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Human Medicines Division

Assessment report for paediatric studies submitted according to Article 46 of the Regulation (EC) No 1901/2006

Neupro

rotigotine

Procedure no: EMEA/H/C/000626/P46/047

Note

Assessment report as adopted by the CHMP with all information of a commercially confidential nature deleted.

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1. Introduction

On 12 September 2023 the MAH submitted the results of the prematurely terminated paediatric study SP1006: fixed dose administration of the rotigotine transdermal system in adolescents, 13 to 17 years of age, with idiopathic Restless Legs Syndrome (RLS), in accordance with Article 46 of Regulation (EC) No1901/2006, as amended.

SP1006 was prematurely terminated by UCB due to unsatisfactory enrolment. A total of 138 study participants were planned to be randomised in this study; however, over a period of 3.5 years, only 23 study participants were randomised. Despite extensive and diligent outreach efforts to increase enrolment, there appeared to be low interest from the population of adolescents with idiopathic RLS, which contributed to the insufficient enrolment..

On 23 November 2022, UCB received a response from the Food and Drug Administration (FDA) about a Type C meeting regarding two studies in adolescents with idiopathic RLS (SP1006 and its open-label extension study, RL0007). In this response, the FDA recognized the difficulties of recruiting participants for studies SP1006 and RL0007 and offered UCB the option to request to be released from the post-marketing requirements for these studies, along with a request for the MAH to provide an updated assessment of the prevalence of RLS in adolescents.

On 13 February 2023, UCB notified the FDA that both SP1006 and RL0007 would be prematurely terminated. At this time there were no study participants actively receiving treatment in either study (all enrolled study participants had either completed or discontinued treatment). Initially the end of the study was defined as Last Patient Last Visit (LPLV); however, due to premature termination, the end of SP1006 and RL0007 was rather 07 April 2023, which corresponds to the date when the Institutional Review Board approved the closure of these studies. In addition, in June 2023, UCB submitted a request to the FDA to be released from the post-marketing requirements for both SP1006 and RL0007, supported by an updated assessment of the prevalence of RLS in adolescents, as requested.

A short critical expert overview has also been provided.

2. Scientific discussion

2.1. Information on the development program

The MAH stated that study SP1006, A remote, double-blind, Randomised, placebo-controlled study of rotigotine transdermal system in adolescent subjects with idiopathic restless legs syndrome, and its open-label extension study RL0007, are stand-alone studies.

2.2. Information on the pharmaceutical formulation used in the study

Rotigotine, a dopamine agonist, has been formulated as a transdermal delivery system and is designed to continuously provide rotigotine over a 24-hour period.

The rotigotine transdermal system has been approved in the EU for the treatment of the signs and symptoms of early-stage idiopathic Parkinson’s disease as monotherapy, and as adjunctive therapy in combination with levodopa over the course of the disease through to late stages when the effect of levodopa wears off or becomes inconsistent and fluctuations of the therapeutic effect occur. In addition, the rotigotine transdermal system is approved for the symptomatic treatment of moderate-

to-severe idiopathic RLS in adults in the EU. In the US, the rotigotine transdermal system is approved for the treatment of the signs and symptoms of early and advanced-stage idiopathic Parkinson's disease and for the treatment of moderate-to-severe primary RLS. In Japan, the rotigotine transdermal system is approved for the treatment of Parkinson's disease and for the symptomatic treatment of moderate-to-severe idiopathic RLS in adults.

Overall, UCB or licensed partners hold marketing authorization for the rotigotine transdermal system in approximately 70 countries for the treatment of Parkinson's disease, and in approximately 40 countries for the treatment of RLS. The specific indication statement(s), approved formulation(s), and dosages for the rotigotine transdermal system may differ based on the country; thus, local labels should be consulted for further information.

In SP1006 study, the rotigotine transdermal patch was administered in the following doses: 1mg/24h, 2mg/24h, and 3mg/24h.

2.3. Clinical aspects

2.3.1. Introduction

The MAH submitted a final report for SP1006.

2.3.2. Clinical study

SP1006 - A Remote, Double-Blind, Randomised, Placebo-Controlled Study of Rotigotine Transdermal System in Adolescent Subjects With Idiopathic Restless Legs Syndrome.

Description

SP1006 was a Phase 3, remote, double-blind, randomised, adaptive placebo-controlled study of fixed dose administration of the rotigotine transdermal system. A total of 138 study participants were planned to be randomised during the study. The study was conducted in adolescents (13 to 17 years of age) with idiopathic RLS. Study participants were randomised to 1 of 3 treatment groups: rotigotine 2mg/24h, rotigotine 3mg/24h, or placebo.

Methods

Study participants

The study was conducted in adolescent (13 to17 years of age) with idiopathic RLS.

Treatments

Rotigotine transdermal system.

Objective(s)

In SP1006, the primary objective was to demonstrate the efficacy of rotigotine against placebo in adolescent study participants with idiopathic RLS over a 12-week Maintenance Period. The secondary objectives were to investigate the safety and tolerability of rotigotine in adolescent study participants with idiopathic RLS.

Outcomes/endpoints

Efficacy variables

The co-primary efficacy variables were change from Baseline to the End of Maintenance (EoM) Period in International Restless Legs Rating Scale (IRLS) sum score and change from Baseline in Clinical Global Impressions (CGI) Item 1 to the EoM Period.

The secondary efficacy variable was change from Baseline in Restless Legs-6 Rating Scales (RLS-6) to the EoM Period.

The other efficacy variables were as follows:

- Change from Baseline in IRLS sum score by visit
- Change from Baseline in CGI Item 1 by visit
- Change from Baseline in RLS-6 by visit
- (For IRLS sum score, CGI Item 1, and RLS-6, the EoM Visit was already covered under primary or secondary efficacy variables.)
- IRLS responder
  (A responder was defined as a study participant with a decrease of ≥50% in IRLS sum score from Baseline.)
- IRLS remitter
- (Two definitions for IRLS remitter were used in the study; a remitter was defined as a study participant with an IRLS sum score of 10 or less or a study participant who was symptom free [ie, IRLS sum score of 0 points].)
- CGI Item 1 responder
  (A responder was defined as a study participant with a decrease of ≥50% in CGI Item 1.)
- Restless Legs Syndrome-Quality of Life Questionnaire (RLS-QoL)
  Protocol-defined responder/remitter variables were not calculated or summarized because of premature termination of the study.

Safety variables

The primary safety variables were as follows:

- Occurrence of treatment-emergent adverse events (TEAEs)
- TEAEs leading to withdrawals

The other safety variables were as follows:

- Changes from Baseline (Visit 1) in 12-lead electrocardiograms (ECGs)
- Changes from Baseline (Visit 1) in vital signs (including assessment of orthostasis)
- Changes from Baseline (Visit 1) in laboratory data (haematology, blood chemistry, and urinalysis)
- Changes from Baseline (Visit 1) in hormone status
- Changes from Baseline (Visit 1) in body weight, height, and body mass index (BMI)

- Changes in Modified Minnesota Impulsive Disorder Interview (mMIDI)
- Changes in menstrual function for all female study participants

Pharmacokinetic variable

The pharmacokinetic (PK) variable was plasma concentrations of rotigotine.

Study design

SP1006 was a Phase 3, remote, double-blind, randomised, adaptive placebo-controlled study of fixed dose administration of the rotigotine transdermal system. A total of 138 study participants were planned to be randomised during the study. The study was conducted in adolescents, 13 to 17 years of age, with idiopathic RLS. Study participants were randomised to 1 of 3 treatment groups: rotigotine 2mg/24h, rotigotine 3mg/24h, or placebo.

A remote clinical study model was utilized and included telemedicine technology (ie, PLATFORM) for interactions between the investigator/study staff and study participants/legal representatives. Mobile study personnel visited study participants'/legal representatives' homes to complete certain study procedures (e.g., neurological exams, physical exams, ECGs, lab collections, and vital signs).

The study consisted of a Screening Period, a Titration Period, a Maintenance Period, a Taper Period, and a Safety Follow-Up (SFU) Visit.

The Screening Period was at least 7 days (maximum of 28 days) prior to Visit 2/Baseline to ensure homogeneous Baseline conditions were established for all study participants. Study participants with prior intake of any dopamine agonists or taking L-dopa had to discontinue the therapy at least 7 days prior to Visit 2/Baseline. Discontinuation of therapy was driven by the study participant's medical need and not undertaken for the purpose of making a potential study participant eligible for the study.

The study began with a 3-week Titration Period. Study participants received their first dose of investigational medicinal product (IMP) at Visit 3/Day 1. Study participants were initiated either on placebo or rotigotine 1mg/24h. The dose of rotigotine taken by study participants randomised to rotigotine was then up-titrated on a weekly basis by 1mg/24h at a time to 2mg/24h or 3mg/24h, depending on the study participant's assigned dose level. Study participants were allowed to back-titrate 1 dose level during the Titration Period. Study participants who did not tolerate the assigned dose in the first week (placebo or rotigotine 1mg/24h) were withdrawn from the study.

The Titration Period was followed by a 12-week Maintenance Period, during which study participants were to remain at the assigned (or back-titrated) dose level. During the Maintenance Period, visits were scheduled every 4 weeks. Plasma samples were collected at the beginning (Visit 6) and end (Visit 9) of the Maintenance Period, and the plasma concentration of unconjugated rotigotine was to be summarized by dose level and visit.

At the EoM Period, study participants entered a Taper Period lasting up to a maximum of 4 days, starting on the day after Visit 9 and consisting of a telemedicine call. The de-escalation dose(s) of IMP to be taken during the Taper Period were dispensed at Visit 9.

The visit window for the SFU Period was 30 days ±5 days relative to the end of the Taper Period. Following dose de-escalation, study participants were eligible to participate in the open-label, long-

term follow-up study (RL0007) at any time prior to the SFU Visit. The SFU Visit was for study participants not entering RL0007.

Results

Overall, 48 study participants were screened: 25 study participants were screen failures and 23 study participants were randomised. The most common reason for screen failures was ineligibility. The most common reasons for ineligibility due to inclusion criteria not being met or exclusion criteria being met were: low serum ferritin level at Visit 1/Screening (9 study participants), suicidal ideation or behaviour as determined by the Columbia-Suicide Severity Rating Scale at Visit 1/Screening (6 study participants), and/or not indicating moderate-to-severe RLS as determined by an IRLS score of ≥15 at Baseline (6 study participants).

A total of 23 study participants were included in the Randomised Set (RS), which consisted of all enrolled study participants (i.e., participants with a signed Informed Consent/Assent form and any demographic data) who were randomised: 8 study participants were randomised to the rotigotine 2mg/24h group, 7 study participants were randomised to the rotigotine 3mg/24h group, and 8 study participants were randomised to the placebo group. All study participants in the RS were included in the Safety Set (SS), which consisted of all study participants from the RS who had at least 1 patch (rotigotine or placebo) applied. No study participants received rotigotine 1mg/24h group after the Titration Period, and thus results are only presented for 2 rotigotine dose groups (rotigotine 2mg/24h and rotigotine 3mg/24h) for this study.

A total of 21 study participants (91.3%) were included in the Full Analysis Set (FAS), which consisted of all study participants from the SS who had a valid IRLS score at Baseline paired with a valid post-Baseline IRLS score or a valid CGI Item 1 score at Baseline paired with a valid post-Baseline CGI Item 1 score. One study participant in the rotigotine 2mg/24h group discontinued before completing any post-Baseline efficacy assessments and subsequently was not included in the FAS. One study participant in the placebo group had no valid post-Baseline assessments during the Treatment Period and subsequently was excluded from the FAS.

Among the 23 study participants included in the RS, 18 study participants (78.3%) completed the study, and 5 (21.7%) discontinued the study. Two study participants (8.7%) discontinued the study during the Titration Period, and 3 (13.0%) discontinued the study during the Maintenance Period. There were no study discontinuations during the Taper Period or the SFU Period.

The most common primary reason for study discontinuation was withdrawal by parent/guardian and occurred for 2 study participants (8.7%); other primary reasons for study discontinuation were adverse event (AE), lost to follow up, and withdrawal by study participant (1 study participant [4.3%] each).

Study participant demographics

Overall, the mean age of study participants was 15.7 years (range: 13 to 17 years), and the median age of participants was 16.0 years. Three out of the 23 study participants were under 15 years of age. There were no meaningful differences in age between treatment groups.

Fourteen out of the 23 study participants (60.9%) were female. The rotigotine 3mg/24h group had a higher percentage of males (71.4%) compared with the other treatment groups (25.0% each).

Twenty out of the 23 study participants were White (87.0%). One study participant (4.3%) was in each of the following racial groups: American Indian/Alaskan Native, Black or African American, and

Other/Mixed. All the study participants were not of Hispanic or Latino ethnicity, and there were no meaningful differences in racial group or ethnicity between treatment groups.

The mean weight, height, and BMI of study participants were 76.54kg, 167.14cm, and 27.24kg/m2, respectively. All 3 treatment groups had 3 study participants with BMIs ≥30kg/m2.

Baseline characteristics

The number of years since first diagnosis of RLS ranged from -0.1 to 8.6 years. The median number of years since first diagnosis of RLS (range:0 to 0.05 years across treatment groups) indicates that most study participants had diagnosis durations of <1 year.

Most study participants (16 of 23) reported that other family members were affected by RLS, and 14 of these study participants reported that at least 1 first-degree relative was affected.

Efficacy results

Because of the study's premature termination, no statistical tests of efficacy data were performed; however, descriptive summaries of a subset of efficacy data were produced. No imputation rules for missing data were applied.

For all efficacy measurements (i.e., IRLS, CGI Item 1, RLS-6, and RLS-QoL), higher scores indicate worse disease.

Because of the small number of study participants, the efficacy observations from this study should be interpreted with caution.

Coprimary efficacy variables

IRLS

Variable Visit	Statistic	Treatment group Placebo N=7	Rotigotine 2mg/24h N=7	Rotigotine 3mg/24h N=7
Visit 2 (Baseline)	n	7	7	7
	Mean (SD)	21.4 (4.0)	24.6 (5.8)	21.4 (2.6)
	Median	22.0	24.0	22.0
	Min, max	17, 28	17, 36	17, 25
Change from Baseline				
Visit 9 Day 106 (EoM)	n	5	7	5
	Mean (SD)	-8.2 (6.8)	-14.0 (8.2)	-6.4 (5.8)
	Median	-9.0	-10.0	-5.0
	Min, max	-18, 0	-25, -6	-16, -1

EoM=End of Maintenance; FAS=Full Analysis Set; IRLS=International Restless Legs Rating Scale; max=maximum; min=minimum; SD=standard deviation

The Baseline mean IRLS sum score was highest in the rotigotine 2mg/24h group (24.6), followed by the rotigotine 3mg/24h group and placebo group (21.4 each).

All treatment groups had a reduction in mean and median IRLS sum score (ie, disease improvement) from Baseline to EoM; the rotigotine 2mg/24h group had the largest reductions in mean and median IRLS sum score from Baseline to EoM:

- The rotigotine 2mg/24h group had a mean change in score of -14.0 and a median change in score of -10.0.
- The rotigotine 3mg/24h group had a mean change in score of -6.4 and a median change in score of -5.0.
- The placebo group had a mean change in score of -8.2 and a median change in score of -9.0.

CGI Item 1

Variable Visit	Statistic	Treatment group		
		Placebo N=7	Rotigotine 2mg/24h N=7	Rotigotine 3mg/24h N=7
Visit 2 (Baseline)	n	7	7	7
	Mean (SD)	4.1 (0.4)	4.4 (0.5)	4.1 (0.4)
	Median	4.0	4.0	4.0
	Min, max	4, 5	4, 5	4, 5
Change from Baseline				
Visit 9 Day 106 (EoM)	n	5	7	5
	Mean (SD)	-1.0 (1.4)	-1.7 (1.1)	-0.8 (0.8)
	Median	-1.0	-1.0	-1.0
	Min, max	-3, 1	-4, -1	-2, 0

EoM=End of Maintenance; FAS=Full Analysis Set; CGI=Clinical Global Impressions; max=maximum; min=minimum; SD=standard deviation

Baseline mean CGI Item 1 scores were similar across all 3 treatment groups.

All treatment groups had a reduction in mean and median CGI Item 1 score (ie, disease improvement) from Baseline to EoM:

- The rotigotine 2mg/24h group had a mean change in score of -1.7 and a median change in score of -1.0.
- The rotigotine 3mg/24h group had a mean change in score of -0.8 and a median change in score of -1.0.
- The placebo group had a mean change in score of -1.0 and a median change in score of -1.0.

Secondary efficacy variable

RLS-6

The Baseline mean RLS-6 scores were higher in the rotigotine 2mg/24h group compared with the rotigotine 3mg/24h and placebo groups for 4 of the 6 subscales.

All treatment groups had a reduction in mean and median RLS-6 scores (ie, disease improvement) from Baseline to EoM. The rotigotine 2mg/24h group had the largest reduction in mean RLS-6 scores from Baseline to EoM across all 6 subscales.

Other efficacy variables

Most study participants in each treatment group had reductions in RLS-QoL total score (ie, disease improvement) from Baseline to EoM.

Safety results

Extent of exposure

The investigational medicinal product duration was calculated including 1 additional day after the final patch removal. Overall, the median IMP duration was 110.0 days (range: 2 to 119 days) and was similar across treatment groups.

Adverse Events

Summary of all TEAEs

	Treatment group			
Category	Placebo N=8 n (%)	Rotigotine 2mg/24h N=8 n (%)	Rotigotine 3mg/24h N=7 n (%)	Total Rotigotine N=15 n (%)
Any TEAEs	7 (87.5)	7 (87.5)	5 (71.4)	12 (80.0)
Serious TEAEs	0	0	1 (14.3)	1 (6.7)
Discontinuations due to TEAEs	1 (12.5)	0	0	0
Permanent withdrawal of IMP due to TEAEs	1 (12.5)	0	0	0
IMP-related TEAEs	3 (37.5)	6 (75.0)	3 (42.9)	9 (60.0)
Severe TEAEs	1 (12.5)	1 (12.5)	1 (14.3)	2 (13.3)
All deaths	0	0	0	0

IMP=investigational medicinal product; SS=Safety Set; TEAE=treatment-emergent adverse event
Note: n=number of study participants reporting at least 1 TEAE in that category.

Overall, 12 study participants (80.0%) in the total rotigotine group and 7 study participants (87.5%) in the placebo group reported TEAEs. Two study participants (13.3%) in the total rotigotine group and 1 study participant (12.5%) in the placebo group reported severe TEAEs. Nine study participants (60.0%) in the total rotigotine group and 3 study participants (37.5%) in the placebo group reported TEAEs that were considered IMP-related by the investigator.

One study participant (14.3%) in the rotigotine 3mg/24h group reported a serious TEAE. In the placebo group, 1 study participant (12.5%) reported a TEAE that led to study discontinuation, and 1 study participant (12.5%) reported a TEAE that led to permanent withdrawal of IMP; both of these incidences were reported by the same study participant.

No deaths were reported during the study.

Most common TEAEs

MedDRA (version 25.1) SOC PT	Treatment group			Total Rotigotine N=15 n (%)
	Placebo N=8 n (%)	Rotigotine 2mg/24h N=8 n (%)	Rotigotine 3mg/24h N=7 n (%)	
Any TEAE	7 (87.5)	7 (87.5)	5 (71.4)	12 (80.0)
Gastrointestinal disorders	3 (37.5)	2 (25.0)	1 (14.3)	3 (20.0)
Abdominal pain	2 (25.0)	0	0	0
Nausea	1 (12.5)	2 (25.0)	0	2 (13.3)
Vomiting	1 (12.5)	2 (25.0)	0	2 (13.3)
General disorders and administration site conditions	2 (25.0)	5 (62.5)	2 (28.6)	7 (46.7)
Application site erythema	1 (12.5)	4 (50.0)	1 (14.3)	5 (33.3)
Application site pruritus	0	3 (37.5)	1 (14.3)	4 (26.7)
Infections and infestations	3 (37.5)	0	3 (42.9)	3 (20.0)
Upper respiratory tract infection	1 (12.5)	0	3 (42.9)	3 (20.0)
Nasopharyngitis	2 (25.0)	0	0	0
Nervous system disorders	2 (25.0)	1 (12.5)	3 (42.9)	4 (26.7)
Headache	0	1 (12.5)	1 (14.3)	2 (13.3)
Dizziness	2 (25.0)	0	1 (14.3)	1 (6.7)
Skin and subcutaneous tissue disorders	1 (12.5)	3 (37.5)	2 (28.6)	5 (33.3)
Skin irritation	0	2 (25.0)	0	2 (13.3)
Pruritus	0	2 (25.0)	1 (14.3)	3 (20.0)

MedDRA=Medical Dictionary for Regulatory Activities; PT=preferred term; SOC=system organ class; SS=Safety Set; TEAE=treatment-emergent adverse event
Note: n=number of study participants reporting at least 1 TEAE within the SOC/PT.

In the total rotigotine group, the most commonly reported TEAEs by PT were application site erythema (5 study participants [33.3%]), application site pruritus (4 study participants [26.7%]), pruritus (3 study participants [20.0%]), and upper respiratory tract infection (3 study participants [20.0%]); no other TEAEs were reported by >2 study participants.

In the placebo group, the most commonly reported TEAEs were abdominal pain, dizziness, and nasopharyngitis (2 study participants [25.0%] each); no other TEAEs were reported by >1 study participant.

TEAEs by maximum intensity

In the total rotigotine group, 2 study participants (13.3%) reported severe TEAEs that were not considered IMP related by the investigator and were resolved: 1 study participant in the rotigotine 2mg/24 group (diarrhoea) and 1 study participant in the rotigotine 3mg/24h group (Type 2 diabetes mellitus).

In the placebo group, 1 study participant (12.5%) reported a severe TEAE of vertigo that was considered IMP-related by the investigator and resolved.

IMP-related TEAEs

In the total rotigotine group, 9 study participants (60.0%) reported IMP-related TEAEs. The most reported IMP-related TEAEs were application site erythema (5 study participants [33.3%]), application site pruritus (4 study participants [26.7%]), pruritus (3 study participants [20.0%]), and skin irritation (2 study participants [13.3%]); no other IMP-related TEAE was reported by >1 study participant.

In the placebo group, 3 study participants (37.5%) reported IMP-related TEAEs; no IMP-related TEAE was reported by >1 study participant.

Deaths

No deaths were reported during the study.

Other serious AEs

One study participant (14.3%) in the rotigotine 3mg/24h group reported a serious TEAE of Type 2 diabetes mellitus. The TEAE was of severe intensity, was not considered IMP related by the investigator, and resolved.

Discontinuation due to AEs

No study discontinuations due to TEAEs were reported in the total rotigotine group.

One study participant (12.5%) in the placebo group reported a TEAE leading to study discontinuation and permanent withdrawal of IMP. The study participant reported a TEAE of moderate insomnia, which was not serious and not considered IMP-related by the investigator.

Clinical laboratory evaluation

Overall, there were no clinically relevant mean changes from Baseline or notable shift patterns observed for any of the haematology, endocrinology, or clinical chemistry parameters evaluated during the study for the SS. In addition, no clinically relevant changes in urinalysis parameters were observed for the SS.

No study participants in the SS met the criteria for potential Hy's Law, defined as ≥3xULN ALT or AST with coexisting ≥2xULN total bilirubin in the absence of ≥2xULN ALP, with no alternative explanation for the biochemical abnormality.

Other observations related to safety

Overall, there were no clinically relevant findings related to ECGs, vital signs, physical and neurological examinations, mMIDI data, or menstrual function and libido assessment for the SS.

Eight study participants in the SS reported suicidal ideation at their Screening Visit. No study participants reported suicidal ideation at any post-Baseline visits.

2.3.3. Discussion on clinical aspects

SP1006 was a Phase 3, remote, double-blind, randomised, adaptive placebo-controlled study of fixed dose administration of the rotigotine transdermal system. The study was conducted in adolescents (13 to 17 years of age) with idiopathic RLS. Study participants were randomised to 1 of 3 treatment groups: rotigotine 2mg/24h, rotigotine 3mg/24h, or placebo.

A total of 138 study participants were planned to be randomised in SP1006 per the protocol; however, over a period of 3.5 years, only 23 study participants were randomised in the study and only 18 completed the study. Due to unsatisfactory enrolment, SP1006 was prematurely terminated by UCB.

A descriptive summary of a subset of efficacy data were provided. No statistical tests of efficacy data were performed.

Improvements in IRLS sum score, CGI Item 1 score, and RLS-6 score were observed in the rotigotine 2mg/24h, rotigotine 3mg/24h, and placebo groups over the 12-week Maintenance Period, with the largest mean differences in these efficacy parameters occurring in the rotigotine 2mg/24h group.

The safety profile was consistent with previous studies of the rotigotine transdermal system, and no new or unexpected safety concerns were observed. There were no deaths, only 1 serious TEAE that was not related to rotigotine, and no study participants who received rotigotine discontinued from the study due to an AE. These safety data suggest that both rotigotine 2mg/24hr and rotigotine 3mg/24hr were well tolerated in adolescent study participants with idiopathic RLS.

The safety profile of the adolescent participants who received rotigotine transdermal system treatment was consistent with the established safety profile of rotigotine transdermal system in adults. No new safety concerns were identified in these participants and the results of the study do not impact the current benefit-risk balance of rotigotine transdermal system.

Because of the small number of study participants, the efficacy and safety results from this study should be interpreted with caution.

3. CHMP overall conclusion and recommendation

Paediatric RLS is a rare disorder and may be self-limited if related to a transient comorbidity, such as iron deficiency. The difficulties reported by the MAH to enrol study participants in this study are understood.

The safety profile of the adolescent participants who received rotigotine transdermal system treatment was consistent with the established safety profile of rotigotine transdermal system in adults. No new safety concerns were identified in this study. These safety data suggest that both rotigotine 2mg/24hr and rotigotine 3mg/24hr were well tolerated in the adolescent study participants with idiopathic RLS. However, due to the small number of subjects, the findings of this study should be interpreted with caution.

The results of SP1006 are being submitted in accordance with Article 46 of Regulation (EC) No 1901/2006 (The Paediatric Regulation). No changes to the approved EU Product Information (PI) for NEUPRO are being proposed based on SP1006 results.

☒ PAM Fulfilled

No regulatory action required