The study listed may include approved and non-approved uses, formulations or treatment regimens. The results reported in any single study may not reflect the overall results obtained on studies of a product. Before prescribing any product mentioned in this Register, healthcare professionals should consult prescribing information for the product approved in their country.

Study No.: WXL101497
Title: A Multi-Centre, Randomised, Double-Blind, Parallel-Group, Placebo- and Active-Controlled, Flexible Dose Study Evaluating the Efficacy, Safety and Tolerability of Extended-Release Bupropion Hydrochloride (150mg - 300mg once daily), Extended-Release Venlafaxine Hydrochloride (75mg - 150mg once daily) and Placebo in Subjects with Major Depressive Disorder.
Rationale: The purpose of this study was to evaluate the efficacy, safety and tolerability of extended-release bupropion hydrochloride (bupropion XL), extended-release venlafaxine hydrochloride (venlafaxine XR) and placebo in the treatment of subjects with major depressive disorder (MDD) as defined by the 4th edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV).
Phase: III
Study Period: 27 May 2004 to 14 June 2005
Study Design: Multi-centre, randomised, double-blind, double-dummy, parallel-group, placebo- and active-controlled, flexible dose study. The study, which could last up to a total of 14 weeks, was divided into four Phases: Screening (up to 2 weeks), Treatment (8 weeks), Taper (up to 1 week), and Follow-up (up to 3 weeks).
Centres: 49 centres in Austria (3), Belgium (3), Bulgaria (5), Croatia (2), Estonia (3), Finland (4), Greece (3), Ireland (2), Latvia (3), Netherlands (2), Poland (2), Portugal (3), Russia (3), Slovakia (4), Spain (3), Sweden (4) and Mexico (1).
Indication: Major Depressive Disorder
Treatment: For the first 4 weeks, subjects received dose level (DL) 1 (i.e. bupropion XL 150mg once daily, venlafaxine XR 75mg once daily, or placebo once daily) in a double-blind, double-dummy manner. At Week 4, study medication could be increased to DL 2 (bupropion XL 300mg once daily, venlafaxine XR 150mg once daily or placebo once daily), at the discretion of the investigator. At the end of the Treatment Phase, subjects on DL 2 were tapered for one week. Taper medication consisted of venlafaxine XR at DL 1 for subjects randomised to venlafaxine XR, and placebo for those randomised to bupropion XL or placebo.
Objectives: The primary objective was to evaluate the antidepressant efficacy of extended-release bupropion hydrochloride (150mg - 300mg od), extended-release venlafaxine hydrochloride (75mg - 150mg od) and placebo, in subjects with MDD.
Primary Outcome/Efficacy Variable: The primary endpoint was the change from baseline in the Montgomery-Asberg Depression Rating Scale (MADRS) total score at the Week 8 Last Observation Carried Forward (LOCF) endpoint.
Secondary Outcome/Efficacy Variable(s): Secondary endpoints were: Change from baseline in the MADRS total score at Weeks 1, 2, 4, 5, 6 and 8 Observed Cases (OC). Change from baseline in the MADRS Item 2 score (Reported Sadness) for OC at Weeks 1, 2, 4, 5, 6 and 8 and for Week 8 LOCF. Change from baseline in the MADRS Item 6 score (Concentration Difficulties) for OC at Weeks 1, 2, 4, 5, 6 and 8 and for Week 8 LOCF. Change from baseline in the MADRS Item 7 score (Lassitude) for OC at Weeks 1, 2, 4, 5, 6 and 8 and for Week 8 LOCF. Percentage of MADRS "responders" (subjects with a 50% or greater reduction from baseline in their MADRS total score) at Week 8 OC and LOCF endpoints. Percentage of MADRS “remitters” (subjects with a MADRS total score ≤ 11) at Week 8 OC and LOCF endpoints. Percentage of subjects with a Clinical Global Impression - Global Improvement (CGI-I) score of 1 ("very much improved") or 2 ("much improved") at Weeks 1, 2, 4, 6 and 8 OC and at Week 8 LOCF endpoint. Change from baseline in the CGI-S score at Weeks 1, 2, 4, 6 and 8 OC and at Week 8 LOCF endpoints. Change from baseline in the Hamilton Anxiety Rating Scale (HAMA) total score for OC at Weeks 1, 2, 4, 5, 6 and 8 and for Week 8 LOCF.
Health Outcome Variable(s): Change from baseline in the Sheehan Disability Scale (SDS) total score at Week 8 OC and LOCF endpoints. Change from baseline in the SDS work, family and social item scores at Week 8 OC and LOCF endpoints. Change from baseline in the Short Form Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q-SF) at Week 8 OC and LOCF endpoints. Change from baseline in the 18-item Motivation and Energy Inventory (MEI) total score at Week 8 OC and LOCF endpoints. Summary of subject satisfaction with study medication. Change from baseline in the subject-completed Change in Sexual Functioning Questionnaire (CSFQ) total score and sub-scores for pleasure, desire, arousal, and orgasm at Week 8 OC and LOCF endpoints.
Statistical Methods: The primary hypotheses of interest were tested sequentially, for inferential purposes, using the closed testing approach. First, the mean change from baseline in MADRS total score at Week 8 was compared between bupropion XL and placebo at the nominal 0.05 level of significance. If this null hypothesis was rejected then the mean change from baseline in MADRS total score at Week 8 was compared between bupropion XL and

venlafaxine XR (by confidence intervals (CIs)), and between placebo and venlafaxine XR. Both comparisons were conducted at the nominal 0.05 level of significance and did not require adjustment since the overall type I error was controlled by the closed testing principle. All three pair-wise comparisons were reported for descriptive purposes, regardless of their statistical significance. In this regard, if the test for bupropion XL versus placebo failed to show significance, the extent to which the placebo versus venlafaxine XR comparison also failed to have a p value below 0.05 was of interest for understanding the assay sensitivity of the study to detect the difference between effective treatment and placebo.

Analysis of covariance (ANCOVA) with baseline MADRS total score and centre as covariates was used to perform the between-treatment-group pair-wise comparisons. For the comparison between bupropion XL and venlafaxine XR, a 95% CI for the mean difference was constructed.

The secondary comparisons were performed pair-wise, between bupropion XL and placebo, and between venlafaxine XR and placebo. Continuous efficacy and health outcome measures were examined via ANCOVA with baseline value and centre as the covariates; categorical efficacy measures were examined via non-parametric analysis of covariance adjusting for the centre effect.

A sample of 173 subjects per treatment arm (total N=519) would provide a power of 90% to detect a difference of 3.5 units in the mean change from baseline MADRS total score at Week 8 using an estimate of the standard deviation of 10.0, at a two-sided significance level of 0.05. This sample size was computed using a two-sample t-test. Assuming a dropout rate of 5%, 182 subjects were to be randomised per treatment group (total N=546).

The safety population consisted of all subjects who were randomised and received at least one dose of study medication. The intent-to-treat (ITT) population consisted of all subjects in the safety population with baseline and at least one post-baseline assessment of MADRS total score.

Study Population: Male or female outpatients aged between 18 and 64 years (inclusive) who had: a diagnosis of MDD, as defined by DSM-IV (296.2/296.3); an interactive voice response system 17-Item Hamilton Depression Rating Scale (IVRS HAMD-17) total score of ≥18, at both the Screening Visit and the Baseline Visit, and no increase or decrease in the IVRS HAMD-17 total score of more than 25% between Screening and Baseline, irrespective of the actual IVRS HAMD-17 score; and a Clinical Global Impression Severity of Illness (CGI-S) score of ≥4 at both the Screening Visit and the Baseline Visit.

Number of Subjects:	**Placebo**	**Bupropion XL**	**Venlafaxine XR**
Planned, N	182	182	182
Randomised, N	199	188	189
Randomised and treated, N	197	187	187
Completed Treatment Phase, n (%)	167 (85)	154 (82)	164 (88)
Number Subjects Withdrawn from Treatment Phase, n (%)	30 (15)	33 (18)	23 (12)
due to Adverse events, n (%)	10 (5)	7 (4)	7 (4)
due to lack of efficacy, n (%)	7 (4)	9 (5)	3 (2)
due to other reasons, n (%)	13 (7)	17 (9)	13 (7)
Completed study, n (%)	163 (83)	154 (83)	161 (86)
Number Subjects Withdrawn after Treatment Phase, n (%)	4 (2)	0	3 (2)
due to other reasons, n (%)	4 (2)	0	3 (2)
Demographics: (Safety Population)	**Placebo**	**Bupropion XL**	**Venlafaxine XR**
N	197	187	187
Females: Males	142: 55	138: 49	128: 59
Mean Age, years (SD)	41.8 (11.56)	41.8 (11.68)	42.7 (11.48)
White, n (%)	189 (96)	180 (96)	182 (97)
Primary Efficacy Results: (ITT Population)			
LOCF MADRS Total Score at Week 8	**Placebo**	**Bupropion XL**	**Venlafaxine XR**
N	197	187	185
Baseline mean (SE)	30.4 (0.34)	30.4 (0.33)	30.0 (0.34)
Change from baseline: LS Mean (SE)	-13.5 (0.65)	-16.0 (0.66)	-17.1 (0.68)
Difference from placebo: LS Mean (95% CI)	-	-2.5 (-4.2, -0.7)	-3.6 (-5.4, -1.8)
p-value	-	0.006	<0.001
Difference from venlafaxine XR: LS mean (95% CI)	-	1.1 (-0.7, 2.9)	-
Secondary Efficacy Variable(s): (ITT Population)	**Placebo**	**Bupropion XL**	**Venlafaxine XR**
N	197	187	185
OC MADRS Total Score			
Week 1 Change from baseline: LS Mean (SE)	-3.5 (0.32)	-2.6 (0.33)	-3.4 (0.34)

	Difference from placebo:	LS Mean (95% CI)	-	0.9 (0.1, 1.8)	0.1 (-0.7, 1.0)
Week 2	Change from baseline:	LS Mean (SE)	-6.2 (0.41)	-6.4 (0.42)	-7.1 (0.43)
	Difference from placebo:	LS Mean (95% CI)	-	-0.3 (-1.4, 0.8)	-0.9 (-2.0, 0.2)
Week 4	Change from baseline:	LS Mean (SE)	-9.9 (0.54)	-11.1 (0.55)	-11.1 (0.55)
	Difference from placebo:	LS Mean (95% CI)	-	-1.1 (-2.6, 0.3)	-1.2 (-2.7, 0.2)
Week 5	Change from baseline:	LS Mean (SE)	-11.8 (0.58)	-13.7 (0.59)	-14.2 (0.58)
	Difference from placebo:	LS Mean (95% CI)	-	-1.9 (-3.5, -0.4)	-2.5 (-4.0, -0.9)
Week 6	Change from baseline:	LS Mean (SE)	-14.1 (0.60)	-15.6 (0.62)	-16.2 (0.61)
	Difference from placebo:	LS Mean (95% CI)	-	-1.5 (-3.1, 0.1)	-2.1 (-3.7, -0.5)
Week 8	Change from baseline:	LS Mean (SE)	-15.8 (0.60)	-18.2 (0.63)	-18.5 (0.61)
	Difference from placebo:	LS Mean (95% CI)	-	-2.4 (-4.1, -0.8)	-2.7 (-4.3, -1.1)
MADRS Item 2 Score (Reported Sadness)			**Placebo**	**Bupropion XL**	**Venlafaxine XR**
Baseline	Mean (SD)		3.9 (0.71)	3.9 (0.63)	3.8 (0.69)
Week 1 OC	Change from baseline:	LS Mean (SE)	-0.5 (0.06)	-0.4 (0.06)	-0.5 (0.06)
	Difference from placebo:	LS Mean (95% CI)	-	0.1 (-0.1, 0.2)	0 (-0.1, 0.2)
Week 2 OC	Change from baseline:	LS Mean (SE)	-0.9 (0.07)	-0.9 (0.07)	-1.0 (0.07)
	Difference from placebo:	LS Mean (95% CI)	-	0 (-0.2, 0.1)	-0.2 (-0.3, 0)
Week 4 OC	Change from baseline:	LS Mean (SE)	-1.3 (0.09)	-1.4 (0.09)	-1.5 (0.09)
	Difference from placebo:	LS Mean (95% CI)	-	-0.1 (-0.4, 0.1)	-0.2 (-0.4, 0)
Week 5 OC	Change from baseline:	LS Mean (SE)	-1.6 (0.09)	-1.8 (0.09)	-1.9 (0.09)
	Difference from placebo:	LS Mean (95% CI)	-	-0.2 (-0.4, 0.1)	-0.3 (-0.6, -0.1)
Week 6 OC	Change from baseline:	LS Mean (SE)	-1.9 (0.09)	-2.0 (0.10)	-2.2 (0.09)
	Difference from placebo:	LS Mean (95% CI)	-	-0.1 (-0.4, 0.1)	-0.3 (-0.5, 0)
Week 8 OC	Change from baseline:	LS Mean (SE)	-2.0 (0.09)	-2.5 (0.09)	-2.5 (0.09)
	Difference from placebo:	LS Mean (95% CI)	-	-0.5 (-0.7, -0.2)	-0.5 (-0.7, -0.2)
Week 8 LOCF	Change from baseline:	LS Mean (SE)	-1.7 (0.10)	-2.2 (0.10)	-2.3 (0.10)
	Difference from placebo:	LS Mean (95% CI)	-	-0.5 (-0.7, -0.2)	-0.6 (-0.8, -0.3)
MADRS Item 6 Score (Concentration Difficulties)			**Placebo**	**Bupropion XL**	**Venlafaxine XR**
Baseline	Mean (SD)		3.2 (0.85)	3.4 (0.81)	3.4 (0.86)
Week 1 OC	Change from baseline:	LS Mean (SE)	-0.3 (0.05)	-0.3 (0.05)	-0.4 (0.06)
	Difference from placebo:	LS Mean (95% CI)	-	0 (-0.1, 0.2)	-0.1 (-0.2, 0.1)
Week 2 OC	Change from baseline:	LS Mean (SE)	-0.5 (0.06)	-0.7 (0.06)	-0.7 (0.07)
	Difference from placebo:	LS Mean (95% CI)	-	-0.1 (-0.3, 0)	-0.2 (-0.3, 0)
Week 4 OC	Change from baseline:	LS Mean (SE)	-0.9 (0.08)	-1.1 (0.08)	-1.1 (0.08)
	Difference from placebo:	LS Mean (95% CI)	-	-0.2 (-0.4, 0)	-0.2 (-0.4, 0)
Week 5 OC	Change from baseline:	LS Mean (SE)	-1.2 (0.08)	-1.4 (0.08)	-1.5 (0.08)
	Difference from placebo:	LS Mean (95% CI)	-	-0.2 (-0.5, 0)	-0.3 (-0.5, -0.1)
Week 6 OC	Change from baseline:	LS Mean (SE)	-1.5 (0.08)	-1.7 (0.09)	-1.7 (0.08)
	Difference from placebo:	LS Mean (95%	-	-0.2 (-0.4, 0.1)	-0.2 (-0.4, 0)

	CI)				
Week 8 OC	Change from baseline:	LS Mean (SE)	-1.7 (0.08)	-2.0 (0.08)	-2.0 (0.08)
	Difference from placebo:	LS Mean (95% CI)	-	-0.3 (-0.5, -0.1)	-0.3 (-0.5, -0.1)
Week 8 LOCF	Change from baseline:	LS Mean (SE)	-1.4 (0.08)	-1.8 (0.08)	-1.9 (0.08)
	Difference from placebo:	LS Mean (95% CI)	-	-0.3 (-0.5, -0.1)	-0.4 (-0.7, -0.2)
MADRS Item 7 Score (Lassitude)			**Placebo**	**Bupropion XL**	**Venlafaxine XR**
Baseline	Mean (SD)		3.5 (0.81)	3.5 (0.80)	3.4 (0.83)
Week 1 OC	Change from baseline:	LS Mean (SE)	-0.4 (0.06)	-0.3 (0.06)	-0.4 (0.06)
	Difference from placebo:	LS Mean (95% CI)	-	0.1 (0, 0.3)	0.1 (-0.1, 0.2)
Week 2 OC	Change from baseline:	LS Mean (SE)	-0.7 (0.07)	-0.7 (0.07)	-0.7 (0.07)
	Difference from placebo:	LS Mean (95% CI)	-	0 (-0.2, 0.1)	0 (-0.2, 0.2)
Week 4 OC	Change from baseline:	LS Mean (SE)	-1.1 (0.08)	-1.3 (0.08)	-1.2 (0.08)
	Difference from placebo:	LS Mean (95% CI)	-	-0.2 (-0.4, 0)	-0.1 (-0.4, 0.1)
Week 5 OC	Change from baseline:	LS Mean (SE)	-1.3 (0.08)	-1.6 (0.08)	-1.6 (0.08)
	Difference from placebo:	LS Mean (95% CI)	-	-0.2 (-0.4, 0)	-0.3 (-0.5, -0.1)
Week 6 OC	Change from baseline:	LS Mean (SE)	-1.6 (0.08)	-1.7 (0.09)	-1.8 (0.09)
	Difference from placebo:	LS Mean (95% CI)	-	-0.2 (-0.4, 0.1)	-0.2 (-0.4, 0)
Week 8 OC	Change from baseline:	LS Mean (SE)	-1.8 (0.09)	-1.9 (0.09)	-2.0 (0.09)
	Difference from placebo:	LS Mean (95% CI)	-	-0.1 (-0.4, 0.1)	-0.2 (-0.5, 0)
Week 8 LOCF	Change from baseline:	LS Mean (SE)	-1.5 (0.09)	-1.7 (0.09)	-1.8 (0.09)
	Difference from placebo:	LS Mean (95% CI)	-	-0.2 (-0.4, 0.1)	-0.3 (-0.6, -0.1)
MADRS Responders and Remitters at Week 8			**Placebo**	**Bupropion XL**	**Venlafaxine XR**
Percentage of OC Responders (%)			53	65	70
Percentage of LOCF Responders (%)			46	57	65
Percentage of OC Remitters (%)			38	53	56
Percentage of LOCF Remitters (%)			32	47	51
CGI-I Responders			**Placebo**	**Bupropion XL**	**Venlafaxine XR**
Week 1 OC	Percentage of Responders (%)		6	6	6
Week 2 OC	Percentage of Responders (%)		17	22	25
Week 4 OC	Percentage of Responders (%)		37	48	47
Week 6 OC	Percentage of Responders (%)		60	67	68
Week 8 OC	Percentage of Responders (%)		61	79	70
Week 8 LOCF	Percentage of Responders (%)		53	68	65
CGI-S Score			**Placebo**	**Bupropion XL**	**Venlafaxine XR**
Baseline	Mean (SD)		4.7 (0.63)	4.7 (0.68)	4.7 (0.68)
Week 1 OC	Change from baseline:	LS Mean (SE)	-0.3 (0.04)	-0.2 (0.04)	-0.2 (0.04)
	Difference from placebo:	LS Mean (95% CI)	-	0.1 (0, 0.2)	0 (-0.1, 0.1)
Week 2 OC	Change from baseline:	LS Mean (SE)	-0.6 (0.06)	-0.5 (0.06)	-0.6 (0.06)
	Difference from placebo:	LS Mean (95% CI)	-	0 (-0.1, 0.2)	0 (-0.2, 0.1)
Week 4 OC	Change from baseline:	LS Mean (SE)	-1.0 (0.08)	-1.1 (0.08)	-1.1 (0.08)
	Difference from placebo:	LS Mean (95% CI)	-	-0.1 (-0.3, 0.1)	-0.1 (-0.4, 0.1)
Week 6 OC	Change from baseline:	LS Mean (SE)	-1.5 (0.09)	-1.8 (0.09)	-1.8 (0.09)
	Difference from placebo:	LS Mean (95% CI)	-	-0.3 (-0.5, 0)	-0.3 (-0.5, -0.1)

Week 8 OC	Change from baseline:	LS Mean (SE)	-1.8 (0.09)	-2.2 (0.09)	-2.3 (0.09)
	Difference from placebo:	LS Mean (95% CI)	-	-0.4 (-0.7, -0.2)	-0.4 (-0.7, -0.2)
Week 8 LOCF	Change from baseline:	LS Mean (SE)	-1.5 (0.10)	-1.9 (0.10)	-2.1 (0.10)
	Difference from placebo:	LS Mean (95% CI)	-	-0.4 (-0.7, -0.1)	-0.5 (-0.8, -0.3)
HAMA Total Score			**Placebo**	**Bupropion XL**	**Venlafaxine XR**
Baseline	Mean (SD)		21.8 (6.70)	22.0 (6.49)	22.6 (6.06)
Week 1 OC	Change from baseline:	LS Mean (SE)	-2.5 (0.31)	-2.1 (0.32)	-2.9 (0.33)
	Difference from placebo:	LS Mean (95% CI)	-	0.4 (-0.4, 1.3)	-0.4, (-1.3, 0.4)
Week 2 OC	Change from baseline:	LS Mean (SE)	-4.0 (0.39)	-4.7 (0.40)	-5.4 (0.41)
	Difference from placebo:	LS Mean (95% CI)	-	-0.7 (-1.8, 0.3)	-1.4 (-2.4, -0.3)
Week 4 OC	Change from baseline:	LS Mean (SE)	-7.4 (0.45)	-8.3 (0.47)	-8.1 (0.47)
	Difference from placebo:	LS Mean (95% CI)	-	-0.9 (-2.1, 0.3)	-0.7 (-1.9, 0.5)
Week 5 OC	Change from baseline:	LS Mean (SE)	-8.7 (0.48)	-10.2 (0.50)	-10.2 (-1.5)
	Difference from placebo:	LS Mean (95% CI)	-	-1.5 (-2.7, -0.2)	-1.5 (-2.7, -0.2)
Week 6 OC	Change from baseline:	LS Mean (SE)	-10.4 (0.47)	-11.7 (0.50)	-11.6 (0.49)
	Difference from placebo:	LS Mean (95% CI)	-	-1.3 (-2.6, 0)	-1.2 (-2.4, 0)
Week 8 OC	Change from baseline:	LS Mean (SE)	-11.6 (0.49)	-13.7 (0.52)	-13.1 (0.51)
	Difference from placebo:	LS Mean (95% CI)	-	-2.1 (-3.4, -0.8)	-1.5 (-2.8, -0.2)
Week 8 LOCF	Change from baseline:	LS Mean (SE)	-9.8 (0.54)	-11.5 (0.56)	-12.3 (0.58)
	Difference from placebo:	LS Mean (95% CI)	-	-1.7 (-3.2, -0.3)	-2.5 (-4.0, -1.1)
Health Outcome Variable(s): (ITT Population)			**Placebo**	**Bupropion XL**	**Venlafaxine XR**
N			197	187	185
SDS Score at Week 8					
Total Score	Baseline mean (SD)		20.0 (4.80)	20.4 (4.64)	20.0 (5.30)
OC	Change from baseline:	LS Mean (SE)	-7.0 (0.54)	-8.9 (0.56)	-9.5 (0.55)
	Difference from placebo:	LS Mean (95% CI)	-	-1.9 (-3.4, -0.5)	-2.5 (-3.9, -1.1)
LOCF	Change from baseline:	LS Mean (SE)	-6.2 (0.53)	-8.4 (0.54)	-9.0 (-2.7)
	Difference from placebo:	LS Mean (95% CI)	-	-2.2 (-3.6, -0.7)	-2.7 (-4.1, -1.3)
Work Score	Baseline mean (SD)		6.7 (2.02)	6.8 (1.93)	6.7 (2.08)
OC	Change from baseline:	LS Mean (SE)	-2.6 (0.18)	-3.0 (0.19)	-3.3 (0.19)
	Difference from placebo:	LS Mean (95% CI)	-	-0.5 (-1.0, 0)	-0.7 (-1.2, -0.2)
LOCF	Change from baseline:	LS Mean (SE)	-2.3 (0.19)	-2.8 (0.19)	-3.0 (0.19)
	Difference from placebo:	LS Mean (95% CI)	-	-0.6 (-1.1, -0.1)	-0.8 (-1.2, -0.3)
Social Score	Baseline mean (SD)		6.8 (1.77)	7.0 (1.89)	6.7 (1.99)
OC	Change from baseline:	LS Mean (SE)	-2.3 (0.20)	-2.9 (0.21)	-3.1 (0.20)
	Difference from placebo:	LS Mean (95% CI)	-	-0.6 (-1.1, -0.1)	-0.7 (-1.3, -0.2)
LOCF	Change from baseline:	LS Mean (SE)	-2.1 (0.20)	-2.8 (0.20)	-2.9 (0.20)
	Difference from placebo:	LS Mean (95% CI)	-	-0.7 (-1.2, -0.2)	-0.9 (-1.4, -0.3)
Family Score	Baseline mean (SD)		6.5 (1.85)	6.6 (1.80)	6.6 (2.06)
OC	Change from baseline:	LS Mean (SE)	-2.1 (0.19)	-2.9 (0.20)	-3.1 (0.20)
	Difference from placebo:	LS Mean (95%	-	-0.8 (-1.3, -0.2)	-1.0 (-1.5, -0.5)

	CI)			
LOCF	Change from baseline: LS Mean (SE)	-1.9 (0.19)	-2.7 (0.19)	-3.0 (0.19)
	Difference from placebo: LS Mean (95% CI)	-	-0.9 (-1.4, -0.4)	-1.1 (-1.6, -0.6)
Q-LES-Q-SF Score at Week 8		**Placebo**	**Bupropion XL**	**Venlafaxine XR**
General Activities	Baseline mean (SD)	32.6 (12.06)	33.1 (11.40)	35.3 (12.19)
OC	Change from baseline: LS Mean (SE)	17.3 (1.32)	22.6 (1.35)	21.7 (1.35)
	Difference from placebo: LS Mean (95% CI)	-	5.4 (1.9, 8.9)	4.5 (1.0, 8.0)
LOCF	Change from baseline: LS Mean (SE)	16.1 (1.26)	21.9 (1.31)	21.1 (1.31)
	Difference from placebo: LS Mean (95% CI)	-	5.8 (2.4, 9.2)	5.0 (1.6, 8.4)
Satisfaction with Medication	Baseline mean (SD)	2.7 (0.88)	2.7 (0.92)	2.8 (0.89)
OC	Change from baseline: LS Mean (SE)	0.8 (0.17)	0.6 (0.15)	0.6 (0.17)
	Difference from placebo: LS Mean (95% CI)	-	-0.2 (-0.6, 0.3)	-0.2 (-0.6, 0.3)
LOCF	Change from baseline: LS Mean (SE)	0.8 (0.18)	0.6 (0.15)	0.6 (0.17)
	Difference from placebo: LS Mean (95% CI)	-	-0.2 (-0.6, 0.2)	-0.2 (-0.6, 0.2)
Life Satisfaction & Contentment	Baseline mean (SD)	2.0 (0.66)	2.0 (0.68)	2.0 (0.75)
OC	Change from baseline: LS Mean (SE)	1.0 (0.07)	1.3 (0.07)	1.3 (0.07)
	Difference from placebo: LS Mean (95% CI)	-	0.3 (0.1, 0.5)	0.3 (0.1, 0.5)
LOCF	Change from baseline: LS Mean (SE)	0.9 (0.07)	1.3 (0.07)	1.2 (0.07)
	Difference from placebo: LS Mean (95% CI)	-	0.4 (0.2, 0.6)	0.3 (0.2, 0.5)
MEI Total Score at Week 8		**Placebo**	**Bupropion XL**	**Venlafaxine XR**
Baseline	Mean (SD)	26.4 (12.79)	26.8 (12.95)	27.1 (13.65)
OC	Change from baseline: LS Mean (SE)	18.5 (1.44)	25.8 (1.47)	27.0 (1.46)
	Difference from placebo: LS Mean (95% CI)	-	7.3 (3.5, 11.1)	8.5 (4.6, 12.3)
LOCF	Change from baseline: LS Mean (SE)	17.4 (1.38)	24.6 (1.44)	25.9 (1.43)
	Difference from placebo: LS Mean (95% CI)	-	7.2 (3.5, 11.0)	8.5 (4.8, 12.2)
Subject Satisfaction with Study Medication at Week 8		**Placebo**	**Bupropion XL**	**Venlafaxine XR**
OC	LS Mean (SE)	4.8 (0.12)	5.3 (0.13)	5.4 (0.13)
	Difference from placebo: LS Mean (95% CI)	-	0.5 (0.2, 0.9)	0.6 (0.3, 1.0)
LOCF	LS Mean (SE)	4.4 (0.13)	4.9 (0.13)	5.2 (0.13)
	Difference from placebo: LS Mean (95% CI)	-	0.5 (0.1, 0.8)	0.8 (0.4, 1.1)
CSFQ Scores at Week 8		**Placebo**	**Bupropion XL**	**Venlafaxine XR**
Total	Baseline mean (SD)	35.9 (9.00)	35.2 (9.18)	35.8 (9.39)
OC	Change from baseline: LS Mean (SE)	5.3 (0.65)	6.3 (0.66)	5.6 (0.63)
	Difference from placebo: LS Mean (95% CI)	-	1.0 (-0.6, 2.6)	0.3 (-1.3, 1.9)
LOCF	Change from baseline: LS Mean (SE)	5.1 (0.61)	6.0 (0.62)	5.2 (0.60)
	Difference from placebo: LS Mean (95% CI)	-	1.0 (-0.5, 2.5)	0.1 (-1.4, 1.6)
Desire / frequency	Baseline mean (SD)	4.3 (1.59)	4.2 (1.65)	4.3 (1.65)
OC	Change from baseline: LS Mean (SE)	1.0 (0.12)	1.0 (0.12)	1.0 (0.12)
	Difference from placebo: LS Mean (95% CI)	-	0.1 (-0.2, 0.4)	0.1 (-0.2, 0.4)
LOCF	Change from baseline: LS Mean (SE)	0.9 (0.12)	1.0 (0.12)	1.0 (0.11)
	Difference from placebo: LS Mean (95% CI)	-	0.1 (-0.2, 0.4)	0.1 (-0.2, 0.4)

Desire / interest	Baseline mean (SD)		5.8 (2.34)	5.6 (2.15)	5.9 (2.39)
OC	Change from baseline:	LS Mean (SE)	1.2 (0.18)	1.7 (0.18)	1.4 (0.18)
	Difference from placebo:	LS Mean (95% CI)	-	0.5 (0.1, 1.0)	0.2 (-0.2, 0.6)
LOCF	Change from baseline:	LS Mean (SE)	1.1 (0.17)	1.6 (0.17)	1.3 (0.17)
	Difference from placebo:	LS Mean (95% CI)	-	0.5 (0.1, 0.9)	0.2 (-0.2, 0.7)
Arousal	Baseline mean (SD)		7.6 (2.70)	7.3 (2.81)	7.5 (2.93)
OC	Change from baseline:	LS Mean (SE)	1.3 (0.19)	1.5 (0.19)	1.3 (0.18)
	Difference from placebo:	LS Mean (95% CI)	-	0.2 (-0.2, 0.7)	0 (-0.4, 0.5)
LOCF	Change from baseline:	LS Mean (SE)	1.2 (0.18)	1.5 (0.18)	1.3 (0.18)
	Difference from placebo:	LS Mean (95% CI)	-	0.3 (-0.2, 0.7)	0 (-0.4, 0.5)
Orgasm	Baseline mean (SD)		7.8 (2.91)	7.6 (3.13)	7.7 (3.00)
OC	Change from baseline:	LS Mean (SE)	1.2 (0.20)	1.3 (0.20)	1.1 (0.19)
	Difference from placebo:	LS Mean (95% CI)	-	0.1 (-0.4, 0.6)	-0.1 (-0.5, 0.4)
LOCF	Change from baseline:	LS Mean (SE)	1.1 (0.19)	1.2 (0.19)	1.0 (0.18)
	Difference from placebo:	LS Mean (95% CI)	-	0.1 (-0.4, 0.6)	-0.2 (-0.6, 0.3)
Pleasure	Baseline mean (SD)		1.8 (0.87)	1.8 (0.89)	1.7 (0.87)
OC	Change from baseline:	LS Mean (SE)	0.8 (0.08)	0.9 (0.08)	0.8 (0.08)
	Difference from placebo:	LS Mean (95% CI)	-	0.1 (-0.1, 0.3)	0 (-0.2, 0.2)
LOCF	Change from baseline:	LS Mean (SE)	0.7 (0.08)	0.8 (0.08)	0.7 (0.08)
	Difference from placebo:	LS Mean (95% CI)	-	0.1 (-0.1, 0.3)	0 (-0.2, 0.2)

Safety Results: (Safety Population) On-therapy AEs and SAEs were defined as having an onset date between the first dose of study medication and the last dose of study medication at the end of the Treatment Phase.

Most Frequent Adverse Events – On-Therapy	**Placebo N=197**	**Bupropion XL N=187**	**Venlafaxine XR N=187**
Subjects with any AE(s), n (%)	95 (48)	88 (47)	93 (50)
Headache	19 (10)	23 (12)	25 (13)
Dry mouth	11 (6)	16 (9)	13 (7)
Nausea	21 (11)	11 (6)	36 (19)
Insomnia	4 (2)	10 (5)	7 (4)
Hyperhidrosis	7 (4)	7 (4)	15 (8)
Dizziness	14 (7)	7 (4)	9 (5)
Constipation	1 (<1)	7 (4)	5 (3)
Nasopharyngitis	5 (3)	7 (4)	2 (1)
Abdominal pain, upper	6 (3)	6 (3)	5 (3)
Fatigue	4 (2)	5 (3)	9 (5)
Anxiety	9 (5)	5 (3)	6 (3)
Diarrhoea	5 (3)	3 (2)	3 (2)
Somnolence	4 (2)	2 (1)	8 (4)
Anorexia	0	2 (1)	6 (3)
Influenza	5 (3)	0	3 (2)
Serious Adverse Events - On-Therapy n (%) [n considered by the investigator to be related to study medication]	**Placebo N=197**	**Bupropion XL N=187**	**Venlafaxine XR N=187**
Subjects with non-fatal SAE(s)	4 (2) [3]	1 (<1) [0]	1 (<1) [0]
Convulsion	1 (<1) [1]	0	0
Major depression	2 (1) [1]	0	0
Syncope	1 (<1) [1]	0	0
Overdose	0	1 (<1) [0]	0

Suicide attempt	0	0	1 (<1) [0]
Subjects with fatal SAE(s)	0	0	0

Conclusion: This study showed a statistical difference between bupropion XL and placebo for the primary efficacy variables; bupropion XL and venlafaxine XR were not statistically different. In the placebo group 95 subjects reported non-serious AEs, with the most frequently reported being nausea and headache. In the bupropion XL group 88 subjects reported non-serious AEs, with the most frequently reported being headache and dry mouth. In the venlafaxine XR group 93 subjects reported non-serious AEs with the most frequently reported being nausea and headache. Four non-fatal SAEs were reported in the placebo group, comprising major depression (two reports), convulsion and syncope. One non-fatal SAE, overdose, was reported in the bupropion XL group. One non-fatal SAE, suicide attempt, was reported in the venlafaxine XR group. There were no fatalities in any group during the study.

Publications:
No publication

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