



## 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 |
|-----------------------|---------------|

##### 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<sub>max</sub>).

Time to reach maximum plasma concentration (T<sub>max</sub>).

Area under the concentration-time curve from time zero to last measured concentration (AUC<sub>0-t</sub>).

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:

| <b>Subjects enrolled per age group</b>    |    |
|-------------------------------------------|----|
| 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 <sup>[1]</sup> |

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         |
| <b>Arm title</b>             | 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

|                  |             |
|------------------|-------------|
| <b>Arm title</b> | 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

|                                                                                                                                                           |              |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------|--------------|
| <b>Arm title</b>                                                                                                                                          | Treatment C  |
| Arm description:<br>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:<br>3 doses to be administered at dosing interval of 3 hours after each dose.                                           |              |
| Notes:<br>[1] - The roles blinded appear inconsistent with a simple blinded trial.<br>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           |

|                                                                                                                                                                                                                                               |                             |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------|
| <b>Period 2</b>                                                                                                                                                                                                                               |                             |
| Period 2 title                                                                                                                                                                                                                                | Treatment Period II         |
| Is this the baseline period?                                                                                                                                                                                                                  | No                          |
| Allocation method                                                                                                                                                                                                                             | Randomised - controlled     |
| Blinding used                                                                                                                                                                                                                                 | Single blind                |
| Roles blinded                                                                                                                                                                                                                                 | Data analyst <sup>[2]</sup> |
| Blinding implementation details:<br>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. |                             |

|                                                                                                                                                                                                                                  |                                    |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------|
| <b>Arms</b>                                                                                                                                                                                                                      |                                    |
| Are arms mutually exclusive?                                                                                                                                                                                                     | Yes                                |
| <b>Arm title</b>                                                                                                                                                                                                                 | Treatment B                        |
| Arm description:<br>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:<br>To be administered at intervals of 3 hours                                                                                                                                                 |                                    |

|                                                                                                                                                |              |
|------------------------------------------------------------------------------------------------------------------------------------------------|--------------|
| <b>Arm title</b>                                                                                                                               | Treatment C  |
| Arm description:<br>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:<br>3 doses to be administered at dosing interval of 3 hours after each dose.                                |              |

|                                                                                                                                                                                                          |                                                 |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------|
| <b>Arm title</b>                                                                                                                                                                                         | Treatment A                                     |
| Arm description:<br>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:<br>3 doses to be administered at dosing intervals of 3 hours after each dose                                                                                          |                                                 |
| Notes:<br>[2] - The roles blinded appear inconsistent with a simple blinded trial.<br>Justification: The data analyst were blinded in the clinical trial.                                                |                                                 |

| <b>Number of subjects in period 2<sup>[3]</sup></b> | 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

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

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.

|                              |     |
|------------------------------|-----|
| <b>Arms</b>                  |     |
| Are arms mutually exclusive? | Yes |

|                                                                                                                                               |              |
|-----------------------------------------------------------------------------------------------------------------------------------------------|--------------|
| <b>Arm title</b>                                                                                                                              | Treatment C  |
| Arm description:<br>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:<br>3 doses to be administered at dosing interval of 3 hours after each dose.                               |              |

|                                                                                                                                                                                                              |                                                 |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------|
| <b>Arm title</b>                                                                                                                                                                                             | Treatment A                                     |
| Arm description:<br>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:<br>3 doses to be administered at dosing intervals of 3 hours after each dose                                                                                              |                                                 |

|                                                                                                                                                                                                                                     |                                    |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------|
| <b>Arm title</b>                                                                                                                                                                                                                    | Treatment B                        |
| Arm description:<br>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:<br>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.

| <b>Number of subjects in period 3</b> | Treatment C | Treatment A | Treatment B |
|---------------------------------------|-------------|-------------|-------------|
| Started                               | 8           | 5           | 4           |
| Completed                             | 8           | 5           | 4           |

## Baseline characteristics

### Reporting groups

|                       |                    |
|-----------------------|--------------------|
| Reporting group title | Treatment Period I |
|-----------------------|--------------------|

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<br>(gestational age < 37 wks) | 0                  | 0     |  |
| Newborns (0-27 days)                                  | 0                  | 0     |  |
| Infants and toddlers (28 days-23<br>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:<br>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:<br>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:<br>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:<br>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:<br>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:<br>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:<br>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:<br>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:<br>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:<br>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:<br>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 <sup>[1]</sup> |
|-----------------|--------------------------------------------------------------------|

End point description:

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

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 <sup>[2]</sup> |
|-----------------|--------------------------------------------------------------------|

End point description:

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

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 <sup>[3]</sup> |
|-----------------|--------------------------------------------------------------------------------------|

End point description:

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

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) <sup>[4]</sup> |
|-----------------|---------------------------------|

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:

[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) <sup>[5]</sup> |
|-----------------|---------------------------------|

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:

[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<sup>[6]</sup>

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)<sup>[7]</sup>

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) <sup>[8]</sup> |
|-----------------|--------------------------------|

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 <sup>[9]</sup> |
|-----------------|----------------------------------------------------------|

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.

| <b>End point values</b>              | Treatment A,<br>EXN-32 (For<br>Levodopa) | Treatment B,<br>EXN-44 (For<br>Levodopa) | Treatment C,<br>SINEMET (For<br>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 (±<br>50923.61)                 | 107661.9 (±<br>57305.41)                 | 78365.4 (±<br>36179.78)                   |  |

### Statistical analyses

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No statistical analyses for this end point



## Adverse events

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### Adverse events information<sup>[1]</sup>

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Timeframe for reporting adverse events:

30 days

|                 |            |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

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### Dictionary used

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|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

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|                    |      |
|--------------------|------|
| Dictionary version | 20.1 |
|--------------------|------|

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Frequency threshold for reporting non-serious adverse events: 5 %

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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

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported