



Clinical trial results:

Efficacy, Safety, Tolerability and Pharmacokinetics of EXN-32 and EXN-44 in patients with Parkinson's Disease experiencing motor fluctuations

Summary

EudraCT number	2017-000262-30
Trial protocol	IT
Global end of trial date	30 May 2018

Results information

Result version number	v1 (current)
This version publication date	28 June 2021
First version publication date	28 June 2021

Trial information

Trial identification

Sponsor protocol code	EXN-32-CD-002
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	NA: NA

Notes:

Sponsors

Sponsor organisation name	Dr. Reddy's Laboratories Ltd.
Sponsor organisation address	8-2-337 Road no. 3, Banjara Hills , Hyderabad , India, 500034
Public contact	Clinical Operation, TFS Trial Form Support, +39 068076072, paola.tiradritti@tfscro.com
Scientific contact	Clinical Operation, TFS Trial Form Support, +39 068076072, paola.tiradritti@tfscro.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	22 May 2019
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	30 May 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate following pharmacodynamic properties of EXN-32 and EXN-44, and compare them with SINEMET®.

Time to resolution of "OFF" period following administration of EXN-32 and EXN-44.

Duration of "ON" period following dosing.

Proportion of patients evaluated to be in the "ON" state at 05, 15, 30, 60, 90, and 120 minutes after administration of EXN-32, and EXN-44.

UPDRS Part III motor score at 10, 20, 30, 60, 90, and 120 minutes after each dose of study medication in each period.

To estimate the pharmacokinetic profiles of levodopa and carbidopa.

Maximum plasma concentration (C_{max}).

Time to reach maximum plasma concentration (T_{max}).

Area under the concentration-time curve from time zero to last measured concentration (AUC_{0-t}).

The secondary objective of the trial is to evaluate PK/PD relationship, safety and tolerability of EXN-32 and EXN-44

Protection of trial subjects:

All subjects will have a full safety evaluation at the end of study visit. For all the subjects, an end of treatment visit was scheduled 7 days after the last dose of study medication. During this visit, clinical laboratory test, urine analysis, urine pregnancy test (for women of child bearing potential only), vital signs, 12-lead ECG, and adverse events were monitored for all the subjects.

Background therapy:

Parkinson's disease is a progressive disorder in which the patient's response to pharmacotherapy decreases overtime, resulting in various motor complications such as inadequate dopaminergic tone ("OFF" time and dose failures) and excess dopaminergic tone (dyskinesia). The prevalence of motor fluctuations, or movement problems, is reported to be as high as 60 - 90% in patients after 5 - 10 years of treatment. There are several non-levodopa therapies like dopamine agonists, MAO-B inhibitors and catechol-O-methyltransferase (COMT) inhibitors available in the market for treatment of Parkinson's disease, but levodopa is the most effective oral pharmacotherapy, and is typically administered in combination with a DDCI inhibitor such as carbidopa.

Evidence for comparator: -

Actual start date of recruitment	20 April 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Italy: 18
Worldwide total number of subjects	18
EEA total number of subjects	18

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	16
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients (male or female, aged 40 years or higher) receiving stable regimen of levodopa for at least one month before screening with or without concomitant therapy with dopamine agonists, COMT inhibitors, MAO-B inhibitors, or amantadine and with at least 3 "OFF" periods per day based on their medical records were selected.

Pre-assignment

Screening details:

25 patients were screened based on IC/EC and 18 patients were selected and randomized. Of the 18 patients, 17 patients completed the study. There were 3 treatment periods; in each period, the patients were treated with 3 doses of either A (EXN-32), B (EXN-44) or C (SINEMET) at 3 hours interval. The treatment sequences were ABC, BCA and CAB.

Period 1

Period 1 title	Treatment Period I
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Data analyst ^[1]

Blinding implementation details:

The evaluator for PD assessments ("ON" and "OFF" assessments) and the laboratory staff in charge of bioanalysis of plasma samples (PK concentration measurements) were blinded to the randomization code.

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment A

Arm description:

1st dose EXN-32, 2nd dose EXN-32, and 3rd dose EXN-32. Each administration will be 5 mL of EXN-32 leading to a dose of 15 / 150 mg of carbidopa / levodopa. Dosing interval is 3 hours after administration of each dose.

Arm type	Experimental
Investigational medicinal product name	EXN-32 (Carbidopa and Levodopa) Oral Suspension
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for oral suspension
Routes of administration	Oral use

Dosage and administration details:

3 doses to be administered at dosing intervals of 3 hours after each dose

Arm title	Treatment B
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Arm description:

1st dose EXN-44, 2nd dose SINEMET®, and 3rd dose EXN-44. Each administration of EXN-44 will be 6.5 mL leading to a dose of 195 mg of levodopa. Dosing interval is of 3 hours after administration of each dose.

Arm type	Experimental
Investigational medicinal product name	EXN-44 (Levodopa) Oral Suspension
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for oral suspension
Routes of administration	Oral use

Dosage and administration details:

To be administered at intervals of 3 hours

Arm title	Treatment C
Arm description: 1st dose SINEMET®, 2nd dose SINEMET®, and 3rd dose SINEMET®. Dosing interval is 3 hours after administration of each dose.	
Arm type	Experimental
Investigational medicinal product name	SINEMET
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 3 doses to be administered at dosing interval of 3 hours after each dose.	
Notes: [1] - The roles blinded appear inconsistent with a simple blinded trial. Justification: The data analyst were blinded in the clinical trial.	

Number of subjects in period 1	Treatment A	Treatment B	Treatment C
Started	8	5	5
Completed	8	5	5

Period 2	
Period 2 title	Treatment Period II
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Data analyst ^[2]
Blinding implementation details: The evaluator for PD assessments ("ON" and "OFF" assessments) and the laboratory staff in charge of bioanalysis of plasma samples (PK concentration measurements) were blinded to the randomization code.	

Arms	
Are arms mutually exclusive?	Yes
Arm title	Treatment B
Arm description: 1st dose EXN-44, 2nd dose SINEMET®, and 3rd dose EXN-44. Each administration of EXN-44 will be 6.5 mL leading to a dose of 195 mg of levodopa. Dosing interval is 3 hours after administration of each dose.	
Arm type	Experimental
Investigational medicinal product name	EXN-44 (Levodopa) Oral Suspension
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for oral suspension
Routes of administration	Oral use
Dosage and administration details: To be administered at intervals of 3 hours	

Arm title	Treatment C
Arm description: 1st dose SINEMET®, 2nd dose SINEMET®, and 3rd dose SINEMET®. Dosing interval is 3 hours after administration of each dose.	
Arm type	Experimental
Investigational medicinal product name	SINEMET
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 3 doses to be administered at dosing interval of 3 hours after each dose.	

Arm title	Treatment A
Arm description: 3 doses EXN-32, each administration will be 5 mL of EXN-32 leading to a dose of 15 / 150 mg of carbidopa / levodopa. Dosing interval is of 3 hours after administration of each dose	
Arm type	Experimental
Investigational medicinal product name	EXN-32 (Carbidopa and Levodopa) Oral Suspension
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for oral suspension
Routes of administration	Oral use
Dosage and administration details: 3 doses to be administered at dosing intervals of 3 hours after each dose	
Notes: [2] - The roles blinded appear inconsistent with a simple blinded trial. Justification: The data analyst were blinded in the clinical trial.	

Number of subjects in period 2 ^[3]	Treatment B	Treatment C	Treatment A
Started	8	5	4
Completed	8	5	4

Notes:
[3] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: The arms are mutually exclusive arms

Period 3	
Period 3 title	Treatment Period III
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Data analyst ^[4]

Blinding implementation details:
The evaluator for PD assessments ("ON" and "OFF" assessments) and the laboratory staff in charge of bioanalysis of plasma samples (PK concentration measurements) were blinded to the randomization code.

Arms	
Are arms mutually exclusive?	Yes

Arm title	Treatment C
Arm description: 1st dose SINEMET®, 2nd dose SINEMET®, and 3rd dose SINEMET. Dosing interval is 3 hours after administration of each dose.	
Arm type	Experimental
Investigational medicinal product name	SINEMET
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: 3 doses to be administered at dosing interval of 3 hours after each dose.	

Arm title	Treatment A
Arm description: 3 doses of EXN-32, each administration will be 5 mL of EXN-32 leading to a dose of 15 / 150 mg of carbidopa / levodopa. Dosing interval is of 3 hours after administration of each dose.	
Arm type	Experimental
Investigational medicinal product name	EXN-32 (Carbidopa and Levodopa) Oral Suspension
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for oral suspension
Routes of administration	Oral use
Dosage and administration details: 3 doses to be administered at dosing intervals of 3 hours after each dose	

Arm title	Treatment B
Arm description: 1st dose EXN-44, 2nd dose SINEMET®, and 3rd dose EXN-44. Each administration of EXN-44 will be 6.5 mL leading to a dose of 195 mg of levodopa. Dosing interval is of 3 hours after administration of each dose.	
Arm type	Experimental
Investigational medicinal product name	EXN-44 (Levodopa) Oral Suspension
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for oral suspension
Routes of administration	Oral use
Dosage and administration details: To be administered at intervals of 3 hours	

Notes:
[4] - The roles blinded appear inconsistent with a simple blinded trial.
Justification: The data analyst were blinded in the clinical trial.

Number of subjects in period 3	Treatment C	Treatment A	Treatment B
Started	8	5	4
Completed	8	5	4

Baseline characteristics

Reporting groups

Reporting group title	Treatment Period I
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Reporting group description: -

Reporting group values	Treatment Period I	Total	
Number of subjects	18	18	
Age categorical			
Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	16	16	
From 65-84 years	2	2	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	65.61		
standard deviation	± 10.32	-	
Gender categorical			
Units: Subjects			
Female	7	7	
Male	11	11	

End points

End points reporting groups

Reporting group title	Treatment A
Reporting group description: 1st dose EXN-32, 2nd dose EXN-32, and 3rd dose EXN-32. Each administration will be 5 mL of EXN-32 leading to a dose of 15 / 150 mg of carbidopa / levodopa. Dosing interval is 3 hours after administration of each dose.	
Reporting group title	Treatment B
Reporting group description: 1st dose EXN-44, 2nd dose SINEMET®, and 3rd dose EXN-44. Each administration of EXN-44 will be 6.5 mL leading to a dose of 195 mg of levodopa. Dosing interval is of 3 hours after administration of each dose.	
Reporting group title	Treatment C
Reporting group description: 1st dose SINEMET®, 2nd dose SINEMET®, and 3rd dose SINEMET®. Dosing interval is 3 hours after administration of each dose.	
Reporting group title	Treatment B
Reporting group description: 1st dose EXN-44, 2nd dose SINEMET®, and 3rd dose EXN-44. Each administration of EXN-44 will be 6.5 mL leading to a dose of 195 mg of levodopa. Dosing interval is 3 hours after administration of each dose.	
Reporting group title	Treatment C
Reporting group description: 1st dose SINEMET®, 2nd dose SINEMET®, and 3rd dose SINEMET®. Dosing interval is 3 hours after administration of each dose.	
Reporting group title	Treatment A
Reporting group description: 3 doses EXN-32, each administration will be 5 mL of EXN-32 leading to a dose of 15 / 150 mg of carbidopa / levodopa. Dosing interval is of 3 hours after administration of each dose	
Reporting group title	Treatment C
Reporting group description: 1st dose SINEMET®, 2nd dose SINEMET®, and 3rd dose SINEMET. Dosing interval is 3 hours after administration of each dose.	
Reporting group title	Treatment A
Reporting group description: 3 doses of EXN-32, each administration will be 5 mL of EXN-32 leading to a dose of 15 / 150 mg of carbidopa / levodopa. Dosing interval is of 3 hours after administration of each dose.	
Reporting group title	Treatment B
Reporting group description: 1st dose EXN-44, 2nd dose SINEMET®, and 3rd dose EXN-44. Each administration of EXN-44 will be 6.5 mL leading to a dose of 195 mg of levodopa. Dosing interval is of 3 hours after administration of each dose.	
Subject analysis set title	Treatment A, EXN-32 (For Carbidopa)
Subject analysis set type	Full analysis
Subject analysis set description: The PK parameters reported here is after the third dose EXN-32	
Subject analysis set title	Treatment B, EXN-44 (For Carbidopa)
Subject analysis set type	Full analysis
Subject analysis set description: The PK parameters reported here is after the second dose, treatment being- SINEMET	
Subject analysis set title	Treatment C, SINEMET (For Carbidopa)
Subject analysis set type	Full analysis

Subject analysis set description:

The PK parameters reported here is after the third dose of SINEMET

Subject analysis set title	Treatment A, EXN-32 (For Levodopa)
Subject analysis set type	Full analysis

Subject analysis set description:

The PK parameters reported here is after the third dose of EXN-32

Subject analysis set title	Treatment B, EXN-44 (For Levodopa)
Subject analysis set type	Full analysis

Subject analysis set description:

The PK parameters reported here is at the third dose, treatment being EXN-44

Subject analysis set title	Treatment C, SINEMET (For Levodopa)
Subject analysis set type	Full analysis

Subject analysis set description:

The PK parameters reported here is after the third dose of SINEMET

Primary: Time to resolution of "OFF" period following dosing

End point title	Time to resolution of "OFF" period following dosing ^[1]
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End point description:

End point type	Primary
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End point timeframe:

Assessed at pre-dose, and at 05, 15, 30, 60, 90, and 120 minutes following each dose

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The analysis set used was modified intent to treat population.

End point values	Treatment A	Treatment B	Treatment C	Treatment B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	5	5	8
Units: minutes				
arithmetic mean (standard deviation)	30.83 (± 16.69)	39.00 (± 24.41)	32.67 (± 14.22)	44.94 (± 26.28)

End point values	Treatment C	Treatment A	Treatment C	Treatment A
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	4	8	5
Units: minutes				
arithmetic mean (standard deviation)	69.33 (± 34.79)	14.58 (± 7.98)	62.29 (± 38.46)	33.00 (± 22.09)

End point values	Treatment B			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: minutes				
arithmetic mean (standard deviation)	33.75 (± 34.67)			

Statistical analyses

No statistical analyses for this end point

Primary: Duration of "ON" periods irrespective of Dyskinesia

End point title	Duration of "ON" periods irrespective of Dyskinesia ^[2]
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End point description:

End point type	Primary
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End point timeframe:

Assessed at pre-dose, and at 05, 15, 30, 60, 90, and 120 minutes following each dose

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The analysis set used was modified intent to treat population.

End point values	Treatment A	Treatment B	Treatment C	Treatment B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	5	5	8
Units: Minutes				
arithmetic mean (standard deviation)	80.42 (± 22.64)	76.00 (± 24.41)	80.33 (± 16.85)	68.13 (± 31.02)

End point values	Treatment C	Treatment A	Treatment C	Treatment A
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	4	8	5
Units: Minutes				
arithmetic mean (standard deviation)	42.67 (± 37.05)	100.42 (± 7.98)	47.71 (± 32.89)	80.00 (± 25.85)

End point values	Treatment B			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: Minutes				
arithmetic mean (standard deviation)	81.25 (± 34.67)			

Statistical analyses

No statistical analyses for this end point

Primary: Unified Parkinson's Disease Rating Scale (UPDRS) Part III Motor score

End point title	Unified Parkinson's Disease Rating Scale (UPDRS) Part III Motor score ^[3]
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End point description:

End point type	Primary
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End point timeframe:

Assessed at 10, 20, 30, 60, 90 and 120 minutes after each dose medication in each period. The results provided is assessed 120 minutes after dose administration in each period.

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The analysis set used was modified intent to treat population.

End point values	Treatment A	Treatment B	Treatment C	Treatment B
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	5	5	8
Units: change from baseline				
arithmetic mean (standard deviation)	-18.44 (± 10.01)	-15.70 (± 14.32)	-15.90 (± 12.26)	-14.13 (± 11.02)

End point values	Treatment C	Treatment A	Treatment C	Treatment A
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	4	8	5
Units: change from baseline				
arithmetic mean (standard deviation)	-8.80 (± 3.81)	-14.58 (± 1.64)	-9.71 (± 6.58)	-15.80 (± 4.27)

End point values	Treatment B			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: change from baseline				
arithmetic mean (standard deviation)	-20.25 (± 5.44)			

Statistical analyses

No statistical analyses for this end point

Primary: Cmax (Carbidopa)

End point title	Cmax (Carbidopa) ^[4]
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End point description:

End point type	Primary
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End point timeframe:

The blood samples were collected at pre-dose and at 5, 15, 30, 60, 90 and 120 minutes after each dose during each treatment period

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The analysis set used was modified intent to treat population. ANOVA with 5% level of significance was employed.

End point values	Treatment A, EXN-32 (For Carbidopa)	Treatment B, EXN-44 (For Carbidopa)	Treatment C, SINEMET (For Carbidopa)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	16	16	13	
Units: nanogram/milliliter				
arithmetic mean (standard deviation)	41.472 (\pm 26.06)	20.350 (\pm 10.46)	34.517 (\pm 15.87)	

Statistical analyses

No statistical analyses for this end point

Primary: Tmax (Carbidopa)

End point title	Tmax (Carbidopa) ^[5]
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End point description:

End point type	Primary
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End point timeframe:

The blood samples were collected at pre-dose and at 5, 15, 30, 60, 90 and 120 minutes after each dose during each treatment period

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The analysis set used was modified intent to treat population. ANOVA with 5% level of significance was employed.

End point values	Treatment A, EXN-32 (For Carbidopa)	Treatment B, EXN-44 (For Carbidopa)	Treatment C, SINEMET (For Carbidopa)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	16	16	13	
Units: minutes				
arithmetic mean (full range (min-max))	62.50 (0.00 to 95.00)	105.00 (60.00 to 135.00)	60.00 (0.00 to 130.00)	

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Curve (AUC(0-t))- Carbidopa

End point title Area Under the Curve (AUC(0-t))- Carbidopa^[6]

End point description:

End point type Primary

End point timeframe:

The blood samples were collected at pre-dose and at 5, 15, 30, 60, 90 and 120 minutes after each dose during each treatment period

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The analysis set used was modified intent to treat population. ANOVA with 5% level of significance was employed.

End point values	Treatment A, EXN-32 (For Carbidopa)	Treatment B, EXN-44 (For Carbidopa)	Treatment C, SINEMET (For Carbidopa)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	16	16	13	
Units: nanogram- minute/ milliliter				
arithmetic mean (standard deviation)	3642.7 (± 2641.46)	1567.6 (± 981.80)	3370.2 (± 1578.30)	

Statistical analyses

No statistical analyses for this end point

Primary: Cmax (Levodopa)

End point title Cmax (Levodopa)^[7]

End point description:

End point type Primary

End point timeframe:

The blood samples were collected at pre-dose and at 5, 15, 30, 60, 90 and 120 minutes after each dose during each treatment period

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The analysis set used was modified intent to treat population. ANOVA with 5% level of significance was employed.

End point values	Treatment A, EXN-32 (For Levodopa)	Treatment B, EXN-44 (For Levodopa)	Treatment C, SINEMET (For Levodopa)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	16	16	13	
Units: nanogram/ milliliter				
arithmetic mean (standard deviation)	1456.275 (± 615.53)	1487.935 (± 774.63)	1022.843 (± 515.64)	

Statistical analyses

No statistical analyses for this end point

Primary: Tmax (Levodopa)

End point title Tmax (Levodopa)^[8]

End point description:

End point type Primary

End point timeframe:

The blood samples were collected at pre-dose and at 5, 15, 30, 60, 90 and 120 minutes after each dose during each treatment period

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The analysis set used was modified intent to treat population. ANOVA with 5% level of significance was employed.

End point values	Treatment A, EXN-32 (For Levodopa)	Treatment B, EXN-44 (For Levodopa)	Treatment C, SINEMET (For Levodopa)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	16	16	13	
Units: minutes				
arithmetic mean (full range (min-max))	30.00 (15.00 to 95.00)	30.00 (15.00 to 120.00)	60.00 (0.00 to 120.00)	

Statistical analyses

No statistical analyses for this end point

Primary: Area Under the Curve (AUC(0-t))- Levodopa

End point title Area Under the Curve (AUC(0-t))- Levodopa^[9]

End point description:

End point type Primary

End point timeframe:

The blood samples were collected at pre-dose and at 5, 15, 30, 60, 90 and 120 minutes after each dose during each treatment period

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The analysis set used was modified intent to treat population. ANOVA with 5% level of significance was employed.

End point values	Treatment A, EXN-32 (For Levodopa)	Treatment B, EXN-44 (For Levodopa)	Treatment C, SINEMET (For Levodopa)	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	16	16	13	
Units: nanogram minute/ milliliter				
arithmetic mean (standard deviation)	111841.5 (± 50923.61)	107661.9 (± 57305.41)	78365.4 (± 36179.78)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

30 days

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	20.1
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Frequency threshold for reporting non-serious adverse events: 5 %

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: No serious adverse events were observed

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported