

Supplemental Material 1. Inclusion and exclusion criteria.**Inclusion criteria**

1. Age between 21 and 80 years
2. Diagnosis of Parkinson's disease according to current criteria [1]
3. Disease duration ≥ 5 years from motor symptoms onset
4. Hoehn & Yahr stage $\leq 4/5$ in ON-phase
5. Capable of complying with study procedures (included lumbar puncture)
 - All male and female participants of childbearing age must agree with their partners to use double-barrier contraception, including the following: (a) complete abstinence; (b) combined oral contraceptive (containing estrogen and progestin) associated with ovulation inhibition; (c) Progestin-only oral contraceptive combined with ovulation inhibition; (d) Intrauterine device; (e) Intrauterine hormone delivery system; (f) Bilateral tubal ligation; (g) Male partner vasectomized.

Exclusion criteria

1. Atypical or Secondary Parkinsonism (e.g. Multiple System Atrophy, Progressive Supranuclear Palsy, Normal Pressure Hydrocephalus, Drug-induced parkinsonism, etc.)
2. PD with Dementia [2, 3]
3. Hoehn & Yahr stage $\geq 4/5$ in ON-phase
4. Deep Brain Stimulation (DBS)
5. Any clinically significant or unstable medical condition, which might place the patient at increased risk or interfere with assessments according to the principal investigators or the clinician delegated by the principal investigator's opinion:
 - previous gastric/duodenal peptic ulcer
 - chronic obstructive pulmonary disease
 - severe liver or kidney changes
 - major cardiovascular event (e.g. myocardial infarction, decompensated congestive heart failure, pulmonary embolism occurring within 6 months prior to the screening visit)
 - neoplastic diseases
6. Bronchial asthma
7. Medical conditions that preclude a safe execution of lumbar puncture according to the investigator's opinion, including (a) treatment with anticoagulants, (b) significant bleeding diathesis (coagulopathy, thrombocytopenia), (c) severe abnormalities or malformations of the lower spine or other spinal pathology, (d) hypersensitivity to lidocaine (if used).
8. Pregnant or breastfeeding women
9. Participants at childbearing age who do not agree to use double-barrier birth control during study participation and for 2 weeks after the last dose of study drug
10. Known hypersensitivity to the active ingredient Ambroxol or any of its excipients.

References:

1. Postuma RB, Berg D, Stern M, Poewe W, Olanow CW, Oertel W, Obeso J, Marek K, Litvan I, Lang AE, Halliday G, Goetz CG, Gasser T, Dubois B, Chan P, Bloem BR, Adler CH, Deuschl G. MDS clinical diagnostic criteria for Parkinson's disease. *Mov Disord*. 2015 Oct;30(12):1591-601. doi: 10.1002/mds.26424.
2. Emre M, Aarsland D, Brown R, Burn DJ, Duyckaerts C, Mizuno Y, Broe GA, Cummings J, Dickson DW, Gauthier S, Goldman J, Goetz C, Korczyn A, Lees A, Levy R, Litvan I, McKeith I, Olanow W, Poewe W, Quinn N, Sampaio C, Tolosa E, Dubois B. Clinical diagnostic criteria for dementia associated with Parkinson's disease. *Mov Disord*. 2007 Sep 15;22(12):1689-707; quiz 1837. doi: 10.1002/mds.21507;
3. Barton B, Grabli D, Bernard B, Czernecki V, Goldman JG, Stebbins G, Dubois B, Goetz CG. Clinical validation of Movement Disorder Society-recommended diagnostic criteria for Parkinson's disease with dementia. *Mov Disord*. 2012 Feb;27(2):248-53. doi: 10.1002/mds.24059