A cost-effectiveness-analysis of apomorphine infusion in the treatment of advanced Parkinson’s disease in the UK, Germany and Mexico

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Objectives
Parkinson Disease (PD) is the second commonest cause of neurological disability. Approximately, 5,2 million men and women are affected worldwide. Continuous subcutaneous apomorphine (CSAI) represents an alternative treatment option of advanced PD with motor fluctuation. The purpose of this analysis was to estimate the cost-effectiveness of CSAI compared with levodopa/carbidopa intestinal gel (LCIG), Deep-Brain-Stimulation (DBS) and Standard-of-care (SOC).

Methods
We developed a Markov-Model to simulate the long-term consequences, disease progression (Hoehn&Yahr-stages 3-5, percentage of wakening-time in the OFF-state), complications and adverse-events. The model is based on adopted models which have been published for the UK and Sweden. Complications are different for the alternatives (e.g. pump problems in case of LCIG, temporary/permanent complications in case of DBS). Moderate and severe adverse-events (e.g. motor fluctuation, dyskinesia, nausea, dizziness, hallucination, skin problems, depression, anxiety) and death were included. Including 25 health-states, the model comprises moderate and severe health conditions. Probabilities derived from RCT and open-label studies.

Direct costs (2014) were estimated from the perspective of the national health care systems. The medical resource use and utilities are based on literature research. QALYs, life-years and costs are projected over a life-time horizon and are discounted with local recommended discount rates.

Cohort definition
The model cohort comprises PD patients aged 50 years or older with Hoehn&Yahr (H&Y) stages 3, 4 or 5 experiencing more than 50% of waking-time (14 hour) in the OFF state at treatment initiation. After treatment initiation with CSAI, LCIG or DBS an improvement in health states in the following cycle may arise; or patients continue SOC. During different therapeutic alternative adverse events or complications may arise.

Resource use and costs
The cost assessment is based on the assignment of costs to the health states. The costs of each health state are determined by the resource utilisation associated with a health state. Resource use and monetary values (prices, tariffs and/or opportunity costs) for each unit of medical goods and services were used to calculate the total direct costs. " treatment

Results
Results were presented in the following table:

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Costs €</th>
<th>DC (QALYs)</th>
<th>QALYs</th>
<th>KER €</th>
<th>LYs</th>
</tr>
</thead>
<tbody>
<tr>
<td>CSAI</td>
<td>76,031,49</td>
<td>2.85</td>
<td>6,460.45 vs. SOC</td>
<td>6.28</td>
<td></td>
</tr>
<tr>
<td>LCIG</td>
<td>130,011,29</td>
<td>3.06</td>
<td>2,244,684 vs. CSAI</td>
<td>6.91</td>
<td></td>
</tr>
<tr>
<td>DBS</td>
<td>87,730,21</td>
<td>2.75</td>
<td>-0.10 vs. CSAI</td>
<td>6.38</td>
<td></td>
</tr>
<tr>
<td>SOC</td>
<td>76,031,49</td>
<td>-1.456</td>
<td>2.62</td>
<td>-0.23</td>
<td>5.79</td>
</tr>
</tbody>
</table>

UK life-time costs associated with CSAI amounts to 78,251 € (96,073 €) and generates 2.85 QALYs and 6.28 LYs (104,500 €, 2,92 QALYs and 6,93 LYs in Germany and 1,341,718,06 MXN / 73,633 €, 2,57 QALYs and 5,72 LYs in Mexico). UK costs associated with LCIG are 130,011 € (159,621 €), achieves 3.06 QALYs and 6,93 LYs (175,064 €, 3,18 QALYs and 7,18 LYs in Germany; not available in Mexico).

UK costs for DBS are 87,730 € (124,449 €, 2,85 QALYs and 6,61 LYs in Germany and 1,376,651,37 MXN / 75,551 €, 2,55 QALYs and 5,92 LYs in Mexico).

CSAI dominates DBS. SOC associated UK costs amounts to 76,793 € (94,283 €); 2,62 QALYs and 5,76 LYs were reached (90,012 €, 2,73 QALYs and 6 LYs in Germany and 1,229,878,40 MXN / 67,496 €, 2,34 QALYs and 5,21 LYs in Mexico).

Conclusion
From a health economic perspective, CSAI is a cost-effective therapy and can be seen as an alternative treatment to LCIG or DBS for patients with advanced PD.

Sensitivity Analysis
Probabilistic sensitivity analysis of 500 trial plots revealed the incremental cost and incremental effectiveness of the interventions in question, as shown in Figures 4. This can be used to give an indication of the proportion of iterations that provide results below a prespecified cost-effectiveness threshold. In turn, this can allow the model user to quantify the level of uncertainty around a model's results by showing the percentage likelihood that the cost-effectiveness of the technology will fall below that threshold.

References
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