Cost-Utility Analysis of Apremilast for the Treatment of Moderate to Severe Psoriasis in Spain

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BACKGROUND

Psoriasis is an immune-mediated inflammatory disease that may have a major impact on quality of life, especially in patients with moderate to severe disease.2

Psoriasis is characterized by a rapid buildup of the cells on the surface of the skin (epidermis), which results in thick, silvery, dry scales that are itchy and painful.1

There is evidence of a delay in using systemic agents and biologics in patients with moderate to severe psoriasis; this delay exceeds 3 years in 50% of patients.1

Conventional systemic agents for psoriasis include cyclosporine and methotrexate or psoraliens plus ultraviolet light (PUVA). Biological therapies are used when response to conventional systemic therapies or PUVA is inadequate or intolerable.3

Apremilast is an orally administered, small-molecule phosphodiesterase 4 inhibitor. It has a novel mechanism of action, targeting multiple steps in the pathogenesis of psoriasis. The marketing authorisation from the European Medicines Agency for the use of apremilast in patients with psoriasis and psoriatic arthritis was granted on January 16, 2015.

OBJECTIVE

This cost-utility model was developed from the payer perspective to assess the impact of placing apremilast before biologicals for the treatment of moderate to severe plaque psoriasis in patients in Spain who have failed to respond to, are intolerant of, or have a contraindication to previous systemic treatment.

METHODS

A 20-year Markov model with monthly cycle duration was developed (Figure 1).

Any-cause mortality rates in the Spanish general population were included in order to estimate quality-adjusted life-years (QALYs).

Treatment strategies consisted of an apremilast before biologicals sequence compared with a biologicals-only sequence.

Sequential biologicals, based on Spanish clinical practice, were adalimumab, ustekinumab, etanercept, and infliximab for both strategies. Patients who failed infliximab were assumed to receive best supportive care (BSC).

RESULTS

A 75% reduction in Psoriasis Area and Severity Index (PASI-75) was used as the efficacy measure. PASI-75 response rates for each drug were derived from a meta-analysis: apremilast (29.74%), adalimumab (62.25%), ustekinumab (76.30%), etanercept (45.33%), and infliximab (85.16%). All-cause overall mortality was considered.

Resource consumption was estimated by an expert panel, and biological doses were taken from the summaries of product characteristics. According to the Spanish National Health System (NHS) perspective, the following costs were included:

- Drug acquisition (ex-factory price) with mandatory deduction
- Mean weight from patients included in apremilast pivotal clinical trials was considered to estimate drug consumption of infliximab
- Administration (for parental drugs)
- Monitoring costs
- Unit costs (€, 2014), obtained from national databases (Table 1)

The price of apremilast is that submitted to the Spanish Ministry of Health for the price and reimbursement process (€820.00).

Table 1. Unit Costs (€, 2014)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Ex-factory Price*</th>
<th>Unit cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apremilast (Celgene)</td>
<td>€820.00</td>
<td></td>
</tr>
<tr>
<td>Adalimumab (Humira)</td>
<td>€459.75</td>
<td></td>
</tr>
<tr>
<td>Etanercept (Remicade)</td>
<td>€716.53</td>
<td></td>
</tr>
<tr>
<td>Ustekinumab (Stelara)</td>
<td>€1,358.91</td>
<td></td>
</tr>
<tr>
<td>Infliximab (Remicade)</td>
<td>€969.00</td>
<td></td>
</tr>
</tbody>
</table>

Incremental Costs (€)

Base case ICER

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Base Case Parameters</th>
<th>Sensitivity Analysis Parameters</th>
<th>Incremental Total Cost (€)</th>
<th>Incremental QALY</th>
<th>ICER (€/QALY)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time horizon</td>
<td>10 years</td>
<td>10 years (40 years)</td>
<td>-9,326</td>
<td>0.77</td>
<td>€12,000</td>
</tr>
<tr>
<td>Discount rate</td>
<td>0%</td>
<td>0%</td>
<td>-9,180</td>
<td>0.17</td>
<td>€53,743</td>
</tr>
<tr>
<td>Drug order in biological sequence</td>
<td>A &gt; E &gt; U &gt; I</td>
<td>A &gt; E &gt; U &gt; I</td>
<td>-9,595</td>
<td>0.11</td>
<td>€63,930</td>
</tr>
<tr>
<td>Mean weight of patients</td>
<td>80.5 kg</td>
<td>75 kg</td>
<td>-5,971</td>
<td>0.11</td>
<td>€80,500</td>
</tr>
<tr>
<td>Best supportive care cost</td>
<td>671,536</td>
<td>671,536</td>
<td>0</td>
<td>0.11</td>
<td>671,536</td>
</tr>
<tr>
<td>Hospitalization from non-responding patients</td>
<td>10 days/year</td>
<td>5 days</td>
<td>-8,222</td>
<td>0.11</td>
<td>€133,000</td>
</tr>
<tr>
<td>Inflammatory cost</td>
<td>69,000</td>
<td>69,000</td>
<td>-2,242</td>
<td>0.11</td>
<td>69,000</td>
</tr>
</tbody>
</table>

Figure 2. Cost-Effectiveness Plane

LIMITATIONS

- Response rates for each treatment within the model were assessed at different time points, and no studies including all current therapies were performed. The model assumes that efficacy is maintained over a long time horizon.
- Due to the lack of studies, utilities have been considered from studies conducted in countries other than Spain. However, based on the experience and knowledge of the experts consulted, this information could also be representative of the Spanish population.
- The present model was developed from a third-party payer perspective; thus it did not include indirect costs that could be useful for a societal analysis.

CONCLUSION

- The administration of apremilast before biologics resulted in a dominant strategy for the Spanish NHS in the treatment of patients with moderate to severe plaque psoriasis.

REFERENCES


This study was sponsored by Celgene Corporation.

Presented at the SPIOR 18th Annual European Congress; 7–11 November 2015; Milan, Italy.
Background

- Utilities were estimated from PASI response using a previously published regression equation.\(^9\)
- Psoriasis is a chronic, immune-mediated inflammatory disease that may have a major impact on quality of life, especially in patients with moderate to severe disease.\(^1\)
- Psoriasis is characterised by a rapid buildup of the cells on the surface of the skin (epidermis), which results in thick, red, and scaly patches.

Results

- There is evidence of a delay in using systemic agents and biologicals in patients with moderate to severe psoriasis; this delay exceeds 3 years in 50% of patients.\(^3\)
- In the base-case assumptions, the sequence with apremilast yielded lower total costs than the sequence with biologicals only. (€7,242 vs. €224,359). Under base-case assumptions, placing apremilast before biologicals is a dominant treatment strategy.

Objectives

- This cost-utility model was developed from the payer perspective to assess the impact of placing apremilast before biologicals for the treatment of moderate to severe plaque psoriasis in patients in Spain who have failed to respond to, or who are non-responders to, previous conventional systemic therapies or phototherapy.

Table 1: Unit Costs (€, 2014)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Cost (€)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adalimumab (Enbrel®)</td>
<td>€947.22</td>
</tr>
<tr>
<td>Etanercept (Enbrel®)</td>
<td>€947.5</td>
</tr>
<tr>
<td>In/f/liximab (Remicade®)</td>
<td>€439.75</td>
</tr>
<tr>
<td>Ustekinumab (Stelara®)</td>
<td>€2,747.36</td>
</tr>
</tbody>
</table>

Table 2: One-Way Deterministic Sensitivity Analysis Results

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Incremental QALY ICER (€/QALY)</th>
<th>Effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Discount rate 3%</td>
<td>Non-responder patients 10 days/year</td>
<td>-6,545</td>
</tr>
<tr>
<td></td>
<td>10 years</td>
<td>-4,326</td>
</tr>
<tr>
<td></td>
<td>Lifetime</td>
<td>-8,189</td>
</tr>
</tbody>
</table>

Limitations

- Response rates for each treatment within the model were assessed at different time points, and no studies including all drugs up to the current time frame were available.
- The present model was developed from a third-party payer perspective; thus it did not include indirect costs that could be useful for a societal analysis.
- The price of apremilast is that submitted to the Spanish Ministry of Health for the price and reimbursement process (€820.00).
- The administration of apremilast before biologicals resulted in a dominant strategy for the Spanish NHS in the treatment of patients with moderate to severe plaque psoriasis.

References

5. 2010;11:513-520.
7. 2010;11:513-520.
8. 2010;11:513-520.
• Psoriasis is an immune-mediated inflammatory disease that may have a major impact on quality of life, especially in patients with moderate to severe disease.¹
• Psoriasis is characterised by a rapid buildup of the cells on the surface of the skin (epidermis), which results in thick, silvery, dry scales that are itchy and painful.²
• There is evidence of a delay in using systemic agents and biologicals in patients with moderate to severe psoriasis; this delay exceeds 3 years in 50% of patients.³
• Conventional systemic agents for psoriasis include cyclosporine and methotrexate or psoralen plus ultraviolet A light (PUVA). Biological therapies are used when response to previous conventional systemic therapies or PUVA therapy is inadequate.⁴
• Apremilast is an orally administered, small-molecule phosphodiesterase 4 inhibitor. It has a novel mechanism of action, targeting multiple steps in the pathogenesis of psoriasis. The marketing authorisation from the European Medicines Agency for the use of apremilast in patients with psoriasis and psoriatic arthritis was granted on January 15, 2015.

**OBJECTIVE**

• This cost–utility model was developed from the payer perspective to assess the impact of placing apremilast before biologicals for the treatment of moderate to severe plaque psoriasis in patients in Spain who have failed to respond to, are intolerant of, or have a contraindication to previous systemic treatment.

**METHODS**

• A 20-year Markov model with monthly cycle duration was developed (Figure 1).
• Any-cause mortality rates in the Spanish general population were included in order to estimate quality-adjusted life-years (QALYs).
• Treatment strategies consisted of an apremilast before biologicals sequence compared with a biologicals-only sequence.
• Sequential biologicals, based on Spanish clinical practice, were adalimumab, ustekinumab, etanercept, and infliximab for both strategies. Patients who failed infliximab were assumed to receive best supportive care (BSC).

**RESULTS**

• A ≥75% reduction in Psoriasis Area and Severity Index (PASI-75) was used as the efficacy measure. PASI-75 response rates for each drug were derived from a meta-analysis: apremilast (29.74%), adalimumab (62.25%), ustekinumab (70.30%), etanercept (45.33%), and infliximab (65.16%). All-cause overall mortality was considered.
• Resource consumption was estimated by an expert panel, and biological doses were taken from the summaries of product characteristics. According to the Spanish National Health System (NHS) perspective, the following costs were included:
  – Drug acquisition (ex-factory price⁵ with mandatory deduction⁶)
  – Administration (for parenteral drugs)
  – Monitoring costs
  – Unit costs (€, 2014), obtained from national databases⁷ (Table 1)
• The price of apremilast is that submitted to the Spanish Ministry of Health for the price and reimbursement process (€820.00).

**Table 1. Unit Costs (€, 2014)**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Ex-factory Price⁵</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apremilast (Otsuka®) 30 mg, 56 tablets – oral</td>
<td>€620.00⁷</td>
</tr>
<tr>
<td>Adalimumab (Humira®) 40 mg, 2 injections 0.8 mL – SC</td>
<td>€1,028.29</td>
</tr>
<tr>
<td>Etanercept (Enbrel®) 50 mg, 4 injections 1 mL – SC</td>
<td>€947.22</td>
</tr>
<tr>
<td>Infliximab (Remicade®) 100 mg, 1 vial – IV</td>
<td>€4,390.75</td>
</tr>
<tr>
<td>Ustekinumab (Stelara®) 45 mg, 1 injection 0.5 mL – SC</td>
<td>€2,747.36</td>
</tr>
</tbody>
</table>

Administration for parenteral drugs

<table>
<thead>
<tr>
<th>Drug administration (25 Hour ~ 2 Hours)</th>
<th>Unit cost</th>
</tr>
</thead>
</table>
| Nurse personnel | €105.90
| Dermatologist | €67.00/hour |

Monitoring (detailed consumption provided by an expert panel)

| For apremilast | €115.40 |
| For adalimumab and etanercept | €230.30 |
| For infliximab | €281.81 |
| For ustekinumab | €213.53 |

¹Apremilast price is submitted to the Spanish Ministry of Health for price and reimbursement process. ²Ex-factory price. ³IV=subcutaneous.
• An annual discount rate of 3% was applied for both costs and health benefits.4
• Utilities were estimated from PASI response using a previously published regression equation.4
• One-way deterministic and probabilistic sensitivity analyses (SA) were performed to test the robustness of the model.

RESULTS

• The administration of apremilast before a sequence of biologicals was estimated to provide an additional 0.12 QALYs: 12.37 QALYs vs. 12.25 QALYs for a sequence of biologicals only.
• In the base-case assumptions, the sequence with apremilast yielded lower total costs than the sequence with biologicals only (€2,178,14 vs. €2,244,359). Under base-case assumptions, placing apremilast before biologicals is a dominant treatment strategy.
• Results of one-way deterministic SA confirm the robustness of the model: the sequence that included apremilast demonstrated higher effectiveness and lower total costs than the sequence with biologicals only in all analyses (Table 2).
• In the probabilistic SA, the administration of apremilast before biologicals was dominant in 100% of the simulations (Figure 2).

Table 2. One-Way Deterministic Sensitivity Analysis Results

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Base Case Parameters</th>
<th>Sensitivity Analysis Parameters</th>
<th>Incremental Total Cost (€)</th>
<th>Incremental QALY</th>
<th>ICER (€/QALY)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time horizon</td>
<td>20 years</td>
<td>10 years</td>
<td>-6,689</td>
<td>0.04</td>
<td>Dominant</td>
</tr>
<tr>
<td>Discount rate</td>
<td>3%</td>
<td>5%</td>
<td>-6,539</td>
<td>0.11</td>
<td>Dominant</td>
</tr>
<tr>
<td>Drug order in biologicals sequence</td>
<td>A &gt;U &gt;E &gt;I</td>
<td>U &gt;A &gt;E &gt;I</td>
<td>-6,743</td>
<td>0.11</td>
<td>Dominant</td>
</tr>
<tr>
<td>Mean weight of patients</td>
<td>92.4 kg</td>
<td>80 kg</td>
<td>-7,921</td>
<td>0.11</td>
<td>Dominant</td>
</tr>
<tr>
<td>Best supportive care cost</td>
<td>€1,358.91</td>
<td>€1,562.75</td>
<td>0</td>
<td>0.11</td>
<td>Dominant</td>
</tr>
<tr>
<td>Hospitalization from non-responder patients</td>
<td>10 days/year</td>
<td>5 days</td>
<td>-7,336</td>
<td>0.11</td>
<td>Dominant</td>
</tr>
<tr>
<td>Infliximab cost</td>
<td>€498.06</td>
<td>€596.77</td>
<td>-7,242</td>
<td>0.11</td>
<td>Dominant</td>
</tr>
</tbody>
</table>

LIMITATIONS

• Response rates for each treatment within the model were assessed at different time points, and no studies including all current therapies were performed. The model assumes that efficacy is maintained over a long time horizon.
• Due to the lack of studies, utilities have been considered from studies conducted in countries other than Spain. However, based on the experience and knowledge of the experts consulted, this information could also be representative of the Spanish population.
• The present model was developed from a third-party payer perspective; thus it did not include indirect costs that could be useful for a societal analysis.

CONCLUSION

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REFERENCES


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