Characteristics Table for The Clinical Question: In the treatment of generalised anxiety disorder what treatment dose improves outcome?

Comparisons Included in this Clinical Question

Anticonvulsants versus Anticonvulsants
FELTNER2003
MONTGOMERY2006
PANDE2003
POHL2005
RICKELS2005

Duloxetine (SNRI) vs Duloxetine (SNRI)
KOPONEN2007
NICOLINI2009

SSRIs versus SSRIs
BALDWIN2006
RICKELS2003

Venlafaxine (SNRI) vs Venlafaxine (SNRI)
ALLGULANDER2001
DAVIDSON1999
HACKETT2003
RICKELS2000A

Characteristics of Included Studies

Methods	Participants	Outcomes	Interventions	Notes
ALLGULANDER2001 Study Type: RCT Study Description: ITT: all eligible participants with at least one efficacy evaluation made whilst receiving study medication Type of Analysis: ITT/LOCF Blindness: Double blind Duration (days): Mean 168 Setting: Belgium, Finland, France, Sweden, UK Outpatient (14 centres) Notes: RANOMISATION: not reported. ALLOCATION CONCEALMENT: not addressed Info on Screening Process: 541 randomised, 529 met ITT criteria for inclusion.	n= 529 Age: Mean 45 Range 18-86 Sex: 201 males 328 females Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-IV Exclusions: - DSM-IV diagnosis of GAD - HAMA score < 20 - HAMA (anxious mood & tension items) < 2 - MDD or other psychiatric disorder - Clinically important medical disease - Non-pharmacological drugs with psychotropic effects Notes: 74% had received prior treatment for anxiety (mostly benzodiazepines & antidepressants); 85% received non-anxiolytic concomitant therapy during the study (26 had beta-blocker, 52 on zolpidem or chloral hydrate) Baseline: HAMA baseline depression score (approx): 26.48 (range 20 to 52). No significant differences between groups at baseline. Venlafaxine 37.5mg/d: 26.6 (range 20 to 44). Venlafaxine 75mg/d: 26.3 (range 20 to 43). Venlafaxine 150mg/d: 26.3 (17 to 38). Placebo: 26.7 (20 to 52).	**Data Used** HAMA Leaving the study due to inefficacy Leaving the study due to adverse events Leaving the study early for any reason **Data Not Used** Response (50% reduction in HAMA score) - not extractable Notes: TAKEN AT: 1,2,3,4,6,8,10,12,16,20,24,25 weeks. Efficacy looked at 8 & 24 weeks. DROP OUTS: 36% CHANGE SCORES USED.	**Group 1 N= 137** Venlafaxine (extended release). Mean dose 150mg/d - Single blind wash-out period & discontinuation period. 24 week treatment. Fixed doses. Once daily. **Group 2 N= 134** Venlafaxine (extended release). Mean dose 75mg/d - Single blind wash-out period & discontinuation period. 24 week treatment. Fixed doses. Once daily. **Group 3 N= 130** Placebo - No further information **Group 4 N= 138** Venlafaxine (extended release). Mean dose 37.85mg/d - Single blind wash-out period & discontinuation period. 24 week treatment. Fixed doses. Once daily.	Funding: Wyeth-Ayerst Research. Quality assessed: +.
BALDWIN2006 Study Type: RCT Study Description: ITT: patients who took at least one dose of the study medication & at least one baseline efficacy assessment were included in analysis Type of Analysis: LOCF/ITT Blindness: Double blind Duration (days): Mean 84 Setting: UK Notes: RANDOMISATION: computer-generated randomisation list. ALLOCATION CONCEALMENT: sealed opaque envelopes. Info on Screening Process: Details not provided.	n= 682 Age: Mean 41 Sex: 244 males 438 females Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-IV-TR Exclusions: - not primary diagnosis of GAD (DSM-IV-TR) - not between 18 and 65 - HAMA score < 20 - HAMA (anxious mood & tension items) < 2 - MADRS >15 - Diagnosis of: MDD, panic disorder, social anxiety, PTSD, bipolar, OCD, body dysmorhpic disorder, substance abuse, personality disorder - suicide risk - receiving psychosocial interventions (i.e. CBT, ECT) - physical health problems (i.e. vascular)	**Data Used** HAMA Leaving the study due to inefficacy Leaving the study due to adverse events Leaving the study early for any reason DESS (modified) Response (50% reduction in HAMA score) **Data Not Used** Remission (less than 7 on HAMA) - not extractable Notes: TAKEN AT: 1,2,4,6,8,10,12,13,14 weeks.DROP OUTS: 14% (98) MEAN CHANGE SCORES.	**Group 1 N= 133** Escitalopram. Mean dose 20 mg/ day - 1 week, single blind placebo lead-in period, 12 weeks of treatment with fixed doses. 2 week placebo wash-out period. **Group 2 N= 134** Escitalopram. Mean dose 5 mg/ day - 1 week, single blind placebo lead-in period, 12 weeks of treatment with fixed doses. 2 week placebo wash-out period. **Group 3 N= 140** Paroxetine. Mean dose 20 mg/ day - 1 week, single blind placebo lead-in period, 12 weeks of treatment with fixed doses. 2 week placebo wash-out period.	Received support from Lundbeck and sponsored by GlaxoSmith Kline. Quality assessed: +.

	- concomittant medication (i.e. psychoactive substances, antidepressants, benzodiazepines, antipsychotics) Baseline: HAMA scores at baseline (approx): 27.04 (4.46); No significant differences at baseline		**Group 4 N= 136** Escitalopram. Mean dose 10 mg/ day - 1 week, single blind placebo lead-in period, 12 weeks of treatment with fixed doses. 2 week placebo wash-out period. **Group 5 N= 139** Placebo - Identical appearance, taste and smell. Oral administration.	
DAVIDSON1999 Study Type: RCT Study Description: ITT: all eligible participants with at least one efficacy evaluation made whilst receiving study medication Type of Analysis: ITT/LOCF Blindness: Double blind Duration (days): Mean 56 Setting: US Outpatient (17 centres) Notes: RANDOMISATION: details not provided. ALLOCATION CONCEALMENT: not addressed. Info on Screening Process: 405 patients completed placeb run-in period & received study drug, 36 had no primary efficacy evaluations & 4 randomised at one site were excluded for administrative reasons.	n= 365 Age: Mean 38 Sex: 224 males 141 females Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-IV Exclusions: - Not 18 years or older - Primary diagnosis not GAD (DSM-IV) - HAMA score < 18 - HAMA (anxious mood & tension items) < 2 - Raskin depression score > 9 or > Covi anxiety score or any item > 3 - Presence of clinically significant psychiatric disorder other than GAD - use of other pharmacology except for chloral hydrate Notes: No. of participants taking chloral hydrate: placebo (N=7), venlafaxine 75mg/d (N = 2), venlafaxine, 150mg/d, buspirone (N=2) Baseline: HAMA scores at baseline (approx) total: 23.55 (4.23); venlafaxine 75mg/ day: 23.7 (4.1), 150 mg/d: 23.0 (4.0); buspirone: 23.8 (4.6); placebo; 23.7 (4.2). No significant differences at baseline.	**Data Used** HAMA Leaving the study due to adverse events Compliance Response (50% reduction in HAMA score) Notes: TAKEN AT: 1, 2, 3, 4, 6, 8 weeks & 4 to 10 days after drug taper. DROP OUTS: 27%. MEAN CHANGE SCORES.	**Group 1 N= 102** Venlafaxine (extended release). Mean dose 75mg/ day - 1 week placebo run-in phase; 8 weeks of treatment. Fixed dose of 75mg/d. **Group 2 N= 104** Placebo - Matched placebo. **Group 3 N= 98** Buspirone. Mean dose 30 mg/ day - 1 week placebo run-in phase; 8 weeks of treatment. Fixed doses. Daily 3 divided doses. Days 1 & 2: 15 mg/d. Days 3 & 4: 20 mg/d. Days 5-7: 25mg/d. Days 8-56: 30 mg/d. **Group 4 N= 101** Venlafaxine (extended release). Mean dose 150 mg/ day - 1 week placebo run-in phase; 8 weeks of treatment. Fixed doses. Weel 1: 75mg/d. Week 2: 150 mg/d.	Funding: Wyeth-Ayerst Research. Quality assessed: +.
FELTNER2003 Study Type: RCT Study Description: ITT included all randomised participants who received at least one dose of study medication Type of Analysis: ITT Blindness: Double blind Duration (days): Mean 28 Setting: Four study centres, USA Outpatients Notes: RANDOMISATION: procedure not reported Info on Screening Process: Not reported	n= 271 Age: Mean 38 Range 18-74 Sex: 128 males 143 females Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-IV Exclusions: - Did not meet DSM-IV criteria for GAD, or GAD not the primary diagnosis in the case of comorbidity and HAMA >20 - Aged <18 years - Suffering from another other Axis I disorder except dysthymia, simple phobia, social phobia, somatization disorder or a histpry pf MDD - Current MDD - Severe personality disorders, drug or alcohol abuse / dependence (active within 6 months of study) - Suicide risk - Covi anxiety scale <9 Raskin depression > 7 Notes: Participants with a dual comorbid psychiatric disorders were required to have GAD as a primary disorder as judged by the psychiatrist, considering relative severity and time of onset Baseline: HAMA: Pregabalin (50mg) 24.9(3.9), Pregabalin	**Data Used** Remission (less than 7 on HAMA) CGI-I HAMA Adverse events Serious Adverse events Leaving the study due to adverse events Leaving the study early for any reason Response (50% reduction in HAMA score) Notes: TAKEN AT: Baseline and end of active treatment (4 weeks) DROPOUTS: total drop outs not reported	**Group 1 N= 68** Lorazepam. Mean dose 6MG - Fixed dose regimen with 2 mg TID. Study medication was tirated during days 1-6 of double-blind treatment. **Group 2 N= 70** Pregabalin. Mean dose 150mg - Fixed dose regimen with 50 mg TID. Study medication was tirated during days 1-6 of double-blind treatment. **Group 3 N= 66** Pregabalin. Mean dose 600mg - Fixed dose regimen with 200 mg TID. Study medication was tirated during days 1-6 of double-blind treatment. **Group 4 N= 67** Placebo	The ITT population was 271, this included all randomised participants who received at least one dose of study medication. No details given on the original number randomised to each condition. Funding: no details. Quality assessment score = +

	(200mg) 25.4(4.6), Lorazepam 24.7(3.7), Placebo 24.8(4.1)			
HACKETT2003 Study Type: RCT Study Description: Randomised, double-blind, placebo-controlled, parallel-group study. Followed by long-term phase study that is reported separately. Type of Analysis: ITT (LOCF method) Blindness: Double blind Duration (days): Mean 56 Setting: Outpatients. Multicentre: France. Notes: RANDOMISATION: no further details Info on Screening Process: 564 entered study, 16 did not receive any medication before dropping out	n= 540 Age: Mean 44 Sex: 175 males 365 females Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-IV Exclusions: - <18 years of age - HAM-A <20 - HAMA <2 for items 1 and 2 - MDD - more than 2 panic attacks in last month Baseline: HAM-A: Placebo =27.6 Venlafaxine 75mg = 27.9 Venlafaxine 150mg = 27.9 Diazepam = 28.4. Doesn't report SDs or SEs.	**Data Used** CGI-I HAMA Leaving the study due to adverse events Leaving the study early for any reason Response (50% reduction in HAMA score) Notes: Rating scales were administered at baseline, and again after 7, 14, 21, 28, 42 and 56 days.	**Group 1 N= 179** Venlafaxine (extended release). Mean dose 150mg - 150mg/day. **Group 2 N= 191** Venlafaxine (extended release). Mean dose 75mg - 75mg/day. **Group 3 N= 97** Placebo - No details given. **Group 4 N= 89** Diazepam. Mean dose 15mg/d - 15 mg/day.	Funded by Wyeth. Quality assessed +.
KOPONEN2007 Study Type: RCT Study Description: ITT analysis included all randomised participants with >=1 postbaseline analysis. Safety analysis included all randomised participants Type of Analysis: ITT Blindness: Double blind Duration (days): Mean 63 Setting: outpatient clinics. Multicentre - 7 countries Notes: RANDOMISATION: procedure not reported. Participants were stratified by baseline HAM-A score. Info on Screening Process: 639 participants were screened for the study with 126 failing to meet the inclusion criteria.	n= 513 Age: Mean 44 Sex: 165 males 348 females Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-IV Exclusions: -<18 years - No primary DSM-IV diagnosis of GAD - CGI-S <4 - HADS anxiety subscale <10 - Covia Anxiety score <9 or not greater and then Raskin depression total score. Raskin depression scale item rated >3 - Medical illness that would contraindicate use of duloxetine - Women of childbearing age not using adequate contraception - recent diagnosis of depression or substance abuse/depence - past year history of panic disorder, PTSD or eating disorder - lifetime history of psychotic, bipolar, OCD or psychosis - lack of response of GAD to 2 prior adequate trails of antidepressants or benzodiazepine treatments - psychotherapy iniated 6 weeks prior to study enrollment Baseline: HAMA (total) Dulox (60mg) 25.0(7.1); Dulox (120mg) 25.2(7.3); Placebo 25.8(7.6)	**Data Used** Q-LES-Q-SF Response (50% reduction in HAMA score) Remission (less than 7 on HAMA) Leaving the study early for any reason PGI-I Leaving the study due to adverse events Significant improvement (30% reduction) EQ-5D CGI-I Symptom Questionnaire-Somatic subscale (SQ-SS) Leaving the study due to inefficacy Serious Adverse events Sheehan Disability Scale (SDS) Visual Analog Scale (VAS) HAMA Discontinuation adverse events (DAEs) Notes: TAKEN AT: baseline and endpoint DROP OUT: Dul 60 33/168 (19.6%); Dul 120 46/170 (27.1%); Placebo 45/175 (25.7%)	**Group 1 N= 175** Placebo **Group 2 N= 168** Duloxetine. Mean dose 60mg/d - Participants were started with 60mg/d, if there were tolerability concerns this was lowered to 30mg/d with all participants gradually increased to their randomised dose within the first 2 study weeks. **Group 3 N= 170** Duloxetine. Mean dose 120mg/d - Participants were started with 60mg/d, if there were tolerability concerns this was lowered to 30mg/d with all participants gradually increased to their randomised dose within the first 2 study weeks.	Drug company funded - Eli Lilly studyF1J-MC-HMBR (NCT00122824) - trial report collected All participants underwent a single-blind placebo lead-in week, 9 week acute phase and a 2 week discontinuation tapering phase. Quality assessment score = + / ++
MONTGOMERY2006 Study Type: RCT Study Description: ITT: all randomized patients who received at least 1 dose of study drug. LOCF used on all primary and secondary outcome measures. Type of Analysis: ITT Blindness: Double blind Duration (days): Mean 42 Followup: None	n= 421 Age: Mean 44 Sex: 160 males 261 females Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-IV Exclusions: Diagnosis of any other current Axis 1 disorders except depression not otherwise specificied, dysthymia, simple phobia or somatisation disorder. Additional exclusion	**Data Used** Remission (less than 7 on HAMA) CGI-I HAMA Adverse events Serious Adverse events Leaving the study early for any reason Response (50% reduction in HAMA score) **Data Not Used**	**Group 1 N= 97** Pregabalin. Mean dose 400mg/day - 100mg/day for 2 days then 200mg/day for 2 days, before receiving the full dosage of 400mg/day on day 5. All administered twice-per-day (b.i.d.). **Group 2 N= 113** Venlafaxine (extended release). Mean dose 37.5mg/day - Began treatment at full 37.5mg/day (b.i.d.) dosage.	Funded by pharma (Pfizer Inc, New York). This study involved a 1 week screening period. 6 weeks of double-blind treatment were followed up by a 1-week, double-blind taper and follow-up phase. Quality assessment score = +

Setting: Multicentre (76): Austria, Belgium, Germany, the Netherlands and the United Kingdom. Outpatients attending primary care or psychiatric practices. Notes: Randomisation procedure not reported. Parallel-group design. Info on Screening Process: 543 ppts entered baseline phase; 421 were randomised and received study medication. Reasons for exclusion: did not meet entry criteria, lost to follow-up, withdrew consent, other/administrative and randomised but did not take study medication.	criteria: clinically relevant hematologic, autoimmune, endocrine, cardiovascular, renal, hepatic, gastrointestinal, or neurologic disorders; a history of seizure disorder; borderline, avoidant or antisocial personality disorder; alcohol or substance use disorder within the past 6 months; and patients considered at risk of suicide. Women who were pregnant or lactating, and women of childbearing potential who were not using a reliable method of contraception. Use of gabapentin or a benzodiazepine within 1 week of first baseline visit, the use of other psychotropic medications within 2 weeks prior to study entry, or ongoing psychodynamic or cognitive-behavioural psychotherapy for GAD. Use of corticosteroids (except topical or inhaled corticosteroids < 1000mg/day), antihypertensive agents, captopril, beta-blockers and psychotropic medication was not permitted during the study. Patients were allowed to take zolpidem for insomnia but not for more than 2 nights per week or the night before clinic visits. Notes: Ppts were diagnosed using the Mini-International Neuropsychiatric Interview (MINI). Baseline: Pregabalin 400mg/day (N=97, 23%), Pregabalin 600mg/day (N=110, 26%), Venlafaxine (N=113, 27%) and Placebo (N=101, 24%). HAM-A baseline: Pregabalin 400mg/day 26.3 (4.4), Pregabalin 600mg/day 26.5 (4.6), Venlafaxine 26.0 (4.6) and Placebo 27.4 (5.5). TOTAL: 26.6 (4.8). HAM-D baseline: Pregabalin 400mg/day 12.2 (3.6), Pregabalin 600mg/day 12.2 (4.0), Venlafaxine 12.0 (3.4) and Placebo 12.8 (4.9). TOTAL: 12.3 (4.0).	Leaving the study due to adverse events - not extractable Significant improvement (30% reduction) - not required Notes: HAM-D outcome scores also reported. TAKEN AT: baseline, 1 week and endpoint. DROP OUTS: Pregabalin 400mg/day 16/97, Pregabalin 800mg/day 29/110, Venlafaxine 34/113 and Placebo 20/101.	**Group 3 N= 101** Placebo - No details given. **Group 4 N= 110** Pregabalin. Mean dose 600mg/day - 150mg/day for 2 days, 300mg/day for 2 days and 450mg/day for 2 days before receiving the full dosage of 600mg/day after day 7. All administered twice-per-day (b.i.d.).	
Results from this paper:				
NICOLINI2009 Study Type: RCT Type of Analysis: ITT (LOCF) Blindness: Double blind Duration (days): Mean 70 Setting: Australia, Argentina, Belgium, Canada, Mexico, Russia, Taiwan, UK Outpatients Notes: RANDOMISATION: computer-generated ALLOCATION CONCEALMENT: interactive voice response system Info on Screening Process: Patients entered (N=771); did not meet criteria/concent (N=190)patients randomised (N=581); patients completed trial (N=396)	n= 581 Age: Mean 43 Sex: 43 males 57 females Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-IV Exclusions: -<18 years - No primary DSM-IV diagnosis of GAD - CGI-S <4 - HADS anxiety subscale <10 - Covia Anxiety score <9 or not greater and then Raskin depression total score. Raskin depression scale item rated >3 - Medical illness that would contraindicate use of duloxetine - Women of childbearing age not using adequate contraception - recent diagnosis of depression or substance abuse/depence - past year history of panic disorder, PTSD or eating disorder - lifetime history of psychotic, bipolar, OCD or psychosis - lack of response of GAD to 2 prior adequate trails of antidepressants or benzodiazepine treatments - psychotherapy iniated 6 weeks prior to study enrollment Notes: Duration of GAD M(S.D.) = 4.37 (8.19) years Baseline: BASELINE HAMA scores = 27.4 (total); 27.33 (7.33) (placebo); 27.65 (7.99) - dul 20mg; 27.74 (7.32) - dul 60-120mg); 27.36 (7.57) - ven 75-125mg)	**Data Used** CGI-I HAMA Sheehan Disability Scale (SDS) Hospital Anxiety and Depression Scale (anxiety) Leaving the study due to inefficacy Leaving the study due to adverse events PGI-I Leaving the study early for any reason Remission (less than 7 on HAMA) Response (50% reduction in HAMA score) Notes: DROP OUTS: 21/84 (25%) - DULOX 20mg; 49/158 (31%) - DULOX 60-120 mg; 47/122 (39%) - VENLAFAXINE; 68/170 (40%) - PLACEBO.	**Group 1 N= 169** Venlafaxine (extended release). Mean dose 151.3mg/day - 75 - 225 mg/day; flexible dosing of an increase of 75mg/day. Dose increase required if CGI-I score > 4 after 3 weeks. Dosed could be decreased no more than twice. Dose stabilised after 6 weeks. **Group 2 N= 84** Duloxetine 20mg. Mean dose 20mg/day - Once daily fixed dose of 20mg. Those who required dose increase received additional placebo capsules. **Group 3 N= 170** Placebo **Group 4 N= 158** Duloxetine. Mean dose 90mg/day - 60-120 mg/day flexible dosing of an increase of 30mg/day. Dose increase required if CGI-I score > 4 after 3 weeks. Dosed could be decreased no more than twice. Dose stabilised after 6 weeks.	FUNDED BY ELI LILLY: Trial report collected (#7106). Quality assessed: +
PANDE2003				

Study Type: RCT Study Description: 1 week placebo lead-in followed by 4 weeks of treatment and then a 1-week dose taper. Type of Analysis: ITT (LOCF method) Blindness: Double blind Duration (days): Mean 28 Setting: Outpatients. Multicentre: USA (Seattle, Portland, Lansing, Los Angeles and Durham). Notes: RANDOMISATION: no details provided. Info on Screening Process: Recruited via clinic referrals or from advertisements. 361 screened; 84 excluded because didn't meet inclusion criteria (N=31), experienced an adverse event (N=1) or because of other administrative reasons (N=52).	n= 276 Age: Mean 36 Sex: 112 males 164 females Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-IV Exclusions: Any axis I disorder except dysthymia, simple phobia, social phobia, somatisation disorder, or a history of MDD. Patients at suicide risk. No psychotropic medications for 2 weeks before enrollment. Score >=2 on HAM-D item 3. Notes: Administered Mini International Neuropsychiatric Interview. Divergent findings between clinical interview and MINI were resolved by judgement of principal investigator. Had to have Covi Anxiety Scale >=9 and Raskin Depression Scale score <=7. HAMA >20. Baseline: HAMA at baseline. Placebo: 22.90 (3.88), Pregabalin 150: 22.35 (2.68), Pregabalin 600: 23.16 (2.73) and Lorazepam: 23.85 (3.24). Slightly more females in placebo and lorazepam groups at baseline.	**Data Used** CGI-I HAMA Adverse events Leaving the study due to adverse events Leaving the study early for any reason Remission (less than 7 on HAMA) Response (50% reduction in HAMA score)	**Group 1 N= 69** Placebo - Day 1 received 1/6 of dose, which was increased daily until targeted dose was reached. **Group 2 N= 70** Pregabalin. Mean dose 600mg/day - 200mg three times a day. Day 1 received 1/6 of dose, which was increased daily until targeted dose was reached. **Group 3 N= 69** Pregabalin. Mean dose 150mg/day - 50mg three times a day. Day 1 received 1/6 of dose, which was increased daily until targeted dose was reached. **Group 4 N= 68** Lorazepam. Mean dose 6mg/day - 2mg three times a day. Day 1 received 1/6 of dose, which was increased daily until targeted dose was reached.	Funding: no details provided. Pfizer Global Research are involved. Quality assessed: +.
PFIZER2005 Study Type: RCT Blindness: Double blind Duration (days): Mean 28 Followup: No Info Setting: No Info Notes: No Info Info on Screening Process: No Info	n= 266 Age: Sex: no information Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-IV Exclusions: No information provided Baseline: HAMA Placebo 23.9, Pregablin 150mg 25.5, Pregablin 600mg 24.4, Lorazepam 6mg 24.3	**Data Used** HAMA Leaving the study early for any reason Remission (less than 7 on HAMA) Response (50% reduction in HAMA score) **Data Not Used** Discontinuation adverse events (DAEs) - not extractable	**Group 1 N= 67** Placebo **Group 2 N= 64** Lorazepam. Mean dose 6mg **Group 3 N= 69** Pregabalin. Mean dose 600mg **Group 4 N= 66** Pregabalin. Mean dose 150mg	Funding: Pfizer
POHL2005 Study Type: RCT Study Description: Comparison of the efficacy and tolerability of BID versus TID dosing of pregabalin. 1-week drug-free screening phase followed by 6 weeks DB treatment. Type of Analysis: ITT (LOCF) Blindness: Double blind Duration (days): Mean 42 Setting: 19 centres: USA. Ppts recruited via clinic referrals and adverts in the local media. Notes: RANDOMISATION: randomised in a 1:1:1:1 fashion. Info on Screening Process: 605 screened: 174 did not meet entry criteria, 22 were lost to follow-up, 36 withdrew consent, 3 were randomised but did not take study medication and 29 were lost for other or administrative reasons.	n= 344 Age: Sex: Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-IV Exclusions: Other current Axis I disorders except dysthymia or simple phobia, patients at suicide risk, patients with any clinically significant, serious or unstable hematologic, autoimmune, endocrine, vardiovascular, renal, hepatic, gastrointestinal, or neurological disorder and patients with prior exposure to pregabalin. Notes: Ppts scored >=20 on the HAM-A, >=9 on Covi Anxiety Scale and >=7 on the Raskin Depression Scale. Diagnosis made via MINI. Baseline: No details provided.	**Data Used** Remission (less than 7 on HAMA) CGI-I Adverse events Leaving the study due to adverse events Leaving the study early for any reason Response (50% reduction in HAMA score) Notes: Ppts were assessed at baseline and study weeks 1, 2, 3, 4 and 6.	**Group 1 N= 89** Pregabalin. Mean dose 400mg/day - Treatment was initiated at 200mg/day and were titrated to 400mg/day on day 4. **Group 2 N= 86** Placebo **Group 3 N= 88** Pregabalin. Mean dose 450mg/day - Treatment was initiated at 300mg/day and titrated to 450mg/day on day 4. **Group 4 N= 78** Pregabalin. Mean dose 200mg/day - Treatment was initiated at 200mg/day and ppts were maintained on this dosage.	Funding: Pfizer, Inc. Quality assessed: +.
RICKELS2000A				

Study Type: RCT Study Description: ITT: all eligible participants with at least one efficacy evaluation made whilst receiving study medication Type of Analysis: ITT/LOCF Blindness: Double blind Duration (days): Mean 56 Setting: US Outpatient (15 centres) Notes: RANDOMISATION: not reported. ALLOCATION CONCEALMENT: not addressed Info on Screening Process: 370 completed placebo run-in period & received study drug, 21 of these were excluded as they had no primary outcome.	n= 349 Age: Mean 41 Range 20-75 Sex: 154 males 195 females Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-IV Exclusions: - Less than 18 years of age - DSM-IV criteria for GAD - No MDD - HAMA score < 18 - HAMA (anxious mood & tension items) < 2 - Reduction of at least 20% in the HAMA total score between screening visit & baseline - Lower scores on the Covi Anxiety scale than the Raskin Depression Scale - Raskin Depression Scale score greater than 3 on any item - Use of other pharmacology (i.e. benzodiazepine, antipsychotic, antidepressants; patients were allowed to take chloral hydrate) - Other clinically significant psychiatric disorder Notes: 6.9% had a history of MDD; 0.5% had a history of dysthymia Baseline: HAMA baseline depression score (approx): 24.23 (4.10). No significant differences between groups at baseline. Venlafaxine 75mg/d: 24.7 (4.4). Venlafaxine 150mg/d: 24.5 (4.1). Venlafaxine 225mg/d: 23.6 (3.7). Placebo: 24.1 (4.2).	**Data Used** HAMA Leaving the study due to inefficacy Leaving the study due to adverse events Compliance Leaving the study early for any reason Notes: TAKEN AT: week 1, 2, 3, 4, 6, 8 weeks 4-10 days after drug tapered. DROP OUTS: 29% CHANGE SCORES USED.	**Group 1 N= 92** Venlafaxine (extended release). Mean dose 75mg/d - 8-week intervention. Fixed doses. Week 1 to 8: 75mg/d. One pill in the morning. **Group 2 N= 90** Venlafaxine (extended release). Mean dose 225mg/d - 8-week intervention. Fixed doses. Week 1: 75mg/d. Week 2: 150mg/d. Week 3 to 8: 225mg/d. **Group 3 N= 91** Venlafaxine (extended release). Mean dose 150mg/d - 8-week intervention. Fixed doses. Week 1: 75mg/d. Week 2 to 8: 150mg/d. **Group 4 N= 97** Placebo - No informtaion given.	Funding: Wyeth-Ayerst Laboratories. Quality assessed: -.
Results from this paper: +				
RICKELS2003 Study Type: RCT Blindness: Double blind Duration (days): Mean 56 Setting: Outpatients, 50 sites in US and Canada Notes: RANDOMISATION: no further details Info on Screening Process: 661 eligible, 35 lost to follow up, 10 adverse events, 6 protocol violations, 44 for other reasons	n= 566 Age: Mean 40 Sex: 253 males 313 females Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-IV Exclusions: - <18 years - HAM-A <20 - HAM-A items 1 and 2 <2 - another other psychiatric condition including MDD - using other psychoactive drugs Baseline: HAM-A: Placebo 24.4 (3.7) 20mg Parox 24.1 (3.6) 40mg Parox 23.8 (3.4)	**Data Used** HAMA Adverse events Leaving the study due to adverse events Leaving the study early for any reason Remission (less than 7 on HAMA) **Data Not Used** Response (50% reduction in HAMA score) - not extractable Notes: Response based on CGI score of 1 or 2.	**Group 1 N= 180** Placebo - No details given. **Group 2 N= 197** Paroxetine. Mean dose 40mg - Starting dose 10mg/day, increased 10mg/day each week until reach 40mg **Group 3 N= 188** Paroxetine. Mean dose 20mg - Starting dose 10mg, followed by 20mg at week 2	Funding: GSK. Quality assessed -.
RICKELS2005 Study Type: RCT Study Description: 1 week drug-free screening period before 4 weeks of double-blind treatment. This was followed by a 1 week taper period and then 1 week drug-free. Type of Analysis: ITT (LOCF method) Blindness: Double blind Duration (days): Mean 28 Setting: Recruited via clinic referrals and from	n= 454 Age: Mean 39 Sex: 165 males 289 females Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-IV Exclusions: Raskin Depression Scale score >7, being a fertile woman having a positive pregnancy test result, not using a medically accepted contraceptive or currently	**Data Used** CGI-I HAMA Adverse events Leaving the study due to adverse events Leaving the study early for any reason Remission (less than 7 on HAMA) Response (50% reduction in HAMA score)	**Group 1 N= 91** Placebo - Three treatments a day. **Group 2 N= 91** Pregabalin. Mean dose 300mg/day - Pregabalin was initiated at 300mg/day and kept constant throughout the study. Three treatments a day.	Funding: Pfizer, Inc. Quality assessed: +.

advertisements in the local media. Outpatients. Multicentre: USA. Notes: RANDOMISATION: ppts were randomised in blocks of 10. No further details. Info on Screening Process: 696 screened: 454 randomised (242 excluded). Reasons for exclusion not provided.	nursing, a current or past history of bipolar, schizophrenic, schizoaffective, psychotic or factitious disorder and dementia, current but not lifetime MDD, social anxiety disorder, panic disorder with or without agoraphobia, OCD, posttraumatic or acute stress disorders, and eating disorders at the diagnostic threshold but not subthreshold level and alcohol or other substance dependence and/or abuse, positive urine drug screen result, any clinically significant acute or unstable medical condition or clinically significant ECG result or laboratory abnormalities, concurrent psychotherapy for GAD, unless undergoing stable treatment for longer than 3 months, concomitant treatment with a psychotropic medication during the study and for at least 2 weeks before the screening visit, current or past history of a seizure disorder or requiring anticonvulsant therapy for any indication, or suicide risk either currently or based on history. Notes: Diagnosis was based on structured Mini-International Neuropsychiatric Interview. Had HAMA scores >9 and Covi Anxiety Scale scores >9. Baseline: HAMA at baseline: Pregabalin 300: 25.0 (SE 0.4), Pregabalin 450: 24.6 (SE 0.4), Pregabalin 600: 25.2 (SE 0.4), Alprazolam: 24.9 (SE 0.4) and Placebo: 24.6 (SE 0.4).	Notes: Assessments were performed at screening, baseline and at study weeks 1, 2, 3 and 4.	**Group 3 N= 89** Pregabalin. Mean dose 600mg/day - Pregabalin was initiated at 300mg/day and titrated to 450mg/day on day 4. Dosage was titrated to 600mg/day on day 7. Three treatments a day. **Group 4 N= 90** Pregabalin. Mean dose 450mg/day - Pregabalin was initiated at 300mg/day and then titrated to 450mg/day on day 4. Three treatments a day. **Group 5 N= 93** Alprazolam. Mean dose 1.5mg/day - Initiated at 0.5mg/day and increased to 1.0mg/day on day 4 and 1.5mg/day on day 7. Three treatments a day.	

Characteristics of Excluded Studies

Reference ID	Reason for Exclusion
BORISON1990	N<10 in each treatment arm

References of Included Studies

ALLGULANDER2001 (Published Data Only)

Allgulander, C., Hackett, D. & Salinas, E. (2001) Venlafaxine extended release (ER) in the treatment of generalised anxiety disorder. British Journal of Psychiatry, 179, 15-22.

BALDWIN2006 (Published Data Only)

Baldwin, D.S., Huusom, A.K.T. & Maehlum, E. (2006) Escitalopram and paroxetine in the treatment of generalised anxiety disorder: randomised, placebo-controlled, doube-blind study. British Journal of Psychiatry, 189, 264-272.

DAVIDSON1999 (Published Data Only)

Davidson, J.R.T., DuPont, R.L., Hedges, D. et al. (1999) Efficacy, safety, and tolerability of venlafaxine extended release and buspirone in outpatients with generalized anxiety disorder. Journal of Clinical Psychiatry, 60, 528-535.

FELTNER2003 (Published Data Only)

Feltner, D.E., Crockatt, J.G., Dubovsky, S.J. et al. 2003 A randomized, double0blind, placebo-controlled, fixed-dose, multicentre study of Pregabalin in patients with geralized anxiety disorder. Journal of Clinical Psychopharmacology, 23, 240-249

HACKETT2003 (Published Data Only)

Hackett, D., Haudiquet, V., Salinas, E. (2003) A method for controlling for a high placebo response rate in a comparison of venlafaxine XR and diazepam in the short term treatment of patients with generalised anxiety disorder. European Psychiatry, 18, 182-187.

KOPONEN2007 (Published Data Only)

Koponen, H., Allgulanderm C., Erickson, J., et al. (2007) Efficacy of Duloxetine for the treatment of generalized anxiety disorder: Implications for primary care physicians. Primary Care Companion yo the Journal of Clinical Psychiatry, 9, 100-107.

MONTGOMERY2006 (Published Data Only)

Montgomery, S.A, Tobias, K., Zornberg, G.L., Kasper, S. & Pande, A.C. (2006) Efficacy and safety of Pregabalin in the treatment of Generalized Anxiety Disorder: A 6-week, multicenter, randomized, double-blind, placebo-controlled comparison of Pregabalin and Venlafaxine. Journal of Clinical Psychiatry, 67, 771-782.

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Nicolini, H., Bakish, D., Duenas, H. et al. (2009) Improvement of psychic and somatic symptoms in adult patients with generalized anxiety disorder: examination from a duloxetine, venlafaxine extended-release and placebo-controlled trial. Psychological Medicine, 39, 267-276

PANDE2003 (Published Data Only)

Pande, A.C., Crockatt, J.G., Feltner, D.E., Janney, C.A., Smith, W.T., Weisler, R., Londborg, P.D., Bielski, R.J., Zimbroff, D.L., Davidson, J.R.T., & Liu--Dumaw, M. (2003) Pregabalin in generalized anxiety disorder: a placebo-controlled trial. American Journal of Psychiatry, 160, 533-540.

PFIZER2005 (Unpublished Data Only)

EMEA 2006, European assessment report: LYRICA. London: EMEA.

POHL2005 (Published Data Only)

Pohl, R.B., Feltner, D.E., Fieve, R.R. & Pande, A.C. (2005) Efficacy of pregabalin in the treatment of generalized anxiety disorder. Double-blind, placebo-controlled comparison of BID versus TID dosing. Journal of Clinical Psychopharmacology, 25, 151-158.

RICKELS2000A (Published Data Only)

*Rickels, K., Pollack, M.H., Sheehan, D.V. et al. (2000) Efficacy of extended-release venlafaxine in nondepressed outpatients with generalized anxiety disorder. American Journal of Psychiatry, 157, 968-974.

Sontheimer, D., & Ables, A. (2000) Is imipramine or buspirone treatment effective in patients wishing to discontinue long-term benzodiazepine use? The Journal of Family Practice, 50, INCOMPLETE.

RICKELS2003 (Published Data Only)

Rickels, K., Zaninelli, R., McCafferty, J. et al. (2003) Paroxetine treatment of generalized anxiety disorder: a double-blind, placebo-controlled study. American Journal of Psychiatry, 160, 749-756.

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Rickels, K., Pollack, M.H., Feltner, D.E., Lydiard, B., Zimbroff, D.L., Bielski, R.J., Tobias, K., Brock, J.D., Zornberg, G.L., & Pande, A.C. (2005) Pregabalin for treatment of generalized anxiety disorder. A 4-week, multi-center, double-blind, placebo-controlled trial of pregabalin and alprazolam. Archives of General Psychiatry, 62, 1022-1030.

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Borison, R.L., Albrecht, J.W. & Diamond, B.I. (1990) Efficacy and safety of a putative anxiolytic agent: Ipsapirone. Psychopharmacologuy Bulletin, 26, 2, 207-210