Cost-effectiveness analysis of inhaled levodopa for managing OFF episodes in patients with Parkinson's Disease from a UK payer perspective

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INTRODUCTION

- Parkinson's disease (PD) is a chronic, progressive neurodegenerative disorder characterised by motor symptoms including bradykinesia, tremors, rigidity and postural instability.[1,2]
- PD is the most common neurodegenerative movement disorder, affecting approximately 108-257 per 100,000 individuals in Europe.[1] As PD advances, patients experience fluctuations in symptom control, with OFF time occurring when medication effects wear off.[3]
- Levodopa (LD) and carbidopa (CD) are the mainstays of treatment, but their efficacy diminishes over time due to disease progression and delayed gastric absorption, leading to prolonged OFF periods.
- Presently, the only on-demand therapy options available are apomorphine subcutaneous injections (APO-SC) and sublingual tablets (APO-SL), both of which are associated with side effects and administration challenges.
- There is an unmet need for fast-acting interventions to restore reliable symptom control for patients whose current treatment regimen no longer provides adequate relief.
- Inbrija, an inhaled levodopa (IL) powder, was developed as an on-demand treatment to address OFF periods in PD patients treated with CD/LD. IL is administered via a breath-actuated inhaler, making it non-invasive and bypasses the gastrointestinal tract, enabling rapid symptom relief.

OBJECTIVE

- This study assesses the cost-effectiveness of inhaled levodopa compared to apomorphine sublingual (APO-SL), apomorphine subcutaneous injection (APO-SC), dispersible levodopa (LD) and no on-demand treatment (no-ODT) in a UK population.

METHODS

- **Model structure:** A 12 state Markov model (Figure 1) was developed with health states based on one-hour increments of OFF ranging from ON to OFF10+ plus death, based on the model submitted in the National Institute for Health and Care Excellence (NICE) appraisal, TA934.[5]
- The cost-effectiveness of inhaled levodopa versus standard of care was assessed over a lifetime horizon from a National Health Service (NHS) and Personal Social Services (PSS) perspective. The base case of this cost effectiveness model (CEM) includes a discount rate of 3.5% per annum for costs and outcomes.
- The first year of the model consists of the following cycle lengths aligned with when outcomes were reported in the SPAN-PD clinical trial: 4, 8, 12, 12, and 16 weeks. Following the first year of the model, subsequent cycles are 3-months (13 weeks) and follow the beyond trial model structure (Figure 1b).[5]
- **Clinical inputs:** OFF time reported in pivotal trial SPAN-PD informed inhaled levodopa clinical efficacy; a network meta-analysis informed APO-SL and APO-SC relative efficacy. The natural history of progression (NH) of PD was assumed equal to that of baseline LD-CD treatment, informing efficacy for no-ODT. There is no statistical difference between LD and baseline LD-CD treatment in latency to ON, resulting in an assumption that efficacy of LD is equal to NH given data limitations.
- In the beyond trial period, last observation caried forward was utilized for the short-term extrapolation (years 1-3) with NH progression informing the long-term extrapolation of efficacy outcomes (years 3+). This is in line with NICE TA934.[5]
- Due to a lack of head-to-head trial data, the efficacy and safety of comparators relative to IL has been calculated via an NMA and implemented within the model.
- **Discontinuation:** After discontinuing treatment (discontinuation rates sourced from pivotal clinical trials), patients received a basket of subsequent therapies including APO-SC, duodopa and deep brain stimulation.
- **Cost inputs:** Where possible, unit costs were obtained for the 2023/24 cost year. If 2023/24 cost data was not available, then costs were sourced from earlier sources and were inflated to 2023/2024.

RESULTS

- Base-case results show IL is associated with 6.648 quality-adjusted life years (QALY), and £153,378 total costs (Table 1). IL dominates when compared to dispersible LD and no-ODT.
- As mortality was assumed constant over all health states, there is no difference in life years gained between any comparators.
- The incremental difference in costs between IL and APO-SC or APO-SL is -£8,592 and -£25,008, respectively. The incremental QALYs between IL and APO-SC or APO-SL are -0.166 and -0.108, respectively.
- Under the willingness-to-pay (WTP) of £30,000, the net monetary benefit (NMB) to the NHS of incorporating IL would be £3,602 compared to APO-SC, £21,756 compared to APO-SL, £11,655 compared to dispersible LD and £34,128 compared to no-ODT.
- Results form the probabilistic sensitivity analysis (PSA) align with the base case results demonstrating the robustness of the model. IL was associated with the lowest total costs of all the comparators considered, which a total cost of £157,806 and total QALY benefit of 6.689.
- The incremental cost-effectiveness plane (ICEP) shows the largest proportion of iterations for IL vs no-ODT and dispersible LD are in the south-east quadrant, whereas the largest proportion of iterations for IL vs APO-SC and APO-SL are in the south-west quadrant (Figure 2a).
- Results from the cost-effectiveness acceptability curve (CEAC) show that, at a WTP of £30,000 per QALY, the probability of being cost-effective is 51.5% for IL, 35.6% for APO-SC, 10.9% for dispersible LD, 1.0% for APO-SL, and 1.0% for no-ODT (Figure 2b).
- Results from the one-way sensitivity analyses (OWSA) showed that across each of the comparisons, the most common parameter that the model results were most sensitive to were the daily IL subsequent therapy costs, IL discontinuation rate at week 12, age of patients and average number of administration per day of IL.

Table 1: Base case pairwise results of the economic model

Intervention	Total costs (£)	Total LYG	Total QALYs	Incremental costs (£)	Incremental QALYs	ICER (£/QALY)	NMB (£)
IL	153,378	11.284	6.648	-	-	-	-
APO-SC	161,970	11.284	6.815	-8,592	-0.166	51,657	3,602
APO-SL	178,386	11.284	6.757	-25,008	-0.108	230,670	21,756
Dispersible LD	162,235	11.284	6.555	-8,857	0.094	Dominating	11,665
No-ODT	184,264	11.284	6.540	-30,886	0.108	Dominating	34,128

Figure 1: Structure of the economic model (a) within trial and (b) beyond trial

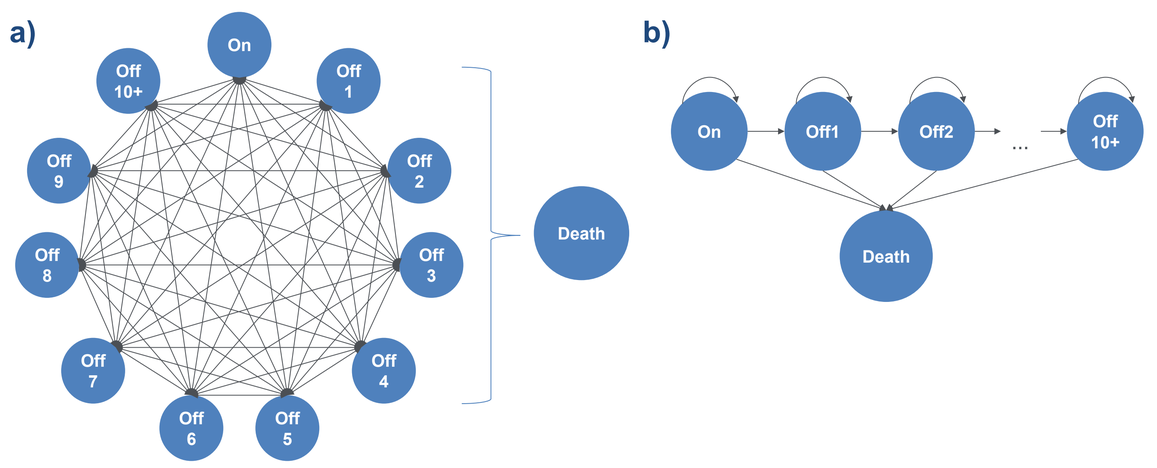


Figure 2a: PSA results plotted on ICEPs showing results of Inhaled levodopa vs APO-SC (i), APO-SL (ii), dispersible LD (iii) and no-ODT (iv)

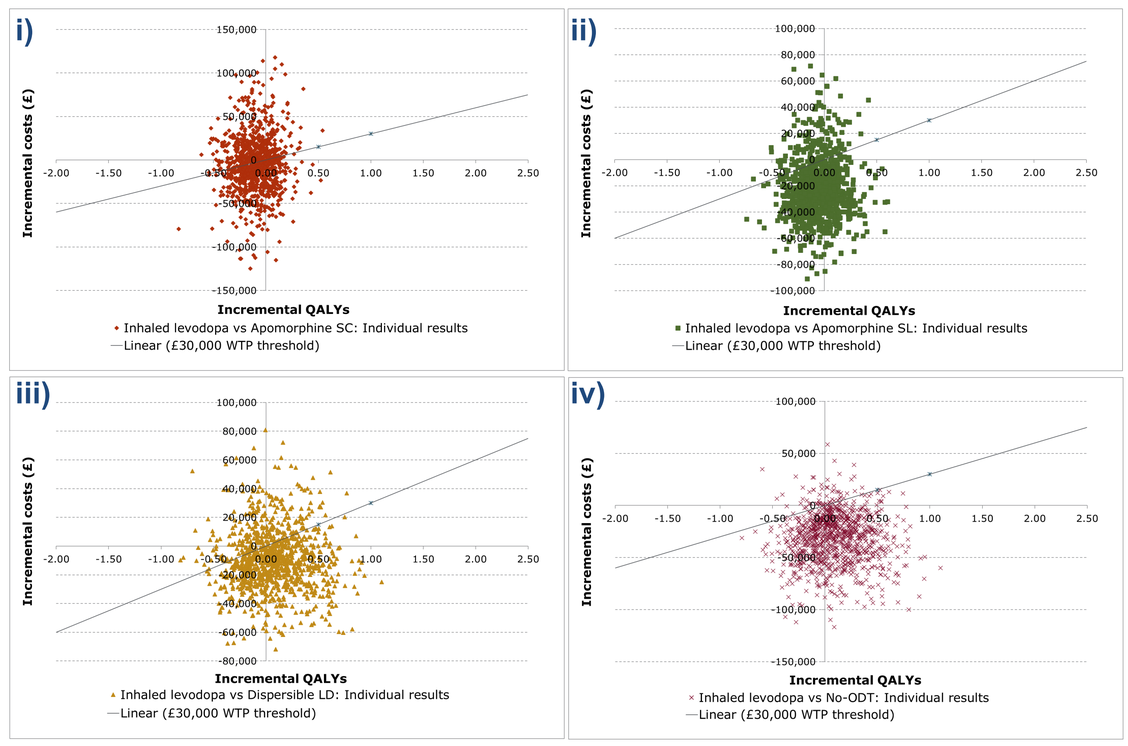
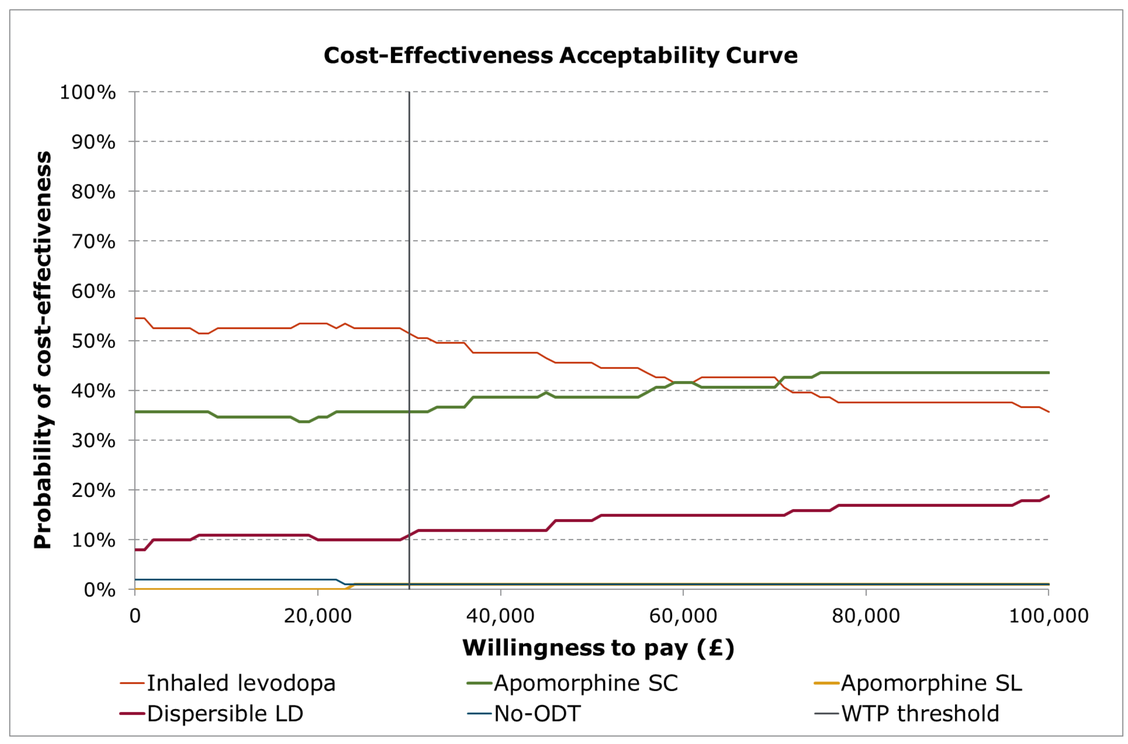


Figure 2b: PSA results plotted on the CEAC



CONCLUSIONS

- The cost-effectiveness analysis results, alongside the NMB, indicate IL could be a cost-saving alternative in the management of OFF episodes in PD patients for the UK population.
- The lower discontinuation rate of IL compared to APO-SC, APO-SL and dispersible LD results in sustained efficacy and a reduction in cost associated with progression to more costly subsequent therapies.

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Abbreviations: APO-SC: apomorphine subcutaneous; APO-SL: apomorphine sublingual; CD: Carbidopa; CEM: Cost-effectiveness model; HCRU: Healthcare resource use; IL: Inhaled levodopa; LD: Levodopa; NH: Natural history; NHS: National Health Service; NICE: National Institute for Health and Care Excellence; NMB: Net monetary benefit; no-ODT: no on-demand treatment; OWSA: One-way sensitivity analysis; PD: Parkinsons Disease; PSA: Probabilistic sensitivity analysis; PSS: Personal Social Services; QALY: Quality-adjusted life year; UK: United Kingdom; WTP: Willingness to pay

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