Appendix Table 3: Main results* of RCTs assessing the benefits and harms of pregabalin in the management of neuropathic pain

		Pain			Sleep Disturbance				
Study ID	**NRS**	**VAS Score**	**SF-MPQ VAS**	**SF-MPQ PPI**	**Sleep Interference Scores**	**MOS-Sleep**	**Quality of Life (EQ-5D)**	**PGIC**	**CGIC**
Arezzo 2008			Significantly favoured PGB over PLA (MD -11.06, 95% CI, -18.89 to -3.22; P = 0.006)					Significant improvement with PGB compared to PLA, P= 0.002	
Cardenas 2013						Significant improvement with PGB over PLA on domains of sleep disturbance, awaken short of breath, sleep quantity, and optimal seep subscales (P<0.05)		PGIC reported as binary outcome; significantly improved with PGB compared with PLA, P<0.001	Significant improvement in the PGB arm (P= 0.0294)
Dworkin 2003			Significantly favoured PGB over PLA (MD -17.62, 95% CI, -25.37 to -9.86; P = 0.0001		Significantly favoured PGB over PLA (MD -1.58, 95% CI, -2.19 to -0.97; P = 0.0001)	Significantly favoured PGB over PLA (MD -9.80, 95% CI, -14.49 to -5.11; P = 0.0001)		Significantly improved with PGB versus PLA, P = 0.001	
Freynhagen 2005	Both flexible- and fixed-dose PGB significantly reduced endpoint mean pain score versus PLA (P=0.002 and P<0.001 respectively)				Significantly improved at endpoint in each PGB treatment group over PLA (P<0.001)	Significantly favoured PGB over PLA (P<0.05)			
Guan 2011			Significantly improved with PGB vs PLA LSMD -6.56, 95% CI -11.65 to -1.47, P=0.012		Significantly improved with PGB vs PLA: LSMD -0.5, 95% CI -0.93 to -0.07, P=0.023				
Holbech 2015					Significantly improved with PGB vs PLA LSMD -0.55, 95% CI -0.93 to -0.17, P=0.004				
Huffmann 2015	Significant treatment difference favouring PGB over PLA for DPN pain (P=0.034) and DPN pain on walking (P=0.001)							Significant improvements with PGB compared to PLA (P=0.002)	
Kanodia 2011		Significantly improved with PGB compared to PLA: MD -21, 95% CI: -23.8 to -18.2; P = 0.004)							
Kim 2011					Significantly favoured PGB over PLA (P<0.05)	Significant improvement with PGB over PLA in sleep quantity (P=0.03), sleep adequacy (P=0.13), snoring (P=0.39), and reduced the sleep problems index (P=0.049)	No significant difference between groups at endpoint, MD 0 (95% CI -0.1, 0,1) P= 0.566	No significant difference between groups at endpoint, -0.2 (95% CI -0.5, 0.1) P=0.144	Significant improvement of in PGB group vs PLA: MD -0.3 (95% CI -0.6, 0) (P=0.049)
Krcevski Škvarč 2010	No significant difference between groups, P values not reported								
Lesser 2004					Significantly favoured PGB over PLA (P=0.0001)				
Liu 2015			Significant decrease with PGB compared with PLA: MD -8.18, 95% CI: -11.99 to -4.37; P<0.0001)	Significant decrease in with PGB compared with PLA: MD -0.37, 95% CI: -0.58 to -0.16; P=0.0007).		Significantly greater improvements with PGB in subscales of sleep disturbance (P=0.0039) and quantity of sleep (P=0.0035) compared with PLA		Significantly improved with PGB versus PLA: LSMD -0.49 95% CI -0.72 to -0.27, P<0.0001	Significant improvement with PGB versus PLA, LSMD -0.62 95% (CI -0.86, -0.39), P<0.0001
Mathieson 2017									
Moon 2010					Significantly favoured PGB over PLA: LSMD -0.51 (95% CI, -0.96 to -0.07; P = 0.024)	Significantly greater improvements with PGB in subscales of sleep disturbance (P=0.0034) and quantity of sleep (P=0.018) compared with PLA	No significant differences in endpoint scores of EQ-5D utility score least squares means 0.03, 95% CI -0.04, 0.09 P= 0.429, or EQ-5D VAS at endpoint LSMD 3.50 (95% CI -1.18, 8.18) P= 0.142	No statistically significant difference between groups	No statistically significant difference between groups
Rauck 2013					No significant difference between groups: MD 0.11 (95% CI -0.60 to 0.82)				
Richter 2005			Significantly favoured PGB 600mg/day over PLA (MD -14.67, 95% CI, -21.92 to -7.41; P = 0.0002). No significant	Significantly favoured PGB 600mg/day over PLA (MD -0.66, 95% CI, -0.97 to -0.35; P = 0.0002). No significant difference	Significantly favoured PGB over PLA: LSMD -1.152; 95% CI -1.752 to -0.551; P=0.0004				

			difference between PGB 150mg/day and PLA (MD -4.78, 95% CI, -12.20 to -2.64; P = 0.20)	between PGB 150 mg/day and PLA (MD -0.17, 95% CI, -0.49 to 0.14; P = 0.28)					
Rosenstock 2004			Significantly favoured PGB over PLA (MD -16.19, 95% CI, -24.52 to -7.86; P = 0.0002)	Significantly favoured PGB over PLA (MD -0.37, 95% CI, -0.72 to -0.02; P = 0.036)	Significantly favoured PGB over PLA: LSMD -1.54, 95% CI -2.28 to -0.80, P=0.0001				
Sabatowski 2004					Significantly favoured PGB over PLA: LSMD -1.11, 95% CI -1.71 to -0.51, P=0.0003 for 150 mg/day; LSMD -1.43, 95% CI -2.04 to -0.82, P=0.0001 for 300 mg/day				
Satoh 2011			Significantly favoured PGB 300 mg/day and 600 mg/day over PLA (P < 0.05)		Significantly improved in the 300 and 600 mg⁄ day PGB groups compared with PLA (P < 0.0001 and P = 0.0273 respectively)				
Shabbir 2011	Significant improvement in pain of DPN was observed in patients receiving PGB (48.1%) and compared to those receiving PLA (10.5%), P values not reported								
Siddall 2006			Significantly favoured PGB over PLA (MD -17.6, 95% CI, -25.2 to -10.0; P<0.001)	Significantly favoured PGB over PLA (MD -0.66, 95% CI, -0.99 to -0.32; P<0.001)					
Simpson 2010								Significant self-reported improvement favouring PGB over PLA: 82.8% vs 66.7% (P= 0.008)	
Simpson 2014					No significant difference between groups: LSMD 0.04, 95% CI 0.43 to 0.35, P =0.840			No significant differences between groups: (P=0.505)	No significant differences between groups (P=0.427)
Stacey 2008		Significant improvement in VAS allodynia scores with PGB compared to PLA (flexible-dose: MD -14.4 mm [P<0 .0001] and fixed-dose, MD -8.98 mm [P =0.0075])	Significant improvement in with PGB compared to PLA (flexible-dose: MD -16.33 mm [P<0 .0001] and fixed-dose, MD -11.97 mm [P =0 .0008])		Significant improvements with flexible- and fixed-dose PGB. Results of between-group differences not reported		Fixed or flexible dose PGB demonstrated significant improvement in VAS anxiety scores over PLA (fixed-dose, 19.95, P = 0.025, and flexible-dose, -17.81; P= 0.024)	Patients treated with any PGB treatment regimen were significantly more likely to rate themselves as minimally, much, or very much improved on the PGIC at end point compared with PLA	
Tolle 2008							Significant improvements in utility scores for 150, 300, 600mg/day respectively compared to PLA, all P ≤ 0.0263	Significant improvement with 600 mg/day PGB versus PLA in subjects reporting “improved” or “much improved” (50.5% vs 33.3%, P = 0.02)	Significant superiority of PGB 600 mg/day over PLA (P= 0.009)
van Seventer 2006						Significant improvement in MOS sleep scale problems with PGB compared with PLA MD – 7.54, 95% CI -11.52 to -3.56, P<0.001		Patients in the 150 mg/day (P = 0.02) and 600 mg/day (P = 0.003) groups were more likely to report global improvement than those in the PLA group	
van Seventer 2010								Significant improvement in favour of PGB over PLA (P = 0.006)	
Vranken 2008		Significant decrease in with PGB compared with PLA: MD 2.18, 95% CI: 0.57 to 3.80; P = 0.01)					Statistically significant improvement for both the EQ-5D utility score (p<0.001) and EQ-5D VAS score with PGB compared to PLA (P<0.001)		

ABBREVIATIONS: CGIC: Clinician global impression of change; LSMD: Least square mean difference; MD: Mean difference; MOS-Sleep: Medical Outcomes Study Sleep Scale; NRS: numerical rating scale; PGB: Pregabalin; PGIC: Patient global impression of change; PLA: Placebo; SF-MPQ PPI: Short-Form McGill Pain Questionnaire personal pain intensity; SF-MPQ VAS: Short-Form McGill Pain Questionnaire visual assessment scale; VAS: Visual assessment scale

*These outcome results have been presented narratively because there was inadequate data to pool results across studies