Economic Evaluation of Apremilast in the Treatment of Moderate to Severe Psoriasis in the United States

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Disclosures

- Vidya Damera and Sandrine Cure are employees of MAPI Group and consultants for Celgene Corporation.
- Dr. Steve Feldman has received honoraria and research grants as an investigator, speaker, and/or consultant for Abbott Labs, Amgen, Anacor Pharmaceuticals, Baxter, Caremark, Celgene, Galderma, Gerson Lehrman Group, Guidepoint Global, Hanall Pharmaceutical, Janssen, Kikaku, LEO Pharma, Lilly, Merck, Merz, Mylan, Novartis, Pfizer, Qurient, Stiefel/GSK, Suncare Research, Taro, and Xenoport; and has received royalties or owns stock in Causa Technologies, Informa Healthcare, Medical Quality Enhancement Corporation, UpToDate, and Xlibris.
- Dr. Tom Tencer, Dr. Zoe Clancy, and Dr. Frank Zhang are employees of Celgene Corporation.
Abstract

**Background:** Previous studies have shown sub-optimal persistence to systemic and biologic therapies in the treatment of psoriasis. Apremilast, an oral PDE4 inhibitor that works intracellularly to regulate inflammatory mediators, is currently being studied in the treatment of moderate to severe psoriasis.

**Objectives:** We assessed the cost-effectiveness of placing apremilast before biologics for patients with moderate to severe plaque psoriasis.

**Methods:** A 10-year Markov state transition cohort model was developed to compare 2 treatment sequences in the base case: (1) apremilast followed by adalimumab followed by etanercept, and (2) adalimumab followed by etanercept (ETN). Patients who failed ETN were assumed to receive best supportive care (BSC). BSC is defined as total healthcare costs following failure of biologic treatment. Response was assessed using 75% improvement in Psoriasis Area and Severity Index (PASI-75) at the end of the trial periods (12 to 16 weeks, depending on study drug). Non-responders moved to the next line of therapy. A 20% annual dropout rate was assumed for each drug. Efficacy inputs were obtained from a network meta-analysis (31.9% for APR, 52.6% for ETN, 65.9% for ADA). Drug costs were sourced from 2014 wholesale acquisition cost, and a 3% annual discount rate was applied to costs and quality-adjusted life-years (QALYs). BSC costs were sourced from a published US study. Apremilast was assumed to be priced at an approximately 35% discount to biologics. Utilities were estimated from PASI response using published economic evaluations.

**Results:** Apremilast was estimated to provide an additional 0.74 years (5.00 vs. 4.26 years) in which patients achieved a PASI-75 and an additional 0.14 QALYs (6.87 vs. 6.73 QALYs). Total time on biologics was reduced by 0.56 years (4.26 vs. 4.82 years) and time spent in BSC was reduced by 1.04 years (3.96 vs. 5.00 years). Under base-case assumptions, placing apremilast before biologics was dominant (lower costs, higher QALYs). Sensitivity analyses indicated that several parameters (e.g., utility gains by PASI response, BSC costs, discount rate) influence the incremental cost-effectiveness ratio, with results ranging from dominant to cost-effective (<50k/QALY). Similar results were obtained when different combinations of ETN, ADA, and ustekinumab were used.

**Conclusion:** Placing apremilast before biologics results in more QALYs and is potentially cost-saving in the treatment of moderate to severe plaque psoriasis.
Psoriasis is a chronic, systemic inflammatory disease that affects approximately 1% to 3% of the world’s population.\(^1\)\(^-\)\(^3\)

In patients with psoriasis, the immune response is uncontrolled, resulting in a chronic imbalance in the production of pro- and anti-inflammatory cytokines.\(^4\)\(^,\)\(^5\)

Conventional oral systemic therapies, such as methotrexate, cyclosporine, and acitretin, as well as biologics, are typically used for the treatment of moderate to severe plaque psoriasis.\(^6\)

In the United States, psoriasis is estimated to cost $112B annually.\(^7\)

In the treatment of psoriasis, switching between alternative biologic treatments for patients treated with biologics is common; however, little is known about the optimal cost-effective strategy in sequencing treatment.

• We assessed, from a US payer perspective, the cost-effectiveness of placing apremilast before biologics for patients with moderate to severe plaque psoriasis.
  – Apremilast was approved by the FDA in 2014 and by the EC in 2015 for the treatment of psoriasis and psoriatic arthritis.¹,²

EC=European Commission; FDA=US Food and Drug Administration.

Methods

- A 10-year Markov state transition cohort model was developed to compare 2 treatment sequences in the base case: (1) apremilast followed by adalimumab followed by etanercept, and (2) adalimumab followed by etanercept (Figure 1).

- Patients who failed etanercept were assumed to receive best supportive care (BSC) as the last line of treatment. BSC is defined as total healthcare costs following failure of conventional and biologic treatment.

- Response to therapy and treatment continuation was assessed using the Psoriasis Area and Severity Index (PASI) at the end of the clinical trial periods (12 to 16 weeks, depending on the study drug).

- Non-responders moved to the next line of therapy.

- A 20% annual dropout rate was assumed for each study drug.

- Treatment efficacy inputs were obtained from a meta-analysis and trial results.

- Drug costs were sourced from wholesale acquisition costs on November 15, 2014, and a 3% annual discount rate was applied to costs and quality-adjusted life-years (QALYs).

- Costs for BSC were sourced from a published US-based study. Apremilast was assumed to be priced at a discount compared with biologics.¹

- Utilities were estimated from PASI response using previously published economic evaluations.

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Figure 1. Model Structure: Analysis of the Effect of Delaying Biologic Therapy

**Apremilast arm**
- Apremilast
  - Trial period
  - Continued use
- Adalimumab
  - Trial period
  - Continued use
- Etanercept
  - Trial period
  - Continued use
- BSC
  - Death

**Non-apremlast arm**
- Adalimumab
  - Trial period
  - Continued use
- Etanercept
  - Trial period
  - Continued use
- BSC
  - Death
Treatment Efficacy

- Clinical efficacy data were obtained from an internal Bayesian network meta-analysis.
- At Week 16, the adjusted PASI-75 response rate was 32% for apremilast; the efficacy of comparator treatments is shown in Table 1.

Table 1. Efficacy of Comparator Treatments for Psoriasis

<table>
<thead>
<tr>
<th>Treatment</th>
<th>PASI-75</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adalimumab</td>
<td>66%</td>
<td>Network Meta-Analysis</td>
</tr>
<tr>
<td>Etanercept</td>
<td>53%</td>
<td>Network Meta-Analysis</td>
</tr>
</tbody>
</table>

Utilities

- Utilities were based on changes in European Quality of Life-5 Dimensions Questionnaire (EQ-5D) scores by PASI response.¹

Model Inputs

Resource Utilization

• Monthly biologic dosing schedules were based on the recommended doses presented in Table 2.
• Healthcare resource use associated with patient monitoring was based on expert opinion and a published study.1

Costs

• Drug costs were sourced from wholesale acquisition cost prices on November 15, 2014 (Table 2).2,3
• Laboratory tests and other costs related to patient monitoring were obtained from the Clinical Diagnostic Laboratory Fee Schedule (2012) and the National Physician Fee Schedule (2012).
• Hospitalizations were based on estimates from Anis et al.4

Discounting

• Costs and QALYs were discounted at an annual rate of 3%.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage Description</th>
<th>Trial Period</th>
<th>Pack Cost</th>
<th>First Month</th>
<th>Second Month</th>
<th>Third Month</th>
<th>Continued Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adalimumab</td>
<td>80 mg initial dose, then 40 mg every other week starting 1 week after initial dose</td>
<td>12 weeks¹</td>
<td>$1,350.16</td>
<td>$5,400.64</td>
<td>$2,700.32</td>
<td>$2,700.32</td>
<td>$2,700.32</td>
</tr>
<tr>
<td>Etanercept</td>
<td>50 mg twice weekly for 3 months, then 50 mg weekly</td>
<td>12 weeks²</td>
<td>$675.20</td>
<td>$5,401.60</td>
<td>$5,401.60</td>
<td>$5,401.60</td>
<td>$2,700.80</td>
</tr>
<tr>
<td>Apremilast</td>
<td>30 mg BID</td>
<td>16 weeks³</td>
<td>$30.82</td>
<td>$862.96</td>
<td>$1,725.92</td>
<td>$1,725.92</td>
<td>$1,725.92</td>
</tr>
</tbody>
</table>

• Apremilast was estimated to provide an additional 0.74 years (5.00 vs. 4.26 years) in which patients achieved a 75% reduction from baseline in PASI score (PASI-75) and an additional 0.14 QALYs (6.87 vs. 6.73 QALYs) (Table 3).

• Total time spent on biologics was reduced by 0.56 years (4.26 vs. 4.82 years) and time spent in BSC was reduced by 1.04 years (3.96 vs. 5.00 years).

• Under base-case assumptions, placing apremilast before biologics was found to be the dominant (lower costs, higher QALYs) strategy (costs reduced by $9,072.39).

• Similar results were obtained when combinations of etanercept, adalimumab, and ustekinumab were used in the 2-drug sequence.
## Results

### Table 3. Base-Case Results

<table>
<thead>
<tr>
<th>Base-Case Results</th>
<th>Apremilast Sequence</th>
<th>Comparator Sequence</th>
<th>Incremental</th>
</tr>
</thead>
<tbody>
<tr>
<td>Costs / patient (overall)</td>
<td>$234,293</td>
<td>$243,365</td>
<td>-$9,072</td>
</tr>
<tr>
<td>Life-years / patient (undiscounted)</td>
<td>9.82</td>
<td>9.82</td>
<td>0.0</td>
</tr>
<tr>
<td>QALYs / patient (discounted)</td>
<td>6.86</td>
<td>6.72</td>
<td>+0.14</td>
</tr>
<tr>
<td>Average time spent on biologics, years</td>
<td>4.26</td>
<td>4.82</td>
<td>-0.56</td>
</tr>
<tr>
<td>Average time spent with PASI-75 response, years</td>
<td>5.00</td>
<td>4.26</td>
<td>+0.74</td>
</tr>
<tr>
<td>Average time spent in BSC, years</td>
<td>3.96</td>
<td>5.00</td>
<td>-1.04</td>
</tr>
<tr>
<td>Incremental cost / QALY gained</td>
<td>Dominant</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Limitations

- Treatment efficacy was assumed to be independent of past treatments due to lack of data in the literature.
- Costs of monitoring were based on expert opinion of monitoring frequency.
- Dropout rates were assumed to be the same across all treatments, both during the trial period and during continued use, while these might be different across regimens.
• Placing apremilast before biologics results in more QALYs and is potentially cost-saving in the treatment of moderate to severe plaque psoriasis.