Clinical Study Summary (CSS)

CT Registry ID#: *NCT00498108*
Study No.: SP791

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Proprietary Drug Name	**INN**	**Therapeutic area and indication(s)**
Neupro® transdermal patch	**Rotigotine**	Restless Legs Syndrome

Name of Sponsor/Company: SCHWARZ BIOSCIENCES, INC. A member of the UCB group.

Title of Study:
An open-label extension trial to investigate the safety and tolerability of long-term treatment with transdermal rotigotine in subjects with idiopathic Restless Legs Syndrome (RLS)

Investigator(s) (number only): 44

Study Center(s) (number only): 44

Length of Study:	~13 months	Phase of Development: 3
Date first subject enrolled:	11 Jan 2006	
Date last subject completed:	08 Sep 2007	

Abstract:
SP791 was a multicenter, open-label (OL) extension trial to assess the safety and tolerability of rotigotine in subjects with idiopathic RLS, administered at an optimal dose for up to 1 year in subjects who previously participated in SP790 (6-month pivotal trial) or SP794 (sleep laboratory trial).

The following safety variables (primary outcome of the study) were measured: adverse events (AEs) reported spontaneously by the subject or observed by the investigator, changes in laboratory tests, changes in vital signs, physical and neurological examination findings, changes in 12-lead electrocardiograms (ECGs), changes in menstrual and sexual function, subject's rating of daytime sleepiness as measured by the Epworth Sleepiness Scale, Global Subject Rating of Tolerability, Clinical Global Impressions (CGI) Item 4, change from Baseline in the Augmentation Severity Rating Scale at the end of the Maintenance Period, changes in the Self-Rating Depression Scale, application site assessment, and patch adhesiveness.

Subjects who completed trial SP790 or SP794 and who had given their written informed consent were included in this trial. Subjects were excluded if they had an ongoing serious adverse event (SAE) from SP790 or SP794 that was assessed as related to trial medication by the investigator and/or the sponsor.

The treatment duration of this trial was approximately 13 months and consisted of a Titration Period of up to 21 days (±3 days), a 1-year Maintenance Period, a Taper Period of up to 4 days, and a Safety Follow-Up Period of 30 days. In fact, the individual Treatment Period including Taper Period amounted to up to 418 days during this trial.

Number of Subjects:	
Planned, N:	420
Enrolled, N:	341 (100.0)
Completed, n (%):	250 (73.3)
Number of Subjects Withdrawn, n (%):	91 (26.7)
Withdrawn due to Adverse Events, n (%):	58 (63.7)
Withdrawn for Other Reasons, n (%):	33 (36.3)
Demography:	
Gender (Females/Males):	246/95
Age (years), mean (SD):	58.6 (10.7)
Race : White	341 (100.0)

Safety Outcomes:

Overall, rotigotine was well tolerated during the trial. Most AEs were consistent with stimulation of dopamine receptors and the use of a transdermal patch. The majority of AEs were mild or moderate in intensity. During the trial, the most common AEs were application site reactions, nausea, fatigue, nasopharyngitis, and headache. A total of 16% of subjects withdrew from the trial due to an AE, the most common AEs being application site reactions. Eleven percent of subjects experienced an SAE during treatment and the SAEs occurred across multiple SOCs with no obvious grouping. Two deaths were reported during the trial resulting from multiple cardiac disorders and myocardial infarction, but these AEs were considered to be not related to trial medication. No clinically relevant changes in vital signs were noted. There was no indication for rotigotine to cause any ECG abnormalities or changes in this trial. Overall, there was no relevant difference in the incidence of AEs or in laboratory, vital signs, and ECG findings between the subjects who completed SP790 and the subjects who completed SP794.

A summary of AEs is provided below:

Treatment Emergent AEs (TEAE):

TEAEs occurring in ≥5% of subjects:

Preferred Term	N=341 n (%)
Any AE	256 (75.1)
Application and instillation site reactions[a]	111 (32.6)
Nausea	25 (7.3)
Fatigue	24 (7.0)
Nasopharyngitis	20 (5.9)
Headache	19 (5.6)

a. MedDRA High Level Term

Drug-related TEAEs (as assessed by the Investigator) :

Drug-related TEAEs occurring in ≥5% of subjects:

Preferred Term	N=341 n (%)
Any AE	182 (53.4)
Application and instillation site reactions[a]	111 (32.6)
Nausea	22 (6.5)
Fatigue	18 (5.3)

a. MedDRA High Level Term

Death, SAEs, and Other SAEs:	
Death, n (%):	2 (0.6)
Subjects with treatment-emergent SAEs Preferred Terms, n (%):	33 (9.7)
Myocardial infarction	2 (0.6) [0]
Angina pectoris	1 (0.3) [0]
Cardiac disorder	1 (0.3) [0]
Tachycardia	1 (0.3) [0]
Cardiac arrest	1 (0.3) [0]
Hiatus hernia	1 (0.3) [0]
Gastritis	1 (0.3) [0]
Diverticulitis	2 (0.6) [0]
Sialoadenitis	1 (0.3) [0]
Pneumonia	1 (0.3) [0]
Humerus fracture	2 (0.6) [0]
Excoriation	1 (0.3) [0]
Sternal fracture	1 (0.3) [0]
Osteoarthritis	3 (0.9) [0]
Lumbar spinal stenosis	1 (0.3) [0]
Spinal column stenosis	1 (0.3) [0]
Collagen disorder	1 (0.3) [0]
Intervertebral disc protrusion	1 (0.3) [0]
Periarthritis	1 (0.3) [0]
Myalgia	1 (0.3) [0]
Bladder cancer	1 (0.3) [0]
Bladder neoplasm	1 (0.3) [0]
Uterine leiomyoma	1 (0.3) [0]
Sleep attacks	2 (0.6) [3]
Depression	1 (0.3) [1]
Insomnia	1 (0.3) [1]
Pathological gambling	1 (0.3) [1]
Stress urinary incontinence	1 (0.3) [0]
Hypoventilation	1 (0.3) [0]
Nasal cyst	1 (0.3) [0]
Breast cosmetic surgery	1 (0.3) [0]
Aortic valve replacement	1 (0.3) [0]
Varicose vein	1 (0.3) [0]
Primary & Secondary Efficacy Outcomes: This was an open-label exploratory trial with no specified primary or secondary efficacy endpoints.	
Publication Reference(s) based on the study: None at this time.	
Date of report: 05-Dec-2008	