**INTRODUCTION**

- Chronic spontaneous urticaria (CSU) is a dermatological condition characterised by rapid appearance of wheals, angioedema or both, with no obvious cause and with symptoms lasting over six weeks. CSU exhibits natural remission typically within 1-5 years, though in some cases the condition may persist for over 20 years.
- Omalizumab is a humanised monoclonal antibody targeting immunoglobulin E and is the only therapy licensed in the European Union for the treatment of CSU with inadequate response to H1 antihistamines.a
- The National Institute for Health and Care Excellence (NICE) has recommended omalizumab for the treatment of severe CSU patients with an inadequate response to H1 antihistamines and leukotriene receptor antagonists (LTRA).b Prior to the approval of omalizumab, standard of care (SOC) amongst this patient group was considered anti-H1, antihistamines +/- CTRA (1–14), antihistamines, due to the lack of licensed alternatives.
- CSU is associated with a considerable negative impact on patient quality of life and also reduces patient productivity through absenteeism and presenteeism.1-7 No previous economic evaluation of omalizumab in the UK has considered the wider societal perspective that accounts for these indirect costs associated with the condition.

**OBJECTIVE**

- To assess the potential cost utility of add-on omalizumab treatment compared to SOC in patients with moderate or severe CSU with an inadequate response to SOC, from the UK societal perspective.

**METHODS**

**Model Structure**

- The model consisted of five health states based on Urticaria Activity Score (UAS7) and states for relapse, spontaneous remission and death (Figure 1).
- UAS7 is an established measure of disease severity and the UAS7 ranges used have been previously evaluated as effective to model CSU health states.
- Model cycle length was four weeks and total model lifetime was 20 years.
- In the base case, response to omalizumab was assessed at 16 weeks.
- Non-responders (UAS7=28–42) were assigned to treatment failure.
- Responders (UAS7=0–15) were in a treatment state until week 24, at which point omalizumab was discontinued.
- Patients in the "urticaria free" and "well-controlled urticaria" states were at risk of relapse from their respective timepoints of omalizumab discontinuation.
- Patients experiencing relapse were re-treated with a 14-week course of omalizumab assuming an appropriate response to the initial treatment.
- All patients were also associated with a probability of entering a spontaneous remission state (UAS7=0), which if reached they received no treatment.

**Model Inputs**

- Patient-level data from the GLACIAL trial provided the basis for several clinical inputs to the model.4,8
- Distribution of patients between UAS7-based health states at each 4-week time point across the treatment period.
- Data from the follow-up periods between 24 and 40 weeks provided relapse rates for patients in each health state at 24 weeks; extrapolations were made for rates beyond 40 weeks.
- Relapse was defined as an un-sustained improvement of the UAS7 that recurred in the inclusion criteria of the phase III trials at omalizumab in CSU.b5
- Risk of discontinuation from omalizumab.
- The observed dataset (no imputation) from the GLACIAL trial was used in the base case.
- Probabilities of spontaneous remission were based on a log-logistic model constructed from natural history data published by Nebess et al.8
- The model assumed CSU-related mortality; all cause mortality was based on annual mortality rates for each age group, obtained from the UK Office for National Statistics life tables.
- Omalizumab trial data informed the selection of adverse events (AEs) for the model (Table 1).
- Health utilities and direct costs associated with AEs were presented in Table 2. Costs included in the model were direct costs (drug acquisition and monitoring costs), AE costs and health state costs. (Table 2) and indirect health care productivity costs. Table 3.

**Sensitivity Analyses**

- One-way sensitivity analyses (OWSA), scenario analyses and probabilistic sensitivity analysis (PSA) were conducted to explore the impact of key model inputs and assumptions on results.

**RESULTS**

**Base Case Analysis**

- In the base case analysis, the deterministic incremental cost-effectiveness ratio (ICER) was £3,183 per quality-adjusted life year (QALY); omalizumab was associated with increased costs (£69.69) and increased benefit (0.202 QALYs) relative to SOC.

**Sensitivity and Scenario Analyses**

- OWSA found the ICER to be most sensitive to assumptions around productivity costs, relapse probabilities and the assumption of omalizumab being associated with spontaneous remission (Table 4).
- The PSA produced a mean probabilistic ICER of £2,586. The majority of ICERs were found to be in the north-east quadrant (Figure 2).
- At a willingness-to-pay threshold of £20,000, the probability of omalizumab being cost-effective was 68% (Figure 3).
- The results of scenario analyses exploring key assumptions around model structure and parameters are presented in Table 4.

**DISCUSSION**

- In the UK, the first economic evaluation of omalizumab in CSU from a UK societal perspective, productivity costs were a major driver of cost-effectiveness results.6–11 Several health technology assessment bodies (eg. NICE) do not consider the broader societal perspective. When excluding indirect costs from the analysis and considering a narrower perspective, such as that of the NICE/PSS, the incremental costs and resultant ICER associated with omalizumab are higher.
- Omalizumab has a high probability of being a cost-effective treatment option in this patient population at conventional willingness-to-pay thresholds.
- Cost-effectiveness of omalizumab was consistently demonstrated when evaluating a range of different scenarios.

**CONCLUSIONS**

- Omalizumab represents a cost-effective treatment for patients with moderate or severe CSU inadequately controlled by SOC from a societal perspective.
- Productivity costs were a particular driver of model results in this indication, which is perhaps unsurprising given the considerable impact of the condition on patients work productivity. This research highlights the relevance of including wider societal considerations in future CSU economic evaluations.

**REFERENCES**


**Figure 1. Model structure**

**Figure 2. Scatterplot for probabilistic sensitivity analysis (PSA)**

**Figure 3. Cost-effectiveness acceptability curve (CEAC) for omalizumab**

**Table 1. Utility inputs applied in the model**

<table>
<thead>
<tr>
<th>Health state</th>
<th>Utility value</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urticaria free</td>
<td>0.65</td>
<td>Sullivan</td>
</tr>
<tr>
<td>Well controlled urticaria</td>
<td>0.71</td>
<td>Sullivan</td>
</tr>
<tr>
<td>Mild urticaria</td>
<td>0.80</td>
<td>Sullivan</td>
</tr>
<tr>
<td>Moderate/severe urticaria</td>
<td>0.55</td>
<td>Sullivan</td>
</tr>
</tbody>
</table>

**Table 2. Direct costs applied in the model**

<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>COST</th>
<th>SOURCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Omalizumab</td>
<td>£254.57 (£172.69)</td>
<td>PSSRU 2013 day-ward nurse time, inflated to 2014</td>
</tr>
<tr>
<td>Injections</td>
<td>£22.22 (£4.38)</td>
<td>BNF July 2014</td>
</tr>
<tr>
<td>Monitoring for AEs</td>
<td>£71.49 (£68.85)</td>
<td>PSSRU 2013 day-ward nurse time, inflated to 2014</td>
</tr>
<tr>
<td>Omalizumab monitoring</td>
<td>£0.33 (£0.07)</td>
<td>NHS Reference Cost Schedule</td>
</tr>
<tr>
<td>Medication AEs</td>
<td>£0.00 (N/A)</td>
<td>N/A</td>
</tr>
<tr>
<td>Medication treatment</td>
<td>£6.26 (£1.25)</td>
<td>PSSRU 2013 day-ward nurse time, inflated to 2014</td>
</tr>
<tr>
<td>Monitoring for relapse</td>
<td>£0.00 (N/A)</td>
<td>N/A</td>
</tr>
</tbody>
</table>

**Table 3. Indirect costs applied in the model**

<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>COST</th>
<th>SOURCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medication</td>
<td>£304.60 (£531.09)</td>
<td>PSSRU 2013 day-ward nurse time, inflated to 2014</td>
</tr>
<tr>
<td>Food</td>
<td>£7.84 (£1.57)</td>
<td>PSSRU 2013 day-ward nurse time, inflated to 2014</td>
</tr>
<tr>
<td>Travel</td>
<td>£7.84 (£1.57)</td>
<td>PSSRU 2013 day-ward nurse time, inflated to 2014</td>
</tr>
<tr>
<td>Cost of identifying a relapse</td>
<td>£254.57 (£172.69)</td>
<td>PSSRU 2013 day-ward nurse time, inflated to 2014</td>
</tr>
<tr>
<td>Cost of monitoring for AEs</td>
<td>£22.22 (£4.38)</td>
<td>BNF July 2014</td>
</tr>
<tr>
<td>Cost of monitoring for relapse</td>
<td>£0.00 (N/A)</td>
<td>N/A</td>
</tr>
</tbody>
</table>

**Table 4. Results of scenario analyses**

- All results presented at 23 May 2014
- Scenario analyses exploring key assumptions around model structure and parameters are presented in Table 4.

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