Characteristics Table for The Clinical Question: In the treatment of generalised anxiety disorder does pharmacology improve outcome?

Comparisons Included in this Clinical Question

Anticonvulsants versus Placebo
FELTNER2003
KASPER2009
MONTGOMERY2006
MONTGOMERY2008
PANDE2003
PFIZER2005
POHL2005
RICKELS2005

Anticonvulsants vs Venlafaxine (SNRI) vs Placebo
KASPER2009
MONTGOMERY2006

Antihistamine vs Placebo
DARCIS1995
LADER1998
LLORCA2002

Benzodiazepines versus Anticonvulsants
FELTNER2003
PANDE2003
PFIZER2005
RICKELS2005

Benzodiazepines versus Azapirones
BOURIN1992

Benzodiazepines versus Placebo
ANDREATINI2002
ANSSEAU2001
CUTLER1993A
FELTNER2003
FRESQUET2000
HACKETT2003
LYDIARD1997
MCLEOD1992
MOLLER2001
PANDE2003
PFIZER2008
RICKELS2000B
RICKELS2005

Buspirone vs Placebo
DAVIDSON1999
LADER1998
MAJERCSIK2003
POLLACK1997
SRAMEK1996

Duloxetine (SNRI) vs. placebo
HARTFORD2007
KOPONEN2007
NICOLINI2009
RYNN2008

Duloxetine (SNRI) vs. Venlafaxine (SNRI)
HARTFORD2007
NICOLINI2009

Quetiapine versus Placebo
ASTRAZENECA2007A
ASTRAZENECA2007B
ASTRAZENECA2007C
ASTRAZENECA2008

SSRI vs Venlafaxine
BOSE2008

SSRIs versus Placebo
ALLGULANDER2004
ASTRAZENECA2007A
ASTRAZENECA2007B
BALDWIN2006
BOSE2008
BRAWMAN-MINTZER2006
DAVIDSON2004
GOODMAN2005
GSK2002
GSK2005
HEWETT2001
LENZE2005
LENZE2009
PFIZER2008
POLLACK2001
RICKELS2003

SSRIs versus SSRIs
BALDWIN2006
BALL2005
BIELSKI2005

TCA vs Placebo
MCLEOD1992

Venlafaxine (SNRI) versus Azapirones
DAVIDSON1999

Venlafaxine (SNRI) versus placebo
ALLGULANDER2001
BOSE2008
DAVIDSON1999
GELENBERG2000
HACKETT2003
HARTFORD2007
KASPER2009
LENOXSMITH2003
MONTGOMERY2006
NICOLINI2009
NIMATOUDIS2004
RICKELS2000A

Venlafaxine vs Benzo
HACKETT2003

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: +.
ALLGULANDER2004 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 84 Setting: Australia, Canada, Denmark, Norway, Sweeden	n= 373 Age: Mean 41 Sex: 167 males 206 females Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-IV Exclusions: - Less than 18 years of age - No DSM-IV primary diagnosis of GAD - HAMA score < 18	**Data Used** CGI-I HAMA Adverse events Hospital Anxiety and Depression Scale (anxiety) Leaving the study due to adverse events Leaving the study early for any reason Remission (less than 7 on HAMA) QoL	**Group 1 N= 188** Placebo - No details given. **Group 2 N= 182** Sertraline - 1 week placebo lead-in period. 12 weeks treatment. Taper period. Flexible doses. Week 1: 25mg/d. Week 2,3,4: 50mg/d. Week 5,6 flexible doses in range of 50 - 150mg/g.	Funding: Pzifer, Inc. Quality assessed: +

Outpatient (21 centres) Notes: RANDOMISATION: procedure not reported. ALLOCATION CONCEALMENT: not addressed. Info on Screening Process: 562 screened, 378 randomised, 5 did not receive study medication.	- HAMA (anxious mood & tension items) < 2 - No current use of medically accepted contraception in fertile women - Other psychiatric diagnosis - MADRS score > 15 - Concurrent psychotherapy for GAD - Clinically significant acute/ unstable medical condition - Treatment with any other psychotropic drug (other than infrequent use of chloral hydrate) - Suicide risk - Previous failure to respond to antidepressant drug treatment Notes: 14% reported a previous diagnosis of depression. 30% reported previous treatment with a psychotropic medication. Baseline: HAMA baseline depression score (approx): 24.80 (4.75). Sertraline: 24.6 (4.6). Placebo: 25.0 (4.9). No significant differences between groups at baseline.	Response (50% reduction in HAMA score) Notes: TAKEN AT: 1, 2, 4, 6, 8, 12 weeks. DROP OUTS: 23%. CHANGE SCORES.		
Results from this paper:				
ANDREATINI2002 Study Type: RCT Study Description: ITT using LOCF included all those who completed at least 1 week of treatment Type of Analysis: ITT Blindness: Double blind Duration (days): Mean 28 Setting: Sao Paulo ,BRAZIL Notes: RANDOMISATION: used a computer programme Info on Screening Process: 132 people were interviewed of which 96 were excluded and 36 participated in the study. Participants were excluded due to the presence of another mental illness, refusal, marked reduction in HAMA prior to study, use of other medications.	n= 36 Age: Mean 41 Sex: 17 males 19 females Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-III-R Exclusions: - No DSM-III-R diagosis of GAD - current or previous MDD, manic episode, panic disorder, OCD, drug dependence or any psychotic symptoms - major medical disorders (e.g. CVD, renal disorders etc.) - drug treatment apart from over the counter drugs - receiving psychotherapy - Patients under treatment with Benzodiazepines were excluded if: 1) they had a clinical response or no evidence of side effects to the curent drug 2) they did not undergo a gradual reduction of medication followed by a 2 week wash-out period - Social phobia or simple phobia excluded if anxiety was secondary to these disorders - females not using a medically accepted form of birth control Notes: All participants were evaluated using the SCI-R Baseline: HAMA - Placebo: 25.1(7.5), Diazepam: 25.2(4.5), Valepotriates: 22.8(7.6)	**Data Used** STAI-trait HAMA Leaving the study due to inefficacy Leaving the study due to adverse events Notes: TAKEN AT: baseline, end of treatment (4 weeks) DROPOUTS:Diazepam 1/12 (8.3%), Valepotriate 2/12 (16.6%), Placebo 2/12 (16.6%)	**Group 1 N= 12** Diazepam. Mean dose 6.5mg/day - Following a two week washout period, study drugs were administered in identical capsules containing 2.5mg. The capsules were adminstered three times a day with thelowest dose consisting of two placebo and one active capsules based on response. 4 week **Group 2 N= 12** Placebo - Following a two week washout period, study drugs were administered in identical capsules. The capsules were adminstered three times a day. **Group 3 N= 12** Valepotriates. Mean dose 81.3mg/day - Following a two week washout period, study drugs were administered in identical capsules containing 50mg. The capsules were adminstered three times a day with thelowest dose consisting of two placebo and one active capsules based on response.	Drug company funded: BYK Quimica e Farmaceutica Ltds (Brazil). Quality assessment score = + The study included a number of participants with current social phobia and simple phobias in addition to GAD
ANSSEAU2001 Study Type: RCT Study Description: 6 parallel groups. 1 week placebo run-in period following by 4 weeks treatment. Type of Analysis: ITT Blindness: Double blind Duration (days): Mean 28 Setting: Outpatients. France. Notes: RANDOMISATION: no details provided. Info on Screening Process: 341 entered: 325 went on to DB treatment phase (16 excluded - 9	n= 325 Age: Mean 42 Sex: 133 males 208 females Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-III-R Exclusions: Could not have a score >2 on item 6 of the Hamilton Anxiety Scale, and score could not be higher than 8 on the Raskin Depression Scale. Evidence of contraindication for an anxiolytic benzodiazepine or serious or uncontrolled medical illness. Notes: Ppts scored >20 on HAMA and >9 on Covi Anxiety	**Data Used** HAMA Adverse events Leaving the study due to adverse events Leaving the study early for any reason Response (50% reduction in HAMA score) Notes: Assessments made at baseline and after 1, 2 and 4 weeks.	**Group 1 N= 56** Suriclone. Mean dose 0.2mg/day - No details provided. **Group 2 N= 57** Suriclone. Mean dose 0.1mg/day - No details provided. **Group 3 N= 54** Diazepam. Mean dose 5mg/day - No details provided. **Group 4 N= 57** Placebo - No details provided.	Funding: no details provided. Quality assessed +.

did not fit inclusion criteria and 7 improved more than 25% on HAMA scale during placebo week).	Scale. Baseline: HAMA at baseline: Suriclone 0.1 29.0 (5.6), Suriclone 0.2 28.6 (5.0), Suriclone 0.3 30.1 (5.2), Suriclone 0.4 30.0 (5.7), Diazepam 29.9 (5.2) and Placebo 29.4 (5.7).		**Group 5 N= 58** Suriclone. Mean dose 0.3mg/day - No details provided. **Group 6 N= 59** Suriclone. Mean dose 0.4mg/day - No details provided.	
ASTRAZENECA2007A Study Type: RCT Blindness: Double blind Duration (days): Mean 56 Setting: Europe, Argentina, Canada, Mexico, South Africa Notes: Randomisation: no further details Info on Screening Process: 1054 screened, 873 randomized	n= 873 Age: Mean 41 Sex: 306 males 567 females Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-IV Exclusions: - <18 years >65 years - HAM-A <20, and items 1 and 2 <2 - CGI <4 - MADRS >16	**Data Used** Discontinuation adverse events (DAEs) Leaving the study early for any reason Remission (less than 7 on HAMA) Response (50% reduction in HAMA score) **Data Not Used** HAMA - no SD	**Group 1 N= 218** Quetiapine. Mean dose 150mg **Group 2 N= 217** Placebo **Group 3 N= 217** Paroxetine. Mean dose 20mg **Group 4 N= 221** Quetiapine. Mean dose 50mg	Funding: Astra Zeneca
ASTRAZENECA2007B Study Type: RCT Blindness: Double blind Duration (days): Mean 56 Setting: US Notes: Randomisation: no further details Info on Screening Process: 1344 screened, 854 randomized	n= 854 Age: Mean 38 Sex: no information Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-IV Exclusions: - <18 years >65 years - HAM-A <20, and items 1 and 2 <2 - CGI <4 - MADRS >16	**Data Used** 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) **Data Not Used** HAMA - no SD	**Group 1 N= 213** Escitalopram. Mean dose 10mg **Group 2 N= 207** Quetiapine. Mean dose 300mg **Group 3 N= 219** Quetiapine. Mean dose 150mg **Group 4 N= 215** Placebo	Funding: Astra Zeneca
ASTRAZENECA2007C Study Type: RCT Blindness: Double blind Duration (days): Mean 56 Setting: US Notes: Randomisation: no further details Info on Screening Process: 1364 screened, 951 randomized	n= 951 Age: Mean 40 Sex: no information Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-IV Exclusions: - <18 years >65 years - HAM-A <20, and items 1 and 2 <2 - CGI <4 - MADRS >16	**Data Used** 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) **Data Not Used** HAMA - no SDs	**Group 1 N= 235** Placebo **Group 2 N= 234** Quetiapine. Mean dose 50mg **Group 3 N= 241** Quetiapine. Mean dose 300mg **Group 4 N= 241** Quetiapine. Mean dose 150mg	Funding: Astra Zeneca
ASTRAZENECA2008 Study Type: RCT Blindness: Double blind Duration (days): Mean 64 Setting: Estonia, Polland, Russia, Ukraine, United States	n= 556 Age: Mean 70 Range 65-87 Sex: 132 males 316 females Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-IV	**Data Used** 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) **Data Not Used** HAMA - no SDs	**Group 1 N= 222** Quetiapine - Flexible dosing (50mg-300mg), periodic stepwise increases up to maximum of 300mg **Group 2 N= 216** Placebo	

Notes: Randomisation: no further details Info on Screening Process: 556 screened, 450 randomized	Exclusions: - < 66 years of age - HAM-A <20, and items 1 and 2 <2 - CGI <4 - MADRS >16 Baseline: HAM-A: Quetiapine 25.2 (3.5) Placebo 25.1 (3.5) MADRS: Quetiapine 12.4 (2.6) Placebo 12.3 (2.3)			
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) - concomittant medication (i.e. psychoactive substances, antidepressants, benzodiazepines, antipsychotics) Baseline: HAMA scores at baseline (approx): 27.04 (4.46); No significant differences at baseline	**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. **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.	Received support from Lundbeck and sponsored by GlaxoSmith Kline. Quality assessed: +.
Results from this paper:				
BALL2005 Study Type: RCT Type of Analysis: ITT (LOCF) Blindness: Double blind Duration (days): Mean 56 Setting: US outpatients Notes: Randomisation: no further details Info on Screening Process: 61 ppts; 6 failed for medical or diagnostic reasons.	n= 55 Age: Mean 39 Sex: 14 males 41 females Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-IV Exclusions: - <18 years - HAM-A <18 - GAD not primary diagnosis - HAM-D >20 - history of psychotic or bipolar illness Baseline: HAM-A: Paroxetine 20.8 (2.3) Sertraline 21.4 (3.4)	**Data Used** HAMA Leaving the study early for any reason Remission (less than 7 on HAMA) Response (50% reduction in HAMA score)	**Group 1 N= 28** Sertraline - Starting dose 25mg could be increase up to maximum of 100mg **Group 2 N= 25** Paroxetine - starting dose 10mg and then could be increased up to 40mg	Funding: Pfizer. Quality assessed +.
BIELSKI2005 Study Type: RCT Type of Analysis: ITT (LOCF) Blindness: Double blind Duration (days): Mean 168 Setting: US,outpatients	n= 121 Age: Mean 37 Sex: 76 males 45 females Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-IV	**Data Used** CGI-I HAMA Leaving the study due to adverse events Leaving the study early for any reason QoL **Data Not Used**	**Group 1 N= 61** Escitalopram - 10mg first four weeks, could then be increased to 20mg/day, then every 2 weeks could be increased by 10mg/day	Funding: Forest Laboratories. Quality assessed +.

	Exclusions: - not 18-65 years - HAM-A <18 - HDRS >17 - Axis I psychiatric disorder - Psychosis Baseline: HAM-A: Escitalopram 23.7 (SE =0.5) Paroxetine 23.4 (SE = 0.4)	CGI (Response) - Not critical outcome Notes: Response based on CGI score of 1 or 2.	**Group 2 N= 60** Paroxetine - 20mg/day first 2 weeks, increased every 2 weeks by 10mg/day	
BOSE2008 Study Type: RCT Type of Analysis: ITT Blindness: Double blind Duration (days): Mean 56 Setting: Outpatients from 28 centres, US Notes: RANDOMISATION: no further details Info on Screening Process: 597 screened, 404 randomized, 7 dropped out before start of sudy	n= 404 Age: Mean 38 Sex: 152 males 252 females Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-IV Exclusions: - HAM-A <20 - HAM-A items 1 and 2 <2 - HDRS >15 - pregnant - Any other Axis I diagnosis - Bipolar Disorder, schizophrenia, psychosis, OCD, personality disorder - learning disabilities Baseline: HAM-A: Placebo 23.7 (SE = 0.3) Escitalopram 24.2 (SE=0.4) Venlafaxine 23.8 (SE=0.3)	**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) Response (50% reduction in HAMA score) Notes: Side effects reported if incidence over 10%.	**Group 1 N= 131** Escitalopram - starting dose of 10mg/day for first week, second week could be increased to 20mg/day **Group 2 N= 140** Placebo - No details given **Group 3 N= 133** Venlafaxine (extended release) - Starting dose of 75mg/day could be increased to maximum of 150mg/day on week 2, and up to 225mg/day in weeks 3-8.	Funded by Forest Laboratories. Quality assessed +.
BOURIN1992 Study Type: RCT Study Description: Compared discontinuation following 8 weeks of treatment. Parallel groups. Type of Analysis: Unclear Blindness: Double blind Duration (days): Mean 56 Setting: Outpatients. France: multicentre. Notes: RANDOMISATION: allocation done before the study (30 ppts in each group). Info on Screening Process: 60 ppts assessed before and after washout period.	n= 43 Age: Range 18-65 Sex: 14 males 29 females Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-III-R Exclusions: Pregnant women or women not using adequate contraception, nursing mothers, use of digitalis or MAOIs and contra-indications to the use of benzodiazepines. No severe somatic illness. No use of psychotropic drugs or agents with anxiolytic activity during the 2 weeks preceding the study. Notes: Ppts had HAM-A score >=18. Baseline: HAM-A at baseline. Lorazepam: 27.55 (1.84) and Buspirone: 26.74 (1.89)	**Data Used** HAMA Adverse events Visual Analog Scale (VAS) Leaving the study early for any reason Notes: Assessments performed at baseline, 2, 4, 6 and 8 weeks (active phase) and 9 and 10 weeks (withdrawal phase).	**Group 1 N= 20** Lorazepam - 3 or 4mg/day. 1mg in 3-4 divided doses. **Group 2 N= 23** Buspirone - 15-20mg/day. 3-4 capsules of 5mg in 3-4 divided doses per day.	Funding: no details proivded. Quality assessed +.
BRAWMAN-MINTZER2006 Study Type: RCT Study Description: ITT: all randomly assigned participants who had at least 1 postbaseline primary outcome measurement. Type of Analysis: ITT Blindness: Double blind Duration (days): Mean 70 Setting: US Outpatient (9 centres) Notes: RANDOMISATION: computerized list	n= 326 Age: Mean 40 Sex: 136 males 190 females Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-IV Exclusions: - Less than 18 years of age - No DSM-IV primary diagnosis of GAD - HAMA score > 20 - HAMA (anxious mood & tension items) < 2	**Data Used** HAMA Leaving the study due to inefficacy Leaving the study due to adverse events Leaving the study early for any reason Response (50% reduction in HAMA score)	**Group 1 N= 165** Sertraline. Mean dose 149.1mg/d - Did not include a placebo run-in phase. 10 weeks of treatment. 1 week taper period. Flexible dose. Week 1: 35mg/d. Weeks: 2,3,4,7 could be increased by 50mg increments. Maximum dose 200mg/d. Dosage reduction permitted. **Group 2 N= 163** Placebo	Financial contributions from Eli Lilly. Quality assessed: +.

ALLOCATION CONCEALMENT: not addressed Info on Screening Process: Patients registered 428; 338 randomly assigned.	- Lower scores on the Covi Anxiety scale than the Raskin Depression Scale - MDD - Other psychiatric diagnosis - MADRS > 17 - Other psychotropic medication - ECT - Women lactating, pregnant or childbearing potential not using an acceptable form of contraception Notes: 53.7% and 51.2% received prior psychotropic medication. 17% reported previous history with depression. Baseline: HAMA scores at baseline (approx) total: 24.3 (3.00); sertraline: 24.5 (3.1); placebo; 24.1 (2.8). No significant differences at baseline.	Notes: TAKEN AT: 1,2,3,4,6,8,10, 11 weeks. DROP OUTS: 26% CHANGE SCORES USED.		
CUTLER1993A Study Type: RCT Study Description: ITT using LOCF only included participants who completed at least 2 out of the 4 weeks of the study and had a 2 week evaluation Type of Analysis: ITT Blindness: Duration (days): Mean 28 Setting: Not reported: study reports single centre results of a multicentre trial Notes: Study comprised of a 4 week acute phase followed by an optional 4 week continuation phase and 2 week placebo washout phase Info on Screening Process: Not reported	n= 90 Age: Mean 31 Sex: 34 males 56 females Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-III Exclusions: - Does not meet DSM-III criteria for GAD and/or HAMD<18, Covi <8 and a depression scale <8 - experienced anxiety < 1 month - <85% compliance during placebo washout phase or >20% improvement in anxiety scores during washout - Females not using acceptable forms of birth control - evidence of drug abuse - clinically significant medical or psychiatic disorder or abnormalities. - Phobic disorder, panic disorder, OCD, MDD Cyclothymic disorder, Bipolar disorder, Briquet's disorder, somatizatio disorder, schizophrenia or psychotic symptoms or any personality disorder Baseline: Analysis only included 79/90 participant HAM-A: Ip: 25.67(3.57) Loz: 25.11(4.00) Plc: 25.72(4.03)	**Data Used** HAMA Adverse events Notes: TAKEN AT: baseline, end of treatment (acute phase) DROP OUTS: Ipsapirone 4/30 (13%), Lorazepam 3/30 (10%), Placebo 6/30 (20%)	**Group 1 N= 30** Ipsapirone - Following a one-week placebo wash-out phase participants received 4 weeks acute treatment. Dose ranged from 10-30 mg/day. Starting dose 5mg with titrated increments of 5mg **Group 2 N= 30** Lorazepam - Following a one-week placebo wash-out phase participants received 4 weeks acute treatment. Dose ranged from 2mg to 6 mg daily t.i.d Starting dose 1mg with titrated increments of 1mg **Group 3 N= 30** Placebo - Participants in the placebo group received identical capsules. Capsules were titrated one at a time.	No information about study funding. Quality assessment score = +
Results from this paper:				
DARCIS1995 Study Type: RCT Study Description: Ppts were randomly allocated to either hydroxyzine or placebo for 4 weeks, followed by a treatment-free period of 1 week. Type of Analysis: ITT (LOCF) Blindness: Double blind Duration (days): Mean 28 Followup: 1 week Setting: No details provided. Notes: RANDOMISATION: no details provided. Info on Screening Process: 133 assessed but 9 were excluded. No details provided.	n= 124 Age: Mean 44 Sex: 55 males 69 females Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-III-R Exclusions: No details provided. Baseline: HAM-A at baseline. Hydroxyzine: 25.9 (4.2) and Placebo: 24.1 (3.9).	**Data Used** Adverse events Hospital Anxiety and Depression Scale (anxiety) Leaving the study due to adverse events Notes: Ppts were assessed at the start of the study, after 1 and 4 weeks of treatment, and one week after stopping therapy.	**Group 1 N= 60** Hydoxyzine. Mean dose 50mg/day - 12.5mg at breakfast and at lunchtime, and 25mg at bedtime. **Group 2 N= 64** Placebo. Mean dose 2 tablets/day - 3 doses a day. 1/2 tablet at breakfast and lunch and one tablet at bedtime.	Funding: no details provided. Quality assessed +.
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: +.
DAVIDSON2004 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 Blindness: Double blind Duration (days): Mean 56 Followup: None Setting: US Outpatient Notes: Randomisation procedure not reported. Allocation consealment not addressed. Info on Screening Process: Details not provided.	n= 315 Age: Mean 40 Sex: 149 males 166 females Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-IV Exclusions: - not between the ages of 18 and 80 - did not meet DSM-IV criteria for GAD - abnormal physical/ laboratory examination - Less than 18 on the HAMA - At least 2 on the HAMA tension & anxiety items - 17 + on the HAMD - Lower scores on the Covi Anxiety scale than the Raskin Depression Scale - Bipolar disorder, schizophrenia, any psychotic disorder, OCD, learning disability, any pervasive developmental disorder or cognitive disorder - Axis I disorder other than GAD - Use of psychoactive medications, neuroleptics 6 months prior to study entry - Any neuroleptic, antidepressant, anxiolytic within 2 weeks (5 weeks for fluoxetine) - Daily benzodiazepne therapy within 1 month - Concomitant treatment with any psychotropic drug (except zolpidem for sleep) or any drug with any psychotripic component - women who were pregnant/ breastfeeding/ childbearing potential/ not practising a reliable method of birth control Notes: 34% (placebo), 40% (escitalopram) received prior GAD pharmacotherapy, majority were nonresponders or intolerant to prior treatment Baseline: HAMA scores at baseline (approx): 23.40 (4.40); No significant differences at baseline.	**Data Used** HAMA CGI (Response) Adverse events CGI (Remission Leaving the study due to adverse events QoL Notes: TAKEN AT: 1, 2, 4, 6 and 8 weeks. DROP OUTS: 4/158 (escitalopram),4/157 (placebo). CHANGE SCORES USED.	**Group 1 N= 158** Escitalopram. Mean dose 12.3 mg - 1 week placebo lead-in phase, 8 weeks intervention. 1 tablet/ day. 10 mg first 4 weeks, increased to 20 mg at week 4 or 6 if therapeutic response not achieved. Patients could return to starting dose for tolerability reasons. **Group 2 N= 159** Placebo - Matching placebo	Funding: Forest Laboratories, Inc. 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 (200mg) 25.4(4.6), Lorazepam 24.7(3.7), Placebo 24.8(4.1)	**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 = +
FRESQUET2000 Study Type: RCT Study Description: Phase II study. 1 week placebo lead-in. Received placebo, lesopitron or lorazepam twice daily for 6 weeks followed by 1 week taper period. Type of Analysis: ITT Blindness: Double blind Duration (days): Mean 42 Setting: Outpatients. Single centre (outpatient clinic). Notes: RANDOMISATION: no details provided. Info on Screening Process: No details provided.	n= 161 Age: Mean 37 Range 20-58 Sex: 33 males 35 females Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-IV Exclusions: Ppts whose HAM-A score decreased by >=20% between screening and baseline, other Axis I psychiatric diagnosis, substance abuse disorder within the last 6 months, two or more discrete panic attacks within 4 weeks, clinically significant hematopoeitic, cardiovascular, or autoimmune disease, clinically significant 12-lead electrocardiogram abnormality at screening and baseline, presence or history of clinically significant gastrointestinal, hepatic, renal, endocrine, cerebrovascular or seizure disorders, malignancy within 5 years of baseline or positive urine drug test. Notes: 68 ppts with documented history of GAD or anxiety NOS were included in subgroup. Ppts scored >=18 on HAM-A, >=2 on anxious mood item, <16 on HAM-D and Covi > Raskin. Many ppts used medication before study. Baseline: HAM-A at baseline. Placebo: 20.3 (1.7), Lesopitron: 21.7 (3.0) and Lorazepam: 21.5 (3.2).	**Data Used** CGI-I HAMA Adverse events Leaving the study early for any reason Response (50% reduction in HAMA score) **Data Not Used** Leaving the study due to adverse events - not extractable Notes: Assessments conducted weekly.	**Group 1 N= 18** Other active treatments. Mean dose 63.3mg/day - Lesopitron. Week 1: 40mg/day. Week 2: 60mg/day. Week 4: 80mg/day. These represent maximum titrations allowed. Twice daily. **Group 2 N= 30** Lorazepam. Mean dose 3.4mg/day - Titrated from 2-3mg/day to a maximum of 4mg/day. Titration was allowed during first three weeks according to tolerance but dosage could not be altered in weeks 4-6. Twice daily. **Group 3 N= 20** Placebo - Twice daily.	Funding: Laboratorios Dr. Esteve, S.A., Barcelona, Spain. Quality assessed: +.
GELENBERG2000 Study Type: 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	n= 238 Age: Mean 40 Sex: 98 males 140 females Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-IV	**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**	**Group 1 N= 127** Placebo - Identical appearing capsules.	Funding: likely to be pharma. Quality assessed: +.

Blindness: Double blind Duration (days): Mean 196 Setting: US Outpatients (14 centres) Notes: RANDOMISATION: table of random numbers. ALLOCATION CONCEALMENT: not addressed Info on Screening Process: 261 patients enrolled; 251 randomized, 10 LTFU, 127 placebo, 124 venlafaxine; 4 placebo, 9 venlafaxine no primary outcome measure (not included in ITT); 44 placebo, 60 venlafaxine completed trial	Exclusions: - less than 18 years - MDD - primary diagnosis not GAD (DSM-IV) - 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 - History of previous psychotic illness, bipolar disorder, ASPD or severe Axis II disorder - Previous treatment with venlafaxine - Concomittant medication (i.e. antipsychotic drugs, antidepressant, benzodiazepine) or ECT - Women lactating, pregnant or childbearing potential not using an acceptable form of contraception Baseline: HAMA scores at baseline (approx): 25.00 (5.00); No significant differences at baseline	Response (40% reduction in HAMA score) - does not meet criteria Notes: TAKEN AT: 1, 2, 3, 4, 6, 8, 12, 16, 20, 24 28 weeks. DROP OUTS: 61% but adequately taken account of in ITT (LOCF). CHANGE SCORES - NEED TO CALCULATE SDs	**Group 2 N= 124** Venlafaxine (extended release) - 6 months of treatment. Flexible dose schedule; week 1: 75 mg/d, week 2 to 3 up to 150mg/d, week 3+ 225 mg/d. Minimum dose: 75mg/d.	
Results from this paper:				
GOODMAN2005 Study Type: RCT Study Description: Pooled analysis from 3 RCTs. Single-blind placebo lead-in for 1 week followed by 8 weeks of double-blind treatment with escitalopram or placebo. Type of Analysis: ITT (LOCF) Blindness: Double blind Duration (days): Mean 56 Setting: Multicentre: US. Notes: RANDOMISATION: no details given. Info on Screening Process: No details given.	n= 856 Age: Mean 39 Sex: 377 males 479 females Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-IV Exclusions: Score of >=17 on the HAMD or a lower score on the Covi Anxiety Scale than the Raskin Depression Scale. Patients with a principal diagnosis of any Axis I disorder other than GAD (including MDD) or who met DSM-IV criteria for bipolar disorder, schizophrenia or any psychotic disorder, obsessive compulsive disorder, mental retardation, or any pervasive developmental disorder or cognitive disorder. A history of psychotic features or disorder, or substance abuse or dependence within the past 6 months. Use of any of the following psychoactive medications prior to study entry: depot neuroleptics within 6 months, any neuroleptic, antidepressants or anxiolytic within 2 weeks (5 weeks for fluoxetine), or daily benzodiazepine therapy within 1 month. Use of concomitant treatment with any psychotropic drug (except zolpidem as needed for sleep). Women who were pregnant or breastfeeding, or of child-bearing potential and not practicing a medically reliable method of birth control. Notes: ONLY USING STUDY 1 & 2 (as study 3 is reported already in Davidson 2004) Baseline: HAMA baseline scores: Placebo 22 (0.2) and Escitalopram 23.0 (0.2). Baseline scores are based on the ITT population.	**Data Used** HAMA **Data Not Used** Adverse events - not extractable for individual studies Leaving the study due to adverse events - not extractable for individual studies Leaving the study early for any reason - not extractable for individual studies Remission (less than 7 on HAMA) - Not extractable for individual studies Response (50% reduction in HAMA score) - not extractable for individual studies Notes: TAKEN AT: Baseline and endpoint DROP OUT:13% across both groups.	**Group 1 N= 267** Escitalopram - During the first 4 weeks, patients received a fixed dose of 10mg/day. If the therapeutic response was judged by the investigator to be insufficient at the week4 or 6 visit, the dose could be doubled to 20mg/day. Otherwise went back to 10mg/day. **Group 2 N= 266** Placebo - No details given.	Funding: Forest Laboratories Inc. Quality assessed +.
GSK2002 Study Type: RCT Study Description: Parallel-group study. 1 week single-blind placebo run-in phase. Randomised to either paroxetine or placebo. Type of Analysis: ITT (LOCF)	n= 335 Age: Mean 39 Sex: 119 males 208 females Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-IV	**Data Used** CGI-I HAMA CGI (Response) Adverse events Leaving the study due to inefficacy Leaving the study due to adverse events	**Group 1 N= 168** Paroxetine - Dose range 12.5-37.5mg/day. Weeks 1-2: 12.5mg/day. Dose increases of 12.5mg/day no more frequently than every 7 days were allowed at the discretion of the investigator according to response and tolerability. Max dose was 37.5mg/day.	Funding: GlaxoSmithKline. Quality assessed +.

Blindness: Double blind Duration (days): Mean 56 Setting: Multicentre (32 centres): USA. Notes: RANDOMISATION: no details given. Info on Screening Process: No details given.	Exclusions: Diagnosis of any current Axis I disorder or within the 6 months prior to screening, posed a current suicidal or homicidal risk in the investigator's judgement, had a score of =>18 on the MADRS at screening or at baseline, showed greater than a 20% reduction in the HAM-A total score from screening to baseline, had taken other psychotropic drugs that had not been discontinued within the minimum discontinuation period prior to screening, had received formal psychotherapy either concurrently or in the 12 weeks prior to screening. Notes: Ppts received medication for a maximum of 10 weeks, including a one-week placebo run-in phase followed by an eight-week treatment phase and a double-blind taper phase of up to 1 week. Baseline: HAM-A: Paroxetine 24.43 (3.71) and Placebo 24.83 (3.64).	Leaving the study early for any reason Remission (less than 7 on HAMA) Notes: Response was defined as CGI 1 or 2.	**Group 2 N= 167** Placebo - Received medication identical in appearance to that received by ppts assigned to the active medication.	
GSK2005 Study Type: RCT Study Description: Placebo run-in medication for one week followed by randomisation to paroxetine (20mg/day) or placebo. Type of Analysis: LOCF method used. Blindness: Double blind Duration (days): Mean 56 Setting: Multicentre (58 centres): Japan. Notes: RANDOMISATION: procedure not known. Info on Screening Process: Not known.	n= 361 Age: Mean 40 Sex: 144 males 214 females Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-IV Exclusions: Subjects with suspected history of psychiatric disorder other than GAD or with history or complications of such diseases, subjects who had taken MAOIs within1 week prior to week 1 and subjects with history of complications thatn might affect the subjects' safety. Notes: Subjects classed as non-responders at week 8 continued to receive paroxetine or placebo orally for a further 4 weeks in a flexible dosing schedule. Baseline: Baseline statistics not provided.	**Data Used** CGI-I HAMA Adverse events Sheehan Disability Scale (SDS) Leaving the study due to inefficacy Leaving the study due to adverse events Leaving the study early for any reason Response (50% reduction in HAMA score) Notes: Response was defined as either a CGI score of 1 or 2 or a HAMA score of <=10.	**Group 1 N= 182** Placebo - No details given. **Group 2 N= 179** Paroxetine - Began with 10mg for 1 weeks, followed by forced titration to 20mg/day for 7 weeks.	Funding: GlaxoSmithKline. Quality assessed +.
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 +.
HARTFORD2007 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	n= 487 Age: Mean 41 Sex: 182 males 305 females Diagnosis:	**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	**Group 1 N= 164** Venlafaxine (extended release). Mean dose 183.82mg/d - Started at 37.5mg/d for week 1, increased to 75mg/d week 2 onwards. Dose could be increased to 150mg/d for at least 1 week and then to	Drug company funded - Eli Lilly trial 7107 NCT00122850. Quality assessment score = +/++ All participants underwent a single-blind placebo lead-in

Blindness: Double blind Duration (days): Mean 70 Setting: Outpatients. Multicentre 42 sites in the USA Notes: RANDOMISATION: procedure not reported Info on Screening Process: 707 people were evaluated of which 220 failed to meet the inclusion criteria.	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 - Benzodiazepine use in the 2 weeks before visit 2 - Judged clinically to be a serious suicide risk - Previous duloxetine treatment Baseline: HAMA: Dulox 25.6(5.8) Venl 24.9(5.4) Placebo 25.0(5.8)	PGI-I Leaving the study due to adverse events Significant improvement (30% reduction) EQ-5D CGI-I Leaving the study due to inefficacy Serious Adverse events Hospital Anxiety and Depression Scale (anxiety) Sheehan Disability Scale (SDS) Adverse events HAMA Discontinuation adverse events (DAEs) Notes: TAKEN AT: Baseline and enpoint DROPOUT: Duloxetine: 67/162 (45.7%), Venlafaxine 62/164 (37.8%), Placebo 62/161 (38.5%)	225mg/d based on efficacy and tolerability. **Group 2 N= 161** Placebo **Group 3 N= 162** Duloxetine. Mean dose 107.73mg/d - Started at 30mg/d for week 1, increased to 60mg/d week 2 onwards. After titration to 60mg, flexible dosing was allowed in weekly increments of 30mg/d up to a max of 120mg/d. Dose increases were based on efficacy and tolerability	week, 10 week acute phase and a 2 week discontinuation tapering phase.
HEWETT2001 Study Type: RCT Study Description: Parallel group study. 1 week single-blind placebo run-in phase. Ppts randomised to receive either paroxetine or placebo. Type of Analysis: ITT (LOCF) Blindness: Double blind Duration (days): Mean 56 Setting: Multicentre (50 centres): France, UK, Germany, Ireland, Austria and Italy. Notes: RANDOMISATION: no details given. Info on Screening Process: No details given.	n= 372 Age: Mean 46 Sex: 110 males 262 females Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-IV Exclusions: Following conditions currently or within 6 months prior to screening visit: MDD, panic disorder, social phobia, agoraphobia, PTSD, OCD, and eating disorders. Current diagnosis of dysthymia or within the previous 6 months as a predominant psychiatric condition relative to GAD. Current psychotic disorder or history of psychotic disorder. Current bipolar disorder or history of bipolar disorder, or had a current history of cyclothymic disorder. Posed a current suicidal or homicidal risk. A score of >=18 on the MADRS at either screening or baseline. Had shown a greater than 20% reduction in HAM-A total score from screening to baseline. Had taken other psychotropic drugs which had not been discontinued within the minimum discontinuation periods prior to screening. Had ECT in the 3 months prior to screening. Had received formal psychotherapy, either concurrently or in the 12 weeks prior to screening. Notes: Ppts requiring more than one dose reduction were withdrawn from the study. Gradual reduction of study medication during double-blind taper phase of up to 3 weeks for ppts who completed treatment or withdrew prematurely at dose of 30mg/day or higher. Baseline: HAM-A: Paroxetine 26.0 (0.4) and Placebo 25.9 (0.4).	**Data Used** CGI-I CGI (Response) Adverse events Sheehan Disability Scale (SDS) Hospital Anxiety and Depression Scale (anxiety) Leaving the study due to inefficacy Leaving the study due to adverse events Leaving the study early for any reason Remission (less than 7 on HAMA) Notes: Response was CGI score of 1 or 2. Remission was <=10 on HAM-A.	**Group 1 N= 188** Paroxetine - Weeks 1-2: 20mg/day. Dose could then be uptirated in 10mg/day increments at intervals no more frequently than every 7 days at the discretion of the investigator, according to response and tolerability. Range 20-50mg/day. **Group 2 N= 186** Placebo - No details given.	Funding: GlaxoSmithKline. Quality assessed +.
KASPER2009 Study Type: RCT Study Description: 1 week open-label lead-in period, then randomised to 8 weeks of double-		**Data Used** CGI-I HAMA	**Group 1 N= 121** Pregabalin - Starting dose of 150mg/day for first week, thereafter flexible from 300-	Funded by Pfizer. Quality assessed +.

blind, parallel-group treatment. Blindness: Double blind Duration (days): Mean 56 Setting: 47 sites in Belgium, Canada, France, Ireland, Italy, Netherlands, Spain, Sweden Notes: RANDOMISATION: computer generated randomisation list. Info on Screening Process: 466 screened, 374 met eligibility criteria	n= 374 Age: Mean 41 Sex: 146 males 228 females Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-IV Exclusions: <18 years or >65 years - HAM-A <20 - HAM-A psychic and somatic factors <10 - bipolar disorder, schizophrenia, psychosis - MDD, dysthymia, OCD, PTSD, eating disorder, substance abuse or dependence - pregnant Baseline: HAM-A: Placebo 26.8 (SE=0.8) Venlafaxine 27.4 (SE=0.4) Pregabalin 27.6 (SE=0.4)	Adverse events Sheehan Disability Scale (SDS) Hospital Anxiety and Depression Scale (anxiety) EQ-5D Leaving the study due to adverse events Leaving the study early for any reason Response (50% reduction in HAMA score)	600mg/day **Group 2 N= 125** Venlafaxine (extended release) - starting dose of 75mg/day for first week then flexible thereafter between 75-225 mg/day **Group 3 N= 128** Placebo - No details given.	
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 = + / ++
LADER1998 Study Type: RCT Study Description: 1-week single-blind placebo run-in then 4-week DB treatment with either hydroxyzine, buspirone or placebo followed by 1 week placebo administration. Type of Analysis: ITT (LOCF) Blindness: Double blind Duration (days): Mean 28 Setting: Multicentre (62 centres): France (48 centres) and UK (14 centres). Patients seen by primary care doctors.	n= 244 Age: Mean 41 Range 30-42 Sex: 73 males 171 females Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-IV Exclusions: Depressive disorders according to DSM-IV criteria. Pregnancy or inadequate contraceptive precautions, major depressive disorder, alcohol abuse, organic or psychotic disorders, undergoing long-term psychotherapy or intake of psychotropic medication during the previous 4	**Data Used** CGI-I HAMA Adverse events Hospital Anxiety and Depression Scale (anxiety) Leaving the study early for any reason Response (50% reduction in HAMA score)	**Group 1 N= 81** Hydoxyzine. Mean dose 50mg/day - 12.5mg morning and midday, 25mg evening. **Group 2 N= 81** Placebo. Mean dose 3 capsules/day - 3 capsules throughout the day. **Group 3 N= 82** Buspirone. Mean dose 20mg/day - 5mg morning and midday, 10mg evening.	Funding: UCB, S.A. Quality assessed +.

Info on Screening Process: Excluded anyone who responded in placebo period of showed positive for benzodiazepines at entry. 266 recruited: 20 failed to meet inclusion criteria.	weeks. Notes: Ppts had HRSA score >20. Low levels of depressive symptoms allowed. Baseline: HARS at baseline: Hydroxyzine: 26.6 (4.3), Buspirone: 26.7 (4.1) and Placebo: 26.2 (4.2).	Notes: Assessments carried out weekly.		
LENOXSMITH2003 Study Type: RCT Blindness: Double blind Duration (days): Mean 168 Setting: 31 Primary care centres, UK Notes: RANDOMISATION: no further details	n= 244 Age: Mean 47 Sex: 100 males 144 females Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-IV Exclusions: - HAM-A <20 - <18 years of age - psychosis - substance abuse or dependence - PTSD - pregnant - MADRS >23 Baseline: HAM-A: Venlafaxine 28 Placebo 28	**Data Used** HAMA Hospital Anxiety and Depression Scale (anxiety) Leaving the study early for any reason Remission (less than 7 on HAMA) Response (50% reduction in HAMA score)	**Group 1 N= 122** Placebo **Group 2 N= 122** Venlafaxine (extended release) - Starting dose 75mg, could be increased to 150mg after 2 weeks. At end of 24 weeks patients on 150mg were reduced to 75mg and then the second week all patients received placebo.	Funded by Wyeth. Quality assessed: -.
LENZE2005 Study Type: RCT Blindness: Double blind Duration (days): Mean 56 Setting: Recruited from adverts and in a primary care centre, US Notes: RANDOMISATION: method not reported Info on Screening Process: 791 screened, 47 consented to participate. Of these 10 refused randomization, 1 spontaneous improvement, 1 did not meet diagnostic criteria, 1 had MDD	n= 34 Age: Mean 69 Sex: 13 males 21 females Diagnosis: 90% Generalised Anxiety Disorder (GAD) by DSM-IV Exclusions: - current MDD - dementia - psychosis - unstable medical illness - substance abuse Notes: 2 people in each group did not have GAD. 8 people in Citalopram group and 4 people in placebo group received lorazepam. Baseline: HAMA: Citalopram 21.4(4.6) Placebo 23.1(3.8) HDRS: Citalopram 11.3 (2.1) Placebo 12.4 (3.8)	**Data Used** 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= 17** Citalopram - 10mg /day at first dose, increased after week to 20mg/day, a further increase to 30mg/day after 4 weeks if no response **Group 2 N= 17** Placebo - No details given.	Funded by Forest Pharmaceuticals. Quality assessed +.
LENZE2009 Study Type: RCT Study Description: ITT: all participants who dropped out or were considered non responders were included except for 2 participants who did not receive medication Type of Analysis: ITT Blindness: Double blind Duration (days): Mean 84 Setting: USA Notes: Randomisation: permuted block, 1:1 randomised list generated by study stastistician Info on Screening Process: 550 screened, 293	n= 177 Age: Mean 72 Sex: 58 males 119 females Diagnosis: 14% Major depressive disorder by DSM-IV 100% Generalised Anxiety Disorder (GAD) by DSM-IV Exclusions: - Less than 60 years of age - Without a principal diagnosis of GAD - Less than 17 on the HAMA - Bipolar disorder, dementia - Increased suicide risk	**Data Used** HAMA CGI (Response) Adverse events Leaving the study due to adverse events Leaving the study early for any reason QoL Notes: TAKEN AT: 1, 2, 3, 4, 6, 8, 10, 12 weeks. DROP OUTS: SMDs REPORTED. DROP OUTS 18.5% (escitalopram), 18.4% (placebo)	**Group 1 N= 85** Escitalopram - 12 weeks. 10 mg of escitalopram, 1 pill/ day, 2 pills/ day after 4 weeks for non-responders, as tolerated. **Group 2 N= 92** Placebo	Funded by National Institute of Health grant, drugs provided by Forest Laboratories. Quality assessed +.

excluded, 257 consented to further assessment, 179 randomised, 2 did not receive medication	- Medical instability - Ongoing psychotherapy - Current antidepressant or anxiolytic use (except for benzodiazepines up to 2 mg/ day equivalent of lorazepam) Notes: 17.1% (escitalopram), 13.2% (placebo) were on benzodiazepines. 12.1% of escitalopram and 15.2% of placebo had MDD diagnosis. Baseline: HAMA baseline depression score (approx): 23.00 (2.30). No significant differences between groups at baseline.			
Results from this paper:				
LLORCA2002 Study Type: RCT Study Description: Parallel-group. 2 weeks SB run-in placebo, 12 weeks DB treatment and 4 weeks SB run-out placebo. Type of Analysis: ITT Blindness: Double blind Duration (days): Mean 84 Setting: Multicentre: France. Outpatients. Conducted by French GPs under supervision of psychiatrists. Notes: RANDOMISATION: no details provided. Info on Screening Process: 369 entered recruitment period. 334 entered DB treatment.	n= 334 Age: Mean 43 Sex: 106 males 228 females Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-IV Exclusions: Pregnant, breast-feeding, absence of a contraception method for women, known alcohol or drug dependence, major depressive episode wtihin the preceding 6 months or >=7 on Raskin Severity of Depression and Mania scale, psychotic or delusional disorders within the preceding 3 years, concomitant chronic diseases, closed-angle glaucoma or prostatic adenoma, intolerance or allergy to hydroxyzine, bromazepam, lactose or cellulose, inability to use self-assessment scales, treatment with antidepressants, neuroleptics, mood regulators, morphine or derivatives, hydroxyzine or bromazepam within the preceding 4 weeks, treatment with benzodiazepines >2 days per week during the previous 30 days or benzodiazepine intake during the previous 2 weeks, CNS active treatment within the last week preceding inclusion, need for psychotherapy. Notes: GPs were trained to diagnose GAD. Ppts not diagnosed by psychiatrists. Ppts scored >=20 on HAM-A. Baseline: HAM-A at baseline. Placebo: 25.73 (4.14). Hydroxyzine: 25.49 (3.61). Bromazepam: 25.32 (3.44).	**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= 116** Bromazepam. Mean dose 6mg/day - 1.5mg in the morning and at noon and 3mg in the evening. **Group 2 N= 113** Placebo - Oral capsules divided into 3 daily doses. **Group 3 N= 105** Hydoxyzine. Mean dose 50mg/day - 50mg/day. 12.5mg in the morning and at noon and 25mg in th evening.	Funding: UCB-Pharma. Quality assessed: +.
LYDIARD1997 Study Type: RCT Study Description: 4 weeks treatment with either abecarnil, alprazolam or placebo followed by 1-2 week taper. Type of Analysis: ITT (LOCF) Blindness: Double blind Duration (days): Mean 28 Setting: Multicenter: outpatients. USA. Notes: RANDOMISATION: no details provided. Info on Screening Process: No details provided.	n= 192 Age: Mean 42 Sex: 89 males 103 females Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-III-R Exclusions: No psychotherapeutic medication for at least 1 week and for at least 1 month for therapeutic doses of neuroleptics or antidepressants. History of pytschosis, mania, current major depression, substance abuse, or other Axis I disorders likely to interfere with objectives of study. Any investigational drug taken within 30 days preceding study admission. Women of childbearing potential who were not using medically accepted birth-control methods or who were planning on becoming pregnant. Pregnant women. Notes: Flexible dosage schedules used. Patients who discontinued for reasons unrelated to medication before completing 2 weeks of treatment were replaced. Ppts had	**Data Used** CGI-I HAMA Adverse events Leaving the study early for any reason Notes: Assessed weekly.	**Group 1 N= 67** Abercarnil - 3.0-9.0mg/day. Capsules contained 1.0mg. Dosages were titrated to 1 capsule t.i.d. by day 4, 2 capsules t.i.d. by day 8 and 3 capsules t.i.d. by day 15. Based dosage on clinical judgement. All ppts had to take at least 1 capsule b.i.d. to stay in study. **Group 2 N= 63** Alprazolam - 1.5mg-4.5mg/day. Capsules contained 0.5mg. Dosages were titrated to 1 capsule t.i.d. by day 4, 2 capsules t.i.d. by day 8 and 3 capsules t.i.d. by day 15. Based dosage on clinical judgement. All ppts had to take at least 1 capsule b.i.d. to stay in study.	Funding: no details provided. Likely to be pharma funded. Quality assessed: -.

	HAM-A score >=18 and Covi>Raskin score. Baseline: HAM-A at baseline. Abecarnil: 24.3, Alprazolam: 24.1 and Placebo: 24.8.		**Group 3 N= 62** Placebo - Dosages were titrated to 1 capsule t.i.d. by day 4, 2 capsules t.i.d. by day 8 and 3 capsules t.i.d. by day 15. Based dosage on clinical judgement. All ppts had to take at least 1 capsule b.i.d. to stay in study.	
MAJERCSIK2003 Study Type: RCT Blindness: Double blind Duration (days): Mean 42 Setting: Hungary Notes: randomisation: no further details	n= 52 Age: Mean 81 Sex: all males Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-IV Exclusions: - HAM-A <15 - anxiolytic medication in previous 6 months Baseline: HAM-A Buspirone 19.45 (SE=0.46) Placebo 21.48 (SE=0.47)	**Data Used** HAMA	**Group 1 N= 33** Buspirone - 30mg/day for 6 weeka **Group 2 N= 19** Placebo - 3 tablets a day	
MCLEOD1992 Study Type: RCT Blindness: Double blind Duration (days): Mean 42 Setting: US volunteers recruited through adverts in local newspapers. Notes: RANDOMISATION: no further details. Assignments were made so that the groups were matched according to gender.	n= 42 Age: Mean 41 Sex: 15 males 27 females Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-IV Exclusions: - history of panic attacks, psychosis or substance abuse and could not have taken any medications that affect the autonomic or central nervous systems for at least 2 weeks prior to entry into the study Notes: Ppts were seen weekly for medication pick-up and supportive therapy, in which they discussed how they were coming along and received a sympathetic and understanding response from a therapist. Baseline: HAM-A: Placebo 25.1 (2.0) Imipramine 25.3 (4.0) Alprazolam 28.1 (4.3)	**Data Used** HAMA Blood pressure	**Group 1 N= 14** Imipramine. Mean dose 92.6mg - Starting dose 25mg but could be adjusted according to clinical need. Range 1-12 capsules. **Group 2 N= 14** Alprazolam. Mean dose 2.3mg - Starting dose of 0.5mg but could be adjusted according to clinical need. **Group 3 N= 14** Placebo - Took 1 capsule three times a day unless they developed excessive side effects.	Funded by NIH grant. Quality assessed -.
MOLLER2001 Study Type: RCT Study Description: ITT using LOCF. 307/313 participants were included in the ITT analysis Type of Analysis: ITT Blindness: Double blind Duration (days): Mean 28 Setting: Multicentre, GERMANY. Outpatients Notes: RANDOMISATION: procedure not reported Info on Screening Process: No details reported	n= 313 Age: Mean 48 Sex: 104 males 209 females Diagnosis: 100% Generalised Anxiety Disorder (GAD) by ICD-10 Exclusions: - No ICD-10 diagnosis of GAD - HAM-A <17 and HAMD >20 - Ages <18 or >65 years - Significant other psychiatric disorders such as panic disorder, MDD - Known substance abuse - Relevant comcomitant other diseases such as epilepsy, severe renal or hepatic impairment, cancer - Placebo responders (defined as those showing a decrease >6 points during the washout period)	**Data Used** Plasma concentrations HAMA Adverse events **Data Not Used** Leaving the study due to adverse events - not extractable Leaving the study early for any reason - data not extractable Notes: TAKEN AT: baseline and end of treatment (end of active treatment) DROPOUTS: Opipramol 8/101 (8%), Alprazolam 13/105 (12%), Placebo 18/107 (17%)	**Group 1 N= 107** Placebo - 4 capsules were given, two in the morning and two in the evening **Group 2 N= 105** Alprazolam. Mean dose 2mg/day - Medication was prepared in identical capsules containing 0.5mg. Day 0 1 of the 2 evening capsules was active, day 1, 2 of the evening capsules active, day 2 morning capsules were also active. By Day 3 the final dose of 2mg was given.	No details reported regarding funding. Quality assessed: -. The study included a 7 day placebo washout period, followed by 4 weeks of active treatment. Active treatment was followed by tapering with placebo.

	Notes: ~66% of participants had concomitant diseases Baseline: No relevant differences at baseline HAMA: Opipramol 27.7(7.4), Alprazolam: 29.7(7.6), Placebo: 29.3(7.0)		**Group 3 N= 101** Opipramol. Mean dose 200mg/day - Medication was prepared in identical capsules containing 50mg. Day 0 1 of the 2 evening capsules was active, day 1, 2 of the evening capsules active, day 2 morning capsules were also active. By Day 3 the final dose of 200mg was given.	
Results from this paper:				
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 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.	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 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).	**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** 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 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. **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.).	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 = +
MONTGOMERY2008 Study Type: RCT Study Description: Parallel group study. 1 week drug-free period then 8 week double-blind study, followed by a 1-5 day taper with a final follow-up visit at 1 week. Type of Analysis: ITT (LOCF) Blindness: Double blind Duration (days): Mean 56 Setting: Outpatients. Multicentre study: 13 in the	n= 273 Age: Mean 72 Sex: 63 males 210 females Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-IV Exclusions: Current or past DSM-IV diagnosis of schizophrenia, schizoaffective, psychotic or bipolar disorder, current DSM-IV diagnosis of MDD, social anxiety disorder,	**Data Used** CGI-I HAMA Adverse events SCL anxiety factor 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= 177** Pregabalin - Initiated at 50mg/day, followed by an increase to 100mg/day on day 3 and 150mg/day on day 5. Dosing was flexible from weeks 1-6 in the range of 150-600mg/day administered either two or three times daily. Maintained on the same dose from weeks 6-8. **Group 2 N= 96** Placebo - No details provided.	Funding: Pfizer, Inc. Quality assessed: +.

US and 69 in Europe. Notes: RANDOMISATION: were randomised 2:1 pregabalin: placebo. Info on Screening Process: 366 people screened. 68 did not meet entry criteria, 16 withdrew consent and 11 did not enter for other reasons.	panic disorder, OCD, PTSD, acute stress disorder, borderline or antisocial personality disorder, eating disorder, delirium, dementia, amnestic disorder, alcohol or substance dependence and/or misuse in the past 6 months, positive urine drug screen, any clinically significant acute or unstable medical condition or clinically significant ECG or laboratory abnormalities, alanine/aspartate aminotransferase levels >3 times the upper limit of normal or creatine clearance rates, concurrent psychotherapy for generalised anxiety disorder unless in stable treatment >3 months, concomitant treatment with psychotropic medication during the study and for at least 2 weeks prior to the screening visit, current suicide risk based on the clinical judgement of the investigator, depressive symptoms predominating over anxiety symptoms. Notes: Diagnosis based on MINI interview, HRSA score >=20 and MMSE score >=24. Monitored adherence by counts of returned medication and ppts were counselled if they were found to be non-adherent. Baseline: HRSA at baseline. Pregabalin: 27 (4.8) and Placebo: 26 (4.1).			
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: +
Results from this paper:				
NIMATOUDIS2004 Study Type: RCT Study Description: Venlafaxine vs. Placebo for 8 weeks. 1week placebo run-in phase. Type of Analysis: ITT (LOCF) Blindness: Double blind Duration (days): Mean 56 Followup: 4-10 days	n= 46 Age: Mean 43 Sex: 15 males 31 females Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-III-R Exclusions: Major depressive disorder within 6 months of	**Data Used** CGI-I HAMA Adverse events Leaving the study early for any reason Remission (less than 7 on HAMA) Response (50% reduction in HAMA score)	**Group 1 N= 24** Venlafaxine (extended release). Mean dose 75mg/day - Ppts with a less than 30% decrease in their HAM-A total score at the end of 2 weeks compared to the end of the pre-study period doubled their dose for the rest of the treatment period (150mg/day).	Funding: possibly Wyeth. Quality assessed: -.

Setting: Multicentre: outpatients. Greece. Notes: RANDOMISATION: no details provided. Info on Screening Process: Removed anyone with a 20%+ decrease in HAM-A score during pre-study period.	study day 1, total Raskin depression score >6, if the secondary depressive symptoms item scores on the Raskin Depression scale was >3 or if their total score on the HAM-D >12. Recent history or current diagnosis of drug or alcohol dependence, current suicidal ideation and/or a history of suicide attempt, evidence or an organic mental disorder, presence of uncontrolled congestive heart failure, myocardial infarction within 6 months of screening visit, history or presence of medical disease that might compromise the study, use of any investigational drug or procedure, any antipsychotic drug withint 30 days of study day 1 and presence of any other Axis I disorder or antisocial personality disorder. Women who were pregnant or lactating or women of childbearing potential who were not using a medically acceptable form of contraception. Concomitant use of psychotropic drugs as well as the introduction or change in intensity of psychotherapeutic interventions. Notes: Ppts had HAM-A baseline score >=18 and Covi Anxiety score >=8. Baseline: HAM-A at baseline. Venlafaxine: 27.1 (4.8) and Placebo: 28.5 (6.4)	Notes: Seen at baseline, days 8, 15, 22, 29, 43 and 57.	**Group 2 N= 22** Placebo - No details provided.	
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
PFIZER2008				

Study Type: RCT Type of Analysis: ITT Blindness: Double blind Duration (days): Mean 28 Setting: No Info Info on Screening Process: 237 screened. 169 randomized. 167 ITT. 115 Completed. 104 Not completed.	n= 169 Age: Mean 36 Range 18-64 Sex: 71 males 98 females Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-IV Exclusions: Pregnant and lactating females. No primary diagnosis of GAD. HAMA <20. Covi Anxiety Scale total score <9. Raskin Depression Scale total score >7.Subjects who had past or current DSM-IV Axis I diagnosis or receiving daily benzodiazepines 3 months prior screening. Baseline: HAMA Placebo 24.0 (4.9) Paroxetine 23.5 (3.3) Lorazepam 24.2 (3.6)	**Data Used** HAMA total score	**Group 1 N= 56** Paroxetine. Mean dose 20mg - Capsules for oral administration. 20mg daily for 28 days **Group 2 N= 56** Lorazepam. Mean dose 4.5mg - Capsules for oral administration. 3mg daily for 3 days increasing to 4.5mg dailty from day 4 to day 28. **Group 3 N= 57** Placebo - Double-blind placebo treatment for 28 days.	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: +.
POLLACK1997 Study Type: RCT Study Description: 1 week placebo run-in. 6 week DB treatment followed by a 18 week maintenance period for treatment responders. Type of Analysis: ITT (LOCF) Blindness: Double blind Duration (days): Mean 42 Setting: Outpatients. USA. Notes: RANDOMISATION: no details provided. Info on Screening Process: No details provided.	n= 464 Age: Mean 39 Sex: 181 males 277 females Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-III-R Exclusions: Current diagnosis of or a history of bipolar illness, organic mental syndromes, schizophrenia or other psychotic disorders, or seizure disorders. Notes: Ppts scored >=20 on HAM-A, and a score >=2 on anxious mood item. Had to score Raskin Depression score <= Covi Anxiety score. HRSD score had to be <20. Baseline: HAM-A at baseline. Abecarnil (high): 25.2. Abecarnil (low): 25.4. Buspirone: 24.4. Placebo: 25.1.	**Data Used** HAMA CGI (Response) Adverse events Leaving the study due to adverse events Leaving the study early for any reason Notes: Assessed after 1 week of washout and then weekly during DB treatment. Then assessed at weeks 8, 10, 12, 16, 20 and 24.	**Group 1 N= 115** Buspirone - Started at 15-45mg/day. Increased in first 2 weeks up to 15mg three times a day by day 15. Kept fixed thereafter. **Group 2 N= 116** Abercarnil - Started at 3-9mg/day. Increased during first 2 weeks up to 3mg three times a day by day 15. Kept fixed after day 15. **Group 3 N= 112** Placebo - No details. **Group 4 N= 115** Abercarnil - Started at 7.5-22.5mg/day. Increased during first 2 weeks to be given maximum of 7.5mg three times a day by day 15. Kept fixed after day 15.	Funding: Sandoz and Schering, Berlin. Quality assessed: +.
POLLACK2001				

Study Type: RCT Blindness: Double blind Duration (days): Mean 56 Setting: outpatient clinics, US and Canada Notes: Randomisation: no further details Info on Screening Process: 331 received baseline assessment, 7 withdrew before start of treatment	n= 324 Age: Mean 40 Sex: 118 males 206 females Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-IV Exclusions: - < 18 years of age - HAM-A <20 - HAM-A items 1 and 2 <2 - diagnosis of any other Axis I disorder - MADRS >17 - substance abuse or dependence - women of child bearing potential not using reliable contraception Baseline: HAM-A: Placebo 24.1(0.30) Paroxetine 24.2(0.30)	**Data Used** 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) Notes: Response was based on CGI score 1 or 2	**Group 1 N= 163** Placebo **Group 2 N= 161** Paroxetine - 10mg/day first week, 20mg/day second week, those who could not tolerate the medication during first two weeks were withdrawn. After 2 weeks could be increased every week by 10mg/day up to 50mg/day.	Funding: GSK. 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: +				
RICKELS2000B Study Type: RCT Study Description: ITT using LOCF for all participants who were randomised and received at least one dose of study medication before evaluation. Type of Analysis: ITT	n= 310 Age: Mean 39 Sex: 118 males 192 females Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-III-R Exclusions: Aged <18 or >65	**Data Used** CGI-I HAMA Adverse events Leaving the study due to inefficacy Leaving the study due to adverse events Leaving the study early for any reason Response (50% reduction in HAMA score)	**Group 1 N= 104** Placebo - All medication was supplied in encapsulated tablets. Week 1, fixed dosage escalation of up to 1 capsules three times daily. Week 2, dosage could increase depending on response within range of 3-7 capsules per day.	Quality assessment score = + Drug company sponsored: Schering AG, Berlin and

Blindness: Double blind Duration (days): Mean 42 Setting: Outpatients, 12 sites in US Notes: RANDOMISATION: procedure not reported Info on Screening Process: Not reported	- no diagnosis of GAD according to DSM-III-R criteria - HAMA <20 after 1 week placebo screenign period or HAMA anxious mood <2 - Raskin Depression score higher than a score on the covi anxiety scale -HAMD >20 - Concomitant medical or psychiatric conditions, a history of seizures - Pregnancy - Participants receiving specified medication in the previous week or receiving neuroleptics, TCAs, MAOIs in previous month prior to study Notes: Study consisted of 6 weeks double-blind treatment followed by an optional maintenace period for a total of 24 weeks. During the maintenance period, participants continued to receive double-blind treatment. Baseline: HAMA: Abecarnil: 24.2, Diazepam: 24.0, Placebo: 24.9	Notes: TAKEN AT: baseline and end of active treatment (6 weeks) DROPOUTS: Abercarnil: 32/102 (34%), Diazepam: 24/104 (23%), Placebo: 29/104 (28%)	**Group 2 N= 102** Abercarnil. Mean dose 12mg/day - All medication was supplied in encapsulated tablets. Active capsules contained 2.5mg. Week 1, fixed dosage escalation of up to 1 capsules three times daily. Week 2, dosage could increase depending on response within range of 3-7 capsules per day. **Group 3 N= 104** Diazepam. Mean dose 22mg - All medication was supplied in encapsulated tablets. Active capsules contained 5.0 mg. Week 1, fixed dosage escalation of up to 1 capsules three times daily. Week 2, dosage could increase depending on response within range of 3-7 capsules per day.	
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 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.	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 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	**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) Notes: Assessments were performed at screening, baseline and at study weeks 1, 2, 3 and 4.	**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. **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.	Funding: Pfizer, Inc. Quality assessed: +.

	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).			
RYNN2008 Study Type: RCT Study Description: ITT included all randomised participants with at least one postbaseline evaluation. Safety analysis included all randomised participants. Type of Analysis: Double Blind Blindness: ITT Duration (days): Mean 70 Setting: Outpatients, Multicentre trail across USA Notes: RANDOMISATION: procedure not reported Info on Screening Process: 515 patients were evaluated, 188 failed to meet the inclusion criteria	n= 327 Age: Mean 42 Sex: 125 males 202 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: Duloxetine 22.6(7.4) Placebo 23.5(7.9)	**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 Leaving the study due to inefficacy Serious Adverse events Sheehan Disability Scale (SDS) Visual Analog Scale (VAS) Adverse events HAMA Discontinuation adverse events (DAEs) Notes: TAKEN AT: Baseline and endpoint DROP OUT: Duolxetine: 75/168 (44.6%), Placebo 50/159 (31.4%)	**Group 1 N= 168** Duloxetine. Mean dose 101.94mg/d - Participants were started with 60mg/d, if there were tolerability concerns this was lowered to 30mg/d. Bt week 2 all patients were required to take a minimum of 60mg/d. Patient doses were progressively titrated if the CGI rating was >=3 up to max of 120mg **Group 2 N= 159** Placebo	Drug compnay funded. Eli Lilly trial 6089. NCT00475969 - trial report collected All participants underwent a single-blind placebo lead-in week, 10 week acute phase and a 2 week discontinuation tapering phase.. Quality Assessment Score = + / ++
Results from this paper:				
SRAMEK1996 Study Type: RCT Study Description: Placebo for 7-10 days. Randomised to receive either buspirone or placebo for 6 weeks. Type of Analysis: LOCF method (completed >2 weeks treatment) Blindness: Double blind Duration (days): Mean 42 Setting: Multicentre: USA. Notes: RANDOMISATION: no details provided. Info on Screening Process: 222 patients entered study: 60 dropped out. 34 didn't meet study inclusion criteria.	n= 162 Age: Mean 38 Sex: 72 males 90 females Diagnosis: 100% Generalised Anxiety Disorder (GAD) by DSM-III-R Exclusions: Pregnant or lactating, DSM-III-R diagnosis of MDD, a concurrent DSM-III-R Axis I disorder, a history of two or more panic attacks within 4 weeks of the beginning of screening, score of 3 or more on the suicide item of the HAM-D scale, used benzodiazepines for 14 days or more in the last 2 months or an investigational drug within the past month, received ECT within the last 3 months or treatment with other psychotropics in the previous month. Clinically significant and/or uncontrolled medical conditions, positive urine drug screen, current or recent history of drug or alcohol abuse. Notes: HAM-A score >=18, score of 2 or 3 on the 'depressed mood' item of the HAM-A scale, scored of >=2 on the 'anxious mood' and 'tension' items on the HAM-A. HAM-D score between 12 and 15. Covi > Raskin.	**Data Used** CGI-I HAMA Adverse events Leaving the study due to adverse events Leaving the study early for any reason Notes: Assessed weekly.	**Group 1 N= 82** Placebo - No details. **Group 2 N= 80** Buspirone - Titrated from an initial dosage of 5mg t.i.d. to 10 mg t.i.d. over first week. Dosage increased by 5mg/day every 2-3 days. After 2 weeks of maintenance at 10mg t.i.d., those who didn't show an improvement were titrated to 15mg t.i.d. over next 7 days.	Funding: Bristol-Myers Squibb Pharmaceutical Research Institute. Quality assessed: +.

	Baseline: HAM-A at baseline. Buspirone: 24.9 (4.2) and Placebo: 25.6 (4.4).			

Characteristics of Excluded Studies

Reference ID	Reason for Exclusion
	no extractable data
ANSSEAU1984	pre-DSM-III-R diagnosis
ANSSEAU1985	pre DSM-III-R diagnosis
BJERRUM1992	DSM-III diagnosis
BLANK2006	no comparator
BOND2002	Combination treatment
BORAL1986	DSM-III diagnosis
BORISON1990	N<10 in each treatment arm
BOYER1993	DSM-III diagnosis
BRAMANTI1990	not double blind
BRESOLIN1988	pre DSM-III-R diagnosis
BRESSA1987	DSM-III diagnosis
BUCHSBAUM1985	DSM-III diagnosis
BUCHSBAUM1987	DSM-III diagnosis
BYSTRITSKY1991	N<10
CASTILLO1988	DSM-III diagnosis
CEPHALON2006A	open label study
CEULEMANS1985	DSM-III diagnosis
COHN1986B	Diagnosis pre-DSM-III-R
CUTLER1993A	Pre DSM-III-R diagnosis
CUTLER1994	DSM-III
ENKELMANN1991	DSM-III diagnosis
FEIGHNER1982	DSM-III diagnosis
FONTAINE1983	pre DSM-III-R diagnosis
FONTAINE1984	DSM-III diagnosis
FONTAINE1986	DSM-III diagnosis
FONTAINE1987	DSM-III diagnosis
FONTAINE1990	DSM-III diagnosis
FONTAINE1993	DSM-III diagnosis
GINSBERG1929	no comparator
HOEHNSARIC1988	DSM-III diagnosis
HOGE2008	open label
JACOBSON1985	DSM-III diagnosis
KIM2006c	Design: open label
KINRYS2002	N <10
KRAGHSORENSEN1990	DSM-III diagnosis
LAPIERRE1982A	DSM-III diagnosis
LAPIERRE1983A	DSM-III diagnosis
LINDSAY1987	pre DSM-III-R diagnosis

MANDOS1995	DSM-III diagnosis
MATHEW2005	open label study
MATHEW2008	open label study
MENDELS1986	DSM-III diagnosis
MENZA2007	open label trial
MOKHBER2010	not double blind
MORTON1992A	DSM-III diagnosis
MURPHY1989	DSM-III diagnosis
NAUKKARINEN2005	not relevant intervention
PANGALILARATU1988	DSM-III diagnosis
PEET1986	DSM-III diagnosis
PETRACCA1990	DSM-III diagnosis
POMARA2005	DSM-III diagnosis
POURMOTABBED1996	one group n<10
POWER1985	pre DSM-III-R diagnosis
POWER1989	pre DSM-III-R diagnosis
POWER1990	DSM-III diagnosis
POWER1990A	DSM-III diagnosis
RAMCHANDRAN1990	DSM-III diagnosis
RAPAPORT2006	open label study
REALINI1990	DSM-III diagnosis
RICKELS1972	pre DSM-III-R diagnosis
RICKELS1993	DSM-III diagnosis
RICKELS1997	DSM-III diagnosis
ROCCA1997	open label study
ROLLAND2002	n < 10 per treatment group
ROSENTHAL2003	open label study
SACCHETTI1994	DSM-III diagnosis
SHAH1990	DSM-III diagnosis
SHAH1991	DSM-III diagnosis
SIMON2006A	no comparator
SPENARD1988	DSM-III diagnosis
SPRATLIN2003	not an RCT
SRAMEK1996A	n <10 per arm
STRAND1990	pre DSM-III-R
TSUKAMOTO2004	open label study
WILCOX1994	one group n<10
WINGERSON1992	not RCT
WURTHMAN2006	not RCT
WURTHMANN2006	no comparator

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Allgulander, C., Dahl A.A., & Austin, C. (2004) Efficacy of sertraline in a 12-week trial for generalized anxiety disorder. American Journal of Psychiatry, 161, 1642-1649.

Dahl, A.A., Ravindran, A., Allgulander, C., Kutcher, S.P., Austin, C., & Burt, T. (2005) Sertraline in generalized anxiety disorder: efficacy in treating the psychic and somatic anxiety factors. Acta Psychiatrica Scandinavica, 111, 429-435.

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ASTRAZENECA2007A (Published Data Only)

AstraZeneca (2007) An international, multi-center, randomized, double-blind, parallel-group, placebo-controlled, active-controlled study of the efficacy and safety of sustained-release quetiapine fumarate (Seroquel SR) in the treatment of Generalized Anxiety Disorder (SILVER Study).

ASTRAZENECA2007B (Published Data Only)

AstraZeneca (2007b) A multicenter, randomized, double-blind, parallel-group, placebo-controlled, active-controlled study of the efficacy and safety of sustained-release quetiapine fumarate (Seroquel) compared with placebo in the treatment of generalized anxiety disorder (Gold Study).

ASTRAZENECA2007C (Published Data Only)

AstraZeneca (2007c) A multi-center, randomized, double-blind, parallel-group, placebo-controlled, study of the efficacy and safety of sustained-release quetiapine fumarate (Seroquel) compared with placebo in the treatment of generalized anxiety disorder (Titanium Study)

ASTRAZENECA2008 (Published Data Only)

Astra Zeneca (2008) A multi-center, double-blind, randomized, parallel-group, placebo-controlled phase III study of the efficacy and safety of quetiapine fumarate extended-release (Seroquel XR) as monotherapy in the treatment of elderly patients with generalized anxiety disorder (CHROMIUM STUDY)

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