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.: AK130940
Title: A Multi-Centre, Randomised, Double-Blind, Parallel-Group, Placebo-Controlled, Flexible Dose Study to Evaluate the Efficacy, Safety and Tolerability of Extended-release Bupropion Hydrochloride (150mg-300mg once daily) in Elderly 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) compared with placebo in the treatment of elderly 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: 2 June 2004 to 21 September 2005
Study Design: Multi-centre, randomised, double-blind, parallel group, flexible-dose study. The study, which could last up to a total of 15 weeks, was divided into three Phases: Screening (up to 2 weeks), Treatment (10 weeks) and Follow-up (up to 3 weeks).
Centres: There were 85 centres: Australia (6), Belgium (2), Canada (4), Croatia (2), Finland (5), France (9), Germany (16), India (3), Latvia (3), Netherlands (4), Norway (2), Poland (2), Republic of South Africa (5), Russia (3) and United States (19).
Indication: Major Depressive Disorder
Treatment: For the first 4 weeks, subjects received study medication at Dose Level 1 (150mg bupropion XL or placebo tablets once daily) in a double-blind manner. At Week 4, the dose level of study medication could be increased to Dose Level 2 (300mg bupropion XL or placebo once daily) at the discretion of the investigator. From Week 4 to Week 10, subjects received study medication at either Dose Level 1 or Dose Level 2 in a double-blind manner.
Objectives: The primary objective was to evaluate the antidepressant efficacy of extended-release bupropion hydrochloride (150mg-300mg once daily) compared with placebo in elderly subjects (aged ≥65 years of age) 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 Week 10 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, 8, and 10, Observed Cases (OC). Change from baseline in the MADRS Item 2 score (Reported Sadness) for OC at Weeks 1, 2, 4, 5, 6, 8, and 10, and for Week 10 LOCF endpoint. Change from baseline in the MADRS Item 6 score (Concentration Difficulties) for OC at Weeks 1, 2, 4, 5, 6, 8, and 10, and for Week 10 LOCF endpoint. Change from baseline in the MADRS Item 7 score (Lassitude) for OC at Weeks 1, 2, 4, 5, 6, 8, and 10, and for Week 10 LOCF endpoint. Percentage of MADRS "responders" (subjects with a 50% or greater reduction from baseline in their total MADRS score) at Week 10 OC and LOCF endpoints. Percentage of MADRS "remitters" (subjects with a MADRS total score ≤11) at Week 10 OC and LOCF endpoints. Percentage of subjects with a Clinical Global Impression - Improvement (CGI-I) score of 1 ('very much improved') or 2 ('much improved') for OC at Weeks 1, 2, 4, 5, 6, 8, and 10, and at Week 10 LOCF endpoint. Change from baseline in the Clinical Global Impression - Severity of Illness (CGI-S) score for OC at Weeks 1, 2, 4, 5, 6, 8, and 10, and at Week 10 LOCF endpoint. Change from baseline in the Hamilton Anxiety Rating Scale (HAMA) total score for OC at Weeks 1, 2, 4, 5, 6, 8 and 10 and for Week 10 LOCF endpoint.
Health Outcome Variable(s): Change from baseline in the Sheehan Disability Scale (SDS) total score at Week 10 OC and Week 10 LOCF endpoints. Change from baseline in the SDS work item score at Week 10 OC and Week 10 LOCF endpoints. Change from baseline in the SDS family item score at Week 10 OC and Week 10 LOCF endpoints. Change from baseline in the SDS social item score at Week 10 OC and Week 10 LOCF endpoints. Change from baseline in the Short Form Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q-SF) at Week 10 OC and Week 10 LOCF endpoints. Change from baseline in the 18-item Motivation and Energy Inventory (MEI) total score at Week 10 OC and LOCF endpoints. Summary of subject satisfaction with study medication.
Statistical Methods: For the primary hypotheses of interest, the mean change from baseline in MADRS total score at Week 10 was compared using the analysis of covariance (ANCOVA) with baseline MADRS total score and centre as covariates. The protocol specified analysis was found to be unsuitable because the usual ANCOVA assumptions were not met and outliers were found to have an effect on the results. Therefore, additional more appropriate statistical methods were also used to compare the treatment groups for the primary endpoint (non-parametric rank analysis of

covariance and parametric robust regression analysis).
The secondary comparisons were performed pair-wise between bupropion XL 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.
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 ≥65 years 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 a CGI-S score of ≥4 at both the Screening Visit and the Baseline Visit.

Number of Subjects:			**Placebo**	**Bupropion XL**
Number of Subjects:				
Planned, N			182	182
Randomised, N			208	212
Randomised and treated, N			207	211
Completed Treatment Phase, n (%)			161 (78)	163 (77)
Number Subjects Withdrawn from Treatment Phase, n (%)			46 (22)	48 (23)
due to Adverse events, n (%)			22 (11)	17 (8)
due to lack of efficacy, n (%)			9 (4)	10 (5)
due to other reasons, n (%)			15 (7)	21 (10)
Completed study, n (%)			160 (77)	161 (76)
Number Subjects Withdrawn after Treatment Phase, n (%)			1 (<1)	2 (1)
due to other reasons, n (%)			1 (<1)	2 (1)
Demographics: (Safety Population)			**Placebo**	**Bupropion XL**
N			207	211
Females: Males			144: 63	157: 54
Mean Age, years (SD)			71.3 (5.88)	70.9 (5.55)
White, n (%)			178 (86)	177 (84)
Primary Efficacy Results: (ITT Population)				
LOCF MADRS Total Score at Week 10			**Placebo**	**Bupropion XL**
N			204	210
Baseline mean (SE)			29.8 (0.34)	29.5 (0.34)
Baseline median (range)			30.0 (16 - 47)	29.0 (14 - 43)
Analysis of covariance (protocol specified analysis)				
Change from baseline:	LS Mean (SE)		-12.4 (0.68)	-13.9 (0.66)
Difference from placebo:	LS Mean (95% CI)		-	-1.5 (-3.2, 0.2)
p-value			-	0.085
Rank analysis of covariance (post-hoc analysis)				
Change from baseline:	Median (range)		-11.0 (-31 - 10)	-15.0 (-37 - 8)
p-value			-	0.033
Robust regression analysis (post-hoc analysis)				
Difference from placebo:	Mean (SE)		-	-1.86 (0.80)
p-value			-	0.021
Secondary Efficacy Variable(s): (ITT Population)				
N			204	210
OC MADRS Total Score			**Placebo**	**Bupropion XL**
Week 1	Change from baseline:	LS Mean (SE)	-3.5 (0.33)	-3.1 (0.32)
	Difference from placebo:	LS Mean (95% CI)	-	0.3 (-0.5, 1.2)
Week 2	Change from baseline:	LS Mean (SE)	-6.3 (0.46)	-6.0 (0.45)
	Difference from placebo:	LS Mean (95% CI)	-	0.3 (-0.9, 1.4)
Week 4	Change from baseline:	LS Mean (SE)	-9.2 (0.53)	-10.0 (0.54)
	Difference from placebo:	LS Mean (95% CI)	-	-0.9 (-2.2, 0.5)
Week 5	Change from baseline:	LS Mean (SE)	-11.4 (0.56)	-12.4 (0.57)
	Difference from placebo:	LS Mean (95% CI)	-	-1.1 (-2.5, 0.3)

Week 6	Change from baseline:	LS Mean (SE)	-12.6 (0.59)	-13.9 (0.60)
	Difference from placebo:	LS Mean (95% CI)	-	-1.3 (-2.8, 0.2)
Week 8	Change from baseline:	LS Mean (SE)	-13.9 (0.64)	-15.5 (0.64)
	Difference from placebo:	LS Mean (95% CI)	-	-1.6 (-3.2, -0)
Week 10	Change from baseline:	LS Mean (SE)	-13.6 (0.67)	-16.6 (0.66)
	Difference from placebo:	LS Mean (95% CI)	-	-3.0 (-4.7, -1.4)
MADRS Item 2 Score (Reported Sadness)			**Placebo**	**Bupropion XL**
Baseline	Mean (SD)		3.8 (0.75)	3.8 (0.71)
Week 1 OC	Change from baseline:	LS Mean (SE)	-0.5 (0.06)	-0.5 (0.06)
	Difference from placebo:	LS Mean (95% CI)	-	0 (-0.2, 0.1)
Week 2 OC	Change from baseline:	LS Mean (SE)	-0.9 (0.08)	-0.9 (0.08)
	Difference from placebo:	LS Mean (95% CI)	-	0 (-0.2, 0.2)
Week 4 OC	Change from baseline:	LS Mean (SE)	-1.2 (0.09)	-1.5 (0.09)
	Difference from placebo:	LS Mean (95% CI)	-	-0.3 (-0.5, 0)
Week 5 OC	Change from baseline:	LS Mean (SE)	-1.5 (0.09)	-1.9 (0.09)
	Difference from placebo:	LS Mean (95% CI)	-	-0.4 (-0.6, -0.1)
Week 6 OC	Change from baseline:	LS Mean (SE)	-1.7 (0.09)	-2.0 (0.10)
	Difference from placebo:	LS Mean (95% CI)	-	-0.3 (-0.6, -0.1)
Week 8 OC	Change from baseline:	LS Mean (SE)	-1.8 (0.10)	-2.2 (0.10)
	Difference from placebo:	LS Mean (95% CI)	-	-0.3 (-0.6, -0.1)
Week 10 OC	Change from baseline:	LS Mean (SE)	-1.8 (0.10)	-2.3 (0.10)
	Difference from placebo:	LS Mean (95% CI)	-	-0.5 (-0.8, -0.3)
Week 10 LOCF	Change from baseline:	LS Mean (SE)	-1.6 (0.10)	-2.0 (0.10)
	Difference from placebo:	LS Mean (95% CI)	-	-0.3 (-0.6, -0.1)
MADRS Item 6 Score (Concentration Difficulties)			**Placebo**	**Bupropion XL**
Baseline	Mean (SD)		3.1 (0.96)	3.1 (0.93)
Week 1 OC	Change from baseline:	LS Mean (SE)	-0.3 (0.06)	-0.3 (0.06)
	Difference from placebo:	LS Mean (95% CI)	-	-0.1 (-0.2, 0.1)
Week 2 OC	Change from baseline:	LS Mean (SE)	-0.5 (0.08)	-0.6 (0.07)
	Difference from placebo:	LS Mean (95% CI)	-	-0.1 (-0.3, 0.1)
Week 4 OC	Change from baseline:	LS Mean (SE)	-0.8 (0.08)	-1.0 (0.08)
	Difference from placebo:	LS Mean (95% CI)	-	-0.2 (-0.4, 0.1)
Week 5 OC	Change from baseline:	LS Mean (SE)	-1.0 (0.09)	-1.1 (0.09)
	Difference from placebo:	LS Mean (95% CI)	-	-0.1 (-0.3, 0.2)
Week 6 OC	Change from baseline:	LS Mean (SE)	-1.2 (0.09)	-1.3 (0.09)
	Difference from placebo:	LS Mean (95% CI)	-	-0.1 (-0.3, 0.1)
Week 8 OC	Change from baseline:	LS Mean (SE)	-1.2 (0.09)	-1.4 (0.09)
	Difference from placebo:	LS Mean (95% CI)	-	-0.2 (-0.4, 0)
Week 10 OC	Change from baseline:	LS Mean (SE)	-1.2 (0.09)	-1.5 (0.09)
	Difference from placebo:	LS Mean (95% CI)	-	-0.2 (-0.4, 0)
Week 10 LOCF	Change from baseline:	LS Mean (SE)	-1.1 (0.08)	-1.2 (0.08)
	Difference from placebo:	LS Mean (95% CI)	-	0 (-0.2, 0.2)
MADRS Item 7 Score (Lassitude)			**Placebo**	**Bupropion XL**
Baseline	Mean (SD)		3.4 (0.98)	3.4 (0.92)
Week 1 OC	Change from baseline:	LS Mean (SE)	-0.3 (0.06)	-0.4 (0.06)
	Difference from placebo:	LS Mean (95% CI)	-	-0.1 (-0.2, 0.1)
Week 2 OC	Change from baseline:	LS Mean (SE)	-0.6 (0.08)	-0.6 (0.08)
	Difference from placebo:	LS Mean (95% CI)	-	0 (-0.2, 0.2)
Week 4 OC	Change from baseline:	LS Mean (SE)	-0.9 (0.08)	-1.2 (0.08)
	Difference from placebo:	LS Mean (95% CI)	-	-0.3 (-0.5, -0.1)
Week 5 OC	Change from baseline:	LS Mean (SE)	-1.1 (0.09)	-1.5 (0.09)
	Difference from placebo:	LS Mean (95% CI)	-	-0.4 (-0.6, -0.1)
Week 6 OC	Change from baseline:	LS Mean (SE)	-1.3 (0.09)	-1.6 (0.10)
	Difference from placebo:	LS Mean (95% CI)	-	-0.3 (-0.5, -0.1)
Week 8 OC	Change from baseline:	LS Mean (SE)	-1.5 (0.10)	-1.8 (0.10)

	Difference from placebo:	LS Mean (95% CI)	-	-0.3 (-0.5, -0.1)
Week 10 OC	Change from baseline:	LS Mean (SE)	-1.4 (0.10)	-1.9 (0.10)
	Difference from placebo:	LS Mean (95% CI)	-	-0.5 (-0.8, -0.3)
Week 10 LOCF	Change from baseline:	LS Mean (SE)	-1.3 (0.09)	-1.6 (0.09)
	Difference from placebo:	LS Mean (95% CI)	-	-0.3 (-0.6, -0.1)
MADRS Responders and Remitters at Week 10			**Placebo**	**Bupropion XL**
Percentage of OC Responders (%)			76 (48)	103 (63)
Percentage of LOCF Responders (%)			87 (43)	109 (53)
Percentage of OC Remitters (%)			62 (39)	74 (45)
Percentage of LOCF Remitters (%)			68 (33)	79 (38)
CGI-I Responders			**Placebo**	**Bupropion XL**
Week 1 OC	Percentage of Responders (%)		12 (6)	8 (4)
Week 2 OC	Percentage of Responders (%)		26 (13)	32 (16)
Week 4 OC	Percentage of Responders (%)		49 (26)	74 (40)
Week 5 OC	Percentage of Responders (%)		69 (38)	93 (53)
Week 6 OC	Percentage of Responders (%)		84 (47)	107 (61)
Week 8 OC	Percentage of Responders (%)		90 (53)	119 (70)
Week 10 OC	Percentage of Responders (%)		83 (52)	117 (71)
Week 10 LOCF	Percentage of Responders (%)		93 (46)	124 (60)
CGI-S Score			**Placebo**	**Bupropion XL**
Baseline	Mean (SD)		4.6 (0.62)	4.5 (0.57)
Week 1 OC	Change from baseline:	LS Mean (SE)	-0.2 (0.04)	-0.2 (0.04)
	Difference from placebo:	LS Mean (95% CI)	-	0 (-0.1, 0.1)
Week 2 OC	Change from baseline:	LS Mean (SE)	-0.5 (0.05)	-0.5 (0.05)
	Difference from placebo:	LS Mean (95% CI)	-	0 (-0.2, 0.1)
Week 4 OC	Change from baseline:	LS Mean (SE)	-0.7 (0.07)	-0.9 (0.07)
	Difference from placebo:	LS Mean (95% CI)	-	-0.2 (-0.4, 0)
Week 5 OC	Change from baseline:	LS Mean (SE)	-1.0 (0.07)	-1.1 (0.07)
	Difference from placebo:	LS Mean (95% CI)	-	-0.1 (-0.3, 0.1)
Week 6 OC	Change from baseline:	LS Mean (SE)	-1.2 (0.08)	-1.3 (0.08)
	Difference from placebo:	LS Mean (95% CI)	-	-0.2 (-0.4, 0)
Week 8 OC	Change from baseline:	LS Mean (SE)	-1.4 (0.09)	-1.6 (0.09)
	Difference from placebo:	LS Mean (95% CI)	-	-0.2 (-0.4, 0.1)
Week 10 OC	Change from baseline:	LS Mean (SE)	-1.4 (0.09)	-1.8 (0.09)
	Difference from placebo:	LS Mean (95% CI)	-	-0.4 (-0.6, -0.1)
Week 10 LOCF	Change from baseline:	LS Mean (SE)	-1.3 (0.09)	-1.5 (0.08)
	Difference from placebo:	LS Mean (95% CI)	-	-0.2 (-0.4, 0)
HAMA Total Score			**Placebo**	**Bupropion XL**
Baseline	Mean (SD)		20.3 (5.68)	20.4 (5.47)
Week 1 OC	Change from baseline:	LS Mean (SE)	-2.4 (0.27)	-2.1 (0.26)
	Difference from placebo:	LS Mean (95% CI)	-	0.3 (-0.4, 1.0)
Week 2 OC	Change from baseline:	LS Mean (SE)	-4.1 (0.34)	-3.7 (0.33)
	Difference from placebo:	LS Mean (95% CI)	-	0.4 (-0.4, 1.3)
Week 4 OC	Change from baseline:	LS Mean (SE)	-5.6 (0.41)	-6.7 (0.41)
	Difference from placebo:	LS Mean (95% CI)	-	-1.1 (-2.1, 0)
Week 5 OC	Change from baseline:	LS Mean (SE)	-7.0 (0.40)	-7.8 (0.41)
	Difference from placebo:	LS Mean (95% CI)	-	-0.8 (-1.9, 0.2)
Week 6 OC	Change from baseline:	LS Mean (SE)	-7.7 (0.41)	-8.9 (0.42)
	Difference from placebo:	LS Mean (95% CI)	-	-1.3 (-2.3, -0.2)
Week 8 OC	Change from baseline:	LS Mean (SE)	-8.3 (0.45)	-9.6 (0.46)
	Difference from placebo:	LS Mean (95% CI)	-	-1.3 (-2.5, -0.2)
Week 10 OC	Change from baseline:	LS Mean (SE)	-8.1 (0.48)	-9.7 (0.47)
	Difference from placebo:	LS Mean (95% CI)	-	-1.6 (-2.8, -0.4)
Week 10 LOCF	Change from baseline:	LS Mean (SE)	-7.3 (0.47)	-8.1 (0.46)
	Difference from placebo:	LS Mean (95% CI)	-	-0.8 (-2.0, 0.4)

Health Outcome Variable(s): (ITT Population)				
SDS Score at Week 10			**Placebo**	**Bupropion XL**
Total Score	Baseline mean (SD)		17.8 (5.91)	17.7 (5.63)
OC	Change from baseline:	LS Mean (SE)	-6.2 (0.59)	-8.6 (0.58)
	Difference from placebo:	LS Mean (95% CI)	-	-2.4 (-3.8, -0.9)
LOCF	Change from baseline:	LS Mean (SE)	-5.7 (0.58)	-7.8 (0.55)
	Difference from placebo:	LS Mean (95% CI)	-	-2.1 (-3.6, -0.7)
Work Score	Baseline mean (SD)		5.5 (2.73)	5.3 (2.80)
OC	Change from baseline:	LS Mean (SE)	-1.8 (0.21)	-2.7 (0.20)
	Difference from placebo:	LS Mean (95% CI)	-	-0.9 (-1.4, -0.4)
LOCF	Change from baseline:	LS Mean (SE)	-1.5 (0.20)	-2.4 (0.19)
	Difference from placebo:	LS Mean (95% CI)	-	-0.8 (-1.3, -0.3)
Social Score	Baseline mean (SD)		6.3 (2.15)	6.4 (1.95)
OC	Change from baseline:	LS Mean (SE)	-2.4 (0.20)	-3.1 (0.20)
	Difference from placebo:	LS Mean (95% CI)	-	-0.8 (-1.3, -0.3)
LOCF	Change from baseline:	LS Mean (SE)	-2.3 (0.20)	-2.9 (0.20)
	Difference from placebo:	LS Mean (95% CI)	-	-0.6 (-1.1, -0.1)
Family Score	Baseline mean (SD)		6.0 (2.28)	6.1 (2.07)
OC	Change from baseline:	LS Mean (SE)	-2.0 (0.22)	-2.8 (0.21)
	Difference from placebo:	LS Mean (95% CI)	-	-0.8 (-1.4, -0.3)
LOCF	Change from baseline:	LS Mean (SE)	-1.9 (0.20)	-2.7 (0.20)
	Difference from placebo:	LS Mean (95% CI)	-	-0.7 (-1.3, -0.2)
Q-LES-Q-SF Score at Week 10			**Placebo**	**Bupropion XL**
General Activities	Baseline mean (SD)		37.8 (11.88)	36.9 (12.06)
OC	Change from baseline:	LS Mean (SE)	16.4 (1.31)	20.5 (1.30)
	Difference from placebo:	LS Mean (95% CI)	-	4.1 (0.9, 7.3)
LOCF	Change from baseline:	LS Mean (SE)	15.7 (1.25)	18.7 (1.23)
	Difference from placebo:	LS Mean (95% CI)	-	3.0 (-0.1, 6.1)
Satisfaction with Medication	Baseline mean (SD)		3.2 (0.83)	3.3 (0.85)
OC	Change from baseline:	LS Mean (SE)	0.4 (0.09)	0.3 (0.09)
	Difference from placebo:	LS Mean (95% CI)	-	-0.1 (-0.4, 0.1)
LOCF	Change from baseline:	LS Mean (SE)	0.3 (0.09)	0.1 (0.10)
	Difference from placebo:	LS Mean (95% CI)	-	-0.2 (-0.4, 0.1)
Life Satisfaction & Contentment	Baseline mean (SD)		2.2 (0.76)	2.1 (0.68)
OC	Change from baseline:	LS Mean (SE)	1.0 (0.08)	1.3 (0.08)
	Difference from placebo:	LS Mean (95% CI)	-	0.3 (0.1, 0.5)
LOCF	Change from baseline:	LS Mean (SE)	0.9 (0.08)	1.2 (0.07)
	Difference from placebo:	LS Mean (95% CI)	-	0.3 (0.1, 0.4)
MEI Total Score at Week 10			**Placebo**	**Bupropion XL**
Baseline	Mean (SD)		29.5 (15.16)	29.0 (13.85)
OC	Change from baseline:	LS Mean (SE)	17.7 (1.64)	26.5 (1.63)
	Difference from placebo:	LS Mean (95% CI)	-	8.8 (4.7, 12.8)
LOCF	Change from baseline:	LS Mean (SE)	16.9 (1.60)	23.6 (1.58)
	Difference from placebo:	LS Mean (95% CI)	-	6.7 (2.7, 10.7)
Subject Satisfaction with Study Medication at Week 10			**Placebo**	**Bupropion XL**
OC	LS Mean (SE)		4.6 (0.14)	5.3 (0.14)
	Difference from placebo:	LS Mean (95% CI)	-	0.8 (0.4, 1.1)
LOCF	LS Mean (SE)		4.4 (0.14)	4.9 (0.13)
	Difference from placebo:	LS Mean (95% CI)	-	0.6 (0.2, 0.9)
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=207**	**Bupropion XL N=211**
Subjects with any AE(s), n (%)			122 (59)	121 (57)
Headache			22 (11)	20 (9)

Dry mouth	10 (5)	18 (9)
Nausea	17 (8)	14 (7)
Constipation	7 (3)	13 (6)
Insomnia	8 (4)	13 (6)
Dizziness	13 (6)	12 (6)
Hyperhidrosis	10 (5)	7 (3)
Nasopharyngitis	4 (2)	6 (3)
Fatigue	6 (3)	5 (2)
Diarrhoea	6 (3)	4 (2)
Agitation	2 (<1)	4 (2)
Anorexia	1 (<1)	4 (2)
Back pain	1 (<1)	4 (2)
Tinnitus	1 (<1)	4 (2)
Restlessness	0	4 (2)
Tension	0	4 (2)
Chest pain	7 (3)	2 (<1)
Depression	6 (3)	2 (<1)
Serious Adverse Events - On-Therapy n (%) [n considered by the investigator to be related to study medication]	**Placebo N=207**	**Bupropion XL N=211**
Subjects with non-fatal SAE(s) on therapy	7 (3) [2]	2 (<1) [0]
Depression	2 (<1) [0]	0
Major depression	1 (<1) [1]	0
Suicidal ideation	1 (<1) [0]	0
Arrhythmia supraventricular	1 (<1) [1]	0
Gastrooesophageal reflux disease	0	1 (<1) [0]
Bronchitis	1 (<1) [0]	0
Vaginal inflammation	0	1 (<1) [0]
Chronic obstructive pulmonary disease	1 (<1) [0]	0
Subjects with non-fatal SAE(s) post-treatment[1]	0	1 (<1) [0]
Cerebrovascular accident	0	1 (<1) [0]
Subjects with fatal SAEs on therapy	0	0
Subjects with fatal SAEs post-treatment[2]	2 (<1) [0]	0
Myocardial infarction	1 (<1) [0]	0
Ruptured cerebral aneurysm	1 (<1) [0]	0
Subarachnoid haemorrhage	1 (<1) [0]	0

[1] The post-treatment non-fatal SAE in the bupropion XL group (cerebrovascular accident) occurred 7 days after the last dose of study medication.

[2] The two post-treatment deaths in the placebo group occurred 2 days (myocardial infarction) and 6 days (aneurysm and haemorrhage) after the last dose of study medication.

Conclusion: This study did not show a statistical difference between bupropion XL and placebo for the primary efficacy variables when analysed using analysis of covariance (protocol-specified analysis), however, a statistical difference was observed using rank analysis of covariance and robust regression analysis (post-hoc analyses). In the placebo group 122 subjects reported non-serious AEs with the most frequently reported being headache and nausea. In the bupropion XL group 121 subjects reported non-serious AEs with the most frequently reported being headache and dry mouth. Seven non-fatal SAEs were reported in the placebo group, comprising depression (two reports), major depression, suicidal ideation, arrhythmia supraventricular, bronchitis and chronic obstructive pulmonary disease (one report each). Two non-fatal SAEs were reported in the bupropion XL group, comprising gastrooesophageal reflux disease and vaginal inflammation, and one post-treatment non-fatal SAE of cerebrovascular accident was reported 7 days after the last dose of study medication. There were no on-therapy fatalities in either group. There were two post-treatment fatalities in the placebo group occurring 2 days (myocardial infarction) and 6 days (aneurysm and haemorrhage) after the last dose of study medication; there were no post-treatment fatalities in the bupropion XL group.
Publications: No publication

Date Updated: 16-May-2006