A Cost-Effectiveness Comparison of Icatibant and C1-Esterase Inhibitor Concentrate for the Symptomatic Treatment of Acute Attacks of Types I and II Hereditary Angioedema in the UK Setting

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OBJECTIVES
- Hereditary angioedema (HAE) type I and II are bradykinin-mediated swellings of the skin and mucosal tissues characterised by debilitating, painful and potentially life-threatening acute attacks lasting 2-5 days (Figure 1).1-4
- HAE type I and II are linked to defects in the SERPING1 gene, leading to a deficiency of C1-esterase inhibitor (C1-INH) protein.1
- As both bradykinin and C1-INH are involved in the pathogenesis of HAE, treatment options for HAE attacks include the bradykinin antagonist icatibant (Firazyr®, Shire HGT Inc.) and C1-INH inhibitors (e.g. Berinert®, CSL Behring).

METHODS
- A probabilistic cost-utility model was constructed in Microsoft Excel to estimate the cost-effectiveness of icatibant (30 mg subcutaneous) and C1-INH (Berinert®, CSL Behring) (20 IU/kg) in the UK setting, using data from Scotland and Wales (Figure 2).
- An indirect comparison of three icatibant studies (For Angioedema Subcutaneous Treatment [FAST]-1, -2 and -3)5,6 and one C1-INH (CSL Behring) study (International Multi-center Prospective Angioedema C1-Inhibitor Trial [I.M.P.A.C.T]-1)7 was undertaken to compare treatment efficacy (Poster PSY10).
- These indirect comparison data were input into the model along with the following costs: drug; cost; administration, monitoring and supportive care (taken from NHS reference costs 2009-2010); method and location of administration; number of attacks per year (to include the cost of vaccination and self-administration training); and requirement of hepatitis A and B vaccinations. These variables comprised the base-case scenario.

RESULTS
Cost-effectiveness
- In the base-case analysis, the total costs per attack were estimated as £1,577 for icatibant and £2,169 for C1-INH (CSL Behring) 20 IU/kg (Figure 3).
- This is equivalent to a saving of £592 (95% CI; £349–£715) per attack with icatibant (Table 1).
- The economic analysis demonstrated that the difference in QALYs between treatments was very small, and therefore not significant (Table 1).

Quality-adjusted life years (QALYs) were estimated by combining data for the time-to-onset of symptom relief (the primary endpoint of the majority of relevant trials) and utility weights for two health states: during an attack (the period of time before the onset of symptom relief), and following recovery from the attack (after onset of symptom relief).

QALYs
- The economic analysis demonstrated that the difference in QALYs between treatments was very small, and therefore not significant (Table 1).
- This difference was equivalent to approximately 0.75 quality-adjusted life hours, in favour of icatibant.

CONCLUSIONS
- The health economic analyses presented here demonstrate that icatibant reduces costs versus C1-INH (CSL Behring) 20 IU/kg in the treatment of HAE type I and II attacks in the UK setting.
- Icatibant reduces total treatment costs, mainly due to lower drug acquisition costs, although savings with administration costs are also expected as a higher proportion of icatibant patients self-administer treatment.

Table 1. Comparison of estimated and incremental costs per attack and incremental outcomes per attack of icatibant 30 mg subcutaneous and C1-INH (CSL Behring) 20 IU/kg intravenous.

<table>
<thead>
<tr>
<th>Cost component</th>
<th>Icatibant</th>
<th>C1-INH (CSL Behring)</th>
<th>Incremental cost, £ (Icatibant - C1-INH)</th>
<th>Incremental QALYs, 0.75</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug</td>
<td>1546.20</td>
<td>1954.62</td>
<td>-408.41</td>
<td>-2.54</td>
</tr>
<tr>
<td>Administration, monitoring and supportive care</td>
<td>31.03</td>
<td>211.70</td>
<td>-180.67</td>
<td></td>
</tr>
<tr>
<td>Vaccination</td>
<td>0.00</td>
<td>0.39</td>
<td>-0.39</td>
<td></td>
</tr>
<tr>
<td>Self-administration training</td>
<td>0.15</td>
<td>2.35</td>
<td>-2.20</td>
<td></td>
</tr>
<tr>
<td>Total costs (mean per attack, £)</td>
<td>1577.38</td>
<td>2169.05</td>
<td>-591.67</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Incremental outcome</th>
<th>Icatibant</th>
<th>C1-INH (CSL Behring)</th>
<th>Incremental cost, £ (Icatibant - C1-INH)</th>
<th>Incremental QALYs, 0.75</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean time with symptoms, h</td>
<td>2.54</td>
<td>2.00</td>
<td>-0.54</td>
<td>0.0009852</td>
</tr>
</tbody>
</table>

Incremental utility weights were identical for all comparators. Costs relate to SmPC data only. Patient Access Scheme discounts have not been applied. PSA = Probabilistic Sensitivity Analysis.

In incremental outcome analyses were calculated by subtracting the outcome estimates for the comparator from the outcome estimates for icatibant.

References
10. Lavanya Diwakar received a travel grant from Shire HGT to attend EAACI (2010), UKPIN 2011, and ESID 2012. She also received a travel grant from CSL Behring to attend EAAACI (2008).
18. Lavanya Diwakar received a travel grant from Shire HGT to attend AAAAI (2007) and ESS (2008).

Disclosures
Matthias Hulbert received a travel grant from Shire AG to attend ESD (2010). He also received an innovation payment from Shire HGT to attend an Advisory Board. Frances Pang and Mauricio Alvarez-Reyes are employees of Shire HGT. Steve Dawber and Sorrel Wolowacz are employees of RTI Health Solutions. When the abstract was submitted, Steve Dawber and Sorrel Wolowacz were employees of Shire HGT Inc. Funding and Acknowledgements The symposium review, indirect comparison and economic modelling were performed by RTI Health Solutions, Manchester, UK, and were funded by Shire HGT Inc. Medical writing support was provided by Steve Steakley, Prime Medica Ltd, Knutsford, Cheshire, UK, and was funded by Shire HGT Inc.

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