Additional file 1: Included studies

Lead Author and Year	Condition/ Inclusion criteria	Patient characteristics	Number of patients	Dosing regimen	Other analgesic medication	Study design	Duration of active treatment (weeks)	Quality score	OPVS	50% or more pain relief	Other pain outcomes (detailed data extracted)
Wernicke et al. 2006	Age ≥18 yrs PDN without any psychological disorder Daily pain for ≥6 months Baseline pain ≥4 (BPI 11 point Likert)	Mean age 61 (±11) yrs M/F 204/130 Duration of neuropathy 4 yrs White 78% Hispanic 16%	334	(1) Dulox 60 mg/day. Fixed dose for 12 weeks, then 30 mg for 1 week, n=114 (2) Dulox 60 mg x1 daily for 3 days then x2 daily to 12 weeks then x1 daily for 1 week, n=112 (3) Placebo, n=108	Max 4 g paracetamol/day and 325g aspirin/day	R, DB, PC, parallel	13	R2, DB1, W1	13	(1) 43% (49/114) (2) 53% (59/112) (3) 27% (29/108)	Mean (SE) reduction 24hr APS (1) 2.72 (0.22) (2) 2.84 (0.23) (3) 1.39 (0.23)
Arnold et al. 2004	Age ≥18 yrs Primary fibromalgia with or without depression Baseline pain ≥4 (FIQ 11 point scale)	Mean age 49 (±12) yrs M/F 23/184 White 87% Hispanic 5% Current MDD 38%	207	(1) Dulox 20mg x1 daily for 5 days then 20mg x2 daily ≥3 days,then 40mg x2 daily for ≥2 days then 60mg x2 daily to 12 weeks, n=104 (2) Placebo, n=103	Max 2 g paracetamol/day and 325g aspirin/day	R, DB, PC, parallel	12	R2, DB2, W1	16	(1) 27.7% (29/104) (2) 16.7% (17/103)	Mean reduction in pain FIQ (fibromyalgia impact questionnaire) (1) 1.98 (0.3) (2) 1.35 (0.29)
Raskin et al. 2005	Age ≥18yrs PDN, without any psychological disorder Pain present ≥6 months Baseline pain ≥4 (BPI 11 point Likert)	Mean age 59 (±10) yrs M162/F186 Caucasian 99.7%	348	(1) Dulox 60 mg x1 daily, n=116 (2) Dulox 60mg x1 daily for 3 days then 60mg x2 daily, n=116 (3) Placebo, n=116	Max 4 g paracetamol/day and 325g aspirin/day	R, DB, PC, parallel	12	R2, DB2, W1	16	(1) 50% (58/116) (2) 39% (45/116) (3) 30% (35/116)	Mean reduction (SE) 24hr APS (1) 2.50 (0.18) (2) 2.47 (0.18) (3) 1.6 (0.18)
Goldstein 2005	Age ≥18yrs PDN, without any psychological disorder Pain present ≥6 months Baseline pain ≥4 (BPI 11 point Likert)	Mean age 60 (±11) yrs M281/F176 Caucasian 77% Hispanic 11%	457	(1) Dulox 20 mg x1 daily, n=115 (2) Dulox 60mg x1 daily, n=114 (3) Dulox 40mg x 2daily for 1 week then 60mg x2 daily for 11 weeks, n=113 (4) Placebo, n=115	Max 4 g paracetamol/day No other analgesics	R, DB, PC, parallel	12	R2, DB1, W1	13	(1) 41% (46/115) (2) 49% (55/114) (3) 52% (57/113) (4) 26% (29/115)	Mean reduction (SE) 24hr APS (1) 2.36 (0.21) (2) 2.89 (0.22) (3) 3.24 (0.23) (4) 1.91 (0.22)
Arnold et al. 2005	Age ≥18yrs Primary fibromyalgia with or without depression Baseline pain ≥4 (BPI 11 point Likert)	Mean age 50 (±11) yrs All F Caucasian 90% Hispanic 8% Current MDD 26%	354	(1) Dulox 60 mg x1 daily, n=118 (2) Dulox 60mg x1 daily for 3 days then 60mg x2 daily, n=116 (3) Placebo, n=120	Max 2 g paracetamol/day and 325g aspirin/day	R, DB, PC, parallel	12	R1, DB1, W1	13	(1) 41% (48/116) (2) 41% (47/114) (3) 23% (27/118)	Mean reduction (SE) 24hr APS (1) 2.39 (0.22) (2) 2.40 (0.22) (3) 1.16 (0.21)
Russell et al. 2008	Age ≥18yrs ACR defined fibromyalgia with or without depression Baseline pain ≥4 (BPI 11 point Likert)	Mean age 51 (±11) yrs M 27/F 493 White 84.2% Current MDD 24%	520	(1) Dulox 20 mg daily, n=115 (2) Dulox 30mg daily for 1 week, then 60mg daily, n=114 (3) Dulox 30mg daily for 1 week then 60mg daily for 1 week, then 120 mg daily, n=113 (4) Placebo, n=115	Max 2 g paracetamol/day and 325g aspirin/day	R, DB, parrallel	13	R2, DB1, W1	13	(1) 32% (20/79) (2) 34% (51/150) (3) 40% (59/147) (4) 24% (34/144)	Mean reduction (SE) 24hr APS (1) 1.92 (0.27) (2) 1.99 (0.20) (3) 2.31 (0.20) (4) 1.39 (0.20)

Abbreviations: R=randomised; DB=double blind; W=withdrawals; PC=placebo controlled; BPI=brief pain inventory; AE=adverse event; PDN=painful diabetic neuropathy; Dulox=duloxetine; OPVS=Oxford Pain Validity Score; APS

Other outcomes	Ascertainment and reporting of adverse events	Specific adverse events	Withdrawals-total	Patients with any AE	Serious AE	Withdrawals-LoE	Withdrawals-AE
BPI average interference score SF-McGill HAMD total score CGI severity	Adverse events, vital signs and lab tests evaluated Ten most frequent specific adverse events reported	Nausea (1)32/114 (2)36/112 (3)7/108 Somnolence (1)9/114 (2)17/112 (3)1/108 Dizziness (1)18/114 (2)12/112 (3)6/108 Headache (1)12/114 (2)15/112 (3)7/108 Constipation (1)8/114 (2)21/112 (3)2/108 Insomnia, increased sweating, fatigue, nasopharyngitis also increased Changes in lab tests and vital signs were small and not clinically relevant	(1) 29/114 (2) 34/112 (3) 23/108	(1) 102/114 (2) 96/112 (3) 79/108	(1) 5/114 (2) 2/112 (3) 5/108	(1) 1/114 (2) 3/112 (3) 5/108	(1) 17/114 (2) 20/112 (3) 8/108
BPI average interference score CGI severity PGI-I scale FIQ total score Beck depression inventory Beck anxienty inventory	Adverse events, vital signs and lab tests evaluated	Insomnia, drymouth, constipation more frequent in dulox group than placebo group Changes in lab tests (incl LFT) and vital signs were small and not clinically relevant	(1) 46/104 (2) 37/103	(1) 94/104 (2) 77/103	Not reported	(1) 9/104 (2) 13/103	(1) 18/104 (2) 11/103
BPI average interference score MNSI (michigan neuropathy screening instrument) HAMD total score CGI severity	Vital signs and lab tests checked, and adverse evnets reviewed, at each visit.	Nausea,somnelence,hyperhidrosis and anorexia more frequent in dulox groups than placebo group. Vomiting and constipation more frequent in Dulox 60mg than placebo group. Mean increases in lab tests (incl LFT, glucose, cholesterol) and vital signs were small, tansient and not clinicaly relevant.	(1) 15/116 (2) 21/116 (3) 16/116	(1) 71/116 (2) 73/116 (3) 57/116	(1) 4/116 (2) 2/116 (3) 4/116	Not reported	(1) 5/116 (2) 14/116 (3) 3/116 Most in first 4 weeks
BAI total (beck anxienty inventory) Beck depression inventory CGI severity	Spontaneously reported adverse events and vital signs recorded. Specific events reported if significantly different from placebo	Nausea (1)16/115 (2)19/114 (3)31/113 (4)11/115 Somnolence (1)9/115 (2)23/114 (3)32/113 (4)9/115 Dizziness (1)7/115 (2)11/114 (3)26/113 (4)8/115 Constipation (1)6/115 (2)17/114 (3)12/113 (4)4/115 Dec apetite (1) 3/115 (2) 3/114 (3) 14/113 (4) 0/115 Drymouth, anorexia, weakness also sig different Mean changes in lab tests (incl LFT) and vital	(1) 24/115 (2) 28/114 (3) 33/113 (4) 28/115	Not reported	Total of 19 experienced serious adverse events	(1) 2/115 (2) 1/114 (3) 2/113 (4) 4/115	(1) 5/115 (2) 15/114 (3) 22/113 (4) 7/115
BPI average interference score FIQ total score CGI severity PGI-I HAMD Sheehan Disability Scale Medical Outcomes Study SF-36 QoL Depression Scale	Adverse events, vital signs and lab tests assessed Specific events reported if significantly different from placebo	Nausea (1)52/118 (2)45/116 (3)16/120 Somnolence (1)6/118 (2) 14/116 (3) 5/120 Constipation (1)17/118 (2)20/116 (3)4/120 Dry mouth (1)25/118 (2)27/116 (3)10/120 Dec apetite (1) 6/118 (2) 13/116 (3) 2/120 Diarrhoea, anorexia, nasopharyngitis also increased Changes in lab tests and vital signs were small and not clinically relevant	(1) 41/118 (2) 45/116 (3) 52/120	(1) 109/118 (2) 105/116 (3) 95/120	(1) 1/118 (2) 1/116 (3) 0/120	(1) 7/118 (2) 4/116 (3) 18/120 NB 13 patients in placebo group withdrew consent (vs 1 and 4 in dulox 60 and 120mg groups)	(1) 25/118 (2) 27/116 (3) 14/120
PGI-I (patient global impression of improvement) FIQ total score CGI severity Multidimensional Fatigue Inventory HAMD Sheehan Disability Scale Medical Outcomes Study SF-36 Euro-QoL Questionnaire-5D	Spontaneously reported adverse events, vital signs and weight recorded.	No separate data for first 13 weeks	(1) 30/79 (2) 53/150 (3) 52/147 (4) 84/144	Not reported	No separate data for first 13 weeks	(1) 8/79 (2) 11/150 (3) 6/147 (4) 14/144	(1) 8/79 (2) 22/150 (3) 32/147 (4) 17/144

=average pain score; HAMD=Hamilton depression score; CGI=clinical global impression; PGI-I=patient global improvement; FIQ=fibromyalgia impact questionnaire