Clinical Update:
The Impact of Novel Therapies

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Learning Objectives

• Review recent insights into the pathophysiology of atopic dermatitis (AD)
• Discuss the safety, efficacy and attributes of emerging therapies for the treatment of AD
Atopic Dermatitis: A Chronic Inflammatory Disease

• Estimated prevalence in the US\(^1\)
  ▪ Adults: 18 million (7.2%)
  ▪ Children (<18 years): 9.6 million (13%)
• Onset typically occurs before age 5
  ▪ Onset may also occur during adulthood\(^2,3\)
• Characterized by pruritus and xerosis\(^4\)
• Follows a waxing and waning course\(^2\)
• Significantly impairs quality of life\(^4\)
• Atopic comorbidities\(^4\)
  ▪ Asthma
  ▪ Allergic rhinitis

Genes and the Environment Influence the Natural History of AD

- AD is complex and multifactorial, characterized by genetic mutations, immune dysregulation, skin barrier dysfunction, and abnormal itch response

Genes linked to AD\(^1,2\)
- *FLG* (encodes profilaggrin, a skin barrier protein)
- *CARD11*
- Genes that encode inflammatory cytokines (e.g., IL-4, IL-5, IL-12, IL-13)

• Skin barrier dysfunction and Th2/Th22-deviated immune reactions are the fundamental abnormality in AD

• Antigen-mediated Th2 cell activation leads to cytokine release (eg, IL-4, IL-13) leading to:
  ▪ Further disruptions in the skin barrier by decreased expression of FLG
  ▪ IL-31 activation of nerve terminals that mediate itch
  ▪ Increased Th2 differentiation drives inflammation and immune activation

Mechanisms of Pruritus in AD

- Pruritus in AD is induced by a variety of histamine-dependent and independent pruritogens including
  - IL-4, IL-13, IL-31
  - Proteases
- IL-31 and nerve growth factors stimulate an increase in the number of epidermal sensory nerve fibers
- Novel AD therapies such as IL-4, IL-13, and IL-31 inhibitors exhibit antipruritic properties

H1R = histamine receptor type 1; H4R = histamine receptor type 4; JAK = Janus kinase; NK1R = neurokinin 1 receptor

Comorbidities More Likely to Occur in the AD Population vs Non-AD Controls

Adjusted Odds Ratio of comorbidities stratified by disease severity in a Commercial population

- Adult patients with a diagnosis of AD in a Commercial claims database* (n=83,106) vs non-AD controls
- AD patients were stratified by disease severity
- Comorbidity burden evaluated during a 12-month follow up

*Optum Health, Eden Prairie, MN

### Treatment of AD Has Historically Been Focused on Symptomatic Relief

<table>
<thead>
<tr>
<th>Nonpharmacologic</th>
<th>Topical Agents</th>
<th>Systemic Agents</th>
</tr>
</thead>
</table>
| • Skin moisturizers  
  ▪ Emollients  
  ▪ Occlusive agents  
  ▪ Humectants  
| • Corticosteroids  
  • Calcineurin inhibitors  
  • Antimicrobial and antiseptics  
  • Antihistamines  
| • Systemic corticosteroids  
  • Cyclosporine*  
  • Methotrexate*  
  • Azathioprine*  
  • Mycophenolate mofetil*  
  • Tacrolimus* |

*Not FDA-approved for AD treatment

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New and Emerging Therapies Target Specific Steps in the Th2 Pathway Integral to AD Pathogenesis

Recently Introduced Targeted Therapies Approved for the Treatment of AD

Systemic Therapy

- **Agent:** Dupilumab (Dupixent)
- **MOA:** IL-4 receptor alpha antagonist
- **Approval:** March 2017
- **Indication:** Treatment of adults with moderate-to-severe AD uncontrolled with topical therapies
- **Administration:** Subcutaneous injection (every-other-week)

Topical Therapy

- **Agent:** Crisaborole (Eucrisa 2% ointment)
- **MOA:** Phosphodiesterase (PDE)-4 inhibitor
- **Approval:** December 2016
- **Indication:** Topical treatment of mild-to-moderate AD in patients ≥2 years
- **Administration:** Topical use only (twice daily)

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Recently Approved Therapy: Dupilumab

**Indication:**
Dupilumab is indicated for the treatment of adults (≥18 years) with moderate-to-severe atopic dermatitis uncontrolled with topical therapies.
Dupilumab

Inhibition of IL-4 Intracellular Signaling

• Fully human IL-4α monoclonal antibody

• Binds to the IL-4 receptor α chain, a component of receptors for both IL-4 and IL-13

• Blocks both IL-4 and IL-13 signaling, cytokines that drive Th2-mediated inflammation


Dupilumab is indicated for the treatment of adults (≥18 years) with moderate-to-severe atopic dermatitis uncontrolled with topical therapies.
**Dupilumab Phase 3 SOLO Trials**

Patients with Moderate-to-Severe AD Treated with Dupilumab Experienced Significant Skin Clearing by Week 16

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**Primary Endpoint**

IGA of 0 or 1 and ≥2 points decrease from baseline at Week 16

- *p<0.001 vs placebo

**Key Secondary Endpoint**

EASI-75 at Week 16

- *p<0.001 vs placebo

---

IGA=Investigator’s Global Assessment; EASI-75=75% improvement in the Eczema Area and Severity Index.

IGA 0 = “clear”; IGA =1 = almost clear


Dupilumab is indicated for the treatment of adults (≥18 years) with moderate-to-severe atopic dermatitis uncontrolled with topical therapies.
**Dupilumab Phase 3 CHRONOS Trial**

Combined Treatment with Dupilumab + TCS Elicited Significant Skin Clearing at Week 16 Which Was Maintained Through Week 52

![Graph showing patient percentages for Primary Endpoint and Key Secondary Endpoint](image)

**Primary Endpoint**
IGA of 0 or 1 and ≥2 points decrease from baseline at Week 16

![Week 16 and Week 52 patient percentages for Primary Endpoint](image)

**Key Secondary Endpoint**
EASI-75 at Week 16

![Week 16 and Week 52 patient percentages for Key Secondary Endpoint](image)

IGA=Investigator’s Global Assessment; EASI-75=75% improvement in the Eczema Area and Severity Index; TCS=topical corticosteroids.

IGA 0 = “clear”; IGA 1 = almost clear


Dupilumab is indicated for the treatment of adults (≥18 years) with moderate-to-severe atopic dermatitis uncontrolled with topical therapies.
Safety Profile

**Warning and Precautions**

- **Hypersensitivity**
  - Discontinue treatment
- ** Conjunctivitis and keratitis**
  - Report new onset or worsening eye symptoms
- **Comorbid asthma**
  - Advise patients with comorbid asthma not to adjust or stop their asthma treatment without consultation with their physician

**Most Common Adverse Reactions**

(>1% in Phase 3 Trials)

- Injection site reactions
- Conjunctivitis
- Blepharitis
- Oral herpes
- Keratitis
- Eye pruritus
- Other herpes simplex virus
- Dry eye


Dupilumab is indicated for the treatment of adults (≥18 years) with moderate-to-severe atopic dermatitis uncontrolled with topical therapies.
**Dupilumab Phase 2a Data**

Treatment with Dupilumab Resulted in Extensive Skin Clearing in Children and Adolescents

**EASI in Children (6-11 years) with Severe AD**

- dupilumab 2 mg/kg (n=18): -32.6%
- dupilumab 4 mg/kg (n=19): -36.6%

**EASI in Adolescents (12-17 years) with Moderate-to-Severe AD**

- dupilumab 2 mg/kg (n=20): -33.9%
- dupilumab 4 mg/kg (n=20): -50.9%

EASI-75=75% improvement in the Eczema Area and Severity Index.

Recently Approved Therapy: Crisaborole

**Indication:**
Topical treatment of mild-to-moderate atopic dermatitis in patients ≥2 years.
Crisaborole
A Non-steroidal Phosphodiesterase (PDE)-4 Inhibitor

- PDE-4 modulates production of inflammatory cytokines by its action on cAMP

**Healthy Skin**
- Low PDE-4 → high cAMP → low cytokine release → low inflammation

**Atopic Dermatitis**
- Increase PDE-4 → low cAMP → increase cytokine release → increase inflammation

**PDE-4 Inhibition**
- PDE-4 inhibition increases cAMP and reduces cytokine release

PDE4 = phosphodiesterase 4; cAMP = cyclic adenosine monophosphate; AMP = adenosine monophosphate.


Crisaborole is indicated for the topical treatment of mild-to-moderate atopic dermatitis in patients ≥2 years.
Patients with Mild-to-Moderate AD Treated with Crisaborole Experienced Significant Skin Clearing and Reduction of Itch

Two identically designed, vehicle-controlled, double-blind studies enrolled patients ≥2 years with mild or moderate AD

**Primary Endpoint***

<table>
<thead>
<tr>
<th></th>
<th>Vehicle</th>
<th>Crisaborole</th>
</tr>
</thead>
<tbody>
<tr>
<td>AD-301 Patients Achieving Success at Day 29 (%)</td>
<td>25.4 32.8</td>
<td>18 31.4</td>
</tr>
<tr>
<td>n</td>
<td>256 503</td>
<td>250 513</td>
</tr>
</tbody>
</table>

*ISGA of 0 [clear] or 1 [almost clear] with ≥ 2 grade improvement from baseline.

Crisaborole is indicated for the topical treatment of mild-to-moderate atopic dermatitis in patients ≥2 years.
Crisaborole

Safety Profile

• Warnings and precautions
  ▪ Hypersensitivity reactions

• No treatment-related serious adverse events were reported in patients treated with crisaborole

• Majority of adverse events (AEs) were mild

• Most common AE (occurring in >1% of subjects) was application site pain

<table>
<thead>
<tr>
<th>Adverse event</th>
<th>Study AD-301</th>
<th>Study AD-302</th>
<th>Pooled</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Crisaborole</td>
<td>Vehicle</td>
<td>Crisaborole</td>
</tr>
<tr>
<td></td>
<td>(n=502)</td>
<td>(n=252)</td>
<td>(n=510)</td>
</tr>
<tr>
<td>Application site pain (%)</td>
<td>6.2</td>
<td>1.2</td>
<td>2.7</td>
</tr>
<tr>
<td>Upper respiratory tract infection (%)</td>
<td>2.8</td>
<td>4.0</td>
<td>3.1</td>
</tr>
</tbody>
</table>


Crisaborole is indicated for the topical treatment of mild-to-moderate atopic dermatitis in patients ≥2 years.
Agents in Late Phase Development for the Treatment of Atopic Dermatitis
# Topical Agents in Development for the Treatment of AD

<table>
<thead>
<tr>
<th>Target</th>
<th>Compound</th>
<th>Target Population</th>
<th>Current Status (Phase)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AhR</td>
<td>Tapinarof/Benvitimod</td>
<td>Moderate-to-severe</td>
<td>3</td>
</tr>
<tr>
<td>PDE-4</td>
<td>Roflumilast</td>
<td>Mild-to-moderate</td>
<td>2</td>
</tr>
<tr>
<td>PDE-4</td>
<td>RVT-501</td>
<td>Mild-to-moderate</td>
<td>2</td>
</tr>
<tr>
<td>JAK1, JAK2</td>
<td>Tofacitinib</td>
<td>Moderate-to-severe</td>
<td>2</td>
</tr>
<tr>
<td>JAK1, JAK2</td>
<td>Ruxolitinib</td>
<td>Moderate-to-severe</td>
<td>2</td>
</tr>
<tr>
<td>JAK1, JAK3</td>
<td>LEO 124249/JTE-052</td>
<td>Moderate-to-severe</td>
<td>2</td>
</tr>
</tbody>
</table>

AhR=aryl hydrocarbon receptor; PDE-4=phosphodiesterase-4; JAK=Janus kinase

<table>
<thead>
<tr>
<th>Target</th>
<th>Compound</th>
<th>Target Population</th>
<th>Current Status (Phase)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL-13</td>
<td>Tralokinumab</td>
<td>Moderate-to-severe</td>
<td>3</td>
</tr>
<tr>
<td>IL-13</td>
<td>Lebrikizumab</td>
<td>Moderate-to-severe</td>
<td>3</td>
</tr>
<tr>
<td>TSLP</td>
<td>Tezepelumab</td>
<td>Moderate-to-severe</td>
<td>2</td>
</tr>
<tr>
<td>IL-4</td>
<td>Pitrakinra</td>
<td>Moderate-to-severe</td>
<td>2</td>
</tr>
<tr>
<td>IL-5</td>
<td>Mepolizumab</td>
<td>Moderate-to-severe</td>
<td>2</td>
</tr>
<tr>
<td>IgE</td>
<td>Ligelizumab</td>
<td>Moderate-to-severe</td>
<td>2</td>
</tr>
<tr>
<td>IL-12/IL-23</td>
<td>Ustekinumab</td>
<td>Moderate-to-severe</td>
<td>2</td>
</tr>
<tr>
<td>IL-22</td>
<td>Fezakinumab</td>
<td>Moderate-to-severe</td>
<td>2</td>
</tr>
<tr>
<td>IL-17A</td>
<td>Secukinumab</td>
<td>Moderate-to-severe</td>
<td>2</td>
</tr>
<tr>
<td>IL-31</td>
<td>Nemolizumab</td>
<td>Moderate-to-severe</td>
<td>2</td>
</tr>
</tbody>
</table>

TSLP=thymic stromal lymphopoietin; IgE=immunoglobulin E

Tralokinumab

The IL-13 Inhibitor Tralokinumab + TCS Elicited Improvement in EASI in Patients with Moderate-to-Severe AD: Phase 2 Results

**Phase 2b Results**

**EASI Mean Change from Baseline**

**ECZTRA Phase 3 Trial Program**

- Evaluate the efficacy and safety of tralokinumab in patients with moderate-to-severe AD who are candidates for systemic therapy
- ECZTRA-1
  - Tralokinumab vs placebo (n=780)
- ECZTRA-2
  - Tralokinumab vs placebo (n=780)
- ECZTRA-3
  - Tralokinumab + topical corticosteroids (n=369)

EASI=Eczema Area and Severity Index; TCS=topical corticosteroids; ECZTRA= ECZema TRAlokinumab Trial.

Lebrikizumab
The IL-13 Inhibitor Lebrikizumab + TCS Elicited Skin Clearance in Patients with Moderate-to-Severe AD: Phase 2 TREBLE Trial

- Adults with moderate-to-severe AD; protocol-mandated b.i.d. use of topical corticosteroids
- Lebrikizumab dosed every 4 weeks
- Adverse events were similar between groups

SD=single dose
Q4W=every 4 weeks

Nemolizumab
The IL-31 Inhibitor Nemolizumab Significantly Reduced Itch in a Phase 2 Trial

**Primary Endpoint**
Percent Change From Baseline in the Pruritus Score at Week 12

<table>
<thead>
<tr>
<th>Group</th>
<th>Percent Change in Pruritus Score, baseline to Week 12</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>-20.9</td>
</tr>
<tr>
<td>0.1 mg/kg</td>
<td>-43.7</td>
</tr>
<tr>
<td>0.5 mg/kg</td>
<td>-59.8</td>
</tr>
<tr>
<td>2.0 mg/kg</td>
<td>-63.1</td>
</tr>
</tbody>
</table>

- Adults with moderate-to-severe AD (n=264)
- Nemolizumab dosed every 4 weeks

# Small Molecules in Development for the Treatment of AD

<table>
<thead>
<tr>
<th>Target</th>
<th>Compound</th>
<th>Target Population</th>
<th>Current Status (Phase)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PDE-4</td>
<td>Apremilast</td>
<td>Moderate-to-severe</td>
<td>2</td>
</tr>
<tr>
<td>H4R</td>
<td>ZPL389</td>
<td>Moderate-to-severe</td>
<td>2</td>
</tr>
<tr>
<td>JAK1, JAK2</td>
<td>Baricitinib</td>
<td>Moderate-to-severe</td>
<td>3</td>
</tr>
<tr>
<td>JAK1</td>
<td>PF-04965842</td>
<td>Moderate-to-severe</td>
<td>3</td>
</tr>
<tr>
<td>JAK1</td>
<td>Upadacitinib</td>
<td>Moderate-to-severe</td>
<td>3 (breakthrough therapy)</td>
</tr>
<tr>
<td>NK1R</td>
<td>Tradipitant</td>
<td>Moderate-to-severe</td>
<td>2</td>
</tr>
<tr>
<td>NK1R</td>
<td>Serlopitant</td>
<td>Moderate-to-severe</td>
<td>2</td>
</tr>
</tbody>
</table>

PDE=phosphodiesterase; H4R=histamine receptor type 4; JAK=Janus kinase; NK1R=neurokinin 1 receptor

Upadacitinib
The Oral, Selective JAK1 Inhibitor Upadacitinib Elicited Significant Skin Clearing and Reduction in Itch: Phase 2 Results

Phase 2b dose ranging study in adults patients with moderate-to-severe AD

Primary Endpoint
Mean % Change in EASI-50 From Baseline vs Placebo at Week 16

<table>
<thead>
<tr>
<th>Dose</th>
<th>Mean % Change in EASI-50 at Week 16</th>
<th>p-Value vs Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>23%</td>
<td></td>
</tr>
<tr>
<td>7.5 mg</td>
<td>39%</td>
<td>* p&lt;0.05</td>
</tr>
<tr>
<td>15 mg</td>
<td>62%</td>
<td>** p&lt;0.001</td>
</tr>
<tr>
<td>30 mg</td>
<td>74%</td>
<td>** p&lt;0.001</td>
</tr>
</tbody>
</table>

Pruritus Rating Scale
Mean % Change in Itch From Baseline vs Placebo at Week 16

<table>
<thead>
<tr>
<th>Dose</th>
<th>Mean % Change in Pruritus Score at Week 16</th>
<th>p-Value vs Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>10%</td>
<td></td>
</tr>
<tr>
<td>7.5 mg</td>
<td>40%</td>
<td>* p&lt;0.01</td>
</tr>
<tr>
<td>15 mg</td>
<td>48%</td>
<td>** p&lt;0.001</td>
</tr>
<tr>
<td>30 mg</td>
<td>69%</td>
<td>** p&lt;0.001</td>
</tr>
</tbody>
</table>

Most common AEs: upper respiratory tract infection, atopic dermatitis worsening and acne; Serious AEs occurred in 0/1/2 patients in the 30/15/7.5 mg groups vs 1 patient on placebo. No herpes zoster, malignancies, deaths or cases of pulmonary embolism or deep vein thrombosis occurred in the first 16 weeks of the study. EASI 50=50% improvement in the Eczema Area and Severity Index.

Baricitinib
The Oral, Selective JAK1/2 Inhibitor Baricitinib Elicited Significant Skin Clearing at Week 16: Phase 2 Results

Phase 2 randomized, double-blind, placebo-controlled study in adult patients with moderate-to-severe AD*

Primary Endpoint
% of Patients Achieving EASI-50 at Week 16

<table>
<thead>
<tr>
<th>Patients Achieving EASI-50 at Week 16 (%)</th>
<th>n=49</th>
<th>n=37</th>
<th>n=38</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>37%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baricitinib 2 mg + TCS</td>
<td>57%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baricitinib 4 mg + TCS</td>
<td>61†</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*p<0.027 baricitinib 4 mg vs placebo

Scoring Atopic Dermatitis (SCORAD) Total
% of Patients Achieving EASI-50 at Week 16

*Topical corticosteroids (TCS) were applied for 4 weeks before randomization; use of TCS permitted during the study.
Treatment-emergent AEs reported in 49%, 46%, and 71% of placebo, baricitinib 2 mg, and baricitinib 4 mg treated patients, respectively.

EASI 50=50% improvement in the Eczema Area and Severity Index.
Integrating New Therapies to Improve Disease Control
Where Do Targeted Therapies Fit into the Treatment Algorithm?

Disease Severity
- Severe
- Moderate
- Mild

Non-pharmacologic treatments
- Moisturizers
- Emollients
- Phototherapy

Topical agents
- Corticosteroids
- Calcineurin inhibitors
- Phosphodiesterase-4 inhibitors

Systemic treatments
- Cyclosporine
- Azathioprine
- Methotrexate
- Mycophenolate mofetil
- IL-4/IL-13 inhibitors
- IL-31 inhibitors*
- JAK inhibitors*

*investigational

Improving Disease Control in AD

• Traditionally, AD has been treated reactively, adjusting treatment in response to symptoms.

• Accumulating evidence suggests AD is a chronic systemic disease active even when symptoms are absent.

• Approaches to improving disease control while minimizing treatment-related AEs include:
  ▪ Preventive therapy
  ▪ Scheduled intermittent therapy
  ▪ Alternating therapy

• Targeted therapies may remove a barrier to proactive systemic treatment for moderate-to-severe AD.

Summary

• AD is a chronically relapsing inflammatory skin disease with a complex pathogenesis involving epidermal barrier dysfunction and immune-mediated cutaneous inflammation.

• Improved understanding of AD pathogenesis has led to targeted treatment strategies for moderate-to-severe disease.

• A wide range of biologic agents are under investigation for treatment of AD.

• The availability of targeted biologics may provide additional flexibility and personalization in the treatment in moderate-to-severe AD.

• Proactive treatment has the potential to result in better disease control.
Care Management Strategies to Improve Clinical and Economic Outcomes

Edmund Pezalla, MD, MPH
CEO
Enlightenment Bioconsult, LLC
Learning Objectives

• Evaluate strategies to align diagnosis and treatment strategies with current evidence-based guidelines

• Apply practical approaches to improve adherence to AD treatment
Moderate-to-Severe Atopic Dermatitis Affects More Than the Skin

**Sleep Disruption**
- 32.4% had 1-4 nights of disrupted sleep per week
- 55% had 5-7 nights of disrupted sleep per week

**Persistent Itch**
- 62.9% had itching lasting at least 12 hours a day
- 60.5% had severe or unbearable itching
- 55% had itching for at least 10 years

**Burden of Care**
- Time to access care
- Inconvenience
- Cost
- Managing side effects

**Psychological Distress**
- 22% had Hospital Anxiety and Depression Scale (HADS) scores suggesting clinically relevant anxiety or depression

n=380 patients with moderate-to-severe AD

A Diagnosis of AD is Associated with Increased Use of Health Care Resources

Adjusted mean annual number of health care visits and number of prescriptions per patient in AD patients and matched non-AD controls in a commercial population†

* *p<0.05 vs non-AD population

†Optum Health, Eden Prairie, MN
n=83,106

Disease Severity in Children and Adults with AD

**Children**
(0 to 17 years)

- 67%
- Moderate

- 26%
- Mild

- 7%
- Severe

**Adults**
(≥18 years)

- 67%
- Severe

- 26%
- Moderate

- 7%
- Mild

- Robust population-based estimates of the prevalence of moderate-to-severe AD in adults are lacking

- Extrapolation from other reports:
  - Approximately 0.7–1.2 million adults with diagnosed severe AD are receiving treatment
  - 25% of adults with AD do not seek treatment for their condition

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Assessing the Severity of Atopic Dermatitis

• >20 disease severity scales exist
• No “gold standard” scale
  ▪ Most commonly used is the Scoring Atopic Dermatitis index (SCORAD)
• Others include:
  ▪ Eczema Area and Severity Index (EASI)
  ▪ Patient-Oriented Eczema Measure (POEM)
  ▪ Investigator’s Global Assessment (IGA)
• Scales are primarily research tools; rarely used in clinical practice

• In clinical practice, severity determined by
  ▪ Duration of disease
  ▪ Thickness of skin lesions
  ▪ Duration and intensity of pruritus
  ▪ Body surface area involved
  ▪ Impact on quality of life (sleep, school/work, social life, etc)

The SCORAD is the Only AD Severity Scale that Includes Patient-Reported Subjective Symptoms

<table>
<thead>
<tr>
<th>Scale</th>
<th>Clinical Variables</th>
<th>Body Surface Area Affected</th>
<th>Subjective Symptoms</th>
<th>Endpoint</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Erythema</td>
<td>Edema / Papulation</td>
<td>Oozing / Crusts</td>
<td>Excoriation</td>
</tr>
<tr>
<td>SCORAD</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>EASI</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>IGA</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

Pruritus | Patient-reported itch severity 0 = no itch; 10 = worst imaginable itch

SCORAD = Scoring Atopic Dermatitis; EASI = Eczema Area and Severity Index; IGA = Investigator’s Global Assessment

Atopic Dermatitis is a Clinical Diagnosis

No universally accepted biomarker(s) to define disease stages, severity, or clinical success

<table>
<thead>
<tr>
<th>Essential Features: Rajka-Hanifin Criteria (must be present)</th>
<th>Important Features (seen in most cases, adding support to the diagnosis)</th>
<th>Associated Features (suggestive of AD, but too nonspecific to be definitive on their own)</th>
<th>Exclusionary Conditions (diagnosis of AD depends on excluding these conditions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Pruritus</td>
<td>• Early age of onset</td>
<td>• Atypical vascular response</td>
<td>• Scabies</td>
</tr>
<tr>
<td>• Eczema</td>
<td>• Atopy</td>
<td>• Keratosis pilaris</td>
<td>• Seborrheic dermatitis</td>
</tr>
<tr>
<td>• Typical morphology and age-specific patterns</td>
<td>• Personal and/or family history</td>
<td>• Ocular/periorbital changes</td>
<td>• Contact dermatitis</td>
</tr>
<tr>
<td>• Chronic or relapsing history</td>
<td>• Immunoglobulin E reactivity</td>
<td>• Perifollicular accentuation/lichenification/prurigo lesions</td>
<td>• Ichthyoses</td>
</tr>
<tr>
<td>• Xerosis</td>
<td></td>
<td></td>
<td>• Cutaneous T-cell lymphoma</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Psoriasis</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Immunodeficiency disorders</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Erythroderma of other causes</td>
</tr>
</tbody>
</table>

Management of AD Has Historically Focused on Symptom Relief

**Treatment Goals**

- Reduce symptoms (eg, itch, degree of skin involvement)
- Reduce inflammation
- Reduce frequency and severity of exacerbations (flares)
- Avoid triggers
- Minimize treatment-related adverse events
- Follow severity-directed treatment

**Factors Associated with Poor Prognosis**

- Family history of AD
- Early age of onset
- Body surface area involved
- Atopy

Treatment of AD is Evolving Rapidly

- Treatment has consisted of non-specific anti-inflammatory agents (eg, topical corticosteroids and systemic immunosuppressants*)
- Two targeted therapies (crisaborole, dupilumab) are now approved
- These agents target the immune dysfunction underlying the pathogenesis of AD

*oral immunosuppressants are being used off label

There is a need for practical guidance on the management of patients with moderate-to-severe AD requiring systemic therapy

*not indicated for the treatment of atopic dermatitis


### Evidence Assessment for Systemic Treatments for Adults Inadequately Controlled on Topical Therapy

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Phototherapy</td>
<td>Small</td>
<td></td>
<td></td>
<td>Caution or insufficient evidence</td>
<td></td>
<td>Moderately frequent and/or extensive</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>Moderate</td>
<td></td>
<td></td>
<td>Positive effects</td>
<td></td>
<td>Frequent and/or extensive</td>
</tr>
<tr>
<td>Cyclosporine</td>
<td>Moderate</td>
<td></td>
<td></td>
<td></td>
<td>Negative effects</td>
<td>Frequent and/or extensive</td>
</tr>
<tr>
<td>Azathioprine</td>
<td>Moderate</td>
<td></td>
<td>Caution or insufficient evidence</td>
<td></td>
<td></td>
<td>Frequent and/or extensive</td>
</tr>
<tr>
<td>Mycophenolate</td>
<td>Small</td>
<td></td>
<td></td>
<td>Caution or insufficient evidence</td>
<td></td>
<td>Frequent and/or extensive</td>
</tr>
<tr>
<td>Prednisone</td>
<td>Small</td>
<td>Caution or insufficient evidence</td>
<td></td>
<td></td>
<td></td>
<td>Moderately frequent and/or extensive</td>
</tr>
<tr>
<td>Dupilumab</td>
<td>Large</td>
<td>Positive effects</td>
<td></td>
<td></td>
<td></td>
<td>Infrequent</td>
</tr>
<tr>
<td>Investigational targeted agents</td>
<td>N/A</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>N/A</td>
</tr>
</tbody>
</table>

Desirable attributes of systemic treatments for adult AD include: 1) reduction in the signs/symptoms of disease, 2) established short- and long-term safety, 3) regulatory approval for treatment of AD, and 4) minimal laboratory monitoring.

Identifying Candidates for Systemic Therapy

- Characteristics of patients who are candidates for systemic therapy
  - Itch that disrupts sleep
  - Significant body surface area involvement (BSA ≥10%)
  - Impaired quality of life
  - Low risk for opportunistic infection

Comparative Clinical Effectiveness of Crisaborole and Dupilumab

• Methodology
  ▪ Meta-analysis of evidence from randomized controlled trials, comparative observational studies, and high-quality systematic review
  ▪ Focused on key clinical outcomes common to AD trials as well as symptoms and burden of the disease

• Included two assessments
  • Comparative clinical effectiveness of crisaborole for its indication in the treatment of mild-to-moderate AD in children and adults
  • Evaluation of the comparative clinical effectiveness and value of dupilumab for the treatment of moderate-to-severe AD in adults

Analytic Framework of the Analyses

**Interventions**
- Crisaborole or Dupilumab

**Population**
1. Adults and children with mild-to-moderate AD
2. Adults with moderate-to-severe AD

**Intermediate Outcomes**
- EASI 50, 75, 90
- IGA
- SCORAD

**Key Measures of Clinical Benefit**
- Health-related quality of life
- Functional outcomes
- Other patient-reported outcomes

**Adverse Events**
- Systemic
- Dermatologic
- Ophthalmic
- Endocrine
- Pulmonary
- Others

### Results: Dupilumab Offers Important Clinical Benefits for Adults with Moderate-to-Severe AD

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Dupilumab</th>
<th>Crisaborole</th>
</tr>
</thead>
<tbody>
<tr>
<td>IGA</td>
<td>• Successful outcomes in 30% - 44% of patients vs 1% – 12% placebo</td>
<td>• Modestly increased the likelihood of achieving success at 4 weeks vs vehicle</td>
</tr>
<tr>
<td></td>
<td>• Dosing schedule and concomitant use of topical corticosteroids (TCS) had no impact on results</td>
<td></td>
</tr>
<tr>
<td>EASI</td>
<td>• Increased likelihood of achieving EASI 75 vs placebo</td>
<td>• Not reported</td>
</tr>
<tr>
<td></td>
<td>• Dosing schedule and concomitant use of TCS had no impact on results</td>
<td></td>
</tr>
<tr>
<td>PROs</td>
<td>• Improved quality of life, symptoms scores, and measures of anxiety and depression</td>
<td>• Improved quality of life as measured by DLQI and CLQI, however the differences were smaller than those usually considered clinically meaningful</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Modestly reduced pruritus</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Reduce caregiver burden</td>
</tr>
<tr>
<td>Harms</td>
<td>• Well-tolerated; AEs were rare during treatment up to 16 weeks</td>
<td>• Well-tolerated; AEs were rare during all clinical trials</td>
</tr>
<tr>
<td></td>
<td>• Injection-site reactions, nasopharyngitis, and headache were the most common AEs</td>
<td></td>
</tr>
<tr>
<td>Summary</td>
<td>• Appears to be at least as efficacious as cyclosporine (typically the preferred systemic therapy currently available) and more efficacious than phototherapy</td>
<td>• Inadequate evidence to assess the relative efficacy of crisaborole vs topical calcineurin inhibitors and TCS</td>
</tr>
</tbody>
</table>

Modeling the Long-term Cost-Effectiveness of Dupilumab

- A Markov model was developed to estimate the cost-effectiveness of dupilumab for moderate-to-severe AD vs usual care over a lifetime horizon
- Health state was categorized by the percent decrease in EASI after initiating dupilumab or usual care
  - All patients entered the model in the “non-responder” state
  - Patients could then transition to responder states one cycle after initiation of treatment
- Utility values for quality-of-life and costs were applied to each health state
- An annual list price for dupilumab used in the model: $37,000
- An estimate of the annual cost of care was also included

# Base Case Results: Dupilumab is Cost Effective

<table>
<thead>
<tr>
<th></th>
<th>Usual Care</th>
<th>Dupilumab</th>
<th>Incremental</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total costs</td>
<td>$271,461</td>
<td>$466,168</td>
<td>$194,708</td>
</tr>
<tr>
<td>Drug costs*</td>
<td>--</td>
<td>$224,372</td>
<td>$244,372</td>
</tr>
<tr>
<td>Other health care costs</td>
<td>$271,461</td>
<td>$241,796</td>
<td>-$29,665</td>
</tr>
<tr>
<td>QALYs</td>
<td>14.37</td>
<td>16.28</td>
<td>1.91</td>
</tr>
<tr>
<td>Cost per additional QALY</td>
<td>--</td>
<td>--</td>
<td>$101,830</td>
</tr>
</tbody>
</table>

*Based on the net price for dupilumab.

- Dupilumab provided an additional 1.91 QALYs over the remaining lifetime of patients, leading to an incremental cost-effectiveness ratio of $101,800 per additional QALY gained.
- Cost per additional QALY was lower for patients with severe AD ($78,300) vs those with moderate AD ($130,800)

---

Dupilumab Offers Good Long-term Value for Adults with Moderate-to-Severe AD

<table>
<thead>
<tr>
<th></th>
<th>Moderate</th>
<th></th>
<th>Severe</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Usual Care</td>
<td>Dupilumab</td>
<td>Incremental</td>
<td>Usual Care</td>
</tr>
<tr>
<td>Total costs</td>
<td>$271,356</td>
<td>$482,861</td>
<td>$211,506</td>
<td>$271,579</td>
</tr>
<tr>
<td>Drug costs</td>
<td>--</td>
<td>$243,786</td>
<td>$243,786</td>
<td>--</td>
</tr>
<tr>
<td>Other health care costs</td>
<td>$271,356</td>
<td>$239,075</td>
<td>-$32,281</td>
<td>$271,579</td>
</tr>
<tr>
<td>QALYs</td>
<td>16.00</td>
<td>17.62</td>
<td>1.62</td>
<td>12.52</td>
</tr>
<tr>
<td>Cost per additional QALY</td>
<td>--</td>
<td>--</td>
<td>$130,807</td>
<td>--</td>
</tr>
</tbody>
</table>

- Patients with moderate disease had lower health care costs but higher drug costs vs the total population
- Patients with moderate disease gained fewer QALYs with dupilumab treatment vs severe patients
- Patients with severe disease had higher health care costs but lower drug costs vs the total population

Determining the Cost Per Additional QALY for Dupilumab vs Usual Care

- Sensitivity analysis was used to demonstrate the effects of uncertainty on health care cost and outcomes
- Key drivers of the base case population included
  - Utility values for quality of life (particularly for non-responders)
  - Price of dupilumab
- Probability of dupilumab being cost effective vs usual care at the $150,000 per QALY threshold
  - 88% overall
  - 70% in patients with moderate AD
  - 95% in patients with severe AD

The ICER for Dupilumab is At or Below Commonly Cited Thresholds for Cost-Effectiveness

<table>
<thead>
<tr>
<th></th>
<th>Dupilumab Mean</th>
<th>Credible Range</th>
<th>Usual Care Mean</th>
<th>Credible Range</th>
<th>Incremental Mean</th>
<th>Credible Range</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total</strong></td>
<td>$466,886</td>
<td>$364,604—$714,037</td>
<td>$271,334</td>
<td>$238,690—$303,910</td>
<td>$195,553</td>
<td>$101,073—$436,399</td>
</tr>
<tr>
<td>Total costs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total QALYs</td>
<td>16.28</td>
<td>14.43—18.14</td>
<td>14.37</td>
<td>12.21—16.52</td>
<td>1.91</td>
<td>1.23—2.64</td>
</tr>
<tr>
<td>ICER</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>$105,764</td>
<td>$49,805—$247,604</td>
</tr>
<tr>
<td><strong>Moderate</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total costs</td>
<td>$485,099</td>
<td>$363,682—$883,929</td>
<td>$271,107</td>
<td>$232,554—$312,740</td>
<td>$213,993</td>
<td>$103,512—$612,720</td>
</tr>
<tr>
<td>Total QALYs</td>
<td>17.62</td>
<td>15.34—19.94</td>
<td>16.00</td>
<td>13.11—18.88</td>
<td>1.62</td>
<td>0.64—2.68</td>
</tr>
<tr>
<td>ICER</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>$129,299</td>
<td>$52,763—$492,019</td>
</tr>
<tr>
<td><strong>Severe</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total costs</td>
<td>$446,446</td>
<td>$349,393—$723,588</td>
<td>$271,605</td>
<td>$233,140—$313,696</td>
<td>$174,841</td>
<td>$87,420—$447,697</td>
</tr>
<tr>
<td>ICER</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>$80,772</td>
<td>$36,184—$208,567</td>
</tr>
</tbody>
</table>

Threshold Analysis Results Suggests Patients Who May Benefit From Dupilumab Are Able to Access It

**Annual Net Price of Dupilumab that Would Achieve Cost-Effectiveness**

<table>
<thead>
<tr>
<th>Threshold</th>
<th>Annual Net Price of Dupilumab</th>
</tr>
</thead>
<tbody>
<tr>
<td>$50,000/QALY gained</td>
<td>$17,307</td>
</tr>
<tr>
<td>$100,000/QALY gained</td>
<td>$30,516</td>
</tr>
<tr>
<td>$150,000/QALY gained*</td>
<td>$43,726</td>
</tr>
</tbody>
</table>

*The price of dupilumab would have to increase to reach the $150,000 per QALY cost-effectiveness threshold.

- For moderate patients, the threshold prices to reach $50,000, $100,000, and $150,000 per QALY would be $14,385, $24,665, and $34,946 respectively, vs $21,275, $38,460, and $55,646, respectively, for severe patients.

Budgetary Impact: Dupilumab is Priced In a Way That Aligns Well With the Benefit It Provides Patients

- ~4% of eligible patients could be treated in a given year without crossing the ICER budget impact threshold of $915 million at WAC ($37,000)

- The low proportion of AD patients that could be treated at each price point reflects the impact that a new treatment may have in a condition with few current treatments

- Because dupilumab is not displacing a current therapy, there are fewer offsetting treatment costs for these patients

Summary

- AD is a chronic relapsing-remitting inflammatory skin disease associated with a significant clinical, humanistic, and economic burden
- AD is a clinical diagnosis based on lesion thickness, duration and intensity of pruritus, body surface area involved, and impact on quality of life
- Treatment is dependent on disease severity, but no uniform measure of severity is currently available
- Treatment guidelines are available, but do not include recently approved therapies
- A comparative effectiveness analysis indicated dupilumab appears to be at least as efficacious as cyclosporine whereas there was insufficient evidence to assess the relative efficacy of crisaborole vs other topic therapies
- An economic modeling analysis indicates that dupilumab improves health outcomes compared to usual care, but with additional costs
Benefit Design and Specialty Pharmacy Services for Optimal Management

Jeffrey D. Dunn, PharmD, MBA
Vice President, Clinical Strategy and Programs and Industry Relations
Magellan Rx Management
Learning Objective

• Assess benefit design strategies to improve overall patient outcomes for AD
Atopic Dermatitis (AD) is Associated with Significant Burden

- Characterized by intense itching and recurrent eczematous lesions\(^1\)
- Typically starts in infancy, but also highly prevalent in adults\(^1\)
- Associated with acute flares, intractable pruritus, and comorbid health conditions which may prompt urgent care visits\(^2\)
- Among the top 4 reasons for a visit to a dermatologist or other\(^1\) specialist

---

2. Kwa L, Silverberg JJ. Abstract 7021: Emergency department visits are common and costly in atopic dermatitis in the United States. Oral presentation at American Academy of Dermatology; February 2018; San Diego, Calif.
Managed Care Perspective on the Economic Impact of AD

**Burden of AD**
- Poorer overall health
- Higher out-of-pocket costs
- More physician visits
- More lost work days
- Delayed care

**Impact**
- High demand for care
- High utilization of care
- Need for utilization management strategies
  - To guide appropriate use of therapy
  - To ensure predictable spend

Silverberg JI. *JAMA Dermatol.* 2015;151(7):743-52.
Introduction of Specialty Drugs for AD Requires Careful Consideration of the AD Pharmacy Benefit

- Crisaborole and dupilumab have the potential to change AD care
- These agents are likely to improve health outcomes vs usual and existing care, but at an additional cost
- With ~400,000 adults potentially eligible for treatment with dupilumab, appropriate management strategies will be needed to manage costs


Cost of Treating Atopic Dermatitis

- $30/month Methotrexate
- $150/month Topical Corticosteroids
- $500/month Topical Immunosuppressants
- $2,500-$3,000/month Dupilumab
Robust Pipeline of Targeted AD Drug Candidates Ensures the Specialty Spend Will Continue to Increase

Historic and Projected Specialty Drug Spend

- **2013**: 30% Specialty, 70% Traditional
- **2018**: 50% Specialty, 50% Traditional
- **2021**: 60% Specialty, 40% Traditional

Specialty Drug Trend: Forecasted PMPY Drug Spend

Costs Can Be Effectively Managed by Aligning Distribution, Plan Design and Pharmacy Care Management

Output

Better Outcomes Lower cost

- Cost and Distribution Management
- Plan Design
- Pharmacy Care Management

Incentives and Copay Assistance

Technology and Support Tools
# Basic Tenets of the Specialty Drug Benefit

<table>
<thead>
<tr>
<th><strong>Utilization Management</strong></th>
<th>• Reduce costs by aggressively managing drug utilization</th>
</tr>
</thead>
</table>
| **Preferred Drug Management** | • Establish preferred products and formulary tiers  
• Use cost sharing to drive use of preferred products, but not limit adherence |
| **Contract Management** | • Aggressively negotiate rebates  
• Incent providers to utilize the most cost-effective drugs |
| **Channel Management** | • For pharmacy, optimize the distribution network  
• Optimize site of care |
| **Care Management** | • Provide counseling and education to patients and caregivers  
• Incent coordinated care |

Elements Typically Found in the AD Benefit Design

- **Incentive Programs**
  - Members
  - Prescribers

- **Patient Access Support Programs**
  - Patient assistance
  - Copay coupons

- **Case Management**
  - Efforts to increase patient ownership of their care

- **Special Pharmacy Integration**

- **Coordination**
  - Data management
  - Integrated IT
Value = Cost Effectiveness

- Efficacy
- Price
- Cost per event avoided
- Cost per % improvement
- Helps compare agents
  - When there are no head-to-head trials

### Cost Difference

<table>
<thead>
<tr>
<th>C+</th>
<th>Intervention more effective and more costly than 0; Depends how much effectiveness you are willing to pay for increased effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>E+</td>
<td>Intervention more effective and less costly than 0; Clear Winner</td>
</tr>
<tr>
<td>E-</td>
<td>Intervention less effective and less costly than 0; Clear Loser</td>
</tr>
<tr>
<td>C-</td>
<td>Intervention less effective and more costly than 0; When there are no head-to-head trials</td>
</tr>
</tbody>
</table>
Elements of the AD Benefit Design: Formulary Tiers

• Trend is toward multi-tier formularies
• Patient cost is dependent on the formulary tier
  • Tier 1: lowest cost
  • Tier 2: slightly higher cost
  • Tier 3: higher cost
  • Tier 4 (specialty drugs): highest cost
• Formulary positioning depends on the demonstrated value of the drug as assessed by the plan sponsor

<table>
<thead>
<tr>
<th>Tier 1 Generic</th>
<th>Tier 2 Preferred</th>
<th>Tier 3 Non-preferred</th>
<th>Tier 4 Specialty</th>
</tr>
</thead>
<tbody>
<tr>
<td>$$$</td>
<td>$$$$</td>
<td>$$$$$</td>
<td>$$$$$$$</td>
</tr>
</tbody>
</table>

- Least expensive, including all generics and select brands
- Brand name drugs proven to be most effective in their class
- Non-preferred brand names not considered to be the most effective as well as preferred specialty drugs
- The most expensive drugs; typically non-preferred, branded specialty drugs

### Pharmacy Benefit

<table>
<thead>
<tr>
<th>Tier</th>
<th>Drug</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preferred generic</td>
<td>$5</td>
<td></td>
</tr>
<tr>
<td>Non-preferred generic</td>
<td>$10</td>
<td></td>
</tr>
<tr>
<td>Preferred brand</td>
<td>$50</td>
<td></td>
</tr>
<tr>
<td>Non-preferred brand</td>
<td>$100</td>
<td></td>
</tr>
<tr>
<td>Preferred specialty</td>
<td>10%</td>
<td></td>
</tr>
<tr>
<td>Non-preferred specialty</td>
<td>20%</td>
<td></td>
</tr>
</tbody>
</table>

### Medical Benefit

<table>
<thead>
<tr>
<th>Tier</th>
<th>Drug</th>
<th>Cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-specialty</td>
<td></td>
<td>NA</td>
</tr>
<tr>
<td>Preferred specialty</td>
<td></td>
<td>10%</td>
</tr>
<tr>
<td>Non-preferred specialty</td>
<td></td>
<td>20%</td>
</tr>
</tbody>
</table>
Traditional Versus Potential Value-based Contracting

- 45% of private payers were involved in pay-for-performance and risk-sharing programs in 2010; the number rose to 62% in 2013, and usage of these programs was estimated to be as high as 75% in 2016.

**Traditional Contracting**
- Flat, Volume, or Share-Based
  - Concessions may depend on volume or share
  - Rebate %s for Purchased Brand A

**Value-Based Contracting**
- Indication-Based
  - Rebate specific to an indication
- Regimen-Based
  - Rebate paid when two products used in combination
- “Outcomes” Based
  - Concessions depend on how ‘well’ the drug works for a patient/cohoot

*Drug manufacturers will increasingly find themselves involved in such arrangements with payers when applicable.*

Increasing Data & Complexity

Manufacturers Are Using “Buy Downs” to Offset Increasing Patient Cost Exposure

Copay Coupons Are Used to Reduce Patient Costs But May Potentially Circumvent Formulary Controls

- In 2015, the pharmaceutical industry spent upward of $7 billion to fund coupons.2
- 75% of members prescribed a Tier 3 drug are using a copay coupon3
- Coupon use is expected to increase to 500 million prescriptions by 20214

Coupons May Be Beneficial for Certain Preferred Drugs

• For traditional drugs and non-preferred specialty drugs, coupons often lead to use of therapies with higher net costs

• Coupons may be beneficial for the subset of members who have high-deductible health plans or high coinsurance prescribed certain preferred specialty drugs
  ▪ Coupon programs that reduce monthly cost sharing to >$250 are associated with a lower risk for patient abandonment of biologic anti-inflammatory therapy

• However, as a way to drive greater savings for plan sponsors, two new specialty copay card programs were introduced in 2017: accumulator adjustment and copay allowance maximization
  ▪ These programs may have unintended consequences

Real Savings Come From Providing Optimal Clinical Support and Care Management

\[ \text{Total Pharmacy Cost} = \text{Price} + \text{Management} \]
Components of Care Management

**Assess Safety**
- Adverse events
- Allergies
- Drug interactions

**Verify Clinical Appropriateness**
- Route of administration
- Strength/dose
- Dosing frequency
- REMS

**Adherence**
- Access assistance
- Initial fill
- Refills

**Monitoring**
- Review progress toward goals
- Manage therapy interruptions

**Patient Education**
- Treatment expectations
- Medication administration
- Support programs

Role of Specialty Pharmacy

• Specialty pharmacists can help determine coverage and service levels for individual health plans or specific products, and reimbursement rates.

• Specialty pharmacists have a good appreciation of unique factors of value to managed care:
  ▪ Market pressure
  ▪ Cost
  ▪ Clinical effectiveness and medical evidence
  ▪ Legislated mandate
  ▪ Medical necessity
  ▪ Preventive value
**Specialty Pharmacy is Well-Positioned to Support Care Management Activities**

<table>
<thead>
<tr>
<th>Patient Education</th>
<th>Drug Administration</th>
<th>Drug Dosing</th>
<th>Monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Therapy expectations</td>
<td>• Train patients and caregivers</td>
<td>• Individualization of dosing</td>
<td>• Adherence support</td>
</tr>
<tr>
<td>• Dosing</td>
<td>• Drug preparation</td>
<td>• Dosing frequency</td>
<td>• Concurrent medications</td>
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<tr>
<td>• Adverse events</td>
<td>• Proper administration techniques</td>
<td></td>
<td>• Adverse events</td>
</tr>
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<td>• Follow up</td>
<td>• Proper handling, storage, and disposal</td>
<td></td>
<td>• Drug interactions</td>
</tr>
<tr>
<td>• Shipping and storage requirements</td>
<td></td>
<td></td>
<td>• Comorbidities</td>
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<td>• Patient access/insurance</td>
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Successful AD Pharmacy Management Requires Finding the Appropriate Balance

- Drug Dispensing
- Specialty Drug Management
- Utilization Management
- Contracting Activities
- Coordination of Care
- Benefit Design (Cost Share) & Formulary
Summary

• The AD treatment landscape is evolving rapidly with the introduction of two novel products and several others in late-stage development

• While many patients stand to gain with the growth in the number of therapeutic options, these benefits will come at a higher cost

• To ensure patient access to these innovative therapies, the AD benefit must evolve to maintain a balance between access, appropriate use, and cost management
The Management of Atopic Dermatitis:
Entering a New Paradigm