

Screening Visits

You will be asked to attend two Screening Visits. The procedures and assessments completed at these visits will help study doctors and staff members determine if you can participate in this study.

In the morning before attending the clinic for your second visit, please do not take your normal Levodopa dose and any other Parkinson’s Disease (PD) medication (you can take it before midnight prior to this Screening Visit). You will then receive your Levodopa dose at the clinic visit.

These visits involve:

- Reading and signing a written informed consent form
- Review of the entry criteria for the study
- Movement disorders assessment
- PD assessments
- Review of medical history and demographics
- Complete physical exam, including looking inside of your mouth and throat
- BMI, weight and height assessments
- Vital signs measurements
- Electrocardiogram assessment
- Collection of clinical laboratory tests
- Mental and behaviour assessments
- Subject “OFF” versus “ON” training*
- Take dose of Levodopa and confirm a response to medication*
- PD and movement disorder assessments before and after Levodopa dosing*
- Confirmation of “OFF” or “ON” by both Investigator and subject*
- Post-dose assessment of involuntary muscle movements, like tics (Dyskinesia)*
- Review of side effects or adverse events
- Review of current and previous medication

*Procedures with * will be completed only at SV2. All other procedures can be completed at either visit.*

PART A: Titration Visits

You are requested to take several doses of study drug in order of increasing strength to determine which dose works best for you when treating your “OFF” episodes. This process is referred to as ‘Titration’. You will undergo titration for APL-130277 and apomorphine injection. You will go through the titration for one study drug and then the other.

During your first titration visit you will be assigned the order of treatment you will receive. This determines whether the study doctor will find your optimal dose of APL-130277 first, followed by apomorphine injection, or apomorphine injection first, followed by APL-130277.

Titration Visit 1 for both study drugs:

You will be required to arrive at clinic in an “OFF” state. You should stop taking your PD medication by midnight the night before, and then withhold any other PD medications before you take study drug.

APL-130277:

If the first dose on Titration Visit 1 is **not** effective in achieving a full “ON” response, you will resume your regular PD medications. You will take an increased dose of study drug the next morning at home and will continue to repeat the process until you reach the most effective dose to treat your “OFF” episodes. The study staff will call to monitor your response every day. Once you reach the most effective dose, you will be asked to return to clinic. You will also complete a daily home dosing diary.

Apomorphine Injection:

If the first dose on Titration Visit 1 is **not** effective, you will receive an increased dose around an hour later. This may be repeated once more on Titration Visit 1 (up to a total of 3 doses). If the third dose is not fully effective, you will be asked to return to clinic the following day to receive up to 2 further doses.

If you are currently taking apomorphine injections, then the titration phase would begin at the dose you are currently on.

These visits involve:

- Abbreviated physical exam, including looking inside your mouth and throat and injection site exam
- Vital signs measurements (before taking the study drug and 60 minutes after)
- Electrocardiogram assessment (before taking the study drug and 50 minutes after)
- Movement assessments (before taking the study drug and at 15, 30, 60, 90 and 120 minutes after)
- In-Clinic Dosing of study Drug
- Confirm “OFF” or “ON”

PART A: Titration Visits - continued

- Post-dose assessment of involuntary muscle movements, like tics (Dyskinesia)
- Study medication dispensation for home dosing
- Receive Self-administration Training
- Home dosing diary training
- Receive/return home dosing diary
- Mental and behaviour questionnaires and assessments
- Review of any side effects or adverse events
- Review of previous and current medication

The effective dose of each study drug will used to treat your “OFF” episodes in PART B.

PART B: Clinic Visit 1, 2, 3, 4, 5 and 6 (Days 1, 14, 28, 35, 49 and 63)

During your first visit in Part B you will be assigned which treatment (APL-130277 or apomorphine injection) shall be taken for the first month. The other treatment will then be taken for the second month.

Please remember to stop taking your PD medications by midnight on the evening prior to these visits, and do not take these medications on the morning of these visits.

You will receive a phone call between each of these visits to review any potential side effects, and medications you have taken or are taking.

You will complete a daily Home Dosing diary between visits and an Expanded Home Dosing diary for 3 continuous days before each visit. You will be asked to bring both of these diaries to each of these visits, as well as any used and unused study drug.

These visits involve:

- Abbreviated physical exam
- Vital signs measurements (before taking the study drug and 30 minutes after)
- Electrocardiogram (ECG) assessment (before taking the study drug and 50 minutes after)†
- Collection of Clinical Laboratory Tests**
- Movement assessments (before taking the investigational drug and at 15, 30, 60, 90 and 120 minutes after)
- In-Clinic Dosing of study Drug
- Confirm “OFF” or “ON”

PART B: Clinic Visit 1, 2, 3, 4, 5 and 6 (Days 1, 14, 28, 35, 49 and 63) - continued

- Post-dose assessment of involuntary muscle movements, like tics (Dyskinesia)
- Receive Self-administration Training, if needed**
- Dispensation of study medication§
- Return study medication†
- Home dosing diary training**
- Receive home dosing diary§
- Return home dosing diary†
- Mental and behaviour questionnaires and assessments
- Questions about involuntary muscle movements, like tics (Dyskinesia)*
- Review of any potential side effects or adverse events
- Review of previous or current medications
- Blood sample collection (certain sites only)†


*Visits 3 and 6 only
**Visits 1 and 4 only
†Visits 1, 3, 4 and 6 only
‡Visits 2, 3, 5 and 6 only
§Visits 1, 2, 4 and 5 only (V2 and V5 only: Unused Study Drug (which was dispensed from IXRS at Clinic Visit 1 and 4, respectively) will be resupplied to the subject)

End of Study Visit

This is the final visit of the study. Please remember to bring any used and unused study drug to this visit.

This visit involves:

- Complete physical exam, including looking in your mouth and throat and injection site exam
- Weight assessment
- Vital signs assessment
- Electrocardiogram assessment
- Collection of Clinical laboratory tests
- Mental and behavioural assessment
- Review of side effects or adverse events
- Review of previous or current medication



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