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.

GSK Medicine: Nicotine	
Study No.: S3250493	
Title: Simultaneous fMRI/EEG of the 4 mg Nicotine Lozenge in Relief of Cognitive Impairment Associated with Nicotine Withdrawal	
Rationale: To use blood oxygen level-dependent (BOLD) functional Magnetic Resonance Imaging (fMRI) in abstinent smokers to directly evaluate the effect of the 4 mg nicotine mint lozenge on brain activation associated with visual attention.	
Phase: IV	
Study Period: 30 September 2007 – 15 February 2008	
Study Design: Single-centre, evaluator and subject blind, randomised, placebo-controlled, two-administration, two-period crossover study	
Centre: 1, UK	
Indication: Nicotine pharmacodynamics	
Treatment: Nicotine Polacrilex Mint Lozenge 4mg	
Objectives: To compare the effect of the 4 mg nicotine lozenge to placebo on blood oxygen level-dependent (BOLD) activation associated with attention in abstinent smokers.	
Primary Outcome: Differences in BOLD signal intensity in brain regions of interest (ROI) between conditions of high and low attention during Rapid Visual Information Processing or divided attention tasks.	
Secondary Outcome: Behavioural measures (accuracy and response times) obtained from Rapid Visual Information Processing and Divided (RVIP) and Sustained Attention tasks.	
Statistical Methods: For analysis of the fMRI data, ROIs were identified following blinded examination of the BOLD signal differences between high and low attention conditions from Visit 1, irrespective to the treatment on that visit. The primary outcome variable, the BOLD score, was evaluated with analysis of variance (ANOVA), including subject, treatment (nicotine, placebo), condition (High attention, Low attention), and treatment*condition interaction as factors. This analysis was performed separately for each ROI and each task (RVIP and Divided Attention). Efficacy was determined by a treatment*condition interaction. The secondary variables were also evaluated with the same ANOVA model. This analysis was performed separately for the RVIP and Divided Attention tasks.	
Study Population: Volunteer smokers	
Number of Subjects Screened:	45
Planned, N	30
Randomized, N	23
Completed, N	22
Total Number Subjects Withdrawn, n (%)	1 (4.35)
Withdrawn due to Adverse Events n (%)	1 (4.35)
Withdrawn due to Lack of Efficacy n (%)	0
Withdrawn for other reasons n (%)	0
Demographics	
N (Intent To Treat [ITT] population)	23
Females: Males	5:18
Mean Age, years (SD)	30.82 (8.428)
Caucasian, n (%)	23 (100)
Mean Weight, kg (SD)	77.19 (11.688)

Mean Height, cm (SD)	178.55 (6.536)			
Mean BMI, kg/m^2 (SD)	24.5 (3.159)			
Primary Efficacy Results: Blood Oxygen-Level Dependent (BOLD) signal intensity level during Rapid Visual Information Processing (RVIP)				
Regions of Interest	Low Attention		High Attention	
Percent (%) BOLD signal change parameter estimates	Nicotine N=18	Placebo N=18	Nicotine N=18	Placebo N=18
BOLD – Left anterior insula, Mean (SD)	0.0 (0.21)	0.2 (0.27)	0.7 (0.48)	0.7 (0.39)
BOLD – Left anterior putamen, Mean (SD)	0.0 (0.20)	0.1 (0.36)	0.3 (0.27)	0.3 (0.34)
BOLD – Left dorsal anterior cingulate cortex, Mean (SD)	0.3 (0.39)	0.4 (0.31)	1.4 (0.70)	1.0 (0.66)
BOLD – Left dorsolateral pre-frontal cortex, Mean (SD)	0.0 (0.29)	0.1 (0.25)	0.7 (0.77)	0.7 (0.59)
BOLD – Left parietal cortex, Mean (SD)	0.3 (0.49)	0.2 (0.37)	1.5 (0.90)	1.2 (0.59)
BOLD – Left premotor cortex, Mean (SD)	0.1 (0.27)	0.1 (0.24)	0.9 (0.69)	0.7 (0.46)
BOLD – Left substantia nigra/ventral tegmental area, Mean	0.1 (0.18)	0.1 (0.29)	0.4 (0.28)	0.3 (0.33)
BOLD – Left thalamus, Mean (SD)	0.1 (0.24)	0.1 (0.36)	0.5 (0.36)	0.6 (0.39)
BOLD – Left visual cortex, Mean (SD)	0.9 (0.72)	0.9 (0.73)	1.6 (0.73)	1.9 (0.87)
BOLD – Right anterior insula, Mean (SD)	0.0 (0.18)	0.1 (0.24)	0.5 (0.35)	0.5 (0.40)
BOLD – Right dorsal anterior cingulated cortex, Mean	0.2 (0.34)	0.2 (0.17)	0.8 (0.57)	0.8 (0.49)
BOLD – Right dorsalateral pre-frontal cortex, Mean (SD)	0.2 (0.45)	0.2 (0.37)	1.0 (0.85)	0.8 (0.55)
BOLD – Right parietal cortex, Mean (SD)	0.2 (0.46)	0.2 (0.52)	1.1 (0.62)	1.2 (0.72)
BOLD – Right premotor cortex, Mean (SD)	0.1 (0.47)	0.2 (0.33)	0.7 (0.61)	0.8 (0.62)
BOLD – Right thalamus, Mean (SD)	-0.1 (0.22)	0.0 (0.44)	0.7 (0.44)	0.6 (0.55)
BOLD – Right visual cortex, Mean (SD)	0.0 (0.44)	-0.1 (0.32)	0.4 (0.43)	0.3 (0.32)
Secondary Outcome Variable(s): Summary of Rapid Visual Information Processing (RVIP)				
	Low Attention		High Attention	
	Nicotine N=22	Placebo N=22	Nicotine N=22	Placebo N=22
Response Time (ms), Mean (SD)	0.5 (0.05)	0.5 (0.05)	0.5 (0.08)	0.5 (0.06)
Valid Responses (% correct), Mean (SD)	92.6 (5.27)	91.1 (4.32)	62.4 (18.51)	54.1 (15.38)
Secondary Outcome Variable(s): Summary of Divided Attention				
Percent (%) BOLD signal change parameter estimates	Low Attention		High Attention	
	Nicotine N=19	Placebo N=19	Nicotine N=19	Placebo N=19
BOLD – Left parietal cortex, Mean (SD)	0.0 (0.39)	0.1 (0.33)	0.7 (0.44)	0.6 (0.40)
BOLD – Left superior occipital cortex, Mean (SD)	-0.1 (0.32)	0.0 (0.28)	0.4 (0.40)	0.4 (0.33)
BOLD – Left visual cortex, Mean (SD)	-0.1 (0.48)	-0.1 (0.41)	0.8 (0.42)	0.6 (0.54)
BOLD – Right parietal cortex, Mean (SD)	-0.1 (0.55)	-0.1 (0.63)	0.5 (0.45)	0.5 (0.39)
BOLD – Right premotor cortex, Mean (SD)	0.1 (0.35)	0.2 (0.57)	0.5 (0.33)	0.7 (0.58)
BOLD – Right superior occipital cortex, Mean (SD)	0.0 (0.37)	0.0 (0.46)	0.5 (0.43)	0.5 (0.53)
BOLD – Right visual cortex, Mean (SD)	0.0 (0.54)	0.0 (0.68)	1.0 (1.13)	1.2 (1.21)
Secondary Outcome Variable(s): Divided Attention				
	Low Attention		High Attention	
	Nicotine N=22	Placebo N=22	Nicotine N=22	Placebo N=22
Response Time (ms), Mean (SD)	0.4 (0.04)	0.5 (0.04)	0.5 (0.04)	0.5 (0.04)
Valid Responses (% correct), Mean (SD)	48.2 (0.97)	47.8 (1.15)	96.9 (3.48)	95.9 (3.61
Safety Results: An on therapy adverse event (AE) was defined as an AE with onset on or after the start date of study				

medication or for up to 5 days after the last administration.		
	Nicotine (N=22)	Placebo (N=33)
Subjects with any AE(s), n (%)	7 (31.8)	3 (13.0)
Hiccups	2 (9.1)	0
Nausea	2 (9.1)	0
Headache	1 (4.5)	1 (4.3)
Throat irritation	1 (4.5)	0
Pain	1 (4.5)	0
Dry throat	0	1 (4.3)
Feeling hot	0	1 (4.3)
Thermal burn	0	1 (4.3)
Serious Adverse Events - On-Therapy n (%) [n considered by the investigator to be related to study medication]		
	Nicotine (N=22)	Placebo (N=23)
Subjects with non-fatal SAEs, n (%)	0	0
Subjects with fatal SAEs, n (%)	0	0