Cost-effectiveness of Apremilast in Psoriatic Arthritis in Scotland

Farhan Mughal, MRPharmS, MSc; Hélène Caswton, MSc; Sandrine Cure, MSc; James Morris, MPH; Tom Tencer, PhD; Zhang, ZH, MPH

1Celgene Ltd, London, UK; 2Mapi Group, London, UK; 3Cogentia Healthcare Consulting, Cambridge, UK; 4Celgene Corporation, Warren, NJ, USA

BACKGROUND

Psoriatic arthritis (PsA) is a chronic, inflammatory disease that develops in up to 30% of patients with psoriasis. It is associated with the destruction of bone and joint cartilage, leading to joint damage and disability.1,2

In 2015, the European Medicines Agency approved apremilast, alone or in combination with disease-modifying anti-rheumatic drugs (DMARDs), for the treatment of active PsA in adult patients who have had an inadequate response to or who have been intolerant of conventional DMARD therapy from a Scottish perspective.

OBJECTIVE

This study was designed to assess the cost-effectiveness of apremilast, a new oral treatment, before tumour necrosis factor alpha (TNF-α) inhibitor therapy in PsA patients who have failed to respond to or are intolerant of conventional DMARD therapy.

METHODS

Model Structure

A Markov state- transition cohort model was developed with a 28-day cycle length and a 40-year time horizon based on the Rodgers et al. (2011) model (Figure 1).

Different treatment options were considered as mutually exclusive health states and depicted the treatment pathway and the impact of each treatment option, as measured by the Psoriatic Arthritis Response Criteria (PsARC), at the end of the trial period, ranging from 12 to 15 weeks.

The following treatment sequences were compared: (1) apremilast followed by adalimumab followed by etanercept and (2) etanercept followed by apremilast.

Patients taking unapproved or non-subsidized care were assumed to experience placebo response.

All-cause mortality was adjusted for the increased risk of death associated with PsA, which was included in all health states.

A 16.5% all-cause annual dropout rate was used for each treatment.

Figure 1. Model Structure: Apremilast Prior to TNF-α Inhibitor Therapy

RESULTS

Base Case

Apremilast followed by TNF-α inhibitors is a cost-effective strategy over a 40-year time horizon (Table 6).

The average time spent on TNF-α inhibitor treatments in BSC was also lower in the apremilast sequence compared with those in TNF-α inhibitor sequence (0.34 years vs. 0.80 years).

The average time spent on TNF-α inhibitor treatments and in BSC was estimated as £118,656 and £77,514, respectively.

Table 6. Base Case Results (40-Year Time Horizon)

Table 7. Alternative Scenarios (40-Year Time Horizon)

Scenario 1: Apremilast followed by adalimumab was compared with BSC.

Scenario 2: Apremilast followed by etanercept was compared with BSC.

Utility obtained from regression function (EQ-5D = 0.897 – 0.298 • HAQ-DI -0.004 • PASI).

Alternative utilities obtained from regression function based on published data.

The average incremental cost/QALY gained was £2,790 to £3,026.

Sensitivity Analysis

Results suggested that, with the exception of the PASI-22 score progression when not on treatment, variations in the model parameters did not significantly affect the base-case conclusions (Figure 2) and apremilast is cost-effective based on a willingness-to-pay threshold of £20,000 to £30,000 (Figure 3).

Figure 2. tornado Diagram

Figure 3. Cost-effectiveness Acceptability Curve

CONCLUSION

Apremilast, when used as an additional therapy option in the current treatment pathway before TNF-α inhibitor therapies, is a cost-effective strategy in this health-care system as an additional therapy for PsA in terms of £20,000 to £30,000 in the NHS in Scotland.
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BACKGROUND

- Psoriatic arthritis (PsA) is a chronic, inflammatory disease that develops in up to 30% of patients with psoriasis. It is characterised by inflammation of both the skin and the axial and peripheral terminal interphalangeal joints.1
- PsA has an estimated prevalence of 0.3% to 1.0% in the general population and can result in joint damage, decreased physical function, and impaired activities of daily living and disability.2,3
- Effective treatment of PsA has been shown to improve patient-reported outcomes significantly.4

Apremilast is an oral phosphodiesterase 4 inhibitor that acts intracellularly to regulate inflammatory mediators.5

In 2015, the European Medicines Agency approved apremilast, alone or in combination with disease-modifying anti-rheumatic drugs (DMARDs), for the treatment of active PsA in adult patients who have failed to respond to or are intolerant of conventional DMARD therapy.

OBJECTIVE

This study was designed to assess the cost-effectiveness of placing apremilast, a new oral treatment, before tumour necrosis factor-alpha (TNF-α) inhibitor therapies in PsA patients who have failed to respond to or are intolerant of conventional DMARD therapy, from a Scottish payer perspective.

METHODS

Model Structure

A Markov state-transition cohort model was developed with a 28-day cycle length and a 40-year time horizon based on the Rodgers et al. (2011) model (Figure 9). Different treatment options were considered as mutually exclusive health states and describe the treatment pathway and the impact of each treatment option, as measured by the Psoriatic Arthritis Response Criteria (PsARC), at the end of the trial period, ranging from 12 to 16 weeks.

The following treatment sequences were compared: (1) apremilast followed by adalimumab followed by etanercept and (2) adalimumab followed by etanercept. Patients taking etanercept received best supportive care (BSC) as the last line of treatment in both sequences.

All-cause mortality, adjusted to reflect the increased risk of death associated with PsA, was included in all health states.5

A 16.5% all-cause annual dropout rate was assumed for each treatment.1

Discounting

- The cost-effectiveness evaluation was conducted from the perspective of the National Health Service (NHS) in Scotland.
- A 3.5% annual discount rate was applied to costs and quality-adjusted life-years (QALYs).

Model Inputs

Treatment Efficacy

- In the absence of head-to-head comparisons vs. Scottish Medicines Consortium (SMC)- approved therapies in PsA, network meta-analyses (NMA)4,6,8,9,10,11 were conducted to provide adjusted indirect comparisons and inform the economic model.
- A systematic literature review was undertaken to identify all published evidence on the efficacy, effectiveness, and safety of all treatments considered in the analysis.
- Twelve randomised, controlled trials, including 4 apremilast trials, were considered for the NMA.

The mean PsARC response rate was calculated for apremilast and TNF-α inhibitor therapies (Table 1).

Table 1. PsARC Response Rate

<table>
<thead>
<tr>
<th>Sequence</th>
<th>Mean % (Crl)</th>
<th>PsARC Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apremilast</td>
<td>39.6 (34.5, 46.1)</td>
<td>NMA</td>
</tr>
<tr>
<td>Adalimumab</td>
<td>71.4 (58.4, 84.5)</td>
<td>NMA</td>
</tr>
<tr>
<td>Etanercept</td>
<td>59.8 (54.1, 65.9)</td>
<td>NMA</td>
</tr>
</tbody>
</table>

- A decline in the efficacy of subsequent TNF-α inhibitor therapies in primary TNF-α inhibitor non-responders was assumed, and this decrease was based on the hazard ratio of 2.7 published in Rodgers et al. (2011). The proportion of long-term withdrawals was also assumed to increase by 56%.1
- Patients in BSC were assumed to experience placebo response.

Utilities

The European Quality of Life-Five Dimensions questionnaire (EQ-5D) utilities were obtained as a linear function of the Health Assessment Questionnaire-Disability Index (HAQ-DI), and Psoriasis Area and Severity Index (PASI) scores based on a previously published regression equation (EQ-5D = 0.807 – 0.030 × HAQ-DI -0.004 × PASI).8

The mean change in HAQ-DI scores by PsARC response for each treatment was derived from the NMA.

The mean PASI scores, by 75% reduction from baseline PASI (PASI-75) response, were derived from the PASI-75, PASI-90, and PASI-30 response rules and the baseline PASI score using the method specified in Rodgers et al. (2011) (Table 2).10
A systematic literature review was undertaken to identify all published evidence on the effects of treatment sequences. The following treatment sequences were compared: (1) apremilast followed by adalimumab, (2) adalimumab followed by apremilast, and (3) etanercept followed by adalimumab. The mean change in HAQ-DI scores by PsARC response for each treatment was derived from the combined data of the two cohorts. The mean change in HAQ-DI score for PsARC responders was statistically significant compared with non-responders for the apremilast adalimumab sequence. The mean change in HAQ-DI score was assumed to increase by 36%.

Resource utilisation
- Treatment duration, frequency, and mode of administration were based on product labels and other published sources.
- Additional treatments were assumed to increase by 36%.
- Prescription costs, accounting for 15% of total costs, were excluded to avoid double counting.
- As the above regression function was estimated based on patients with rheumatoid arthritis, it was applied to the analysis of PsA.
- Utilities obtained from regression function (EQ-5D = 0.833 − 0.261 • HAQ-DI -0.002 • age +0.005 • disability +0.003 • QoL) were used in the analysis of PsA.

Costs
- Drug costs were sourced from the British National Formulary (BNF) (Table 4), while drug administration costs and the costs associated with physician visits were obtained from the NHS 2012–2013 reference cost schedule.

Analysis of Uncertainty
- Probabilistic sensitivity analyses and deterministic sensitivity analyses were conducted to assess the possible implications of uncertainty.
- The following scenario analyses were also conducted:
  - Number of anti-TNFα options in the treatment sequence.
  - Other healthcare costs, including resources for secondary care such as hospitalisations, were assumed to increase with the severity of disease and were estimated as a function of the HAQ-DI score.
  - Prescription costs, accounting for 15% of total costs, were excluded to avoid double counting.
  - As the above regression function was estimated based on patients with rheumatoid arthritis, it was applied to the analysis of PsA.
  - Utilities obtained from regression function (EQ-5D = 0.833 − 0.261 • HAQ-DI -0.002 • QoL) were used in the analysis of PsA.
  - Alternative costs were estimated for other healthcare costs and BSC (Proke et al., 2019).
RESULTS

Base Case
- Apremilast followed by TNF-α inhibitors is a cost-effective strategy over a 40-year time horizon (Table 6).
- On average, the time spent with PsARC response was greater among those in the apremilast sequence compared with those in the TNF-α inhibitor sequence (5.34 vs. 3.85).
- The average time spent on TNF-α inhibitor treatments and in BSC was also lower in the apremilast sequence (1.33 years and 1.79 years, respectively).

Table 6. Base Case Results (40-Year Time Horizon)

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Costs/patient (overall)</th>
<th>QALYs/patient (discounted)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>£122,384</td>
<td>9.04</td>
</tr>
<tr>
<td>Apremilast followed by adalimumab</td>
<td>£100,357</td>
<td>8.48</td>
</tr>
<tr>
<td>Apremilast followed by golimumab</td>
<td>£12,027</td>
<td>0.56</td>
</tr>
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Sensitivity Analysis
- Results suggested that, with the exception of the HAQ-DI score progression when on treatment, variations in the model parameters do not significantly affect the base case conclusions (Figure 2), and apremilast is cost-effective based on a willingness-to-pay threshold of £25,000 to £30,000 (Figure 3).

Figure 2. Tornado Diagram

Scenario Analysis
- Results from the alternative scenarios also suggested that variations in the model parameters and structural assumptions do not affect the base case conclusions (Table 7), and apremilast is cost-effective based on a willingness-to-pay threshold of £25,000 to £30,000.

Table 7. Alternative Scenarios (40-Year Time Horizon)

<table>
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</tbody>
</table>

LIMITATIONS
- There is a lack of head-to-head trial data for apremilast vs. the identified TNF-α inhibitor comparators.
- Because of the lack of comparative long-term data on treatment withdrawal rates, these data were assumed to remain constant over time.
- Finally, because of the lack of long-term safety data for apremilast, our model did not explicitly incorporate adverse events and costs or disutilities related to these factors.

CONCLUSION
- Apremilast, when used as an additional therapy step in the current treatment pathway before TNF-α inhibitor therapy, is a cost-effective strategy in the treatment of PsA based on a willingness-to-pay threshold of £25,000 to £30,000 in the NHS in Scotland.

REFERENCES
- Celgene Corporation. PsA Network Meta-Analysis; 2015.

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