression scores	(n = 1041): SMD -0.06 (-0.26 to 0.13, P = 0.54, I^2=60%	(n = 418): SMD -0.16 (-0.41 to 0.10, P = 0.23, I^2=44%	(n = 623): SMD 0.02 (-0.28 to 0.32, P = 0.90, I^2=71%	P = 0.38, I^2=8%
Overall adverse events	(n = 4010): RR 1.33 (1.23 to 1.44), P < 0.00001, I^2=52%	(n = 489): RR 1.33 (1.20 to 1.47), P < 0.00001, I^2=0%	(n = 3225): RR 1.34 (1.21 to 1.47), P < 0.00001, I^2=61%	P = 0.92, I^2=0%
Adverse event: weight gain	(n = 3636): RR 4.58, (2.88 to 7.28), P < 0.00001, I^2=0%	(n = 428): RR 3.77 (0.94 to 15.08), P = 0.06, I^2=0%	(n = 3636): RR 4.69 (2.87 to 7.68), P < 0.00001, I^2=0%	P = 0.77, I^2=0%
Adverse event: somnolence	(n = 5695): RR 2.84, (2.36 to 3.42), P < 0.00001, I^2=0%	(n = 785): RR 3.18 (2.16 to 4.68), P < 0.00001, I^2=0%	(n = 4910): RR 2.74 (2.22 to 3.40), P < 0.00001, I^2=1%	P = 0.51, I^2=0%
Adverse event: dizziness	(n = 5732): RR 2.94 (2.30 to 3.74), P < 0.00001, I^2=63%	(n = 785): RR 3.38 (2.46 to 4.63), P < 0.00001, I^2=0%	(n = 4947): RR 2.89 (2.17 to 3.85), P < 0.00001, I^2=67%	P = 0.48, I^2=0%
Adverse event: peripheral edema	(n = 5001): RR 2.63 (1.86 to 3.73), P < 0.00001, I^2=41%	(n = 439): RR 3.90 (1.63 to 9.36), P = 0.002, I^2=0%	(n = 4562): RR 2.53 (1.74 to 3.68), P < 0.00001, I^2=44%	P = 0.37, I^2=0%
Adverse event: fatigue*	(n = 3958): RR 1.83 (1.32 to 2.54), P = 0.0003, I^2=14%	N/A	N/A	N/A
Adverse event: visual disturbance	(n = 2814): RR 2.50 (1.53 to 4.09), P = 0.0003, I^2=6%	(n = 566): RR 4.05 (1.27 to 12.91), P = 0.02, I^2=0%	(n = 2248): RR 2.36 (1.32 to 4.22), P = 0.004, I^2=16%	P = 0.42, I^2=0%
Adverse event: ataxia**	(n = 1045): RR 5.49 (1.84 to 16.36), P = 0.002, I^2=0%	N/A	N/A	N/A
Adverse event: dry mouth	(n = 3873): RR 2.39 (1.66 to 3.44), P < 0.0001, I^2=16%	(n = 357): RR 3.75 (1.43 to 9.83), P = 0.007, I^2=0%	(n = 3516): RR 2.28 (1.52 to 3.41), P < 0.0001, I^2=20%	P = 0.35, I^2=0%
Adverse event: non-peripheral edema	(n = 2337): RR 3.51 (1.93 to 6.40), P < 0.0001, I^2=0%	(n = 785): RR 3.82 (1.65 to 8.85), P = 0.002, I^2=0%	(n = 1552): RR 3.70 (1.36 to 10.06), P = 0.01, I^2=19%	P = 0.96, I^2=0%
Adverse event: vertigo**	(n = 1031): RR 3.08 (1.01 to 9.40), P = 0.05, I^2=30%	N/A	N/A	N/A
Adverse event: euphoria*	(n = 1274): RR 8.80 (2.72 to 28.54), P = 0.0003, I^2=0%	N/A	N/A	N/A
Discontinuation due to adverse events	(n = 5426): RR 1.91 (1.54 to 2.37), P < 0.00001, I^2=0%	(n = 576): RR 1.42 (0.79 to 2.55), P = 0.24, I^2=0%	(n = 4850): RR 2.00 (1.58 to 2.55), P < 0.00001, I^2=6%	P = 0.29, I^2=12%

Abbreviations: HADS: Hospital anxiety depression scale; NRS: Numerical rating scale; RR: Risk ratio; SMD: Standardized mean difference

*only one RCT on central neuropathic pain reported adequate data
**all RCTs were in patients with peripheral neuropathic pain