ICER Public Meeting: Evaluating Emerging Therapies for Psoriasis and Endometriosis

July 12, 2018
Targeted Immunomodulators for Plaque Psoriasis: Effectiveness and Value Condition Update

Public Meeting – Morning Session
July 12, 2018
Welcome and Introduction

Why are we here this morning?

The 2016 economic analyses resulted in incremental cost-effectiveness ratios across all agents that were well-aligned with commonly-accepted thresholds for cost-effectiveness. [ICER’s Policy] Recommendations encouraged payers to abolish or limit the use of step therapy for these treatments… [Yet,] It is unfortunate that [since the last report] it appears the “access problem” may have gotten worse for individuals living with psoriasis.

- National Psoriasis Foundation

The psoriasis field has grown increasingly crowded over the last few years, thanks to a slew of biologic approvals. Novartis’ Cosentyx kicked off the party back in early 2015, only to be followed by Eli Lilly’s Taltz, Valeant’s Siliq and Johnson & Johnson’s Tremfya. And therapy areas that see waves of pricey new products tend to be the ones payers target to keep costs down.

- Fierce Pharma, Feb 21 2018
Welcome and Introduction

Why are we here this morning?

• Increasing health care costs affecting individuals, state and federal budgets
• New mechanisms of action often raise questions about appropriate use, cost
• Patients can have difficulty accessing drugs
  – Step therapy protocols
  – Requirements to switch drugs with new insurance
  – High out-of-pocket costs
• Need for objective evaluation and public discussion of the evidence on effectiveness and value
• ICER’s first “condition update” – opportunity to evaluate new therapies, update evidence on established medicines, track policy/coverage changes
Welcome and Introduction

• New England Comparative Effectiveness Public Advisory Council (CEPAC)

• The Institute for Clinical and Economic Review (ICER)
Sources of Funding, 2018

- Non-profit foundations: 78%
- Manufacturer grants, contracts, and contributions: 10%
- Contributions from health plans and provider groups: 9%
- Government grants and contracts: 3%

ICER Policy Summit only
Welcome and Introduction

How was the ICER report on therapies for plaque psoriasis developed?

• Scoping with guidance from patient groups, clinical experts, manufacturers, and other stakeholders
• Internal ICER staff evidence analysis
• University of Washington cost-effectiveness modeling
• Public comment and revision
• Expert report reviewers
  – Dr. Alexa Kimball
  – Dr. Joseph Merola
  – Leah McCormick Howard, J.D. (National Psoriasis Foundation)
  – Bram Ramaekers, PhD (health economist)

• How is the evidence report structured to support CEPAC voting and policy discussion?
Goal: Sustainable Access to High-Value Care for All Patients

Long-Term Value for Money
- Comparative Clinical Effectiveness
- Incremental cost-effectiveness
- Other Benefits or Disadvantages
- Contextual Considerations

Short-Term Affordability
- Potential Budget Impact
Morning Agenda

9:00am: Welcome and Opening Remarks

9:15 am: Presentation of the Evidence and Economic Modeling
   • Reiner Banken, MD, MSc, Senior Fellow, ICER
   • David Veenstra, PharmD, PhD, University of Washington

10:15 am: Public Comments

10:30 am: Manufacturer Panel and Discussion

10:45 am: NE CEPAC Vote on Clinical Effectiveness and Value

11:45 am: Reflections from Experts and NE CEPAC Panel

12:00 pm: Break for Lunch
Evidence Review

Reiner Banken, MD MSc
Senior Fellow
Institute for Clinical and Economic Review
**Key review team members:**
Foluso Agboola, MBBS, MPH
Alexandra Ellis, PhD
Katherine Fazioli, BS

**Disclosures:**
We have no conflicts of interest relevant to this report.
Condition Update

• Update from New England CEPAC Meeting on November 18, 2016

• **New therapies**: new class of drugs IL23 (guselkumab, tildrakizumab, risankizumab) and new indication for certolizumab pegol

• Update on clinical data and costs for therapies reviewed in 2016
Topic in Context

• Autoimmune skin disease that causes itchy, red, scaly raised plaques
• Affects 3% of the population
• Associated with
  • Other autoimmune diseases
  • Metabolic syndrome and cardiovascular disease
  • Psoriatic arthritis: in up to 30%
• Moderate-to-severe when affecting 5% to 10% of a patient’s body surface; lesions significantly reducing quality of life
Effect on Lives Can Be Profound

- Life long disease
- Higher likelihood of having depression, anxiety, and suicidal ideation
- Impact of lesions in particular areas: nails, scalp, face, flexural areas, palms, soles of feet, and genitals
Management

• Topical Therapies: emollients, topical steroids and others (effective for 70-80% of patients)
• Older systemic therapies: cyclosporine, methotrexate
• Phototherapy
• Targeted immunomodulators: TNFα, interleukins 17-A, 12 and 23, PDE-4
Insights from Patients and Patient Groups

- Research is not patient-centered
- Patient dissatisfaction
- Challenges of Black and Hispanic patients
- Using treatments can be challenging
- Affects social functioning
- Psychological and emotional effects
- Concern about lack of access
Issues of Focus
Review Scope (PICOTS)

- **Population:** Adults with moderate-to-severe plaque psoriasis
- **Interventions:** Targeted immunomodulators
- **Comparators:** Placebo and head-to-head
- **Main Outcomes:**
  - Psoriasis Area and Severity Index (PASI)
  - Physician Global Assessment (PGA)/ Investigator Global Assessment (IGA)
  - Patient-reported outcomes (DLQI, Symptom measure scales)
  - Treatment-related adverse events
Updated Evidence Base

- 48 key trials included in the update
  - 34 were included in the 2016 review
- 10 of the newly identified trials relates to the four new drugs of interest
- 4 additional trials were identified on the old drugs
  - Placebo controlled adalimumab trial
  - Placebo controlled infliximab trial
  - Head-to-head between infliximab and etanercept (PIECE)
  - Head-to-head between secukinumab and ustekinumab (CLARITY)
## Phase III Trials on New drugs

<table>
<thead>
<tr>
<th>Drug</th>
<th>Trial names</th>
<th>N</th>
<th>Primary endpoints (weeks)</th>
<th>Mean baseline PASI</th>
<th>Age (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guselkumab</td>
<td>VOYAGE 1*</td>
<td>1,829</td>
<td>16</td>
<td>22</td>
<td>44</td>
</tr>
<tr>
<td></td>
<td>VOYAGE 2*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tildrakizumab</td>
<td>RESURFACE 1</td>
<td>1,862</td>
<td>12</td>
<td>20</td>
<td>46</td>
</tr>
<tr>
<td></td>
<td>RESURFACE 2*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Risankizumab†</td>
<td>UltIMMA 1*</td>
<td>1,504</td>
<td>16</td>
<td>20</td>
<td>48</td>
</tr>
<tr>
<td></td>
<td>UltIMMA 2 IMMhance</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>IMMhance</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Certolizumab Pegol</td>
<td>CIMPASI 1</td>
<td>1,020</td>
<td>16/12</td>
<td>20</td>
<td>46</td>
</tr>
<tr>
<td></td>
<td>CIMPASI 2</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>CIMPACT*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Placebo controlled trials with active comparators
†Phase III trials of risankizumab are only available in the grey literature
All targeted immunomodulators had statistically significantly higher PASI 75, 90 and 100 responses compared to placebo.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>PASI 75 (%)</th>
<th>PASI 90 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Treatment</td>
<td>Placebo</td>
</tr>
<tr>
<td>Gusekumab</td>
<td>86-91</td>
<td>6-8</td>
</tr>
<tr>
<td>Tildrakizumab</td>
<td>62-66</td>
<td>6</td>
</tr>
<tr>
<td>Risankizumab</td>
<td>89</td>
<td>8</td>
</tr>
<tr>
<td>Certolizumab Pegol</td>
<td>75-83</td>
<td>4-12</td>
</tr>
</tbody>
</table>
### Direct Comparative Trials: PASI 75 & 90 outcome

<table>
<thead>
<tr>
<th>Trial/Treatment</th>
<th>PASI 75 (%)</th>
<th>PASI 90 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>VOYAGE 1 &amp; 2</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adalimumab</td>
<td>69-73</td>
<td>47-50</td>
</tr>
<tr>
<td>Guselkumab</td>
<td>86-91</td>
<td>70-73</td>
</tr>
<tr>
<td><strong>RESURFACE 2</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Etanercept</td>
<td>48</td>
<td>21</td>
</tr>
<tr>
<td>Tildrakizumab</td>
<td>61</td>
<td>39</td>
</tr>
<tr>
<td><strong>ULTIMMA 1 &amp; 2†</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ustekinumab</td>
<td>Data in confidence</td>
<td>42-48*</td>
</tr>
<tr>
<td>Risankizumab</td>
<td>Data in confidence</td>
<td>75*</td>
</tr>
<tr>
<td><strong>CIMPACT</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Etanercept</td>
<td>53</td>
<td>27</td>
</tr>
<tr>
<td>Certolizumab Pegol 400mg</td>
<td>67</td>
<td>34</td>
</tr>
<tr>
<td>Certolizumab Pegol 200mg</td>
<td>61</td>
<td>31</td>
</tr>
</tbody>
</table>

- Guselkumab was superior to adalimumab in two trials
- Tildrakizumab and 400mg certolizumab pegol were superior to etanercept in one trial each
- Risankizumab was superior to ustekinumab in two trials

*Data obtained from grey literature*
Network Meta-Analysis
RR of Achieving PASI 75 during induction relative to placebo

- Gusekumab
- Risankizumab*
- Tildrakizumab
- Certolizumab
- Adalimumab
- Etanercept
- Infliximab
- Ustekinumab
- Brodalumab
- Ixekizumab
- Secukinumab
- Apremilast
# Other Outcomes: Direct Comparative Trials

<table>
<thead>
<tr>
<th>Head-to-Head comparisons</th>
<th>Trials</th>
<th>N</th>
<th>PASI</th>
<th>IGA/PGA</th>
<th>DLQI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Guselkumab (vs. Adalimumab)</strong></td>
<td>2</td>
<td>1,829</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td><strong>Risankizumab (vs. Ustekinumab)</strong></td>
<td>2</td>
<td>997</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td><strong>Tildrakizumab (vs. Etanercept)</strong></td>
<td>1</td>
<td>1,090</td>
<td>↑</td>
<td>↔</td>
<td>↔</td>
</tr>
<tr>
<td><em><em>Certolizumab Pegol</em> (vs. Etanercept)</em>*</td>
<td>1</td>
<td>559</td>
<td>↑</td>
<td>ND</td>
<td>ND</td>
</tr>
</tbody>
</table>

400mg certolizumab pegol (200mg certolizumab pegol not different to etanercept)

Other Outcomes: Direct Comparative Trials

<table>
<thead>
<tr>
<th>Statistically better (superior)</th>
<th>↑</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not significant (Comparable)</td>
<td>↔</td>
</tr>
<tr>
<td>Statistically worse (Inferior)</td>
<td>↓</td>
</tr>
<tr>
<td>Limited or no data identified</td>
<td>No data</td>
</tr>
</tbody>
</table>
Harms

• **Induction: 10-16 weeks**
  • Serious adverse events rare: 2-4% (3% in placebo)
  • Any adverse effect: 46-58% (50% in placebo)
    • *Nasopharyngitis, upper respiratory tract infections, and headaches were the most common side effects*
  • Discontinuation due to AEs: 0.5-1.3%

• **Long-term safety**
  • 48-52 weeks available data for guselkumab, tildrakizumab, and risankizumab
  • Types and patterns were similar to the placebo-controlled periods
  • Similar to other TNF-α therapies certolizumab pegol has a boxed warning for serious infection and malignancy based on it’s longer term use in RA
Controversies and Uncertainties

• 16 of the 48 key trials are head-to-head comparisons
• Outcomes that patients said were important continue to be underreported
• Clinical outcomes based on short term data
• Subgroup data only for placebo comparisons
• No good evidence on choice of second line targeted immunomodulators
### ICER Evidence Ratings – New agents

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Adalimumab TNFα sc</th>
<th>Etanercept TNFα sc</th>
<th>Certolizumab TNFα sc</th>
</tr>
</thead>
<tbody>
<tr>
<td>Certolizumab pegol</td>
<td>C-</td>
<td>C (1)</td>
<td>-</td>
</tr>
<tr>
<td>Gusekumab</td>
<td>B (2)</td>
<td>C+</td>
<td>C+</td>
</tr>
<tr>
<td>Risankizumab</td>
<td>C+</td>
<td>B</td>
<td>C+</td>
</tr>
<tr>
<td>Tildrakizumab</td>
<td>I</td>
<td>C+ (1)</td>
<td>I</td>
</tr>
</tbody>
</table>

- Indirect comparison
- Direct comparison
- ¥ Based on conference abstract
Potential Other Benefits and Contextual Considerations

• All agents are administered SC except for apremilast (oral) and infliximab (IV)
  • SC may be less burdensome and has reduced complexity
  • Patients may favor the convenience of an oral drug

• New class of drugs that may offer new options for patients who did not achieve adequate control with the other agents
Public Comments Received

• Systematically include patient-reported outcomes (DLQI and others)
  • DLQI and other outcomes are reported when available. Outcomes other than PASI inconsistently reported across trials making cross-drug comparisons difficult. PASI relates closely.

• Add other subpopulations
  • No: Subpopulation analysis limited by available data. Evidence applicable to general patient population.

• Apremilast should not be viewed as part of the broader category of “targeted immunomodulators”
  • No: Apremilast is a targeted immunomodulator. Similar clinical use.

• Modify NMA methods, such as placebo adjustment
  • Scenarios and sensitivity analyses added that did not change the conclusions.
Cost Effectiveness

David Veenstra, PharmD, PhD
Professor
University of Washington
Key Review Team Members
Nathaniel Hendrix, PharmD, PhD student (UW)

Disclosures:
We have no conflicts of interest relevant to this report.
Objective

Estimate the cost-effectiveness of targeted treatment strategies for moderate-to-severe plaque psoriasis in patients who have failed treatment with methotrexate, phototherapy, and/or topical therapy.
Drugs evaluated

Included in CUA

- Adalimumab
- Apremilast
- Brodalumab
- Certolizumab pegol
- Etanercept
- Guselkumab

Threshold price only

- Risankizumab
- Tildrakizumab

- Infliximab
- Ixekizumab
- Secukinumab
- Ustekinumab
Overall Approach

• Population assumptions: mean age 45, mean weight 90 kg
• Payer perspective
• Ten-year time horizon summing costs, QALYs, time spent in PASI 90+ health states, and time spent in PASI 75+ health states
• Discount rate of 3%
Key Model Assumptions

• Patients remain on first-line therapy during the induction period
• All discontinuation in the first year is accounted for by lack of effectiveness at the end of the induction period, except for infliximab
• Of patients discontinuing their first-line targeted treatment, 75% continue to a second-line targeted treatment
• Risk of death is based on age alone
• Subcutaneously administered drugs are given once in the clinic, then subsequently by the patient themselves
Changes since 2016 report

- Updated net prices
- Switched from class-specific to drug-specific discounts
- Changed source of utility weights
- Included calculation of time spent in PASI 75+ and PASI 90+ health states
- Used updated drug discontinuation data
- Made choice of second-line treatment dependent upon first-line treatment
- Did not include adverse events in the base case
## Inputs: Treatment Sequence

<table>
<thead>
<tr>
<th>Initial treatment strategy</th>
<th>Second-line treatment strategy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guselkumab</td>
<td>Market basket average of all IL-17 drugs</td>
</tr>
<tr>
<td>IL-17 drugs</td>
<td>Guselkumab</td>
</tr>
<tr>
<td>Certolizumab and all other drugs</td>
<td>Market basket average of guselkumab plus all IL-17 drugs</td>
</tr>
</tbody>
</table>
Input: Effectiveness

• First-line targeted effectiveness derived from NMA results

• Second-line targeted treatment:
  • Assumed a 10 percentage point reduction in probability of achieving PASI 75 - 100, and a 10 percentage point increase in the probability of achieving PASI < 75.
## Inputs: Annual Discontinuation Rates

<table>
<thead>
<tr>
<th>Drug</th>
<th>Year 1 during initiation</th>
<th>Years 2+</th>
</tr>
</thead>
<tbody>
<tr>
<td>adalimumab</td>
<td>30%</td>
<td>5%</td>
</tr>
<tr>
<td>apremilast</td>
<td>63%</td>
<td>5%</td>
</tr>
<tr>
<td>brodalumab</td>
<td>13%</td>
<td>5%</td>
</tr>
<tr>
<td>certolizumab 200/400</td>
<td>31%</td>
<td>5%</td>
</tr>
<tr>
<td>etanercept</td>
<td>49%</td>
<td>10%</td>
</tr>
<tr>
<td>guselkumab</td>
<td>12%</td>
<td>5%</td>
</tr>
<tr>
<td>infliximab</td>
<td>21%*</td>
<td>10%</td>
</tr>
<tr>
<td>ixekizumab</td>
<td>11%</td>
<td>5%</td>
</tr>
<tr>
<td>secukinumab 300</td>
<td>17%</td>
<td>5%</td>
</tr>
<tr>
<td>ustekinumab 45/90</td>
<td>30%</td>
<td>5%</td>
</tr>
</tbody>
</table>

*An additional 35% of infliximab patients discontinue in the 1st year after initiation phase.

All second-line treatments discontinue at a rate of 15% per year.
Inputs: Dosing Considerations

• Certolizumab pegol
  • 50% receive 200mg dose, 50% 400mg dose

• Ustekinumab
  • 70% receive 45mg dose, 30% 90mg dose
## Inputs: Drug Costs

<table>
<thead>
<tr>
<th>Targeted drug</th>
<th>Maintenance cost per month</th>
</tr>
</thead>
<tbody>
<tr>
<td>infliximab</td>
<td>$2,479</td>
</tr>
<tr>
<td>apremilast</td>
<td>$2,585</td>
</tr>
<tr>
<td>brodalumab</td>
<td>$3,044</td>
</tr>
<tr>
<td>ixekizumab</td>
<td>$3,140</td>
</tr>
<tr>
<td>secukinumab 300</td>
<td>$3,181</td>
</tr>
<tr>
<td>ustekinumab 45/90</td>
<td>$3,549</td>
</tr>
<tr>
<td>adalimumab</td>
<td>$3,641</td>
</tr>
<tr>
<td>etanercept</td>
<td>$3,643</td>
</tr>
<tr>
<td>guselkumab*</td>
<td>$3,700</td>
</tr>
<tr>
<td>certolizumab 200/400</td>
<td>$4,213</td>
</tr>
</tbody>
</table>

*estimated drug discount
## Inputs: Quality of life weights

<table>
<thead>
<tr>
<th>State</th>
<th>Utility weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>PASI 90-100</td>
<td>0.903</td>
</tr>
<tr>
<td>PASI 75-89</td>
<td>0.856</td>
</tr>
<tr>
<td>PASI 50-74</td>
<td>0.827</td>
</tr>
<tr>
<td>PASI 0 – 50</td>
<td>0.718</td>
</tr>
<tr>
<td>Non-targeted</td>
<td>0.660</td>
</tr>
</tbody>
</table>

Derived from mapping the PASI onto the EQ-5D – not based on treatment; average of five submissions to NICE (adalimumab, apremilast, ixekizumab, secukinumab, ustekinumab) (Pickard, 2016)
Results
## Base-Case Results

<table>
<thead>
<tr>
<th>First-line Treatment</th>
<th>Total Cost</th>
<th>Total QALYs</th>
<th>Months spent in PASI 75+</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-targeted treatment</td>
<td>$67,800</td>
<td>5.70</td>
<td>0</td>
</tr>
<tr>
<td>Apremilast</td>
<td>$215,000</td>
<td>6.79</td>
<td>53.5</td>
</tr>
<tr>
<td>Etanercept</td>
<td>$272,000</td>
<td>6.88</td>
<td>57.9</td>
</tr>
<tr>
<td>Infliximab</td>
<td>$238,000</td>
<td>6.98</td>
<td>62.5</td>
</tr>
<tr>
<td>Certolizumab pegol</td>
<td>$341,000</td>
<td>7.16</td>
<td>73.5</td>
</tr>
<tr>
<td>Adalimumab</td>
<td>$308,000</td>
<td>7.17</td>
<td>74.1</td>
</tr>
<tr>
<td>Ustekinumab</td>
<td>$315,000</td>
<td>7.17</td>
<td>74.1</td>
</tr>
<tr>
<td>Secukinumab</td>
<td>$305,000</td>
<td>7.34</td>
<td>82.4</td>
</tr>
<tr>
<td>Brodalumab</td>
<td>$289,000</td>
<td>7.39</td>
<td>84.9</td>
</tr>
<tr>
<td>Guselkumab</td>
<td>$342,000</td>
<td>7.40</td>
<td>85.3</td>
</tr>
<tr>
<td>Ixekizumab</td>
<td>$311,000</td>
<td>7.42</td>
<td>86.1</td>
</tr>
</tbody>
</table>
## Base-Case Results: ICER vs non-targeted

<table>
<thead>
<tr>
<th>First-line Treatment</th>
<th>Cost / QALY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brodalumab</td>
<td>$131,000</td>
</tr>
<tr>
<td>Infliximab</td>
<td>$134,000</td>
</tr>
<tr>
<td>Apremilast</td>
<td>$135,000</td>
</tr>
<tr>
<td>Ixekizumab</td>
<td>$142,000</td>
</tr>
<tr>
<td>Secukinumab</td>
<td>$145,000</td>
</tr>
<tr>
<td>Guselkumab</td>
<td>$161,000</td>
</tr>
<tr>
<td>Adalimumab</td>
<td>$164,000</td>
</tr>
<tr>
<td>Ustekinumab</td>
<td>$169,000</td>
</tr>
<tr>
<td>Etanercept</td>
<td>$175,000</td>
</tr>
<tr>
<td>Certolizumab pegol</td>
<td>$188,000</td>
</tr>
</tbody>
</table>
One-Way Sensitivity Analyses

Guselkumab versus non-targeted

- Guselkumab price ($4,764, $8,848)
- QoL of non-targeted (±0.05)
- QoL of PASI 75 & 90 (±0.05)
- Non-targeted price per month ($313, $940)
- QoL of PASI < 75 (±0.05)
- 2L loss of PASI 75+ (0%, -20%)
- d/c % to 2L (50%, 100%)
- Discount rate (0%, 5%)
- 1L d/c rate (year>1, PASI 75+) [guselk.] (2.5%, 10%)
- Probability of PASI 75 [guselk.] (78%, 98%)
- Annual 2L -> no treatment (10%, 20%)
- 1L switch rate (year 1, PASI 75+) [guselk.] (0%, 10%)
- Cost per in-clinic sub-q inj ($20.67, $31.01)

High parameter value
Low parameter value
One-Way Sensitivity Analyses

Guselkumab versus etanercept

Comparison to etanercept shows comparison to step therapy
Guselkumab dominates at a unit price of $4,764
Probabilistic Sensitivity Analysis
Scenario analyses

• *Inclusion of productivity cost offsets*
  • Reduced ICERs by approximately $20,000, and did not change ordering of drugs
  • Guselkumab: $133,985 (-12%)
  • Certolizumab: $166,162 (-13%)

• *Lower doses for certolizumab and ustekinumab*
  • Assuming similar effectiveness across doses,
  • ICERs are $129,000 and $130,000, respectively
Limitations

• No robust data on treatment patterns and discontinuation rates in the US for most drugs
• The 10% loss of effectiveness for second-line treatment data was derived primarily from observational studies
• Associations between specific treatments and patient utilities not well studied
Comments Received

- Monthly dosing does not capture the correct drug quantities
  - We recalculated monthly cost via average daily dose

- Include dose escalation in model
  - Dose escalation depends heavily on payer policies; for this reason and due to lack of data in the US setting, we have not included it in the model

- Include productivity cost offsets for clinical response
  - Included in a scenario analysis
Summary

• Guselkumab may be cost-effective at a $150K/QALY threshold
  • Primarily dependent on drug price discount

• Dosing for certolizumab pegol reduces its value in the general population
  • Cost-effectiveness may be favorable for patients eligible to receive the lower dose

• Value for tildrakizumab and risankizumab currently unknown due to lack of a published price
  • Threshold analyses suggest value-based prices of ~$25-$40K annually
## Threshold Prices (updated)

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Annual price of maintenance therapy</th>
<th>Price needed for $50k/QALY</th>
<th>Price needed for $100k/QALY</th>
<th>Price needed for $150k/QALY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adalimumab</td>
<td>$43,700</td>
<td>$11,600</td>
<td>$25,700</td>
<td>$39,800</td>
</tr>
<tr>
<td>Apremilast</td>
<td>$31,000</td>
<td>&lt; $0</td>
<td>$17,500</td>
<td>$36,600</td>
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<tr>
<td>Brodalumab</td>
<td>$36,500</td>
<td>$14,900</td>
<td>$28,200</td>
<td>$41,500</td>
</tr>
<tr>
<td>Certolizumab pegol</td>
<td>$50,600</td>
<td>$11,300</td>
<td>$25,500</td>
<td>$39,700</td>
</tr>
<tr>
<td>Etanercept</td>
<td>$43,700</td>
<td>$1,700</td>
<td>$18,500</td>
<td>$35,400</td>
</tr>
<tr>
<td>Guselkumab</td>
<td>$44,400</td>
<td>$15,400</td>
<td>$28,400</td>
<td>$41,500</td>
</tr>
<tr>
<td>Infliximab</td>
<td>$29,700</td>
<td>$2,600</td>
<td>$18,800</td>
<td>$35,000</td>
</tr>
<tr>
<td>Ixekizumab</td>
<td>$37,700</td>
<td>$14,500</td>
<td>$27,100</td>
<td>$39,700</td>
</tr>
<tr>
<td>Risankizumab</td>
<td>NA</td>
<td>$14,700</td>
<td>$27,300</td>
<td>$39,800</td>
</tr>
<tr>
<td>Secukinumab</td>
<td>$38,200</td>
<td>$13,600</td>
<td>$25,500</td>
<td>$39,400</td>
</tr>
<tr>
<td>Tildrakizumab</td>
<td>NA</td>
<td>$9,200</td>
<td>$23,000</td>
<td>$36,800</td>
</tr>
<tr>
<td>Ustekinumab</td>
<td>$42,600</td>
<td>$12,600</td>
<td>$25,200</td>
<td>$37,800</td>
</tr>
</tbody>
</table>

Risankizumab and tildrakizumab costs are calculated without laboratory monitoring. Risankizumab and tildrakizumab assumed to be dosed at weeks 0 and 4, then Q12W, as in RCTs.
Public Comment and Discussion
Conflicts of interest:

- The National Psoriasis Foundation works with all the manufacturers that have a therapy in the psoriatic disease space, including AbbVie, Amgen, Boehringer Ingelheim, Celgene, Eli Lilly, Janssen, Merck, Novartis, Ortho Dermatologics, Pfizer, Sandoz, Sun Pharma, and UCB. A full list of their funders can be found in their Annual Report.
Manufacturer Public Comment and Discussion
Conflicts of interest:

- Receipt or potential receipt of anything of monetary value, including but not limited to, salary or other payments for services such as consulting fees or honoraria in excess of $5,000
- Equity interests such as individual stocks, stock options or other ownership interests in excess of $10,000

Brad Stolsheek is an employee and shareholder of Amgen.
Conflicts of interest:

- Receipt or potential receipt of anything of monetary value, including but not limited to, salary or other payments for services such as consulting fees or honoraria in excess of $5,000

Dr. Kaplan has been a speaker for AbbVie, Pfizer, and Celgene.
Voting Questions

WIFI Network: Student
Password: [Open Network]
0. How many stories is the tallest building in Vermont?

A. 8  
B. 25  
C. 11  
D. 32
Patient Population for all questions:
Patients with moderate-to-severe plaque psoriasis for whom treatment with topical therapies, older systemic therapies, and/or phototherapy has been ineffective, contraindicated, or not tolerated.
1. Is the evidence adequate to demonstrate that the net health benefit of certolizumab pegol is superior to that provided by the other subcutaneous TNFα inhibitors (adalimumab and etanercept)?

A. Yes
B. No
2. Is the evidence adequate to demonstrate that the net health benefit of guselkumab is superior to that provided by all subcutaneous TNFα inhibitors (adalimumab, etanercept, and certolizumab pegol)?

A. Yes
B. No
3. Is the evidence adequate to demonstrate that the net health benefit of risankizumab is superior to that provided by all subcutaneous TNFα inhibitors (adalimumab, etanercept, and certolizumab pegol)?

A. Yes
B. No
4. Is the evidence adequate to demonstrate that the net health benefit of tildrakizumab is superior to that provided by all subcutaneous TNFα inhibitors (adalimumab, etanercept, and certolizumab pegol)?

A. Yes
B. No
5. When compared to non-targeted therapy, do newer treatments for moderate-severe plaque psoriasis offer one or more of the following “potential other benefits”? (select all that apply)

This intervention:
A. Offers reduced complexity that will significantly improve patient outcomes.
B. Will reduce important health disparities across racial, ethnic, gender, socioeconomic, or regional categories.
C. Will reduce caregiver/family burden
D. Is a novel mechanism of action or approach
E. Will have a significant impact on improving return to work/overall productivity
F. Offers other important benefits or disadvantages.
6. Are any of the following contextual consideration important in assessing long-term value for money for the newer targeted immunomodulators? (select all that apply)

A. Intended for care of individuals with condition of high severity in terms of impact on quality and/or length of life

B. Intended for care of individuals with condition with high lifetime burden of illness

C. First to offer any improvement for patients

D. Compared to non-targeted therapies, there is significant uncertainty about long-term risk of serious side effects

E. Compared to non-targeted therapies, there is significant uncertainty about the magnitude or durability of long-term benefits

F. Other important contextual considerations.

___________
7. Given the available evidence on comparative clinical effectiveness and incremental cost effectiveness, and considering other benefits and contextual considerations, what is the long-term value for money of guselkumab compared with non-targeted therapy?

A. Low
B. Intermediate
C. High
8. Given the available evidence on comparative clinical effectiveness and incremental cost effectiveness, and considering other benefits and contextual considerations, what is the long-term value for money of certolizumab pegol compared with non-targeted therapy?

A. Low
B. Intermediate
C. High
Expert and CEPAC Panel Reflections
Next Steps

• Meeting recording posted to ICER website next week
• Final Report published on/about August 2
  • Includes description of CEPAC votes, deliberation; policy roundtable discussion
• Materials available at
  https://icer-review.org/meeting/psoriasis-update/
Break for Lunch.
Reconvene at 1:00pm.