Confronting the Challenge of Managing Moderate-to-Severe *Atopic Dermatitis*

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Integrating Atopic Dermatitis Diagnosis and Treatment Guidelines with Health Plan Algorithms to Optimize Outcomes

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Learning Objectives

- Align diagnosis and treatment strategies with evidence-based guidelines to optimize atopic dermatitis (AD) treatment outcomes
- Apply methods to improve adherence to AD treatment

Atopic Dermatitis: The Most Common Inflammatory Skin Disease

- Chronic, relapsing-remitting course characterized by persistent pruritus[1]
- Affects >30 million Americans[2]
  - ~13% of children[3]
    - ~1/3 with moderate to severe disease[3]
  - 2-3% of adults[1]
    - Severity varies widely in adults[1]
- Multifactorial etiology; commonly associated with asthma and allergies[1]
- High negative impact on quality of life[1]

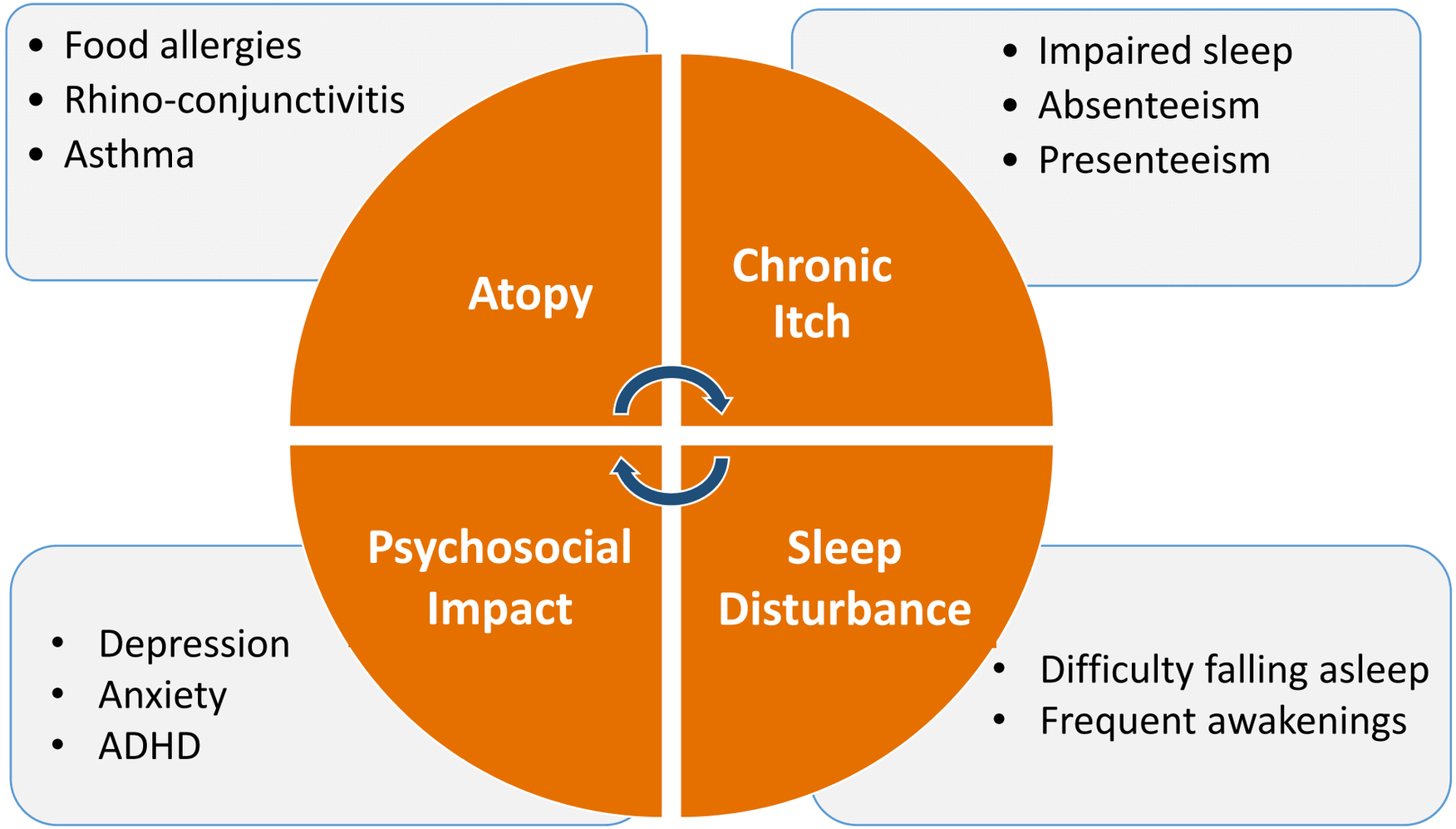
Infants

Children & Adolescents

Adults

1. Eichenfield LF, Tom WL, Chamlin SL, et al. Guidelines of care for the management of atopic dermatitis: section 1. Diagnosis and assessment of atopic dermatitis. *J Am Acad Dermatol*. 2014;70(2):338-51.
2. Hanifin JM, Reed ML. A population-based s2014;70. Survey of eczema prevalence in the United States. *Dermatitis*. 2007;18(2):82-91.
3. Silverberg JI, Simpson EL. Associations of childhood eczema severity: a US population-based study. *Dermatitis*. 2014;25(3):107-14.

Clinical Presentation: AD Impacts More Than the Skin



Simpson EL, Bieber T, Eckert L, et al. Patient burden of moderate to severe atopic dermatitis (AD): Insights from a phase 2b clinical trial of dupilumab in adults. *J Am Acad Dermatol*. 2016;74(3):491-8.

Economic Burden: Increased Use of Health Care Resources

- A diagnosis of AD is associated with increased physician visits, emergency department visits, and hospitalizations[1]
  - 75% of patients with AD visited a doctor at least once in the last year specifically for their AD[1]
- Patients with AD had an average of $371 higher out-of-pocket costs per person/year vs those without AD[1]
- AD causes the highest disability-adjusted life-years among all skin disorders[1]
  - AD patients 53% more likely to have >6 lost workdays vs those without AD[2]

1. Silverberg JI. Health Care Utilization, Patient Costs, and Access to Care in US Adults With Eczema: A Population-Based Study. JAMA Dermatol. 2015;151(7):743-52.
2. Mohan GC, Silverberg JI. Association of Vitiligo and Alopecia Areata With Atopic Dermatitis: A Systematic Review and Meta-analysis. *JAMA Dermato*l. 2015;151(5):522-8.

Prognosis

- In general, individual outcomes are difficult to predict
  - Spontaneous resolution in 40-60% of infants, especially with mild disease
  - 20% of cases resolve by adolescence
- Features of AD associated with a poor prognosis include
  - Family history of AD
  - Early age of onset
  - Body surface area involved
  - Atopy

Unmet Needs

- Need for disease severity and quality of life scales for use in clinical practice
  - >20 instruments to assess disease severity in clinical trials, but these have limited clinical application
- No universally accepted biomarker to define disease stages, severity, or clinical success
- Limited use of effective and safe therapeutic options for long-term treatment of moderate-to-severe disease
- Due to a lack of comparative data, treatment effects of existing therapies cannot be readily compared

Eichenfield LF, Tom WL, Chamlin SL, et al. Guidelines of care for the management of atopic dermatitis: section 1. Diagnosis and assessment of atopic dermatitis. *J Am Acad Dermatol*. 2014;70(2):338-51.

Physician Management of AD

Mild Disease

Managed by pediatricians and primary care providers[1]

Moderate-to-Severe Disease

Referral to dermatology, allergy, multidisciplinary clinics[1,2]

- Multidisciplinary interventions show promise in improving adherence, disease control, and quality of life for patients with AD and their families[2]

1. Eichenfield LF, Boguniewicz M, Simpson EL, et al. Translating Atopic Dermatitis Management Guidelines Into Practice for Primary Care Providers. *Pediatrics*. 2015;136(3):554-65.
2. Lebovidge JS, Elverson W, Timmons KG, et al. Multidisciplinary interventions in the management of atopic dermatitis. *J Allergy Clin Immunol*. 2016;138(2):325-34.

American Academy of Dermatology Diagnostic Criteria

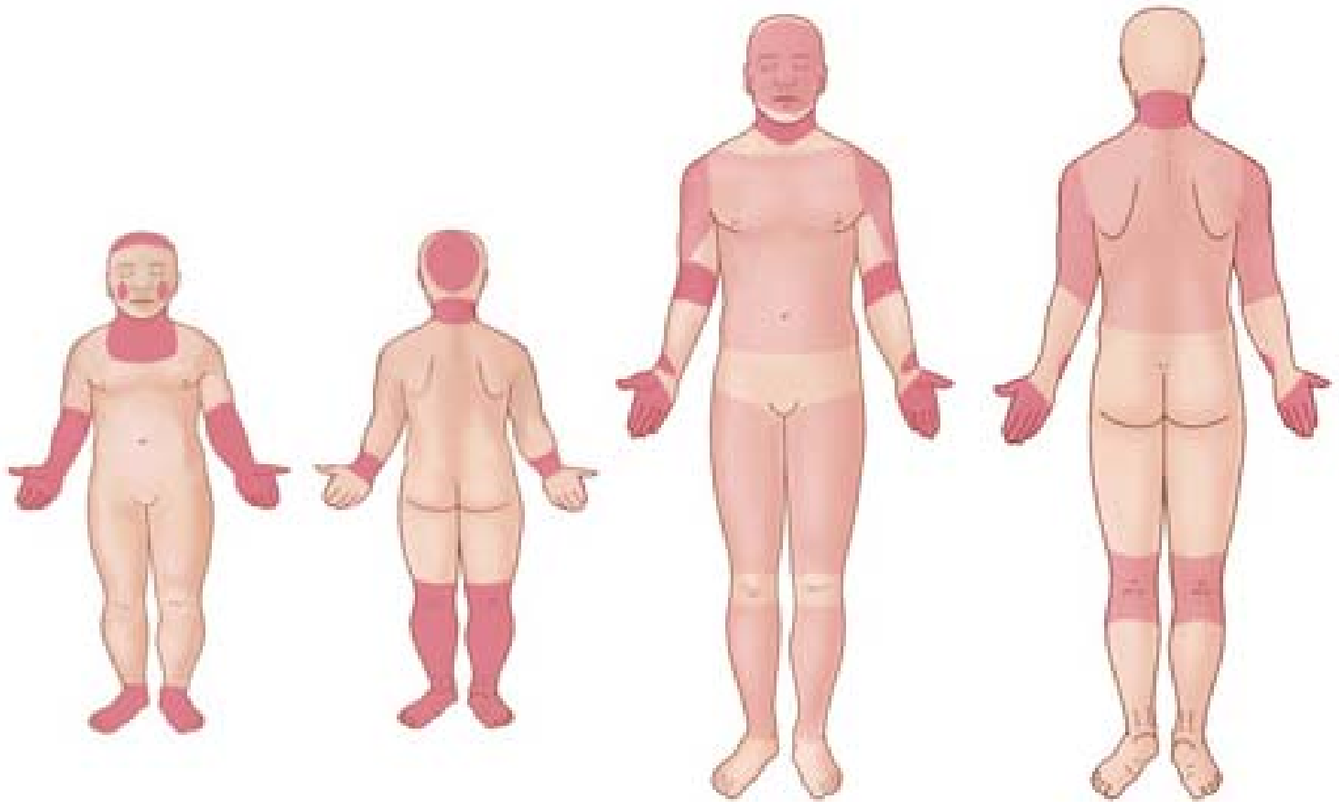
AD is a Clinical Diagnosis

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

Eichenfield LF, Tom WL, Chamlin SL, et al. Guidelines of care for the management of atopic dermatitis: section 1. Diagnosis and assessment of atopic dermatitis. *J Am Acad Dermatol*. 2014;70(2):338-51.

Assessing Severity

- Severity determined by
  - Lesion thickness
  - Duration and intensity of pruritus
  - Body surface area involved
  - Impact on quality of life



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Severity Scales

- >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)
- Scales are used primarily in clinical trials
  - Rarely used in clinical practice

Example of AD Severity Scoring

SCORAD Index	
Objective Signs	**Subjective Symptoms**
• Body surface area	• Itch
• Grading of lesions • Erythema • Swelling • Crusting/oozing • Lichenification • Xerosis • Excoriation	• Sleep loss

SCORAD <25	SCORAD 25-50	SCORAD >50
Mild	Moderate-to-Severe	Severe

Eichenfield LF, Tom WL, Chamlin SL, et al. Guidelines of care for the management of atopic dermatitis: section 1. Diagnosis and assessment of atopic dermatitis. *J Am Acad Dermatol*. 2014;70(2):338-51.

Wollenberg A, Oranje A, Deleuran M, et al. ETFAD/EADV Eczema task force 2015 position paper on diagnosis and treatment of atopic dermatitis in adult and paediatric patients. *J Eur Acad Dermatol Venereol*. 2016;30(5):729-47.Wollenberg A, Oranje A, Deleuran M, et al. ETFAD/EADV Eczema task force 2015 position paper on diagnosis and treatment of atopic dermatitis in adult and paediatric patients. J Eur Acad Dermatol Venereol. 2016;30(5):729-47.

Hill MK, Pishkenari AK, Armstrong AW, Dunnick CA. Current trends in the use of disease severity and quality of life measures for atopic dermatitis: A systematic review. [AAD abstract 2476] *J Am Acad Dermatol*. 2016;74(suppl 1):AB86.

Treatment Goals

- Avoid trigger factors
- Minimize itching
- Reduce inflammation
- Reduce frequency and severity of exacerbations (flares)
- Minimize treatment-related adverse events
- Follow severity-directed treatment

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Treatment Guidelines: American Academy of Dermatology (2014)

- Most current US-based guidelines[1]
  - Recommendations also available from other sources (eg, AAAAI*)[2]
- Includes guidance on[1]
  - Diagnosis and assessment
  - Treatment with topical therapies, phototherapy, and systemic agents
  - Prevention of disease flares
- Recently approved agents (phosphodiesterase-4 and IL-4/IL-13 inhibitors) are not included

FROM THE ACADEMY

Guidelines of care for the management of atopic dermatitis

Section 1. Diagnosis and assessment of atopic dermatitis

Work Group: Co-chair, Lawrence F. Eichenfield, MD,[a] Wynnis L. Tom, MD,[a] Sarah L. Chamlin, MD, MSCI,[b] Steven R. Feldman, MD, PhD,[c] Jon M. Hanifin, MD,[d] Eric L. Simpson, MD,[d] Timothy G. Berger, MD,[e] James N. Bergman, MD,[f] David E. Cohen, MD,[g] Kevin D. Cooper, MD,[h] Kelly M. Cordoro, MD,[e] Dawn M. Davis, MD,[i] Alfons Krol, MD,[d] David J. Margolis, MD, PhD,[j] Amy S. Paller, MS, MD,[k] Kathryn Schwarzenberger, MD,[l] Robert A. Silverman, MD,[m] Hywel C. Williams, PhD,[n] Craig A. Elmets, MD,[o] Julie Block, BA,[p] Christopher G. Harrod, MS,[q] Wendy Smith Begolka, MBS,[q] and Co-chair, Robert Sidbury, MD[r]

San Diego, San Francisco, and San Rafael, California; Chicago and Schaumburg, Illinois; Winston-Salem, North Carolina; Portland, Oregon; Vancouver, British Columbia, Canada; New York, New York; Cleveland, Ohio; Rochester, Minnesota; Philadelphia, Pennsylvania; Burlington, Vermont; Fairfax, Virginia; Nottingham, United Kingdom; Birmingham, Alabama; and Seattle, Washington

Atopic dermatitis (AD) is a chronic, pruritic, inflammatory dermatosis that affects up to 25% of children and 2% to 3% of adults. This guideline addresses important clinical questions that arise in the management and care of AD, providing updated and expanded recommendations based on the available evidence. In this first of 4 sections, methods for the diagnosis and monitoring of disease, outcomes measures for assessment, and common clinical associations that affect patients with AD are discussed. Known risk factors for the development of disease are also reviewed. (J Am Acad Dermatol 2014;70:338-51.)

Key words: assessment scales; atopic dermatitis; biomarkers; clinical associations; criteria; diagnosis; risk factors.

*AAAAI=American Academy of Allery, Asthma, & Immunology

1. Eichenfield LF, Tom WL, Chamlin SL, et al. Guidelines of care for the management of atopic dermatitis: section 1. Diagnosis and assessment of atopic dermatitis. *J Am Acad Dermatol*. 2014;70(2):338-51.
2. Schneider L, Tilles S, Lio P, et al. Atopic dermatitis: a practice parameter update 2012. *J Allergy Clin Immunol*. 2013;131(2):295-9.e1-27.

Treatment: American Academy of Dermatology Guideline Directed Management Approach

Disease Severity

Severe

Moderate

Mild

Non-pharmacologic treatments
- Moisturizers
- Emollients

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

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

*FDA-approved after the publication of the current treatment guidelines.

Eichenfield LF, Tom WL, Chamlin SL, et al. Guidelines of care for the management of atopic dermatitis: section 1. Diagnosis and assessment of atopic dermatitis. *J Am Acad Dermatol*. 2014;70(2):338-51.
Sidbury R, Davis DM, Cohen DE, et al. Guidelines of care for the management of atopic dermatitis: section 3. Management and treatment with phototherapy and systemic agents. *J Am Acad Dermatol*. 2014;71(2):327-49.

Perspectives on the New and Emerging Systemic Therapies

Traditional Systemics

- Non-specific agents
- Results in general immunosuppression
- Requires lab monitoring
- Risk of therapeutic toxicities
- Robust clinical trial data supporting their use is limited

New/Emerging Systemics

- Targeted biologic therapies
- Minimize general immunosuppression
- May not require lab monitoring
- Growing body of robust clinical trial evidence supporting their use

Systemic Therapy: AAD Guideline Recommendations

"…recommended for the subset of *adult and pediatric patients in whom optimized topical regimens* using emollients, topical anti-inflammatory therapies, adjunctive methods, and/or phototherapy *do not adequately control the signs and symptoms of disease…*"

- "…systemic immunomodulating agents may also be used in *patients whose medical, physical, and/or psychological states are greatly affected by their skin disease,* which may include negative impact on work, school performance, or interpersonal relationships."

Sidbury R, Davis DM, Cohen DE, et al. Guidelines of care for the management of atopic dermatitis: section 3. Management and treatment with phototherapy and systemic agents. *J Am Acad Dermatol*. 2014;71(2):327-49.

Candidates for Systemic Therapy

Is the diagnosis correct?

↓

Have topical therapies failed?

↓

Is the patient adherent to treatment?

- Characteristics of patients who are candidates for systemic therapy
  - Itch that disrupts sleep
  - Low risk for opportunistic infections
  - Impaired quality of life

Sidbury R, Davis DM, Cohen DE, et al. Guidelines of care for the management of atopic dermatitis: section 3. Management and treatment with phototherapy and systemic agents. *J Am Acad Dermatol*. 2014;71(2):327-49.

Barriers to Treatment

"Steroid Phobia"	Fear of Side Effects	Few Long-term Therapies	Poor Adherence
• Experienced by both patients and physicians • Limits duration and intensity of treatment	• Experienced by both patients and physicians • Boxed warnings on several therapies	• Options for long-term treatment are limited by effectiveness, safety, and inconvenience	• To guidelines (physicians) • To prescribed therapy (patients and caregivers)

Murota H, Takeuchi S, Sugaya M, et al. Characterization of socioeconomic status of Japanese patients with atopic dermatitis showing poor medical adherence and reasons for drug discontinuation. *J Dermatol Sci*. 2015;79(3):279-87.
Bass AM, Anderson KL, Feldman SR. Interventions to Increase Treatment Adherence in Pediatric Atopic Dermatitis: A Systematic Review. *J Clin Med*. 2015;4(2):231-42.

Treatment Dissatisfaction Often Leads to Poor Adherence

Complicated, Ineffective, and/or Inconvenient Regimens
Treatment-related AEs

Poor Adherence

Adherence assessed in 1327 patients with AD using the Morisky Medication Adherence Scale-8 (MMAS-8)

- **44% of patients were dissatisfied with their AD treatment**
- **Satisfaction may be related to disease severity**

Murota H, Takeuchi S, Sugaya M, et al. Characterization of socioeconomic status of Japanese patients with atopic dermatitis showing poor medical adherence and reasons for drug discontinuation. *J Dermatol Sci*. 2015;79(3):279-87.

Assessment of Interventions to Improve Adherence

Study	N	Intervention	Assessment Tool	Results	Comments
Rork et al. 2012	35	**Written action plan**	Survey of disease severity	Severity was decreased in 80% of patients whose parents utilized a written action plan	Adherence not measured directly; attributed severity improvement to better adherence
Moore et al. 2009	99	**Nurse-led educational workshops**	SCORAD Index	73% improvement in severity in the intervention group vs 40% in the control	Adherence not measured directly; attributed severity improvement to better adherence
Sagransky et al. 2010	20	**Extra office visit each week**	Medication Event Monitoring Systems (MEMS) cap	Decrease in adherence was less in the intervention group (-23%) vs control (-39%)	Direct measurement of dosing events recorded by MEMs cap
Grillo et al. 2006	61	**Educational workshop (2 hour session)**	SCORAD index	54% improvement in severity for the intervention group vs 16% in the control	Adherence not measured directly; attributed severity improvement to better adherence
Staab et al. 2002	204	**Educational program (6 two-hour group sessions)**	SCORAD index	Decrease in adherence was less in the intervention group (-7%) vs control (-25%)	Adherence measured directly by survey

Bass AM, Anderson KL, Feldman SR. Interventions to Increase Treatment Adherence in Pediatric Atopic Dermatitis: A Systematic Review. *J Clin Med*. 2015;4(2):231-42.

Engaging the Patient: Atopic Dermatitis Action Plans

- Written plans can help patients understand how best to manage their AD[1]
- Safeguards against medication errors and therapeutic toxicities[2]
- Use of action plans have been shown to decrease disease severity[2] and may increase adherence[3]

Doctor/NP: _____
To contact Doctor/PA/NP: (617) 355-6117
To contact Doctor on call: (617) 355-6369

Name: _____
DOB: _____
MRN: _____
TODAY'S DATE: _____

DAILY SKIN CARE ROUTINE

- **BATH 10-20 minutes:** ☐ Daily ☐ Every other day
  - **Cleanser:** _____
- **MOISTURIZER:** _____ **twice daily** and more often as needed
- **Antihistamine:** _____

GREEN ZONE (Skin with very mild redness/irritation)

- **Continue Daily Skin Care Routine**

YELLOW ZONE (Skin starting to **FLARE** with **mild to moderate** redness/itching)

- **Continue Daily Skin Care Routine**
- Apply **topical steroid:** _____ **twice daily** to **FACE** for maximum ____ **days**
- Apply **topical steroid:** _____ **twice daily** to **BODY** for maximum ____ **days**

RED ZONE (Skin with **SEVERE** redness/itching/oozing)

- **Continue Daily Skin Care Routine** with any changes made in Yellow Zone
- Apply **topical steroid:** _____ **twice daily** to **FACE** for maximum ___ **days**
- Apply **topical steroid:** _____ **twice daily** to **BODY** for maximum ___**days**
- Call **(617) 355-6117** or Doctor on call **(617) 355-6369** if there is **no improvement** in **3-5 days**

1. Shi VY, Nanda S, Lee K, Armstrong AW, Lio PA. Improving patient education with an eczema action plan: a randomized controlled trial. *JAMA Dermatol*. 2013;149(4):481-3.
2. Rork JF, Sheehan WJ, Gaffin JM, et al. Parental response to written eczema action plans in children with eczema. *Arch Dermatol*. 2012;148(3):391-2.
3. Bass AM, Anderson KL, Feldman SR. Interventions to Increase Treatment Adherence in Pediatric Atopic Dermatitis: A Systematic Review. *J Clin Med*. 2015;4(2):231-42.

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 multimodal, multidisciplinary approach to care may improve adherence and treatment outcomes

Targeted Therapies for the Treatment of Moderate-to-Severe Atopic Dermatitis

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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

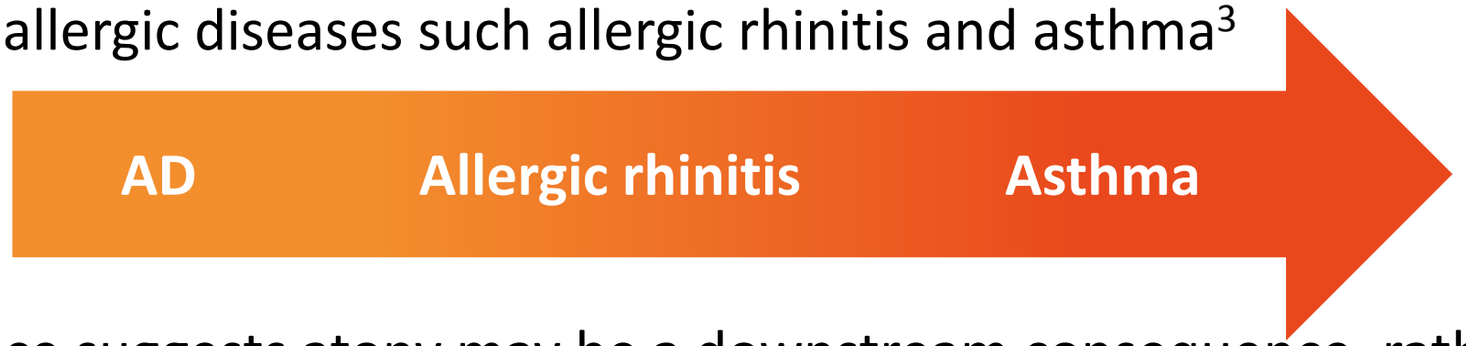
AD is a Chronically Relapsing Inflammatory Skin Disease with a Profound Effect on Patient Quality of Life

- Most common skin disease worldwide[1]
  - 15% to 30% global prevalence in children
  - Up to 10% prevalence in adults
- Heterogeneous clinical presentation[1,2]
  - Intense, often unbearable itching
  - Chronic or recurring eczematous lesions
- Significantly impaired QoL[3]
  - Disrupted sleep patterns
  - Increased rates of mental health disorders
  - Negative social, academic, occupational, and financial effects

1. Udkoff J, Waldman A, Ahluwalia J, Borok J, Eichenfield LF. Current and emerging topical therapies for atopic dermatitis. *Clin Dermatol*. 2017;35(4):375-382.
2. Simpson EL, Bieber T, Eckert L, et al. Patient burden of moderate to severe atopic dermatitis (AD): Insights from a phase 2b clinical trial of dupilumab in adults. *J Am Acad Dermatol*. 2016;74(3):491-8.
3. Drucker, A.M., Wang, A.R., Li, W.Q. et al, The Burden of Atopic Dermatitis: Summary of a Report for the National Eczema Association. *J Invest Dermatol*. 2017;137:26–30.

AD Disease Manifestations are Influenced by Genetic, Immune, and Environmental Factors

- Genes linked to AD[1]
  - *FLG*, a gene that encodes profilaggrin, a skin barrier protein
  - Genes that encode cytokines (e.g., IL-5, IL-12, IL-13)
- About 80% of patients with AD have personal or family history of atopy (elevated IgE)[2]
- AD most often begins in early childhood and is often considered the first step in the "atopic march" to other allergic diseases such allergic rhinitis and asthma[3]

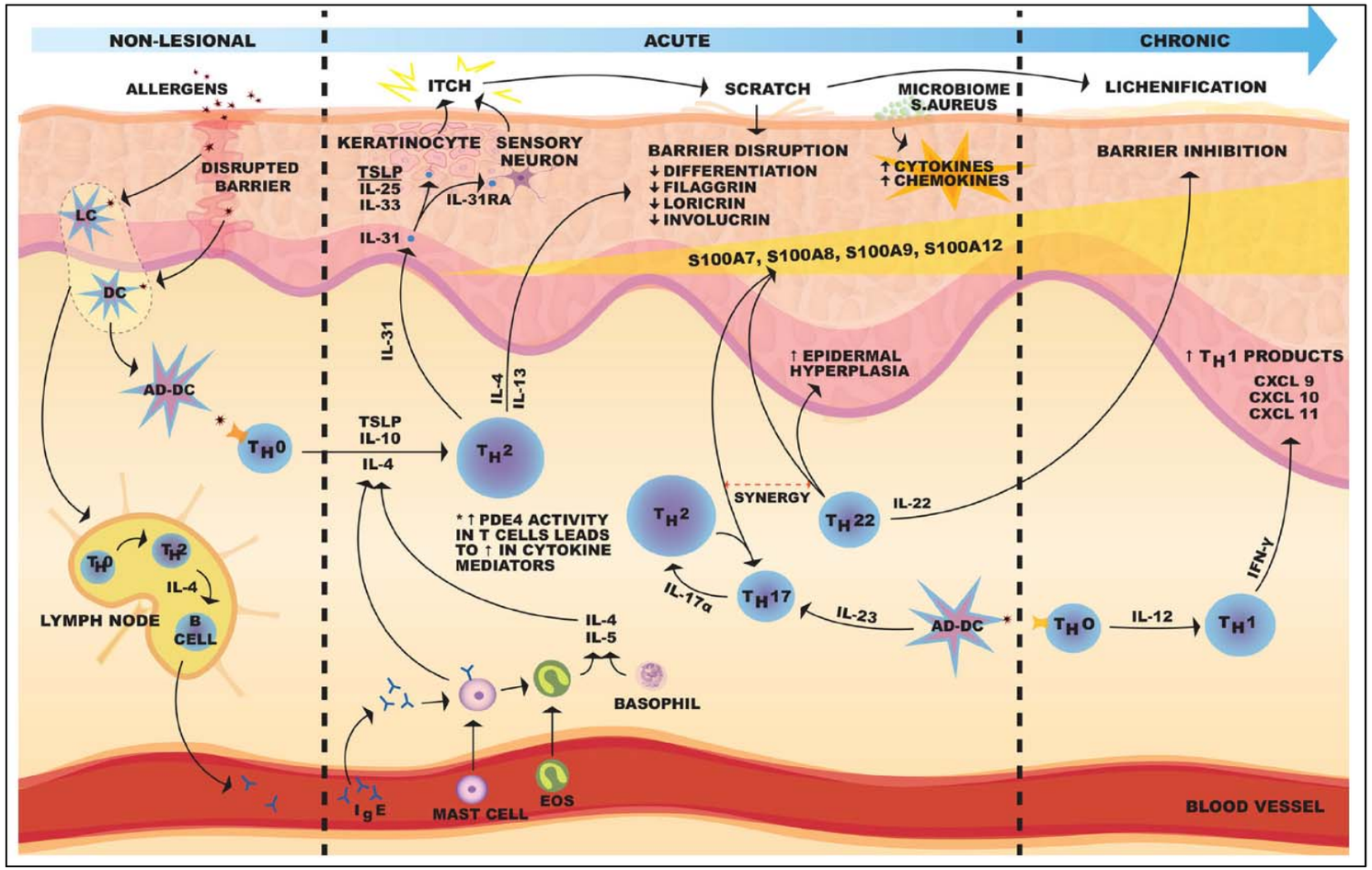


- However, evidence suggests atopy may be a downstream consequence, rather than a cause, of AD in genetically predisposed individuals[3]

1. Lee DE, Clark AK, Tran KA, Shi VY. New and Emerging Targeted Systemic Therapies: A New Era for Atopic Dermatitis. *J Dermatolog Treat*. 2017;:1-44.
2. Guttman-Yassky E, Dhingra N, Leung DY. New era of biologic therapeutics in atopic dermatitis. *Expert Opin Biol Ther*. 2013;13(4):549-61.
3. Nutten S. Atopic dermatitis: global epidemiology and risk factors. *Ann Nutr Metab*. 2015;66 Suppl 1:8-16.

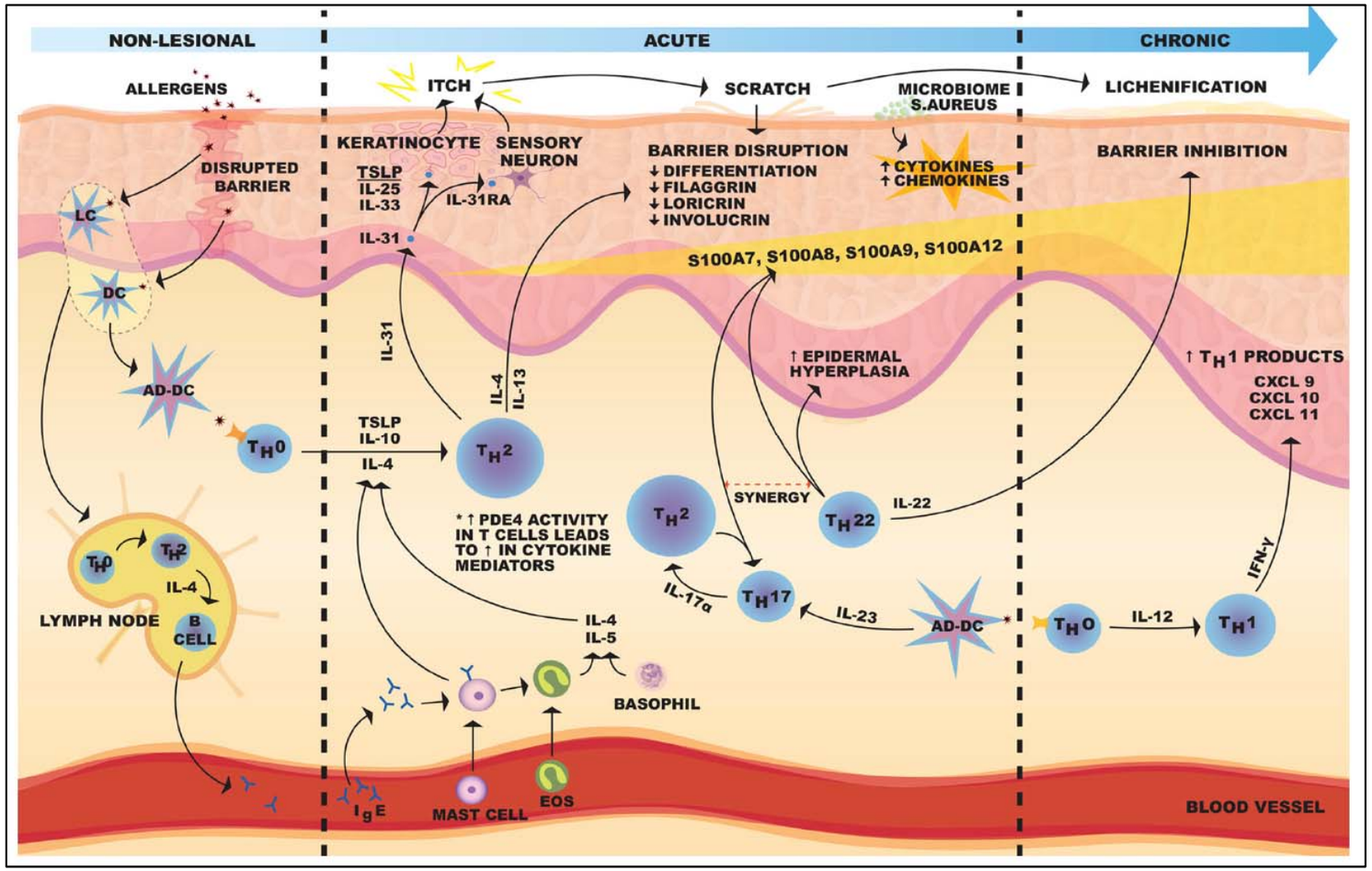
AD Has a Complex Pathogenesis Involving Epidermal Barrier Dysfunction and Immune-mediated Cutaneous Inflammation[1]

- Barrier defects in non-lesional skin allow penetration of allergens
- Antigen-mediated T helper 2 (Th2) cell activation results in cytokine release (eg, IL-4, IL-5, IL-13), inflammatory cell recruitment, and increased IgE production
- IL-4 and IL-13 disrupt the skin barrier by decreasing expression of barrier proteins (eg, filaggrin)



1. Vakharia PP, Silverberg JI. Monoclonal Antibodies for Atopic Dermatitis: Progress and Potential. *BioDrugs*. 2017 [Epub ahead of print].

AD Has a Complex Pathogenesis Involving Epidermal Barrier Dysfunction and Immune-Mediated Cutaneous Inflammation (cont'd)[1]



- IL-23 stimulates production of Th17 and Th22 cells that release IL-17 and IL-22, respectively
  - IL-22 induces epidermal hyperplasia and in concert with IL-17, acts on terminal differentiation proteins that mediate itch
- Epithelial damage releases thymic stromal lymphopoietin (TSLP), IL-25, and IL-33, and these, along with IL-10, further drive Th2 differentiation
- In chronic AD, Th1 cells release interferon-ϒ and stimulate production of chemokines that lead to further support of inflammation and immune activation

1. Vakharia PP, Silverberg JI. Monoclonal Antibodies for Atopic Dermatitis: Progress and Potential. *BioDrugs*. 2017 [Epub ahead of print].

Moderate-to-Severe AD Often Requires Intensive Therapy for Adequate Disease Control[1]

Limitations with currently available therapies create a significant unmet need for safe, effective treatments for patients with moderate-to-severe AD[1]

Systemic immunosuppressants[1,2]

- Variable efficacy
- Tolerability issues and toxicity (eg, nephrotoxicity) with long-term use

Topical corticosteroids[3]

- Irreversible skin atrophy with long-term use
- Potential for adrenal suppression

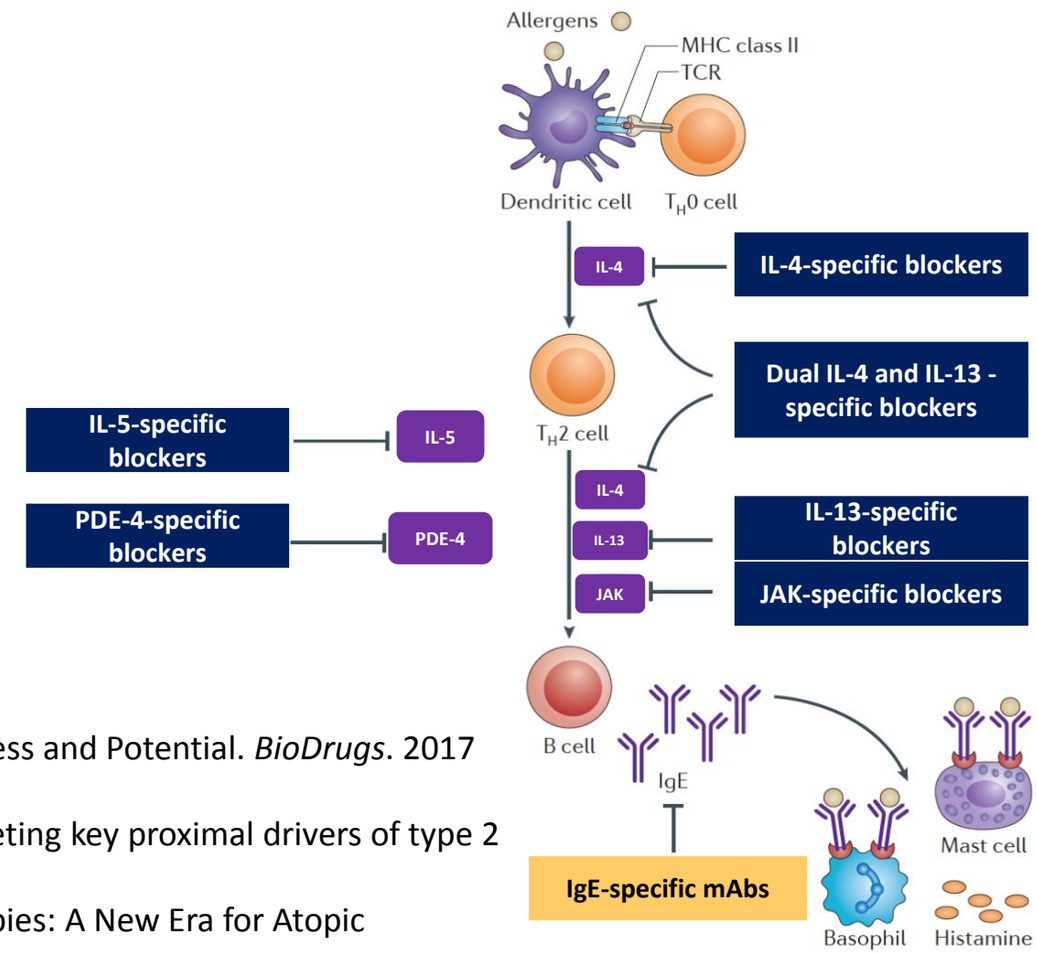
1. Vakharia PP, Silverberg JI. Monoclonal Antibodies for Atopic Dermatitis: Progress and Potential. *BioDrugs*. 2017 [Epub ahead of print].
2. Sidbury R, Davis DM, Cohen DE, et al. Guidelines of care for the management of atopic dermatitis: section 3. Management and treatment with phototherapy and systemic agents. *J Am Acad Dermatol*. 2014;71(2):327-49.
3. Eichenfield LF, Tom WL, Berger TG, et al. Guidelines of care for the management of atopic dermatitis: section 2. Management and treatment of atopic dermatitis with topical therapies. *J Am Acad Dermatol*. 2014;71(1):116-32.

Improved Understanding of AD Pathogenesis Has Led to New Treatment Strategies for Moderate-to-Severe Disease[1]

Emerging biologics specifically target steps in the Th-2 pathway integral to AD pathogenesis[2,3]

Traditional systemic therapies[2]

- Provide generalized immunosuppression (eg, corticosteroids), or
- Target end-product mediators of inflammation (eg, IgE, antihistamines)



1. Vakharia PP, Silverberg JI. Monoclonal Antibodies for Atopic Dermatitis: Progress and Potential. *BioDrugs*. 2017 [Epub ahead of print].
2. Gandhi NA, Bennett BL, Graham NM, Pirozzi G, Stahl N, Yancopoulos GD. Targeting key proximal drivers of type 2 inflammation in disease. *Nat Rev Drug Discov*. 2016;15(1):35-50.
3. Lee DE, Clark AK, Tran KA, Shi VY. New and Emerging Targeted Systemic Therapies: A New Era for Atopic Dermatitis. *J Dermatolog Treat*. 2017;:1-44. [Epub ahead of print].

Several Targeted Agents Have Been Recently Approved or Are in Late-Stage Development for Treatment of AD[1]

Agent	Trade Name	Target	Route	Clinical Trial Phase
IL-4, IL-13				
Dupilumab	Dupixent	IL-4, IL-13	SC	Approved
Tralokinumab		IL-13	SC	3
Lebrikizumab		IL-13	SC	2
JAK				
Tofacitinib	Xeljanz	JAK1, JAK3	PO	
Baricitinib	Olumiant	JAK1, JAK2	PO	2
Pf-04965842		JAK1	PO	2
PDE-4				
Crisaborole	Eucrisa	PDE-4	Topical	Approved
Apremilast	Otezla	PDE-4	PO	2

PDE=phosphodiesterase; JAK=Janus kinase; PO=oral; SC=subcutaneous.

Two of these new agents have received FDA approval for AD

- Dupixent (dupilumab)[2]
- Eucrisa (crisaborole)[3]

1. Lee DE, Clark AK, Tran KA, Shi VY. New and Emerging Targeted Systemic Therapies: A New Era for Atopic Dermatitis. *J Dermatolog Treat*. 2017;:1-44. [Epub ahead of print].
2. Dupixent [package insert]. Tarrytown, NY: Regeneron Pharmaceuticals, Inc; 2017.
3. Eucrisa [package insert]. Palo Alto, CA: Anacor Pharmaceuticals, Inc; 2016.

Additional Agents in Development

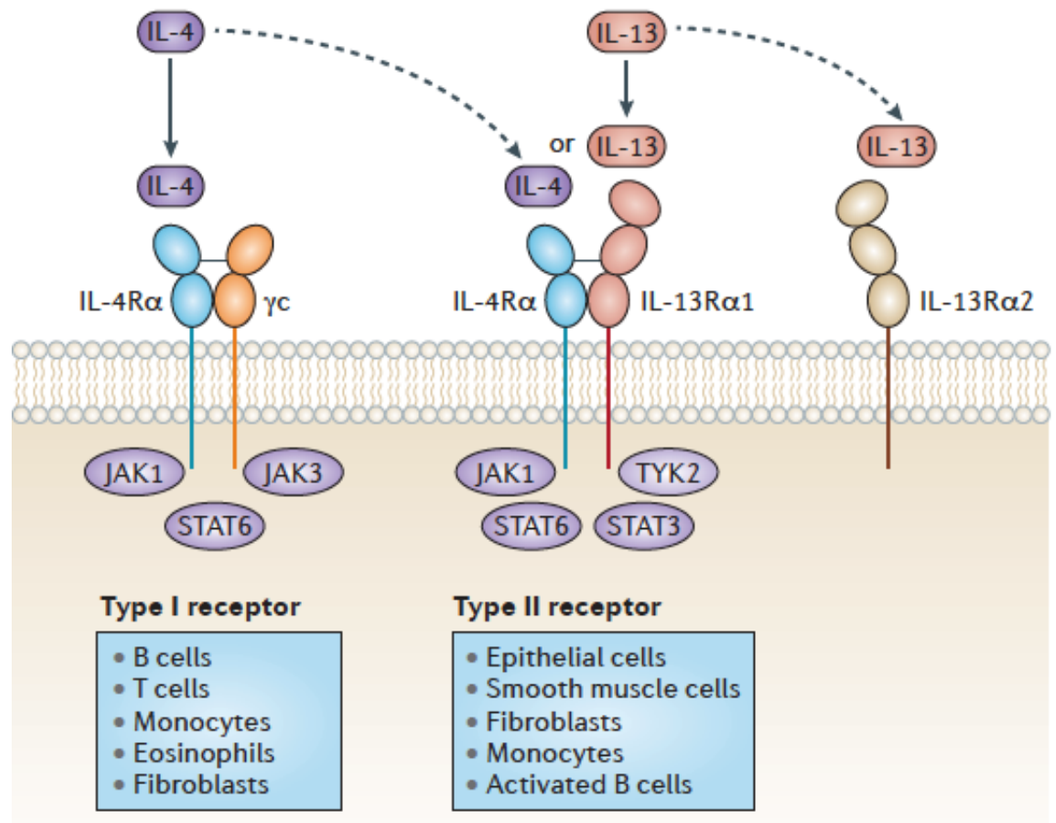
Agent	Trade Name	Target	Route	Clinical Trial Phase
Other cytokines				
Ustekinumab	Stelara	IL-12, IL-23	SC	2
Secukinumab	Cosentyx	IL-17A	SC	2
ILV-094		IL-22	IV	2
Nemolizumab		IL-31RA	SC	2
IgE				
Ligelizumab (QGE031)		IgE	SC	2
Omalizumab	Xolair	IgE	SC	2

IgE=immunoglobulin E; RA=receptor antagonist; SC=subcutaneous; IV=intravenous.

Lee DE, Clark AK, Tran KA, Shi VY. New and Emerging Targeted Systemic Therapies: A New Era for Atopic Dermatitis. *J Dermatolog Treat*. 2017;1-44. [Epub ahead of print].

IL-4 Receptor α Chain (IL-4Rα) Inhibitor

- Mechanism of action
  - Binds to the IL-4 receptor α chain, a component of receptors for both IL-4 and IL-13[1]
  - Blocks both IL-4 and IL-13 signaling, key cytokines that drive Th2-mediated inflammation[2-4]
- Status
  - Approved for adults with moderate-to-severe AD (Dupixent®, March 2017)[4]
  - In Phase 3 trials for pediatric AD[3]



1. Gandhi NA, Bennett BL, Graham NM, Pirozzi G, Stahl N, Yancopoulos GD. Targeting key proximal drivers of type 2 inflammation in disease. *Nat Rev Drug Discov*. 2016;15(1):35-50.
2. Vakharia PP, Silverberg JI. Monoclonal Antibodies for Atopic Dermatitis: Progress and Potential. *BioDrugs*. 2017 [Epub ahead of print].
3. Lee DE, Clark AK, Tran KA, Shi VY. New and Emerging Targeted Systemic Therapies: A New Era for Atopic Dermatitis. *J Dermatolog Treat*. 2017;:1-44. [Epub ahead of print].
4. Dupixent [package insert]. Tarrytown, NY: Regeneron Pharmaceuticals, Inc; 2017.

Dupilumab – An IL-4Rα Antagonist for AD

- Dupixent, Regeneron/Sanofi Genzyme
  - Fully human monoclonal antibody
  - IL-4Rα antagonist
  - Inhibits IL-4 and IL-13 signaling
- US Approval: March 2017
- Indication
  - Treatment of adult patients with moderate-to-severe atopic dermatitis whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable
- Dosage and administration
  - Subcutaneous injection
  - 600 mg (two 300 mg injections in different injection sites), followed by 300 mg given every other week
- Dosage form and strength
  - Injection
  - 300 mg/2 mL solution in a single-dose pre-filled syringe with needle shield

Dupixent [package insert]. Tarrytown, NY: Regeneron Pharmaceuticals, Inc; 2017.

Dupilumab – Safety Profile

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

- Most common adverse reactions (≥1% incidence)
  - Injection site reactions
  - Conjunctivitis
  - Blepharitis
  - Oral herpes
  - Keratitis
  - Eye pruritus
  - Other HSV infection
  - Dry eye

Dupixent [package insert]. Tarrytown, NY: Regeneron Pharmaceuticals, Inc; 2017.

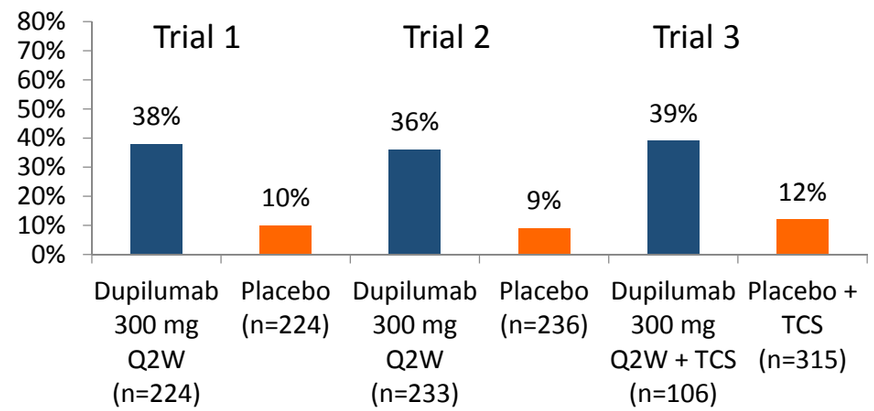
Dupilumab – Pivotal Clinical Trials

- Approved based on 3 randomized, double-blind, placebo-controlled trials (Trials 1, 2, and 3)[1]
  - 2119 subjects ≥18 years of age moderate-to-severe AD not adequately controlled by topical medications
- Treatment[1]
  - Placebo or dupilumab 600 mg at Week 0, followed by 300 mg Q2W)
  - In Trial 3, subjects also received concomitant topical corticosteroids (TCS) or topical calcineurin inhibitors (TCI) for problem areas only
- Primary endpoint[1]
  - Change from baseline to Week 16 in the proportion of subjects with an IGA 0 (clear) or 1 (almost clear) and at least a 2-point improvement
- Other results[2,3]
  - Significant improvements vs placebo in EASI75, pruritus, and patient reported outcomes (eg, QoL)

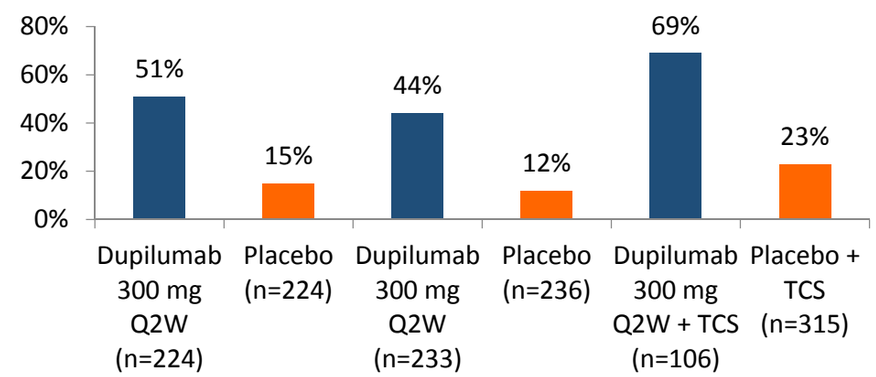
1. Dupixent [package insert]. Tarrytown, NY: Regeneron Pharmaceuticals, Inc; 2017.
2. Simpson EL, Bieber T, Guttman-yassky E, et al. Two Phase 3 Trials of Dupilumab versus Placebo in Atopic Dermatitis. *N Engl J Med*. 2016;375(24):2335-2348.
3. Simpson EL. Dupilumab Improves General Health-Related Quality-of-Life in Patients with Moderate-to-Severe Atopic Dermatitis: Pooled Results from Two Randomized, Controlled Phase 3 Clinical Trials. *Dermatology and Therapy*. 2017;7(2):243-248. doi:10.1007/s13555-017-0181-6.

Efficacy Results With or Without Concomitant TCS at Week 16[1]

IGA Responders*



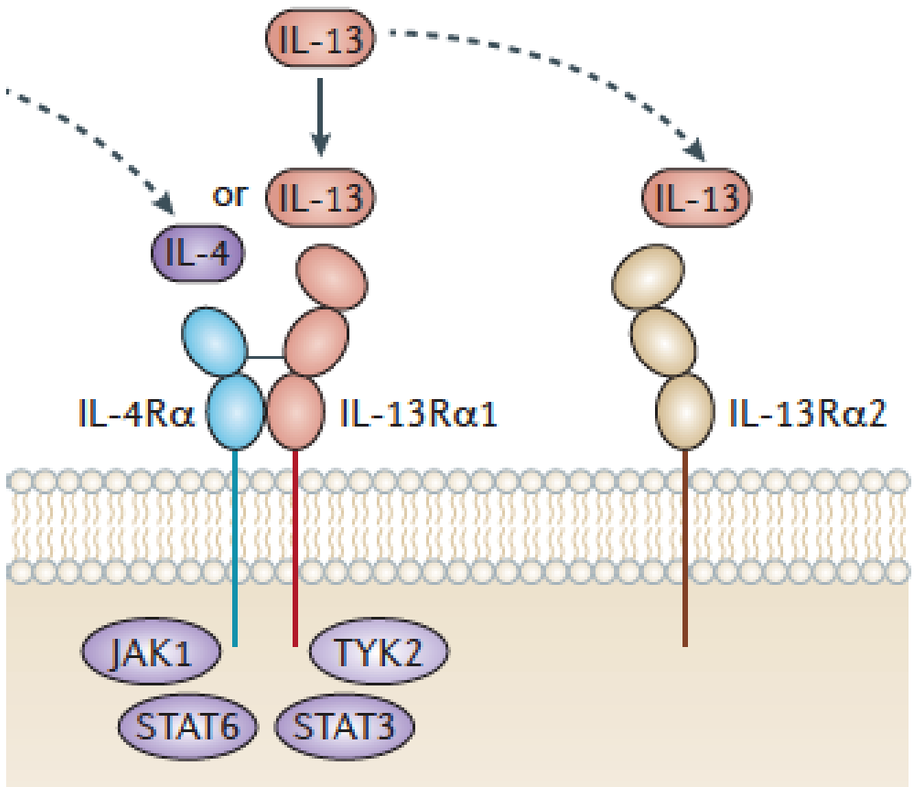
EASI-75



*Responder was defined as a subject with IGA 0 or 1 ("clear" or "almost clear") with a reduction of ≥2 points on a 0-4 IGA scale.

IL-13 Receptor α Chain (IL-13Rα1, IL-13Rα2) Inhibitors

- Mechanism of action
  - Binds to the IL-13 receptor α chains 1 and 2 (IL-13Rα1 and IL-13Rα2) on B-cells and monocytes
  - Blocks IL-13 signaling, a key driver of Th2-mediated inflammation
- Status: two monoclonal antibodies under investigation
  - Phase 3: Tralokinumab
  - Phase 2: Lebrikizumab



1. Lee DE, Clark AK, Tran KA, Shi VY. New and Emerging Targeted Systemic Therapies: A New Era for Atopic Dermatitis. *J Dermatolog Treat*. 2017;1-44. [Epub ahead of print].
2. Vakharia PP, Silverberg JI. Monoclonal Antibodies for Atopic Dermatitis: Progress and Potential. *BioDrugs*. 2017 [Epub ahead of print].
3. Gandhi NA, Bennett BL, Graham NM, Pirozzi G, Stahl N, Yancopoulos GD. Targeting key proximal drivers of type 2 inflammation in disease. *Nat Rev Drug Discov*. 2016;15(1):35-50.

Tralokinumab – Phase 2 Clinical Trial in Adults

- Design
  - Randomized, placebo-controlled, double-blind
- Patients
  - 204 adults with moderate-to-severe AD
- Treatment
  - Tralokinumab (45, 150, or 300 mg) or placebo by SC injection Q2W for 12 weeks
- Primary endpoint: reduction in EASI
- Key efficacy results
  - Significant reduction in EASI scores
    - -15.7 tralokinumab 300 mg
    - -10.8 placebo; *P*=0.011
  - Significant improvement in IGA success, EASI50, EASI75, and pruritus
  - Significant improvement in Dermatology quality of life index
- Most common adverse reactions
  - Nasopharyngitis (17%), upper respiratory tract infection (9%), headache (6%) and AD (6%)

EASI=Eczema Area and Severity Index; EASI50=50% improvement in EASI; EASI75=75% improvement in EASI75; IGA=investigator global assessment; Q2W=every other week; SC=subcutaneous.

Wollenberg A, Oranje A, Deleuran M, Simon D, Szalai Z, Kunz B et al. ETFAD/EADV Eczema task force 2015 position paper on diagnosis and treatment of atopic dermatitis in adult and paediatric patients. *J Eur Acad Dermatol Venereol.* 2016;30(5):729-747.

Lebrikizumab – Phase 2 Clinical Trial in Adults

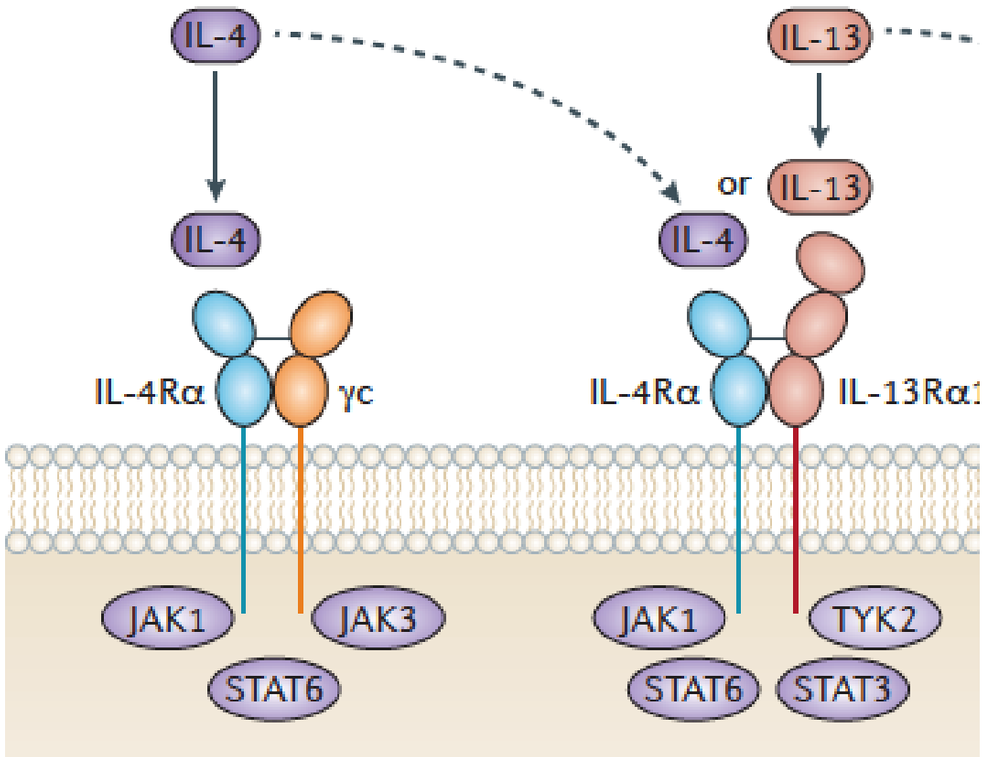
- Design[1]
  - Randomized, placebo controlled, double-blind trial
- Patients[1]
  - 209 adults with moderate-to-severe AD
- Treatment[1]
  - Lebrikizumab (125 mg) or placebo by SC injection Q4W for 12 weeks
- Primary endpoint: EASI50[1]
- Key efficacy results[1]
  - Significant improvement in EASI50 scores
    - 82.4% lebrikizumab
    - 62.9% placebo; $P<0.05$
  - Significant improvements in patient reported outcomes and trend toward improvement in EASI75, EASI90[1,2]
- Notable adverse reactions[2]
  - Conjunctivitis
  - injection-site reaction

EASI=Eczema Area and Severity Index; EASI50=50% improvement in EASI; EASI75=75% improvement in EASI75; EASI90=90% improvement in EASI; IGA=investigator global assessment, Q4W=every four weeks; SC=subcutaneous; TCI=topical calcineurin inhibitors; TCS=topical corticosteroids.

1. Lee DE, Clark AK, Tran KA, Shi VY. New and Emerging Targeted Systemic Therapies: A New Era for Atopic Dermatitis. *J Dermatolog Treat.* 2017;1-44. [Epub ahead of print].
2. Vakharia PP, Silverberg JI. Monoclonal Antibodies for Atopic Dermatitis: Progress and Potential. *BioDrugs*. 2017 [Epub ahead of print].

Janus Kinase (JAK) Inhibitors

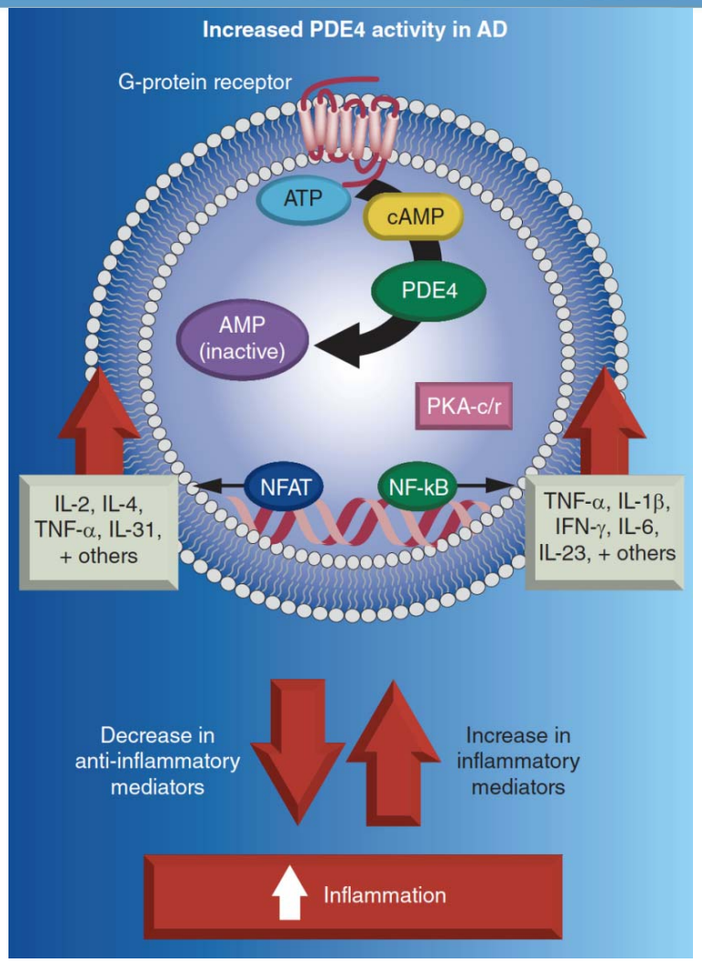
- Mechanism of action[1-3]
  - JAK-STAT signaling is activated by IL-4, IL-5, and IL-13, and in turn up-regulates pro-inflammatory cytokines, activates eosinophils, and suppresses regulatory T cells
  - JAK inhibitors inhibit JAK-STAT signaling by preventing the phosphorylation and activation of STATs
- Status
  - Tofacitinib (Xeljanz) is an oral JAK1 and JAK3 inhibitor currently approved in the US for rheumatoid arthritis (RA) and in early testing for AD[1,2]
  - Baricitinib and Pf-04965842 are JAK inhibitors in phase 2 trials for AD[1]



1. Lee DE, Clark AK, Tran KA, Shi VY. New and Emerging Targeted Systemic Therapies: A New Era for Atopic Dermatitis. *J Dermatolog Treat*. 2017;1-44. [Epub ahead of print].
2. Xeljanz [package insert]. New York, NY: Pfizer Inc; 2012.
3. Gandhi NA, Bennett BL, Graham NM, Pirozzi G, Stahl N, Yancopoulos GD. Targeting key proximal drivers of type 2 inflammation in disease. *Nat Rev Drug Discov*. 2016;15(1):35-50.

Phosphodiesterase 4 (PDE-4) Inhibitors

- Mechanism of action
  - Modulates production of inflammatory cytokines (eg, IL-4, IL-5, IL-10, IL-13 and prostaglandin E2) by its action on cyclic adenosine monophosphate (cAMP)[1,2]
  - PDE-4 inhibitors increase intracellular cAMP levels, reduce release cytokine mediators, and mitigate inflammatory processes in AD[3]
- Status
  - Crisaborole is a topical PDE-4 inhibitor that is approved for patients ≥2 years of age with mild-to-moderate AD[2]
  - Apremilast is an oral PDE-4 inhibitor in phase 2 testing for moderate-to-severe AD[4]



ATP=Adenosine triphosphate; cAMP=cyclic adenosine monophosphate; IFN-γ=Interferon gamma; IL=Interleukin; NFAT=Nuclear factor of activated T cells; NF-κB=Nuclear factor κB; PDE4=Phosphodiesterase 4; PKA-c/r=cAMP-dependent protein kinase catalytic subunits c and r; TNF-α=Tumor necrosis factor alpha.

1. Zane LT, Chanda S, Jarnagin K, Nelson DB, Spelman L, Gold LS. Crisaborole and its potential role in treating atopic dermatitis: overview of early clinical studies. *Immunotherapy*. 2016;8(8):853-66.
2. Eucrisa [package insert]. Palo Alto, CA: Anacor Pharmaceuticals, Inc; 2016.
3. Eichenfield LF, Stein gold LF. Addressing the immunopathogenesis of atopic dermatitis: advances in topical and systemic treatment. *Semin Cutan Med Surg*. 2017;36(2 Suppl 2):S45-S48.
4. Lee DE, Clark AK, Tran KA, Shi VY. New and Emerging Targeted Systemic Therapies: A New Era for Atopic Dermatitis. *J Dermatolog Treat*. 2017;1-44. [Epub ahead of print].

Crisaborole – The First PDE-4 Inhibitor Approved for AD

- Eucrisa 2% ointment, Anacor Pharmaceuticals
  - Small-molecule, boron-based, PDE-4 inhibitor
- US Approval: December 2016
- Indication
  - Topical treatment of mild-to-moderate AD in patients 2 years of age and older
- Warnings and precautions
  - Hypersensitivity reactions
- Pivotal clinical trials
  - In two clinical trials, 1522 subjects were randomized 2:1 to receive crisaborole or placebo twice a day for 28 days
  - The primary endpoint was ISGA success
- Adverse reactions
  - The most common AR occurring in ≥1% of patients is injection site pain

Primary Efficacy Outcomes in Subjects with Mild-to-Moderate AD at Day 29

	Trial 1		Trial 2	
	Crisaborole (N=503)	Vehicle (N=256)	Crisaborole (N=513)	Vehicle (N=250)
ISGA success	32.8%	25.4%	31.4%	18.0%

ISGA, investigator's static global assessment. In two clinical trials, 1522 subjects were randomized 2:1 to receive crisaborole or placebo twice a day for 29 days The primary endpoint was ISGA success, defined as a score of 0 (clear) or 1 (almost clear) with a ≥2 grade improvement over baseline.

Eucrisa [package insert]. Palo Alto, CA: Anacor Pharmaceuticals, Inc; 2016.

Apremilast

- Otezla, Celgene
- Oral PDE-4 inhibitor approved for the treatment of adults with active psoriatic arthritis and for patients with moderate-to severe plaque psoriasis and psoriatic arthritis[1]

Phase 2 trial in moderate-to-severe AD[1]

- Design: randomized, double-blind, placebo-controlled, parallel-group trial
- Patients: 191 adults with moderate-to-severe AD
- Treatment: apremilast (40 mg) or placebo twice daily for up to 24 weeks
- Primary endpoint: Percentage improvement in EASI at week 12
- Key efficacy result at week 12:
  - Apremilast: 31% reduction in EASI
  - Placebo: 11% reduction in EASI; $P = 0.0347$

EASI=Eczema Area and Severity Index; IGA=investigator global assessment, Q4W=every four weeks; SC=subcutaneous; TCI=topical calcineurin inhibitors; TCS=topical corticosteroids.

1. Otezla [package insert]. Summit, NJ: Celgene Corporation; 2014.
2. Lee DE, Clark AK, Tran KA, Shi VY. New and Emerging Targeted Systemic Therapies: A New Era for Atopic Dermatitis. *J Dermatolog Treat*. 2017;1-44. [Epub ahead of print].

Other Agents that Target Th2 Cytokines

Agent	Description/mechanism of action	Results in AD clinical trials
Ustekinumab (Stelara)	• Monoclonal antibody approved for treatment of plaque psoriasis, psoriatic arthritis, and Crohn's disease • IL-12/IL-23 inhibitor	• In 2 randomized controlled trials, treatment did not significantly improve AD disease severity
Secukinumab (Cosentyx)	• Monoclonal antibody approved for treatment of plaque psoriasis, psoriatic arthritis, and ankylosing spondylitis • IL-17 inhibitor	• Secukinumab is early in its AD testing program–a case report of secukinumab for treatment of AD has been published
Fezakinumab (ILV-094)	• Monoclonal antibody • IL-22 inhibitor	• In a randomized, controlled clinical trial of 60 patients with moderate-to-severe AD, patients treated with fezakinumab twice weekly had significantly better improvement in patient-reported outcome scores than patients treated with placebo

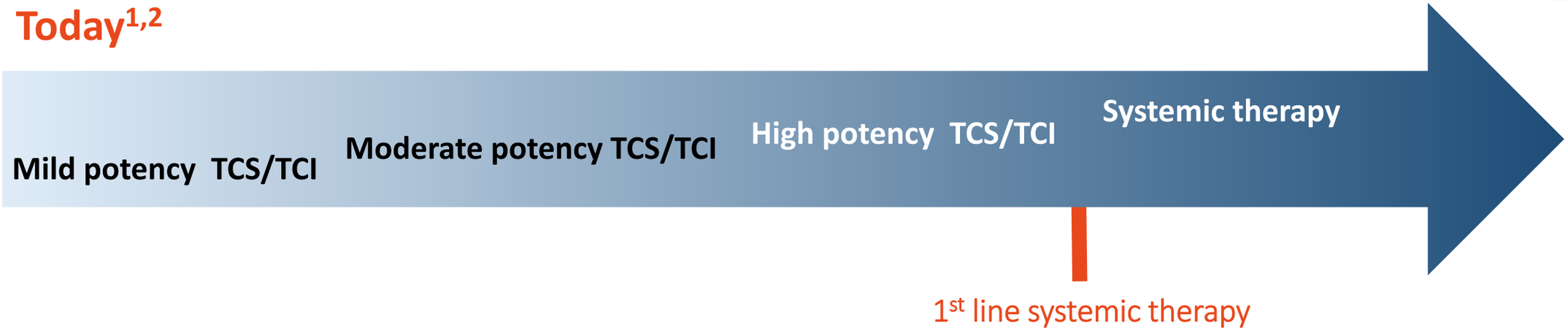
1. Stelara [package insert]. Horsham, PA: Janssen Biotech, 2016.
2. Cosentyx [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation, 2015.
3. Vakharia PP, Silverberg JI. Monoclonal Antibodies for Atopic Dermatitis: Progress and Potential. *BioDrugs*. 2017 [Epub ahead of print].
4. Lee DE, Clark AK, Tran KA, Shi VY. New and Emerging Targeted Systemic Therapies: A New Era for Atopic Dermatitis. *J Dermatolog Treat*. 2017;1-44. [Epub ahead of print].

Other Agents that Target Th2 Cytokines (cont.)

Agent	Description/mechanism of action	Results in AD clinical trials
Nemolizumab[1]	• Monoclonal antibody • IL-31 receptor A (IL-31RA) inhibitor	• In a phase 2, randomized, double-blind, placebo-controlled trial of 216 adults with moderate-to-severe AD, a single subcutaneous dose resulted in ~50% improvement in pruritus and non-significant improvement is EASI score • AEs: exacerbation of AD, peripheral edema, nasopharyngitis • May eventually play an important role in treatment of pruritus associated with AD
Ligelizumab[1]	• Monoclonal antibody • Anti IgE	• In a randomized, double-blind, placebo-controlled, proof of concept study, active treatment was not associated with a significant EASI score improvement
Omalizumab (Xolair)[1,2]	• Monoclonal antibody approved for treatment of allergic asthma and chronic idiopathic urticaria • Anti-IgE	• Despite many studies, the appropriate clinical role of Xolair for AD yet to be determined because the agent has had inconsistent results in clinical trials • Currently undergoing a large phase IV study in pediatric patients with AD

1. Vakharia PP, Silverberg JI. Monoclonal Antibodies for Atopic Dermatitis: Progress and Potential. *BioDrugs*. 2017 [Epub ahead of print].
2. Xolair [package insert]. South San Francisco, CA: Genentech, 2003.

Where Do Emerging Targeted Therapies Fit into the AD Treatment Algorithm?

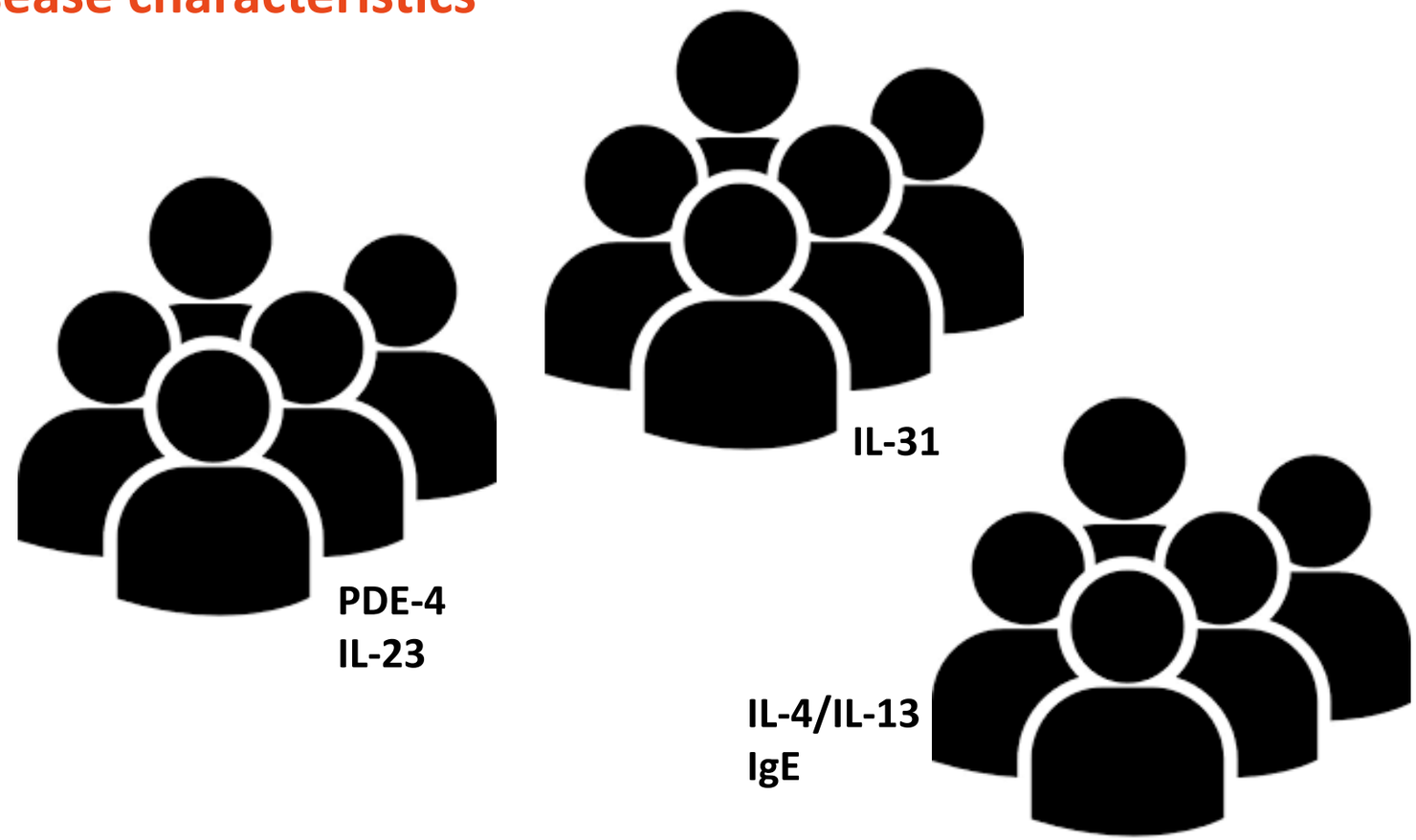


- Currently, only one approved biologic – dupilumab[3]
  - Indicated for treatment of adult patients with moderate-to-severe AD whose disease is not adequately controlled with topical prescription therapies
  - Practically, due to cost concerns, it may first be used in patients with persistent disease on current systemic immunosuppressants

1. Eichenfield LF, Tom WL, Berger TG, et al. Guidelines of care for the management of atopic dermatitis: section 2. Management and treatment of atopic dermatitis with topical therapies. *J Am Acad Dermatol*. 2014;71(1):116-32.
2. Sidbury R, Davis DM, Cohen DE, et al. Guidelines of care for the management of atopic dermatitis: section 3. Management and treatment with phototherapy and systemic agents. *J Am Acad Dermatol*. 2014;71(2):327-49.
3. Dupixent [package insert]. Tarrytown, NY: Regeneron Pharmaceuticals, Inc; 2017.

As Additional Biologics Become Available and As We Gain Deeper Understanding of this Heterogeneous Disease . . .

..treatment will likely be better personalized by patient and disease characteristics



"It is unlikely that any single agent, class of agents, or therapeutic approach can be expected to be universally applicable treatments for all forms of AD. Instead, the choice of agents used in subsets of patients may be best guided by techniques that could include patient stratification based on biomarkers such as transcriptome analysis, immunohistochemistry, and serum cytokine profiling"
—*Friedlander et al, 2016*

1. Udkoff J, Waldman A, Ahluwalia J, Borok J, Eichenfield LF. Current and emerging topical therapies for atopic dermatitis. *Clin Dermatol*. 2017;35(4):375-382.
2. Friedlander SF, Simpson EL, Irvine AD, Eichenfield LF. The Changing Paradigm of Atopic Dermatitis Therapy. *Semin Cutan Med Surg*. 2016;35(5 Suppl):S97-9.

Proactive Treatment Has the Potential to Result in Better Disease Control and Improved Quality of Life

- AD has traditionally been treated reactively, adjusting treatment as symptoms of disease severity change
- However, AD is a chronic systemic disease active even in the absence of symptoms
- Preventive therapy, scheduled intermittent therapy, and alternating therapy are examples of potentially viable approaches to keeping AD under control and preventing reappearance of symptoms while minimizing drug-related risk
- If targeted biologics prove to have fewer long-term toxicities with equal or better efficacy, they may remove a barrier to proactive systemic treatment for moderate-to-severe AD

1. Eichenfield LF, Tom WL, Berger TG, et al. Guidelines of care for the management of atopic dermatitis: section 2. Management and treatment of atopic dermatitis with topical therapies. *J Am Acad Dermatol*. 2014;71(1):116-32.
2. Eichenfield LE, et al. Perspectives from the American Academy of Dermatology Meeting 2017: Clinical Strategies and Scientific Advances in Atopic Dermatitis. June 9, 2017 – June 8, 2018. https://courses.elseviercme.com/aad/712. Accessed September 1, 2017.

Summary

- AD is a chronically relapsing inflammatory skin disease with a profound effect on patient quality of life
- AD has 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 and improved quality of life

Benefit Design Strategies to Remove Barriers and Enhance Overall Value for the Treatment of Atopic Dermatitis

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

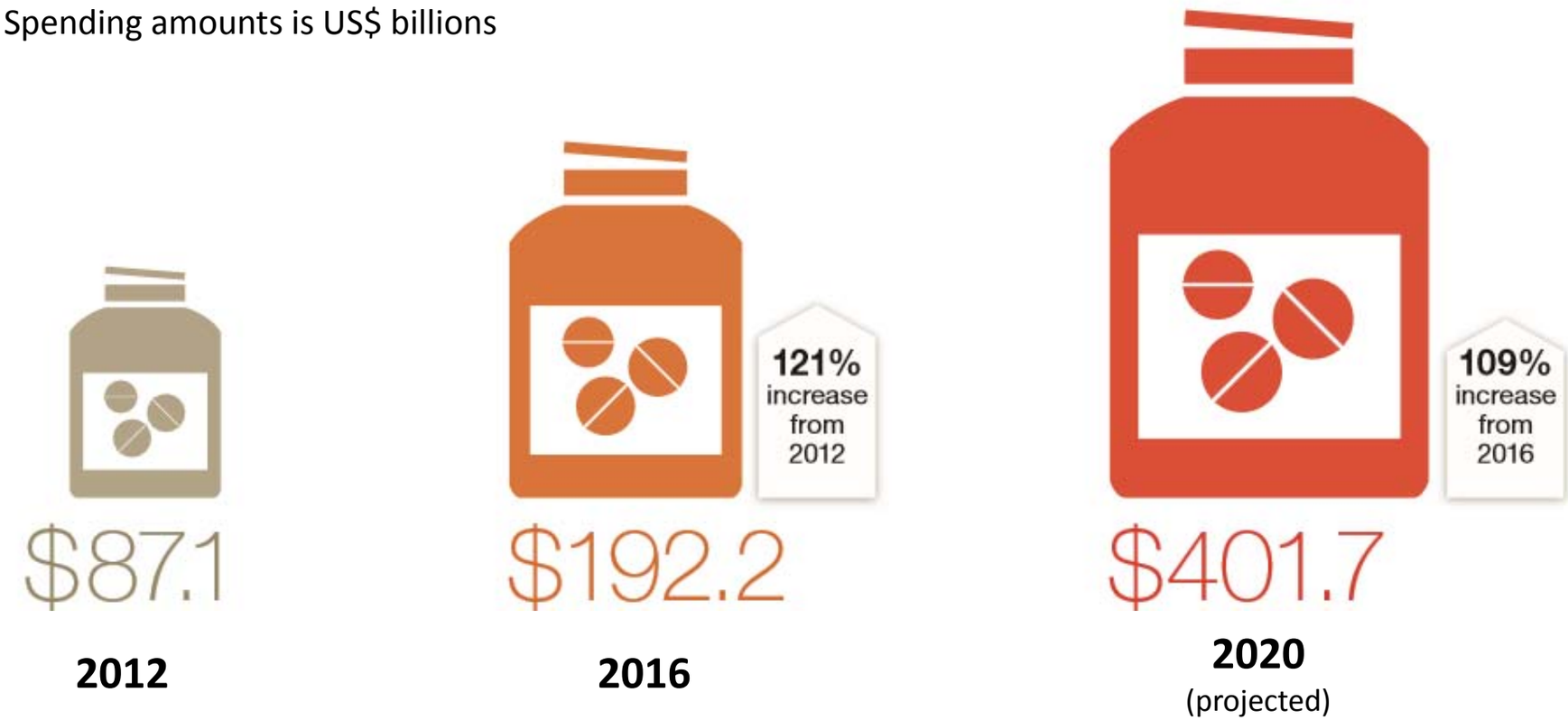
Current Issues

- Several new drugs have been recently approved or are currently in development for AD, including specialty agents (ie, biologics)
- Management of biologics for AD have many similarities to our experience with plaque psoriasis
- New specialty drugs for AD are also being studied for other disease states (eg, asthma)
- With a new AD specialty category, there are no contracts unless semi-open access

Sales of Specialty Drugs Continue to Increase

Projected Specialty Drug Spending from 2012 to 2020

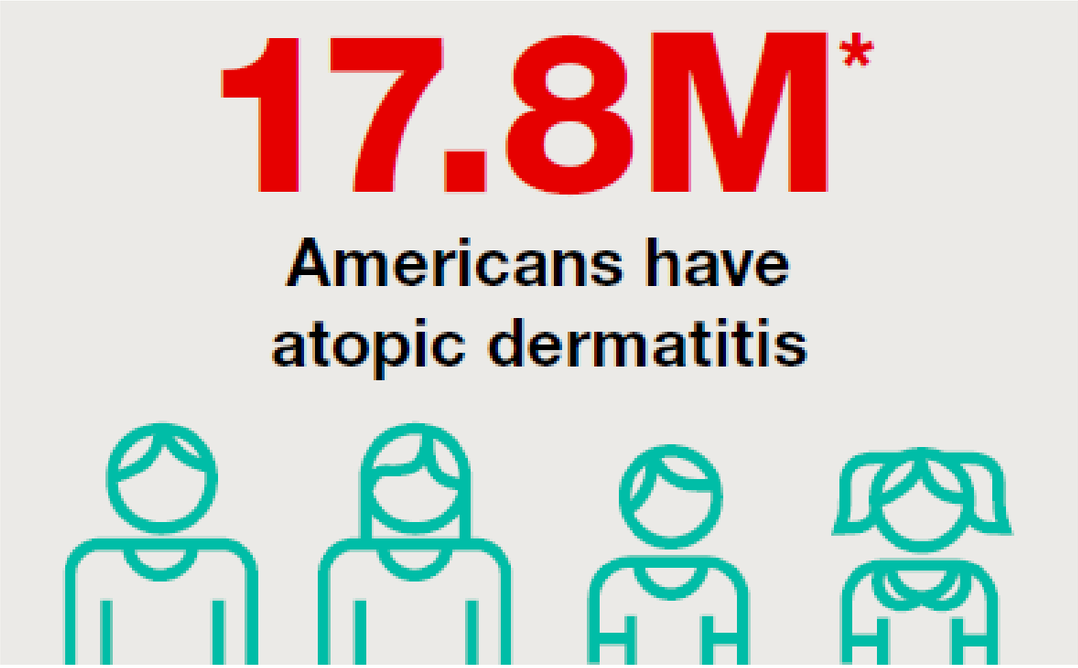
Spending amounts is US$ billions



Medical Cost Trend: Behind the Numbers 2015. PricewaterhouseCoopers. https://www.pwc.com/us/en/health-industries/top-health-industry-issues/assets/pwc-hri-medical-cost-trend-2015.pdf. Accessed August 2017.

Background

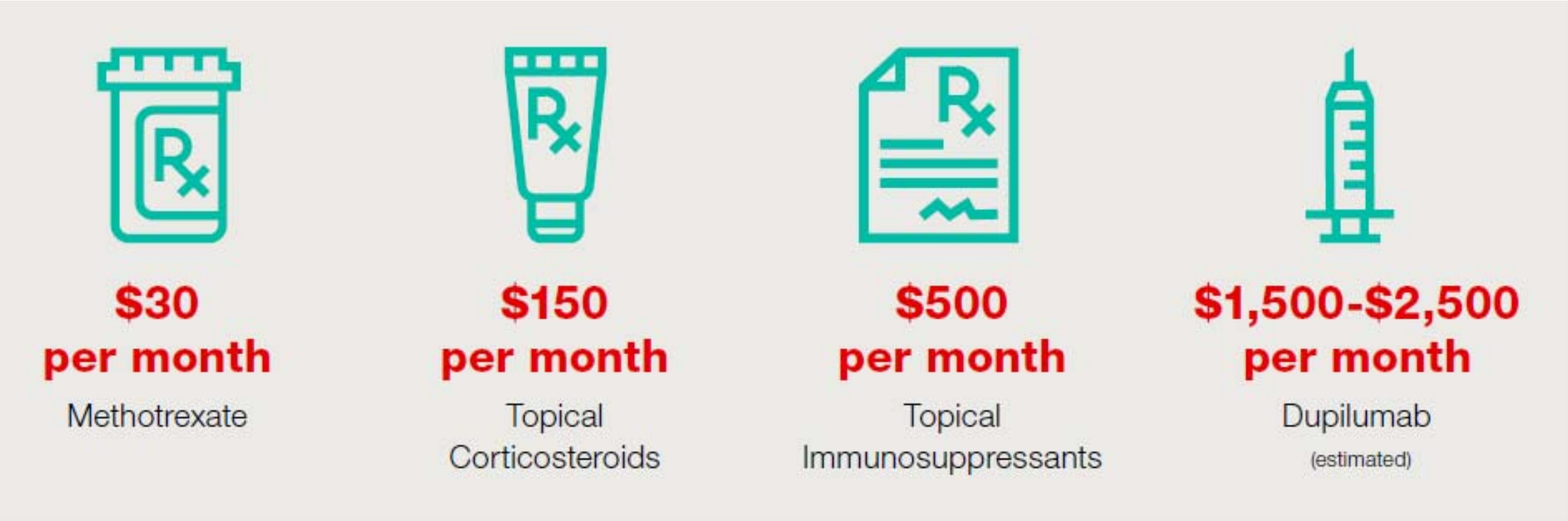
- AD is a chronic pruritic inflammatory skin disease associated with elevated serum level of IgE and a personal or family history of atopy
- Disproportionally more children (10-20%) are affected than adults (1-3%)
- Typically diagnosed in childhood
- The AD that emerges in adults is often different than that in children
- The incidence of AD appears to be increasing



*estimated

New Specialty Drug for Atopic Dermatitis. CVS Health. https://payorsolutions.cvshealth.com/sites/default/files/cvs-health-payor-solutions-insights-feature-new-specialty-drug-for-atopic-dermatitis-october-2016.pdf. Published October 18, 2016. Accessed August 2017.
Atopic Dermatitis Overview. American Academy of Dermatology. https://www.aad.org/public/diseases/eczema/atopic-dermatitis#overview. Accessed August 2017.

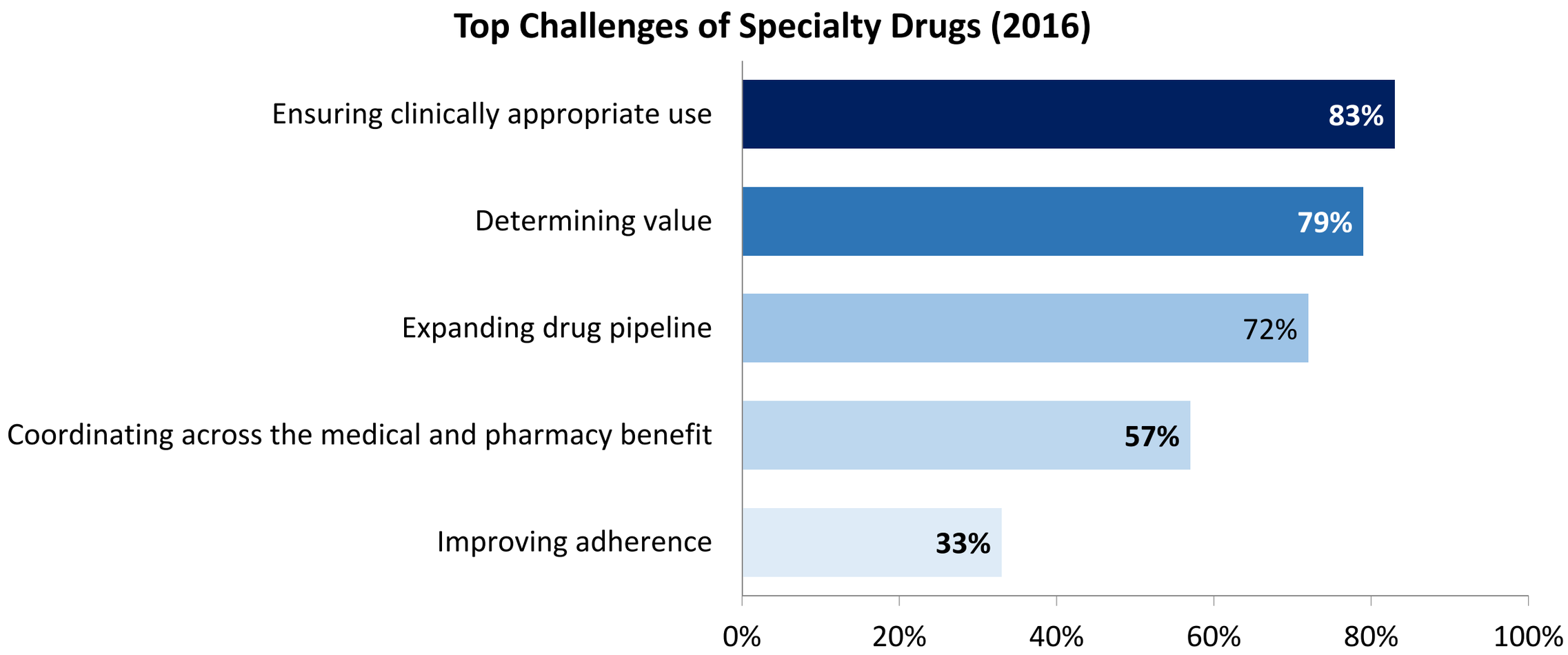
Cost of Treating AD



An estimated 1.6 million patients are expected to be eligible for new AD treatments

New Specialty Drug for Atopic Dermatitis. CVS Health. https://payorsolutions.cvshealth.com/sites/default/files/cvs-health-payor-solutions-insights-feature-new-specialty-drug-for-atopic-dermatitis-october-2016.pdf. Published October 18, 2016. Accessed August 2017.

AD Management Challenges



Specialty Drug Management Performance Overview. EMD Serono Specialty Digest, 13th Edition. https://specialtydigestemdserono.com. Published May 1, 2017. Accessed August 2017.

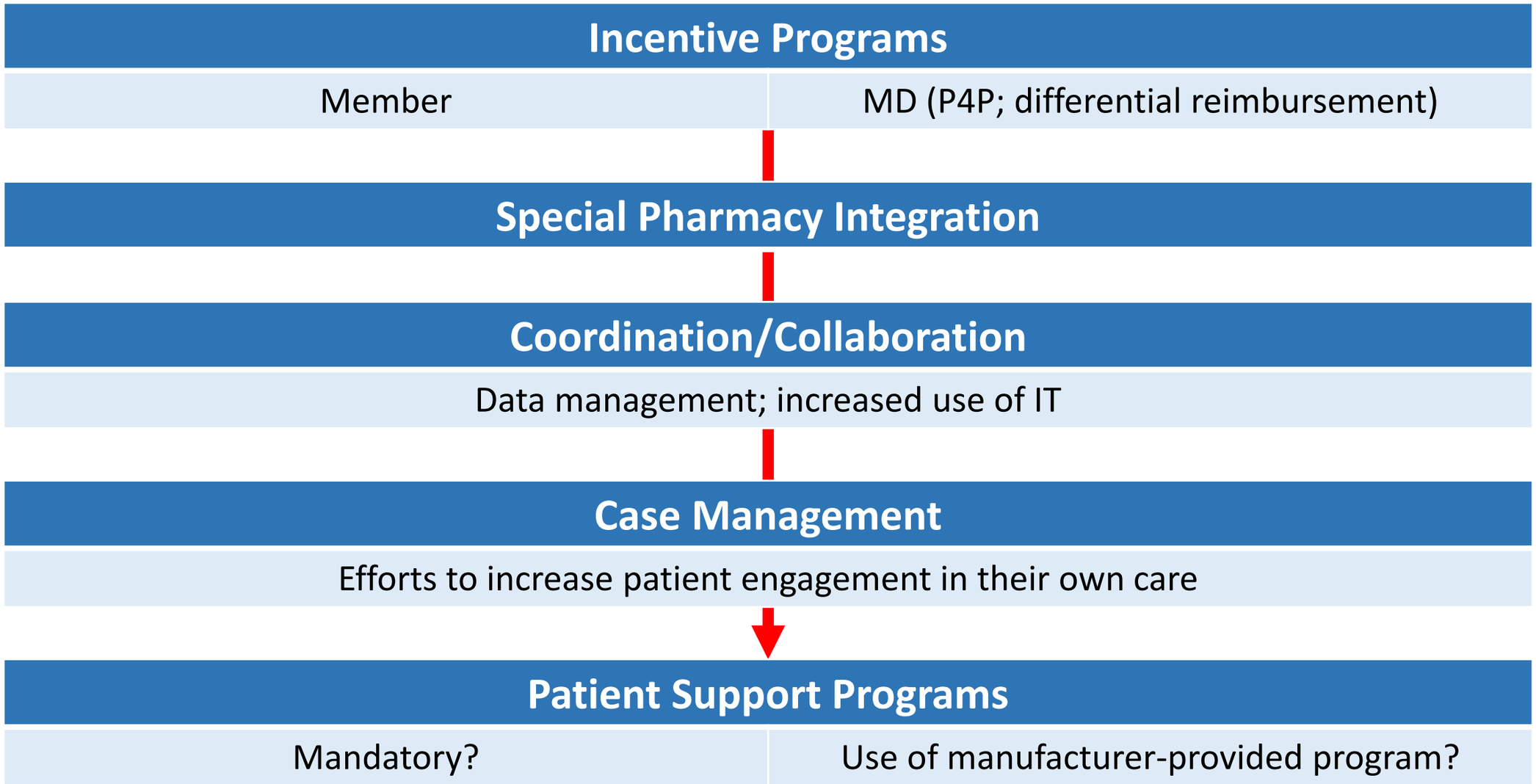
Basic Tenets of a Benefits Plan Design

Manage costs by restricting resource (eg, drug) utilization
Medical and pharmacy designs are usually independent

Cost sharing is used to influence patterns of utilization	
Patient cost-share related to acquisition cost of the drug	Assumes an inelastic demand or willingness to pay

The Management of Specialty Drugs. sPCMA. https://www.spcma.org/wp-content/uploads/2016/06/sPCMA_The_Management_of_Specialty_Drugs.pdf. Published February 2016. Accessed August 2017.

Common Components of an AD Benefit Design



AD Pharmacy Benefit Design Considerations

Benefit Design

Tiers

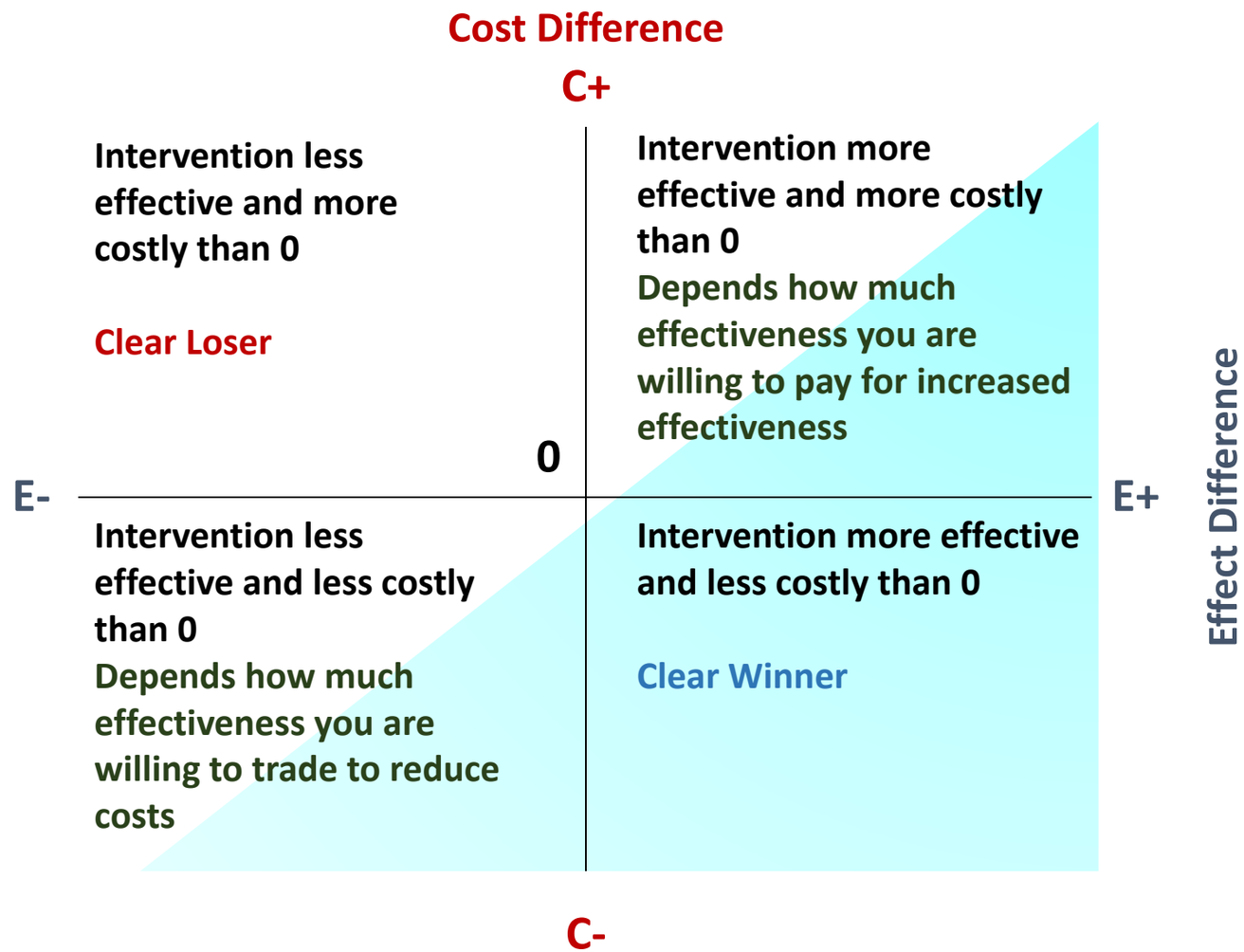
Evaluation of out-of-pocket expenses and distribution

↓

Application of Guidelines, Clinical Pathways, and/or Disease Management

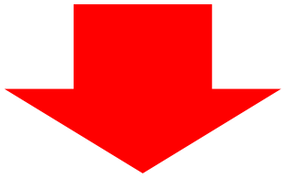
Value = Cost Effectiveness

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



Formulary Management

More Formulary Control			
Need for data/ Use of CER	Levels of evidence for PA	Quantity limits	Stop/start rules



Contracts	
Work with manufacturers; Outcomes-based contracts	Net effective pricing

Formulary Tiers

Pharmacy Benefit Cost Sharing Design Overview	High-Deductible Plans (n=47)		Standard Deductible Plans (n=57)	
	% of Plans	% of Lives	% of Plans	% of Lives
Traditional and specialty in the same tier	**36%**	**21%**	**44%**	**24%**
1-tier or 2-tier plans	29%	71%	8%	41%
3 or more tiers	71%	29%	92%	59%
Traditional and specialty in separate tiers	**64%**	**79%**	**56%**	**76%**
1 specialty tier	70%	62%	69%	41%
2 or more specialty tiers	30%	38%	31%	59%

Specialty Drug Management Performance Overview. EMD Serono Specialty Digest, 13th Edition. https://specialtydigestemdserono.com. Published May 1, 2017. Accessed August 2017.

Special Pharmacy Care Management

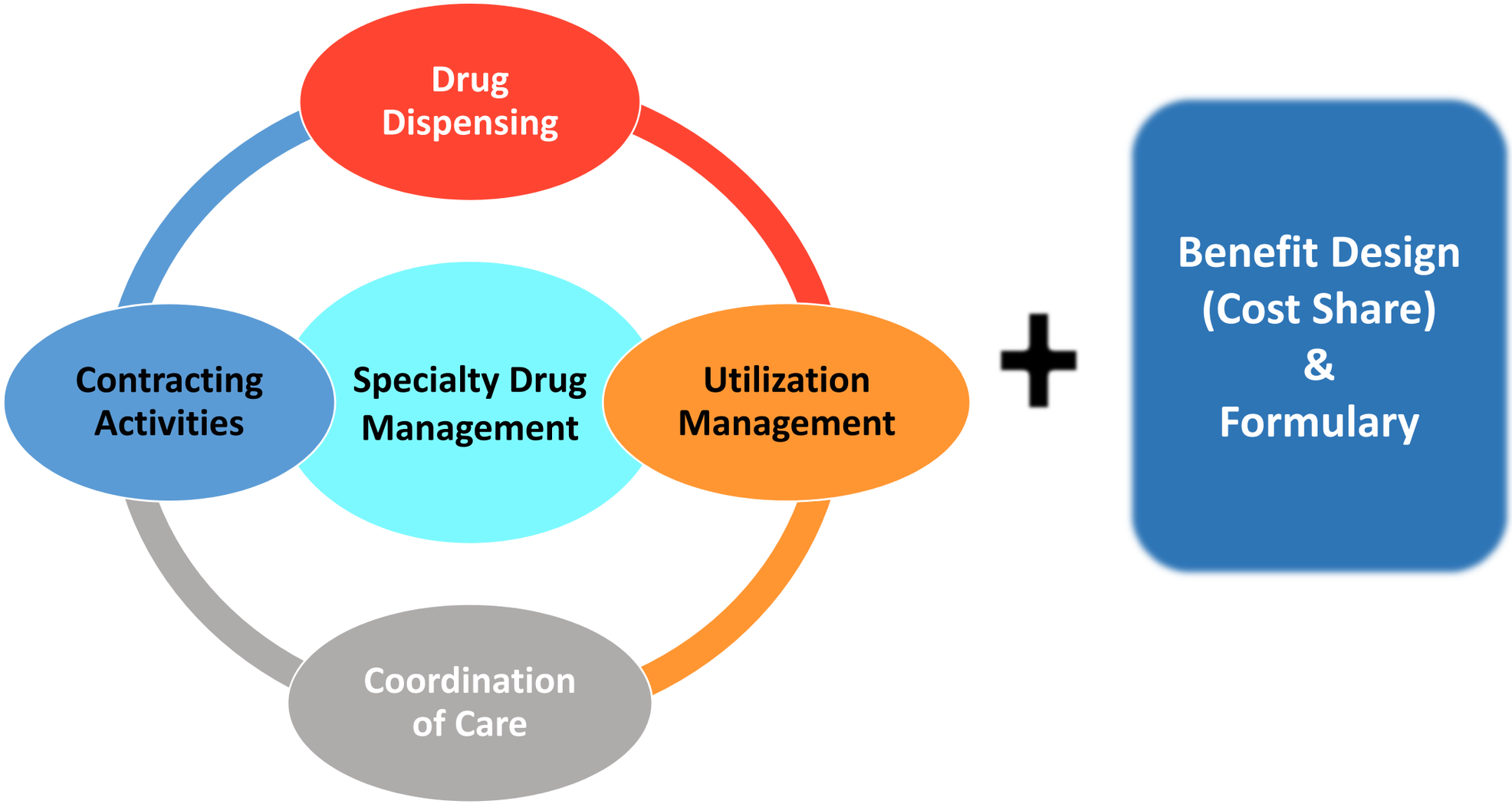
Program

- Specialty Pharmacy Medication Therapy Management (MTM)
  - Integration with Care Management
  - Coordinate site of care
  - Ensure appropriate dosing
  - Adherence
  - Patient education
  - Expectation management

Actions

- Design workflow and integration with Care Management
- Analyze drug utilization patterns to select targeted drugs/disease
- Train personnel
  - Specialty diseases
  - Medications
  - Site of care logistics

AD Pharmacy Management: Finding the Right Balance



Summary

- Several novel agents to treat AD have been recently approved or are in late stage development.
- While the increasing number of treatment options is a great benefit to patients, providers, and payers, these same stakeholders are challenged by the acquisition cost and appropriate use of these therapies.
- New plan designs and care models that emphasize value over volume of care are being implemented to ensure patients continue to have access to these innovative therapies.