Background
- Parkinson's disease (PD) is a progressive chronic disease associated with substantial economic and societal burden.
- Immediate-release carbidopa-levodopa (CD-LD) is the most commonly prescribed treatment for advanced PD patients. However, effectiveness of IR CD-LD treatment declines with long-term treatment and is associated with increased "off" time (increase in off-state symptoms) and the advent of motor complications.
- CD-LD plus entacapone (E) has produced some clinical improvement over IR CD-LD alone.
- Prior to IPX066, carbidopa-levodopa and entacapone were marketed as an extended-release formulation of CD-LD designed to address some of the limitations of IR CD-LD by allowing 5 times levodopa concentrations by 1 hour and maintaining LD concentrations for a prolonged duration. Thus this class is prone to reduce "off" time and increase "on" time without troublesome dyskinesias compared to both IR CD-LD and CD-E.

Objective
- The aim of this study was to evaluate the comparative cost-effectiveness of IPX066 and CD-E from a U.S. payer's perspective. Outcomes measured:
  1. Total costs (including pharmacy and direct medical costs)
  2. Total quality-adjusted life-years (QALYs) (including assessment of length and quality of survival)
  3. Incremental cost-effectiveness ratios (ICERs)

Methods
- A 6-arm Markov state transition model (Figure 1) was designed to compare the cost-effectiveness of treating PD patients with either IPX066 or branded or generic CL+E.
  - The model was calibrated to estimate a patient's progression through three health states (≤25% "off" time, >25% "off" time, and death) at 6-month cycle lengths.
  - Six months cycle was selected to closely approximate the duration of the ≤25% "off" clinical trials.
  - Prior to administration of IPX066, the state of the IPX066 health states was based on age-dependent mortality in the U.S.

Figure 1. Markov model structure

The model was based on published cost-effectiveness models for drug therapy in PD. The baseline evaluation of clinical trial patients was assumed to start in the >25% "off" time health state.

Results
- Table 1. Cost-effectiveness for 5-year base case model

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Pharmacy (drug)</th>
<th>Direct medical costs, ≤25% off time</th>
<th>6-mo cost CL+E branded</th>
<th>6-mo cost CL+E generic</th>
<th>Total Cost 6-mo</th>
<th>Cost per QALY</th>
<th>CER</th>
</tr>
</thead>
<tbody>
<tr>
<td>CL+E branded</td>
<td>$3,032</td>
<td>$4,126</td>
<td>$4,126</td>
<td>$4,126</td>
<td>$6,162</td>
<td>$23,881</td>
<td>-</td>
</tr>
<tr>
<td>CL+E generic</td>
<td>$3,032</td>
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<td>$4,126</td>
<td>$4,126</td>
<td>$6,162</td>
<td>$23,881</td>
<td>-</td>
</tr>
</tbody>
</table>

- Figure 2. Distribution of total costs estimated after 5-year treatment with branded CL+E, generic CL+E, and IPX066

- Figure 3. Sensitivity analysis of IPX066 cost and ICER

- The total 5-year cost of IPX066 (base case: $68,703) was most sensitive to direct medical costs of the >25% "off" time health state: IPX066 drug cost, the probability of health state transitions, and discounting rate.

Conclusions
- A 6-arm Markov state transition model demonstrated the cost-effectiveness of treating PD patients with IPX066 compared to both the branded and generic CL+E.
- IPX066 treatment resulted in a cost savings of $146,947/QALY over branded CL+E and $75,921/QALY over generic CL+E.
- Multiple sensitivity analyses demonstrated the robustness of the model, confirming the robustness of IPX066 in the majority of scenarios.

References