**SUMMARY OF EVIDENCE/POSITION**

This policy addresses the coverage of **Dupixent (dupilumab)** for the treatment of adult patients with **moderate-to-severe atopic dermatitis** when appropriate criteria are met.

The intent of the Dupixent (dupilumab) drug policy is to ensure appropriate selection of patients for therapy based on product labeling, clinical guidelines, and clinical studies. This policy is intended to address coverage criteria that are appropriate for the majority of individuals/members with a particular disease, illness, or condition. Each member's unique clinical circumstances may warrant individual consideration, based on review of applicable medical records.

- **Atopic dermatitis (AD)** is a chronic, pruritic inflammatory skin disease of unknown origin that usually starts in early infancy, but also affects a substantial number of adults. Moderate-to-severe AD is characterized by rashes often covering much of the body, and can include intense, persistent itching and skin dryness, cracking, redness, crusting, and oozing. Itch is one of the most burdensome symptoms for patients and can be debilitating.
  - *Disease severity* may be mild, moderate, or severe and is generally based on type (acute, subacute, chronic) and extent (pattern) of eczema. Approximately 10% to 30% of children, who develop AD, continue to live with the disease into adulthood, and up to 3% of U.S. adults are living with AD (Eichenfield et al., 2014).
  - *Goals of treatment* for atopic dermatitis include: reduction of symptoms (pruritus and dermatitis, clearance of skin lesions), prevention of exacerbations and adverse events and triggers associated with various treatment modalities, and minimizing therapeutic risks. There is no known cure for AD at this time.

- **Dupilumab** (Dupixent) is a human monoclonal antibody that is designed to specifically inhibit overactive signaling of two key proteins, interleukin (IL)-4 and IL-13, which are believed to be major drivers of the persistent underlying inflammation in AD. Inhibition of IL-4 receptor alpha blocks downstream TH2-dependent release of IL-4 and IL-13, with subsequent allergic sensitization that causes skin barrier changes in atopic dermatitis.

- Dupixent (dupilumab) is the first systemic therapy approved for the treatment of moderate-to-severe atopic dermatitis and the first biologic therapy approved in this patient population. Dupixent is a first-in-class monoclonal antibody that inhibits the interleukin-4 receptor, interrupting signaling of key proteins that drive inflammation in atopic dermatitis.
The most common adverse reactions reported in clinical trials with dupilumab were injection site reactions, conjunctivitis, keratitis, and oral herpes.

SUMMARY OF EVIDENCE

LIBERTY AD Clinical Program and Results
The FDA approval was based on data from the global LIBERTY AD clinical program, which included 3 Phase III randomized controlled trials (RCTs): 2 trials of Dupixent monotherapy (SOLO 1 and SOLO 2) and 1 trial of Dupixent plus topical corticosteroids (CHRONOS). The studies enrolled 2,119 total adult patients and evaluated Dupixent either alone (SOLO 1 or SOLO 2) or with topical corticosteroids (CHRONOS) in patients with inadequately controlled moderate-to-severe AD.

- Results demonstrate significant efficacy of Dupixent monotherapy over placebo to reduce AD symptoms in adults with moderate-to-severe disease. SOLO 1 and SOLO 2 trials evaluated efficacy up to 16 weeks and safety up to 28 weeks.
- In both trials, a significantly greater proportion of patients treated with Dupixent versus placebo achieved the primary efficacy endpoint. In SOLO 1, the endpoint was reached by 10% of patients allocated to the placebo group, 38% of those in the Dupixent every-other-week group, and 37% of those in the Dupixent-weekly group (P<0.001). Outcomes in placebo and Dupixent every-other-week/once-weekly groups were similar in SOLO 2 (8% and 36%, respectively; P<0.001).
- Improvement of at least 75% on the EASI was achieved by significantly more patients in Dupixent groups than in placebo groups. Patients treated with Dupixent also demonstrated significantly better measures of pruritus, anxiety, and depression than patients in the placebo groups. Approximately half the patients in both placebo groups required rescue medication, while rescue medication was required by 21% and 23% of patients in the 2 Dupixent groups (every other week and every week, respectively) in SOLO 1, and by 15% and 21% of patients in SOLO 2 Dupixent treatment groups, respectively. Researchers noted that the primary efficacy outcome continued to significantly favor Dupixent when patients who required rescue medication were included in the analysis.
- Across both trials, infectious conjunctivitis occurred in 2 patients given placebo and 36 patients treated with Dupixent; allergic conjunctivitis was reported in 4 placebo group patients and 26 Dupixent-treated patients. An association between Dupixent and conjunctivitis is being investigated.

CLASSIFICATION: Interleukin-4 Receptor Antagonist; Monoclonal Antibody (mAb)

FDA INDICATIONS

Atopic dermatitis
Dupilumab is indicated in adults for the treatment of moderate-to-severe atopic dermatitis not adequately controlled with topical prescription therapies or when those therapies are inadvisable.

Dupilumab may be used with or without topical steroids.

Reserve concomitant use with topical calcineurin inhibitors for problem areas only (e.g., face, neck, intertriginous and genital areas.

Available as: 300mg/2mL Pre-Filled Syringe with Needle Shield Solution for Injection

FDA Approved: March 28, 2017
Dupilumab received FDA priority review* and a breakthrough therapy designation.* Dupixent represents the first time this designation was granted for a dermatological disease, other than in dermatologic cancers.

* FDA priority review is reserved for medications that represent potentially significant improvements in safety or efficacy in treating serious conditions. *Breakthrough Therapy designation expedites the development and review of drugs developed for serious or life-threatening conditions.
Black Box Warnings: None at the time of this writing

REMS: No REMS at the time of this writing

### RECOMMENDATIONS/COVERAGE CRITERIA

**Dupixent (dupilumab)** may be authorized for members who meet **ALL** of the following criteria **[ALL]**

1. **Prescriber specialty [ONE]**
   - Prescribed by, or in consultation with, a board-certified dermatologist, allergist, or pulmonologist. Submit consultation notes if applicable.

   **NOTE:** Consultation notes must be submitted for initial request and for continuation of treatment requests at least **ONCE** annually.

2. **Diagnosis/Indication [ALL]**
   - Clinical documented diagnosis of (includes clinical notes from the member’s medical records including any applicable labs and/or tests, supporting the diagnosis):
     - Diagnosis of moderate-to-severe chronic atopic dermatitis (eczema)
       - No reliable biomarker exists for the diagnosis of AD. Diagnosis is made clinically based on history and physical.
       - A serum immunoglobulin E (IgE) level can be helpful to support the diagnosis
       - There is no agreed-on definition of “mild-to-moderate” or “moderate-to-severe” atopic dermatitis (Roekevisch 2014) even recent trials have used different scaling systems to define severity of disease (Futamura 2016, Paller 2016, Simpson 2016). Severity indices were developed for use in AD clinical trials and are not generally recommended for routine clinical management of patients.

   - Baseline evaluation of **moderate-to-severe disease** using **ONE** (1) of the following documented objective measurements [ONE]
     - Involvement at least 10% body surface area OR flexures of the arms and legs involved accompanied by large lichenified abdominal plaques
     - Investigator’s Global Assessment (IGA) with a score > 3
       - **Moderate-to-severe disease was defined as a score of 3 or 4 in the IGA (scores range from 0 to 4, with higher score indicating greater severity) [as defined by SOLO 1 and 2 RCTs]**
     - Eczema Area and Severity Index (EASI) with a score ≥16

   - **Functional impairment** due to atopic dermatitis, which may include, but is not limited to, documentation of limitation of activities of daily living (ADLs) including but not limited to: sleep disruption; itching and pain that can affect both sleeping and waking hours; individual psychologic effects of illness, including depression, anxiety, suicidal ideation, and loss of self-esteem; effects on performance, including effects on developmental milestones and school attendance in children, missed days of work, disability for one’s chosen profession, effects on school and work performance; effects on life activities, including restrictions on diet, exercise, and recreation

---

Page 3 of 21
3. **Age/Gender/Restrictions [ALL]**

- 18 years of age or older
  - *Safety and efficacy have not been established in pediatric patients*

4. **Conventional Therapy/Concurrent Therapy/Other Requirements [ALL]**

- Member is **NOT** concurrently receiving Dupixent in combination with ANY of the following: [ANY]
  - Live vaccines
  - Another biologic medication for the treatment of atopic dermatitis (e.g., Xolair (omalizumab), Rituxan (rituximab), Enbrel (etanercept), Remicade/Inflectra (infliximab))

- **TOPICAL THERAPY**
  - Documentation of inadequate response, *clinical intolerance, contraindication, or clinical rationale of the inappropriateness to the following topical treatments, or cases where treatment may not be indicated:* [ALL]
    - *Inadequate response is defined as failure to achieve and maintain remission or a low disease activity state despite treatment with a **daily regimen** for the maximum treatment period indicated in the product prescribing information.*
    - *Topical corticosteroids may not be indicated in the following concomitant clinical situations:*
      - Individual has lesions located in sensitive areas (such as face, anogenital area or skin folds)
      - Individual has steroid-induced atrophy
      - History of long-term or uninterrupted topical steroid use

  - Moderate to very high-potency corticosteroid [Refer to Appendix 2]

  **AND**

  - Topical calcineurin inhibitors [ONE]
    - pimecrolimus (Elidel)
    - tacrolimus (Protopic)

- **ONE (1) of the following: [ONE]**

  - Phototherapy (UVB or PUVA): Documentation of failure to achieve and maintain remission of low or mild disease activity state or is contraindicated

  - Systemic treatment: Documentation of failure to achieve and maintain remission of low or mild disease activity state or is contraindicated.
    - Methotrexate (oral)
    - cyclosporine (AAD Strength of Recommendation B, Level II)
    - azathioprine (AAD Strength of Recommendation B, Level II)
Informational Note

- Clinical practice guidelines recommend the use of topical corticosteroids in individuals who have failed to respond to good skin care and regular use of emollients alone. Topical calcineurin inhibitors are recommended as second-line agents. (Eichenfield 2014)

- Guidelines recommend using topical calcineurin inhibitors in the following patients/cases: individuals refractory to topical corticosteroids, use in sensitive areas (e.g., face, axilla, anogenital region, and skin folds), patients with steroid induced-atrophy, and in patients who require long-term treatment.

- There are two topical calcineurin inhibitors available currently: topical tacrolimus (indicated for moderate to severe AD) and pimecrolimus (indicated for mild to moderate disease). Both topical tacrolimus and pimecrolimus are FDA-approved as second-line agents. Topical calcineurin inhibitors are reported as well-tolerated but contain a boxed warning for rare cases of malignancy (e.g., skin cancer and lymphoma).
  - Tacrolimus: Ointment, both 0.03% and 0.1% for adults, and only 0.03% for children 2 to 15 years of age, is indicated as second-line therapy for the short-term and non-continuous chronic treatment of moderate-to-severe AD in non-immunocompromised adults and children who have failed to respond adequately to other topical prescription treatments for AD, or when those treatments are not advisable
  - Pimecrolimus (Elidel): Second-line therapy for short-term and non-continuous long-term treatment of mild to moderate AD in non-immunocompromised patients 2 years and older who have failed to respond adequately to other topical prescription treatments, or when those treatments are not advisable.

5. Contraindications*/Exclusions/Discontinuations

Authorization will not be granted if ANY of the following conditions apply [ANY]

- Non-FDA approved indications
- Hypersensitivity to dupilumab or any component of the formulation
  - Drug Interactions: No formal drug interaction studies have been published.

Exclusions [ANY]

- Concurrent live vaccines
- Concurrent another biologic medication for the treatment of atopic dermatitis [i.e. Xolair (omalizumab), Rituxan (rituximab), Enbrel (etanercept), Remicade/Inflectra (infliximab)]
- Younger than 18 years

6. Labs/Reports/Documentation required [ALL]

All documentation for determination of medical necessity must be submitted for review. Prescriber to submit documentation as indicated in the criteria above, including but not limited to chart notes, applicable lab values and/or tests, adverse outcomes, treatment failures, or any other additional clinical information or clinical notes from the member’s medical records supporting the diagnosis. Letters of support and/or explanation are often useful, but are not sufficient documentation unless ALL specific information required by this MCP is included.

NOTE: Additional documentation, rationale, and/or supporting evidence may be requested for review as deemed necessary or appropriate by Molina Medical/Pharmacy staff.
CONTINUATION OF THERAPY

Dupixent (dupilumab) may be authorized for continuation of therapy if meet ALL of the following criteria are met: [ALL]

1. Initial Coverage Criteria [ALL]
   - Member currently meets ALL initial coverage criteria
   - Subsequent authorizations will require the Member to have an office visit and re-assessment for this condition annually to determine if continuation of treatment with requested medication is medically necessary. Chart notes or consultation notes (if applicable) must be submitted for initial request and for continuation of treatment requests at least ONCE annually.

2. Compliance [ALL]
   N/A

3. Labs/Reports/Documentation required [ALL]
   Dupixent (dupilumab) therapy may be authorized when therapy has demonstrated efficacy as evidenced by an improvement in disease activity after initial therapy documentation by: [ALL]
   - Dupixent (dupilumab) therapy effective as defined by a reduction in body surface area involvement, pruritus severity, skin infections, or sleep disturbances
   - Documented improvement of the condition using ONE (1) of the following documented objective measurements: [ONE]
     - Decrease in the following: [ALL APPLICABLE]
       - Frequency of treatment
       - Frequency of office visits
       - Need for prednisone (acceptable for short-term use)
     - Investigator’s Global Assessment (IGA): decrease from baseline by at least 2 points
     - Eczema Area and Severity Index (EASI): decrease from baseline by at least 75%
       Refer to Appendix 1 for information on ‘ASSESSMENT OF SEVERITY’

   - Member is NOT concurrently receiving Dupixent in combination with ANY of the following:
     - Live vaccines
     - Another biologic medication for the treatment of atopic dermatitis [e.g., Xolair (omalizumab), Rituxan (rituximab), Enbrel (etanercept), Remicade/Inflectra (infliximab)]

Informational Note
SOLO 1 and SOLO 2 clinical trials indicated 2 primary endpoints:
- The proportion of patients with an IGA score of 0 (clear) to 1 (almost clear) and a reduction from baseline of at least 2 points in week 16; and
- The proportion of patients who had a reduction from baseline at week 16 of at least 75% on the EASI-75 (A key secondary in the US; a co-primary end point in Japan and the EU).
4. Discontinuation of Treatment [ANY]
   Discontinue treatment if ANY of the following conditions applies: [ANY]
   - Intolerable adverse effects or drug toxicity
   - Persistent and uncorrectable problems with adherence to treatment
   - Poor response to treatment as evidenced by physical findings and/or clinical symptoms
   - Contraindications
     - Non-FDA approved indications
     - Hypersensitivity to dupilumab or any component of the formulation
       - Drug Interactions: No formal drug interaction studies have been published.
   - Exclusions [ANY]
     - Concurrent live vaccines
     - Concurrent another biologic medication for the treatment of atopic dermatitis [i.e. Xolair (omalizumab), Rituxan (rituximab), Enbrel (etanercept), Remicade/Inflectra (infliximab)]
     - Younger than 18 years

5. Labs/Reports/Documentation required [ALL]
   All documentation for determination of medical necessity must be submitted for review. Prescriber to submit
documentation as indicated in the criteria above, including but not limited to chart notes, applicable lab values and/or
tests, adverse outcomes, treatment failures, or any other additional clinical information or clinical notes from the
member’s medical records supporting the diagnosis. Letters of support and/or explanation are often useful, but are
not sufficient documentation unless ALL specific information required by this MCP is included.
NOTE: Additional documentation, rationale, and/or supporting evidence may be requested for review as deemed
necessary or appropriate by Molina Medical/Pharmacy staff.
Consult the manufacturer’s labeling for more detailed information on dosage and administration of this drug, cautions, precautions, contraindications, potential drug interactions, laboratory test interferences, and acute toxicity.

1. **Recommended Dosage [ALL]**
   The recommended dosage (subcutaneous route) for atopic dermatitis, moderate to severe is an initial dose of 600 mg (two 300 mg subcutaneous injections in different injection sites), followed by 300 mg given every other week.

   *In phase 3 clinical trials (SOLO-1 and SOLO-2), dupilumab was administered by subcutaneous injection as a loading dose of 600 mg and then as 300 mg weekly or every other week.* (Simpson 2016)

   - Initial dosage: Initial, 600 mg subcutaneous, divided in 2 different injection sites *(pre-filled syringe may be self-administered as a subcutaneous injection every other week after an initial loading dose)*
   
   - Maintenance dosage: 300 mg subQ every other week

     ➢ Missed dose: May administer within 7 days of the missed dose and then resume the original schedule. If more time has elapsed, do not administer until next scheduled dose

2. **Authorization Limit [ALL]**

   - Quantity limit: 9 syringes (or 24 syringes in 12 months)

   - Dispensing limit: Only a 1-month supply may be dispensed at a time<sup>a-e</sup>

   - Duration authorization: [ALL]
     - Initial: 3 months
     - Continuation: 6 months

   - Continuation of treatment: Re-authorization is required every 6 months to determine effectiveness of therapy and continued need based on documented positive clinical response. Subsequent renewals will be authorized upon verification of marked clinical improvement demonstrated by objective improvement in these selected markers. Refer to ‘Continuation of Therapy’ section.

3. **Route of Administration [ALL]**

   - Dupixent (dupilumab) is considered a self-administered medication.

     *Dupixent (dupilumab) is deemed appropriate for self-administration or administration by a caregiver (i.e., not a healthcare professional). Therefore, coverage (i.e., administration) in a provider-administered setting such as an outpatient hospital, ambulatory surgical suite, physician office, or emergency facility will not be authorized.*

   - If member meets all criteria and approval for therapy is granted, medication will be dispensed by a specialty pharmacy vendor at the discretion of Molina Healthcare. Self-administered medications may not be dispensed for self-administration and billed through the medical benefit by a provider. These agents must be dispensed through a participating pharmacy.
**COVERAGE EXCLUSIONS**

This policy addresses the coverage of *Dupixent (dupilumab)* for the treatment of adult patients with **moderate-to-severe atopic dermatitis** when appropriate criteria are met.

All other uses of *Dupixent (dupilumab)* that are not an FDA-approved indication or not included in the ‘Coverage Criteria’ section of this policy are considered experimental/investigational or not a covered benefit of this policy. This subject to change based on research and medical literature, or at the discretion of Molina Healthcare.

*Pharmaceutical samples: The use of pharmaceutical samples (from the prescriber or manufacturer assistance program) will not be considered when evaluating the medical condition, prior prescription history, or as continuation of therapy.

*FDA-approved indication does not, in itself, dictate coverage. Molina Clinical Policy may not recommend coverage for all FDA-approved indications. Please review this Policy in its entirety for indications covered by Molina Healthcare.*

**SUMMARY OF EVIDENCE/POSITION**

**Management of AD** includes a variety of treatments, such as pharmacological, topical, phototherapy, and systemic interventions.

- **Moisturizers**
  - Moisturizers (i.e. Petrolatum, Aquaphor, Atopiclair and Mimyx) are an integral part of treatment and there is strong evidence that their use can reduce disease severity and need for pharmacologic intervention (AAD Strength of Recommendation A, Level I)

- **Topical steroids:** Current mainstay of treatment; commonly used in conjunction with moisturizers
  - Treatment guidelines recommend the use of topical corticosteroids in patients who have failed to respond to good skin care and regular use of emollients alone
  - Topical corticosteroids remain **first-line therapy** for inflammation and pruritus (AAD Strength of Recommendation A, Level I)
  - Select potency of topical steroid based on severity and location of atopic dermatitis
  - Hydrocortisone, triamcinolone, or betamethasone; ointment bases are generally preferred, particularly in dry environments
  - All of the systemic treatments other than oral corticosteroids lack approval by the FDA for atopic dermatitis
  - Consider combination topical steroid plus topical calcineurin inhibitor, concomitantly or sequentially, as steroid-sparing regimen (AAD Strength of Recommendation B, Level II)

- **Immunomodulators:** Tacrolimus and pimecrolimus
  - Topical calcineurin inhibitors are recommended as **second-line agents**
  - Guidelines recommend using topical calcineurin inhibitors in the following situations: patients’ refractory to topical corticosteroids, use in sensitive areas (e.g. face, axilla, anogenital region, and skin folds), patients with steroid induced-atrophy, and in patients who require long-term treatment
  - American Academy of Dermatology (AAD) 2014 recommendations for topical calcineurin inhibitors for atopic dermatitis (Section 2)
    - topical calcineurin inhibitors recommended and effective for acute, chronic, or maintenance treatment, and may be preferable to topical steroids for any of the following situations (AAD Strength of Recommendation A, Level I)
      - recalcitrance to steroids
      - sensitive areas (face, anogenital, skin folds)
      - steroid-induced atrophy
      - long-term uninterrupted topical steroid use
• recommended for use on actively-affected areas as a steroid-sparing agent (AAD Strength of Recommendation A, Level I)
• in children < 2 years old with mild to severe disease, off-label use of 0.03% tacrolimus or 1% pimecrolimus ointment may be recommended (AAD Strength of Recommendation A, Level I)
• inform patients of potential skin burning or pruritus with pimecrolimus cream or tacrolimus ointment, and consider initial treatment with topical corticosteroids to minimize application site reactions (AAD Strength of Recommendation B, Level II)
• concomitant use of topical corticosteroid with topical calcineurin inhibitor may be recommended (AAD Strength of Recommendation B, Level II)
• routine blood monitoring of tacrolimus or pimecrolimus levels not recommended (AAD Strength of Recommendation A, Level I)

◆ Interleukin inhibitors: Dupilumab

Other treatments that have been tried include the following:

◆ Ultraviolet (UV)-A, UV-B, a combination of both, psoralen plus UV-A (PUVA), or UV-B1 (narrow-band UV-B) therapy
  ◦ Long-term adverse effects of skin malignancies in fair-skinned individuals should be weighed against the benefits.

◆ For severe atopic dermatitis
  • Consider systemic treatment with: methotrexate, azathioprine, cyclosporine, and mycophenolate mofetil
    ◦ cyclosporine (AAD Strength of Recommendation B, Level II)
    ◦ azathioprine (AAD Strength of Recommendation B, Level II)
    ◦ dupilumab (FDA ‘Breakthrough Therapy Designation’) (level 1 [likely reliable] evidence)
  ◦ Azathioprine can be effective monotherapy for severe AD. Marrow suppression and liver toxicity are major concerns, and blood cell counts and liver function tests should be monitored closely. Azathioprine should be dosed according to thiopurine methyltransferase (TPMT) genotype/levels because low activity correlates with higher risk of marrow suppression

◆ Therapies with insufficient or limited evidence include:
  • Topical antihistamines: not routinely recommended (AAD Strength of Recommendation B, Level II)
  • Oral antihistamines: not routinely recommended (AAD Strength of Recommendation A, Level II)
  • Probiotics: not routinely recommended (AAD Strength of Recommendation B, Level II)
  • Specific laundering products or techniques: not recommended (AAD Strength of Recommendation C, Level III)

American Academy of Dermatology (AAD) Quality of Evidence ratings:

Strength of recommendation
- Strength of Recommendation A: recommendation based on consistent and good-quality patient-oriented evidence
- Strength of Recommendation B: recommendation based on inconsistent or limited-quality patient-oriented evidence
- Strength of Recommendation C: recommendation based on consensus, opinion, case studies, or disease-oriented evidence

Levels of evidence
- Level I: good-quality patient-oriented evidence
- Level II: limited-quality patient-oriented evidence
- Level III: other evidence, including consensus guidelines, opinion, case studies, or disease-oriented evidence

LIBERTY AD Clinical Program and Results
The approval of Dupixent was based on data from the global LIBERTY AD clinical program, which included three randomized Phase 3 pivotal trials known as SOLO 1, SOLO 2 and CHRONOS (enrolled 2,119 total adult patients). The studies examined the use of Dupixent either alone (SOLO 1 or SOLO 2, 1,379 adult patients enrolled) or with topical corticosteroids (CHRONOS, 740 adult patients enrolled) in patients with inadequately controlled moderate-to-severe AD. In all these studies, Dupixent alone or with topical corticosteroids met the primary and key secondary endpoints, specifically:

Published Pivotal Phase III SOLO 1 and 2 RCTs
SOLO-1 and SOLO-2 trials were two randomized, double-blind, placebo-controlled, international, multicenter phase 3 trials used the same study design and enrolled patients from North America, Europe, and Asia (Simpson et al., 2016).

The efficacy of dupilumab was established in 3 randomized, double-blind, placebo-controlled studies (n = 2,119). Moderate-to-severe disease was defined as a score of 3 or 4 in the IGA (scores range from 0 to 4, with higher score indicating greater severity). Both trials randomized patients to receive 16 weeks of therapy with subcutaneous Dupixent 300 mg or placebo as follows:

<table>
<thead>
<tr>
<th></th>
<th>SOLO 1 (n=671)</th>
<th>SOLO 2 (n=708)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dupixent 300 mg every week</td>
<td>n=223</td>
<td>n=239</td>
</tr>
<tr>
<td>Dupixent 300 mg every other week</td>
<td>n=224*</td>
<td>n=233*</td>
</tr>
<tr>
<td>Placebo every week</td>
<td>n=224</td>
<td>n=236</td>
</tr>
</tbody>
</table>

*Placebo administered on alternate week to preserve blinding.

Subjects
Baseline characteristics were similar between treatment groups in both trials. Approximately 68% of participants in the combined population were white, 22% were Asian, 7% were black, and 3% had an unknown ethnicity. The median age was approximately 37 years; most had AD for decades, affecting a median of approximately 50% of their body surface area.

1. 1,379 patients. SOLO-1 (n=671) and SOLO-2 (n=708) trials randomized individuals to one of three trial arms with each arm receiving treatment for 16 weeks.
   1) weekly subcutaneous (SQ) dupilumab injections,
   2) weekly placebo SQ injections or
   3) weekly SQ injections alternating between dupilumab and placebo

2. 18 years and older with moderate to severe atopic dermatitis not adequately controlled with topical therapy

3. Investigator’s Global Assessment (IGA) score of 3 or higher (3=moderate; 4=severe), Eczema Area and Severity Index (EASI) score of 16 or higher, atopic dermatitis involvement over at least 10% of total body surface area (BSA) at screening and baseline, and baseline score on a pruritus numerical rating scale for maximum itch intensity of at least 3.

4. Once enrolled, patients were not permitted concomitant use of topical glucocorticoids or calcineurin inhibitors, immunomodulating biologic agents, or systemic glucocorticoids or nonsteroidal immunosuppressants.

Exclusion
Patients were excluded if they had received treatment with any investigational drug (including dupilumab) within 8 weeks of baseline; immunosuppressive or immunomodulatory medication or phototherapy for atopic dermatitis within 4 weeks of baseline; biologic agent (i.e., cell-depleting agent [e.g., rituximab] within 6 months of baseline, other biologic agent within 16 weeks of baseline); topical corticosteroid or topical calcineurin inhibitor within 1 week of baseline; or live (attenuated) vaccine within 12 weeks of baseline.
Other exclusion criteria included history of HIV; hepatitis B or C antibodies at screening; or skin comorbidity with the potential to interfere with study assessment. Among treatment groups (SOLO 1 and SOLO 2), more than 50% were men, 65% to 71% were white, 19% to 25% were Asian, median age ranged from 34 to 39 years, 47% to 49% had an IGA score of 4 (severe atopic dermatitis), and median peak score for pruritus (a patient-reported measure of maximum itch intensity) ranged from 7.6 to 7.8. Extent of affected BSA and EASI scores were also comparable across all study groups.

Intervention
- Study drugs were administered after patients underwent a 35-day screening and washout period.
- All patients were required to apply moisturizers twice daily for 1 week before randomization, and throughout the trial; concomitant topical glucocorticoids and calcineurin inhibitors were prohibited unless a physician determined that “rescue” therapy was indicated. Patients who required a systemic rescue therapy were considered “nonresponders” and discontinued the trial.
- Subjects were randomized 1:1:1 (stratified according to disease severity [IGA 3 versus 4] and region) to receive subcutaneous injections of placebo weekly, dupilumab weekly, or dupilumab every other week (every 2 weeks) for 16 weeks.
- Dupilumab was administered as a 600 mg loading dose on day 1 and then as 300 mg for all subsequent doses. Patients in the group that received dupilumab every other week received placebo injections on the alternating weeks between dupilumab injections.

Primary End Point(s)
The SOLO 1 and SOLO 2 clinical trials indicated 2 primary endpoints:
- The proportion of patients with an IGA score of 0 (clear) to 1 (almost clear) and a reduction from baseline of at least 2 points in week 16; and
- The proportion of patients who had a reduction from baseline at week 16 of at least 75% on the Eczema Area and Severity Index (EASI-75) (A key secondary in the US; a coprimary end point in Japan and the EU).

Results
- In the SOLO 1 and SOLO 2 studies, treatment with dupilumab as monotherapy significantly improved measures of skin clearing and overall extent and severity of disease:
  - At 16 weeks, for SOLO 1 and SOLO 2, respectively, 38 and 36 percent of patients who received dupilumab 300 mg every two weeks achieved clear or almost clear skin as measured by the 5-point Investigator's Global Assessment (IGA) scale (primary endpoint), compared to 10 and 9 percent with placebo.
  - At 16 weeks, for SOLO 1 and SOLO 2, respectively, 51 and 44 percent of patients who received dupilumab 300 mg every two weeks achieved a 75 percent or greater reduction in their Eczema Area and Severity Index score (EASI-75) from baseline, a key secondary endpoint, compared to 15 and 12 percent with placebo.
  - At 16 weeks, for SOLO 1 and SOLO 2, respectively, 41 and 36 percent of patients who received dupilumab 300 mg every two weeks achieved a greater than or equal to 4 point improvement in the daily intensity of patient-reported itch, as measured by the Pruritus Numerical Rating Scale (NRS), compared to 12 and 10 percent with placebo.

- In the CHRONOS study, treatment with dupilumab with topical corticosteroids (TCS) significantly improved measures of overall disease severity at 16 and 52 weeks, when compared to placebo with TCS:
  - At 16 weeks, 39 percent of patients who received dupilumab 300 mg every two weeks with TCS achieved clear or almost clear skin (IGA 0 or 1), the primary endpoint, compared to 12 percent of patients receiving placebo with TCS.
  - At 16 weeks, 69 percent of patients who received dupilumab 300 mg every two weeks with TCS achieved EASI-75 (key secondary endpoint), a 75 percent reduction on an index measuring eczema severity, compared to 23 percent of patients receiving placebo with TCS.
  - At 16 weeks, 59 percent of patients who received dupilumab 300 mg every two weeks with TCS achieved a greater than or equal to 4 point improvement in the daily intensity of patient-reported itch, as measured by the NRS, compared to 20 percent of patients receiving placebo with TCS.
The study also met additional key secondary endpoints at 52 weeks, showing that 36 percent of patients who received dupilumab 300 mg every two weeks with TCS achieved clear or almost clear skin (IGA 0 or 1), compared to 13 percent of patients receiving placebo with TCS.

The studies also revealed positive results for secondary endpoints, including patient-reported reductions in the severity of itching, and significant reductions in scores on both the Hospital Anxiety and Depression Scale, and the Dermatology Life Quality Index.

CONCLUSION

- Dupilumab was FDA-approved based on clinical trials investigating dupilumab as monotherapy (SOLO 1 and SOLO 2) and in concomitant administration with topical corticosteroids (CHRONOS).
  - Results from the SOLO 1 (n=671) and SOLO 2 (n=708) trials showed 36-38% of patients who received dupilumab had scores of 0 or 1 (clear or almost clear) on the Investigator's Global Assessment scale compared with placebo (8-10%) (P < .001).
  - Additionally, improvement from baseline to week 16 of at least 75% on the Eczema Area and Severity Index was reported in significantly more patients who received each regimen of dupilumab than in patients who received placebo (P < .001). (Simpson et al., 2016)
- Therapy was discontinued if patients received systemic rescue therapy, in which case data at all subsequent time points were treated as no response.
- Overall, patients treated with dupilumab had an improvement in atopic dermatitis symptoms, as well as in quality-of-life measures such as DLQI and POEM, compared to patients treated with placebo. Adverse effects of the study medication included injection-site reactions, nasopharyngitis, upper respiratory tract infection, conjunctivitis, and herpes viral infection (oral herpes being most common). There was also a low incidence of exacerbation of atopic dermatitis (incidence ranged from 10% to 16% in dupilumab groups and was 30% and 35% in placebo groups). Overall incidence of adverse events was similar in the dupilumab and placebo groups. The safety and efficacy results of the SOLO 1 and SOLO 2 trials are similar to findings of previous phase 1 and 2 studies. [Beck 2014; Simpson 2016a; Simpson 2016b; Thaçi 2016]

Limitations

The study protocol allowed for patients to self-administer medication, which may have introduced a potential for non-adherence in those opting to self-administer. The investigators did not detail measures taken to ensure medication adherence in the published information. In addition, rescue medication use was at the investigator’s discretion and reserved for patients who had unacceptable symptoms of atopic dermatitis. However, the protocol did not specify criteria for unacceptable symptoms of atopic dermatitis or the extent of affected BSA. The study was not powered to compare the 2 dosage regimens.

- Efficacy and safety of dupilumab in adults with moderate-to-severe atopic dermatitis inadequately controlled by topical treatments: a randomized, placebo-controlled, dose-ranging phase 2b trial (Thaçi et al., 2016)

The published literature on Dupixent for AD also includes a phase II RCT (NCT01859988) that evaluated 5 Dupixent regimens (Thaçi et al., 2016). Post hoc reports on outcomes in patients enrolled in this trial are published separately (Simpson et al., 2016a; Simpson et al., 2016b). In addition, a collection of 4 small, short-term, phase I and II RCTs are published in a single report (Beck et al., 2014). Also published is a report on the molecular signature in the skin of patients enrolled in 2 of these 4 trials (Hamilton et al., 2014).

HAYES

At the time of this writing in April 2017, a Hayes assessment addressing the management of atopic dermatitis with dupilumab (Dupixent) is not available; however a ‘Prognosis Overview’ is available.
Guidelines of Care for the Management of Atopic Dermatitis (Eichenfield LF, et al. 2014)

NOTE: These guidelines were developed prior to the availability of dupilumab.

Atopic dermatitis manifests as erythema, edema, xerosis, erosions and excoriations, oozing and crusting, and lichenification, and may require a multifaceted treatment approach. Topical agents are the mainstay of therapy.

Non-pharmacologic options include moisturizers, bathing practices, and wet wrap therapy. Anti-inflammatory pharmacologic therapies include topical corticosteroids and topical calcineurin inhibitors.

- **Topical corticosteroids** are first-line anti-inflammatory therapy, typically started when skin lesions are not adequately controlled with good skin care and regular use of moisturizers. They are available in a variety of preparations and potencies and are used for treatment and prevention. Low-potency preparations are generally used for maintenance therapy, while higher-potency preparations are reserved for acute episodes. Recommended application frequency is twice daily; however, once-daily or less frequent administration of some topical corticosteroids may be sufficient in some cases (e.g., maintenance therapy). In addition to adrenal function suppression, cutaneous adverse effects, especially skin atrophy, is a concern with prolonged use of topical corticosteroids; these adverse effects tend to be reduced with mid-potency topical corticosteroid agents and less frequent application (e.g., twice weekly).

- **Topical calcineurin inhibitors** (tacrolimus and pimecrolimus) are approved as second-line anti-inflammatory therapy for atopic dermatitis. They can be used for short-term and non-continuous long-term treatment in immunocompetent individuals who did not respond to other topical prescription therapies. Topical calcineurin inhibitors are not associated with skin atrophy and can be used at sensitive skin sites (e.g., face and skin folds). Similar to topical corticosteroids, topical calcineurin inhibitors offer optimal benefit when applied twice daily, or 2 to 3 times weekly for proactive maintenance therapy. Package labeling advises against use of topical calcineurin inhibitors during acute infections. Although adverse effects are relatively mild (e.g., local stinging and burning), rare cases of skin cancer and lymphoma have been reported. Topical calcineurin inhibitors are typically used as steroid-sparing agents and to prevent relapse after treatment of an acute flare with topical corticosteroids; however, they may be used concomitantly as well.

- **Atopic dermatitis skin lesions** are associated with increased risk of infections, which may require additional antimicrobial or antiseptic treatment.


European guidelines recommend skin care and emollients, bathing techniques, and avoidance of triggers or allergens as initial treatment, especially for mild atopic dermatitis.

- **Topical anti-inflammatory therapies** may be used concurrently with emollients. Topical corticosteroids are first-line and topical calcineurin inhibitors are second-line anti-inflammatory therapy. Co-administration of topical corticosteroids and topical calcineurin inhibitors has not been shown to provide additional benefit. Because topical calcineurin inhibitors are not associated with skin atrophy, they may be favored over topical corticosteroids for use in delicate areas such as the eyelid, perioral skin, genital area, and skin folds, as well as for use in long-term management. Patients using topical calcineurin inhibitors must use proper UV protection (e.g., sunscreen). Additional treatments, specifically for pruritus, addressed by the guidelines include interferon gamma, narrowband UV-B therapy, topical anesthetics, topical cannabinoid receptor agonists, capsaicin, topical doxepin, topical mast cell stabilizers, leukotriene receptor antagonists, and opioid receptor antagonists. However, evidence to support some of these therapies is limited or lacking.
Guidelines of Care for the Management of Atopic Dermatitis

The AAD issued guidelines for the treatment of atopic dermatitis in 2014, updating and expanding their previous guidelines, published in 2004. The guidelines were developed by a working group of recognized atopic dermatitis experts using an evidence-based approach.

The guidelines recommend both non-pharmacologic interventions as well as a range of pharmacological treatment options. The guidelines also discuss the use of systemic agents and the use of phototherapy to treat atopic dermatitis.

Non-pharmacological treatments recommended include the application of moisturizers as a method to reduce the severity of atopic dermatitis and reduce the need for pharmacological treatments. Bathing, with the limited use of non-soap cleansers, followed by moisturizers, is also recommended. For patients with moderate-to-severe atopic dermatitis, use of wet-wraps, used in conjunction with topical corticosteroids at times, was also recommended during flares.

Pharmacological topical treatments recommended include topical corticosteroids and topical immunotherapies (calcineurin inhibitors).

- Topical corticosteroids are recommended for those individuals for whom non-pharmacological interventions have not been successful in controlling symptoms. Topical corticosteroids are recommended as both active treatment and maintenance therapy to prevent relapses.

- Topical calcineurin inhibitors are recommended for patients with atopic dermatitis as a second-line therapy where topical corticosteroids have failed to control symptoms, or when corticosteroids are not an appropriate treatment choice, for example on sensitive areas like the face or genitals.

- Other topical treatments discussed include topical antimicrobials and antiseptics, which are not routinely recommended and topical antihistamines, which are not recommended in any instance.

- Phototherapy is recommended as a second-line treatment, to be used after the failure of topical first-line therapies, such as emollients and topical corticosteroids and calcineurin inhibitors. For those patients with chronic disease, phototherapy is recommended as maintenance therapy.

- Systemic therapies are recommended for those patients with moderate-to-severe atopic dermatitis, particularly those where topical regimens and phototherapy are not adequately controlling the disease or when quality of life is affected. The guidelines identify cyclosporine, methotrexate, mycophenolate mofetil, and azathioprine as the more common and effective systemic options. The guidelines also discourage the use of systemic corticosteroids due to the short- and long-term adverse effects.
DEFINITIONS

N/A

APPENDIX

Appendix 1: Disease Severity Scales

There is no “gold standard” tool for measuring AD severity and though there is no accepted standardized method of classifying disease severity, categorization is usually based upon objective disease features, extent of skin involvement and possibly subjective disease features. Due to the impaired skin integrity, affected individuals are more susceptible to skin infections. The following are some commonly used severity scales:

**Investigator’s Global Assessment (IGA):** An Investigator Global Assessment (IGA) is often used as a standard benchmark comparator tool for other scales. This clinician-reported outcome measure determines severity of atopic dermatitis. The most common versions used in the trials reviewed were static scales (they did not assess changes in severity with treatment; abbreviated in the key crisaborole trials as “ISGA”) and used either a 5-point scale ranging from 0 (clear) to 4 (severe) or a 6-point scale ranging from 0 (clear) to 5 (very severe).

- 0 Clear (no inflammatory signs of AD)
- 1 Almost clear (just perceptible erythema, and just perceptible papulation/infiltration)
- 2 Mild disease (mild erythema, and mild papulation/infiltration)
- 3 Moderate disease (moderate erythema, and moderate papulation/infiltration)
- 4 Severe disease (severe erythema, and severe papulation/infiltration)
- 5 Very severe disease (severe erythema, and severe papulation/infiltration with oozing/crusting)

**Eczema Area Severity Index score (EASI):** The EASI evaluates four anatomical regions for extent and severity of disease signs by: erythema, induration/papulation/edema, excoriations, and lichenification, which are graded systematically for each anatomical region and assembled in a composite score. 

*Link to calculate the eczema area and severity index to determine atopic dermatitis severity: [https://www.easiscore.com/](https://www.easiscore.com/)

- EASI 50: a percentage improvement of EASI score from baseline that is ≥ 50%
- EASI 75: a percentage improvement of EASI score from baseline that is ≥ 75%
- EASI 90: a percentage improvement of EASI score from baseline that is ≥ 90%

**Global Individual Signs Score (GISS):** Individual components of the atopic dermatitis lesions are rated globally (for the whole body, not by anatomical region) on a 4-point scale (0 [none] to 3 [severe]) using the EASI severity grading criteria. The cumulative score, which ranges from 0 to 12, is the sum of the four components.

**Dermatology Life Quality Index (DLQI):** A 10-item, validated questionnaire used in clinical practice and clinical trials to assess the impact of skin conditions on quality of life

**Hospital Anxiety and Depression Scale (HADS):** Likert scale used to detect states of anxiety and depression; anxiety and depression subscales each with 7 items.

**Scoring Atopic Dermatitis (SCORAD):** The extent and severity of atopic dermatitis over the body area and the severity of 6 specific symptoms (erythema, edema/papulation, excoriations, lichenification, oozing/crusts, and dryness) are assessed and scored by the investigator. Subjective assessment of itch and sleeplessness is scored by the patient. The SCORAD score is a combined score of body area affected, and investigator and patient symptom scoring, with a maximum of 103.

**Patient-Oriented Eczema Measure (POEM):** A validated questionnaire, examining seven items, used in clinical settings to assess time spent with symptoms and the impact of symptoms on sleep.
# APPENDIX 2: TOPICAL CORTICOSTEROID PREPARATIONS

Reference: Lexicomp Online, Lexicomp, Inc. All Rights Reserved; and Tadicherla S, Ross K, Shenefelt D, Topical corticosteroids in dermatology; Journal of Drugs in Dermatology 2009; 12:1093. [via UpToDate online subscription]  

<table>
<thead>
<tr>
<th>Potency group*</th>
<th>Corticosteroid</th>
<th>Vehicle type/form</th>
<th>Trade names (United States)</th>
<th>Available strength(s), percent (except as noted)</th>
<th>Generic available in United States†</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Super high potency (group 1)</strong></td>
<td>Betamethasone dipropionate, augmented</td>
<td>Ointment, optimized</td>
<td>Diprolene</td>
<td>0.05</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lotion</td>
<td>Diprolene</td>
<td>0.05</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Gel</td>
<td>Diprolene</td>
<td>0.05</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ointment</td>
<td>Temovate</td>
<td>0.05</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cream</td>
<td>Temovate</td>
<td>0.05</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Clobetasol propionate</td>
<td>Cream, emollient base</td>
<td>Temovate E</td>
<td>0.05</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Gel</td>
<td>Temovate</td>
<td>0.05</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lotion</td>
<td>Clobex</td>
<td>0.05</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>Diflucortolone valerate (not available in United States)</td>
<td>Ointment, oily cream</td>
<td>Nerusone Forte (United Kingdom, others)</td>
<td>0.3</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>Fluocinonide</td>
<td>Cream</td>
<td>Vanos</td>
<td>0.1</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>Flurandrenolide</td>
<td>Tape (roll)</td>
<td>Cordran</td>
<td>4 mcg/cm²</td>
<td>No</td>
</tr>
<tr>
<td><strong>High potency (group 2)</strong></td>
<td>Amcinonide</td>
<td>Ointment</td>
<td>Cyclocort®&lt;sup&gt;A&lt;/sup&gt;, Amcort®&lt;sup&gt;A&lt;/sup&gt;</td>
<td>0.1</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Betamethasone dipropionate</td>
<td>Ointment</td>
<td>Diprosone</td>
<td>0.05</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Desoximetasone</td>
<td>Ointment</td>
<td>Topicort</td>
<td>0.25</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cream</td>
<td>Topicort</td>
<td>0.25</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Gel</td>
<td>Topicort</td>
<td>0.05</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Diflorasone diacetate</td>
<td>Ointment</td>
<td>ApexiCon®&lt;sup&gt;Δ&lt;/sup&gt;, Florone®&lt;sup&gt;Δ&lt;/sup&gt;</td>
<td>0.05</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Cream, emollient base</td>
<td>Ointment</td>
<td>ApexiCon E</td>
<td>0.05</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ointment</td>
<td>Lidex®&lt;sup&gt;A&lt;/sup&gt;</td>
<td>0.05</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Gel</td>
<td>Lidex®&lt;sup&gt;A&lt;/sup&gt;</td>
<td>0.05</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cream anhydrous</td>
<td>Lidex®&lt;sup&gt;A&lt;/sup&gt;</td>
<td>0.05</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Solution</td>
<td>Lidex®&lt;sup&gt;A&lt;/sup&gt;</td>
<td>0.05</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ointment</td>
<td>Halog</td>
<td>0.1</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cream</td>
<td>Halog</td>
<td>0.1</td>
<td>No</td>
</tr>
<tr>
<td><strong>High potency (group 3)</strong></td>
<td>Amcinonide</td>
<td>Cream</td>
<td>Cyclocort®&lt;sup&gt;A&lt;/sup&gt;, Amcort®&lt;sup&gt;A&lt;/sup&gt;</td>
<td>0.1</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lotion</td>
<td>Amcort®&lt;sup&gt;A&lt;/sup&gt;</td>
<td>0.1</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cream,</td>
<td>Diprosone</td>
<td>0.05</td>
<td>Yes</td>
</tr>
<tr>
<td>Steroid</td>
<td>Medium potency (group 4)</td>
<td>Lower mid potency (group 5)</td>
<td>Low potency (group 6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>---------</td>
<td>-------------------------</td>
<td>---------------------------</td>
<td>---------------------</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Betamethasone valerate</td>
<td>Cream, oily cream, ointment</td>
<td>Cream</td>
<td>Ointment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dipropionate</td>
<td>Ointment</td>
<td>Betamethasone dipropionate</td>
<td>DesOwen, 0.05 Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Betamethasone</td>
<td>Ointment</td>
<td>Fluticasone propionate</td>
<td>0.05 Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Desoximetasone</td>
<td>Cream</td>
<td>Mometasone furoate</td>
<td>0.1 Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diflorasone diacetate</td>
<td>Cream</td>
<td>Triamcinolone acetonide</td>
<td>0.1 Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diflucortolone valerate (not available in United States)</td>
<td>Cream, oily cream, ointment</td>
<td>Hydrocortisone butyrate</td>
<td>0.1 Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluocinonide</td>
<td>Cream aqueous emollient</td>
<td>Hydrocortisone probutate</td>
<td>0.1 Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluticasone propionate</td>
<td>Ointment</td>
<td>Hydrocortisone valerate</td>
<td>0.1 Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mometasone furoate</td>
<td>Ointment</td>
<td>Prednicarbate</td>
<td>0.1 Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Triamcinolone acetonide</td>
<td>Cream</td>
<td>Triamcinolone acetonide</td>
<td>0.1 Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medium potency (group 4)</td>
<td></td>
<td>Lower mid potency (group 5)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Betamethasone dipropionate</td>
<td>Spray</td>
<td>Betamethasone valerate</td>
<td>0.1 Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clocortolone pivalate</td>
<td>Cream</td>
<td>Desoximetasone</td>
<td>0.05 Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluocinolone acetonide</td>
<td>Ointment</td>
<td>Diflucortolone valerate (not available in United States)</td>
<td>0.05 Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Flurandrenolide</td>
<td>Ointment</td>
<td>Fluocinonide</td>
<td>0.05 No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hydrocortisone valerate</td>
<td>Cream</td>
<td>Fluticasone propionate</td>
<td>0.005 Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mometasone furoate</td>
<td>Ointment</td>
<td>Mometasone furoate</td>
<td>0.1 Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Triamcinolone acetonide</td>
<td>Cream</td>
<td>Ointment</td>
<td>0.1 Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medium potency (group 4)</td>
<td></td>
<td>Lower mid potency (group 5)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Betamethasone dipropionate</td>
<td>Spray</td>
<td>Betamethasone valerate</td>
<td>0.1 Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clocortolone pivalate</td>
<td>Cream</td>
<td>Desoximetasone</td>
<td>0.05 Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluocinolone acetonide</td>
<td>Ointment</td>
<td>Diflucortolone valerate (not available in United States)</td>
<td>0.05 Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Flurandrenolide</td>
<td>Ointment</td>
<td>Fluocinonide</td>
<td>0.05 No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hydrocortisone valerate</td>
<td>Cream</td>
<td>Fluticasone propionate</td>
<td>0.005 Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mometasone furoate</td>
<td>Ointment</td>
<td>Mometasone furoate</td>
<td>0.1 Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Triamcinolone acetonide</td>
<td>Cream</td>
<td>Ointment</td>
<td>0.1 Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medium potency (group 4)</td>
<td></td>
<td>Lower mid potency (group 5)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Betamethasone dipropionate</td>
<td>Spray</td>
<td>Betamethasone valerate</td>
<td>0.1 Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clocortolone pivalate</td>
<td>Cream</td>
<td>Desoximetasone</td>
<td>0.05 Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluocinolone acetonide</td>
<td>Ointment</td>
<td>Diflucortolone valerate (not available in United States)</td>
<td>0.05 Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Flurandrenolide</td>
<td>Ointment</td>
<td>Fluocinonide</td>
<td>0.05 No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hydrocortisone valerate</td>
<td>Cream</td>
<td>Fluticasone propionate</td>
<td>0.005 Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mometasone furoate</td>
<td>Ointment</td>
<td>Mometasone furoate</td>
<td>0.1 Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Triamcinolone acetonide</td>
<td>Cream</td>
<td>Ointment</td>
<td>0.1 Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medium potency (group 4)</td>
<td></td>
<td>Lower mid potency (group 5)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Betamethasone dipropionate</td>
<td>Spray</td>
<td>Betamethasone valerate</td>
<td>0.1 Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clocortolone pivalate</td>
<td>Cream</td>
<td>Desoximetasone</td>
<td>0.05 Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluocinolone acetonide</td>
<td>Ointment</td>
<td>Diflucortolone valerate (not available in United States)</td>
<td>0.05 Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Flurandrenolide</td>
<td>Ointment</td>
<td>Fluocinonide</td>
<td>0.05 No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hydrocortisone valerate</td>
<td>Cream</td>
<td>Fluticasone propionate</td>
<td>0.005 Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mometasone furoate</td>
<td>Ointment</td>
<td>Mometasone furoate</td>
<td>0.1 Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Triamcinolone acetonide</td>
<td>Cream</td>
<td>Ointment</td>
<td>0.1 Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medium potency (group 4)</td>
<td></td>
<td>Lower mid potency (group 5)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Betamethasone dipropionate</td>
<td>Spray</td>
<td>Betamethasone valerate</td>
<td>0.1 Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clocortolone pivalate</td>
<td>Cream</td>
<td>Desoximetasone</td>
<td>0.05 Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluocinolone acetonide</td>
<td>Ointment</td>
<td>Diflucortolone valerate (not available in United States)</td>
<td>0.05 Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Flurandrenolide</td>
<td>Ointment</td>
<td>Fluocinonide</td>
<td>0.05 No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hydrocortisone valerate</td>
<td>Cream</td>
<td>Fluticasone propionate</td>
<td>0.005 Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mometasone furoate</td>
<td>Ointment</td>
<td>Mometasone furoate</td>
<td>0.1 Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Triamcinolone acetonide</td>
<td>Cream</td>
<td>Ointment</td>
<td>0.1 Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Least potent (group 7)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>--------------------------------------------------------------------------------------</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluocinolone acetonide</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lotion</td>
<td>Tridesilon&lt;sup&gt;Δ&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Foam</td>
<td>DesOwen, LoKara</td>
<td>0.05</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cream</td>
<td>Verdeso</td>
<td>0.05</td>
<td>No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Solution</td>
<td>Synalar&lt;sup&gt;Δ&lt;/sup&gt;</td>
<td>0.01</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shampoo</td>
<td>Capex</td>
<td>0.01</td>
<td>No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oil (scalp)&lt;sup&gt;◊&lt;/sup&gt;</td>
<td>Derma-Smoother/FS</td>
<td>0.01</td>
<td>No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oil (body)&lt;sup&gt;◊&lt;/sup&gt;</td>
<td>Derma-Smoother/FS</td>
<td>0.01</td>
<td>No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Triamcinolone acetonide</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cream</td>
<td>Kenalog&lt;sup&gt;Δ&lt;/sup&gt;, Aristocort&lt;sup&gt;Δ&lt;/sup&gt;</td>
<td>0.025</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lotion</td>
<td>Kenalog&lt;sup&gt;Δ&lt;/sup&gt;</td>
<td>0.025</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hydrocortisone (base, ≥2%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ointment</td>
<td>Hytone</td>
<td>2.5</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cream</td>
<td>Hytone, Nutracort&lt;sup&gt;Δ&lt;/sup&gt;</td>
<td>2.5</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lotion</td>
<td>Hytone, Ala Scalp, Scalacort</td>
<td>2.5 or 2</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Solution</td>
<td>Texacort</td>
<td>2.5</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hydrocortisone (base, &lt;2%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ointment</td>
<td>Coptraid, Hytone, Nutracort</td>
<td>1</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cream</td>
<td>Coptraid, Hytone, Synacort</td>
<td>1</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lotion</td>
<td>Aquaniel HC, Sarnol-HC, Cortizone 10</td>
<td>1</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spray</td>
<td>Coptraid</td>
<td>1</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Solution</td>
<td>Coptraid, Noble, Scalp relief</td>
<td>1</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ointment</td>
<td>Coptraid</td>
<td>0.5</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cream</td>
<td>Coptraid</td>
<td>0.5</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hydrocortisone acetate with pramoxine 1% combination</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ointment</td>
<td>Pramosone</td>
<td>1 or 2.5</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cream</td>
<td>Pramosone, Analpram-HC</td>
<td>1 or 2.5</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lotion</td>
<td>Pramosone, Analpram-HC</td>
<td>1 or 2.5</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aerosol foam</td>
<td>Epifoam</td>
<td>1</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Listed by potency according to the US classification system: group 1 is the most potent, group 7 is the least potent. Other countries use a different classification system with only four or five groups.

† Vehicle and base ingredient(s) for generic products, in some cases, may not be identical to trade version.

Δ Inactive United States trade name for specific product; brand may be available outside United States.

◊ 48% refined peanut oil.
### CODING INFORMATION

The codes listed in this clinical policy are for informational purposes only. Listing of a service or device code in this policy does not imply that the service described by this code is a covered or non-covered. Coverage is determined by the benefit document. This list of codes may not be all inclusive and inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

<table>
<thead>
<tr>
<th>CPT</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>NA</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HCPCS</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>J3490</td>
<td>Unclassified drugs [when specified as dupilumab (Dupixent)]</td>
</tr>
<tr>
<td>J3590</td>
<td>Unclassified biologics [when specified as dupilumab (Dupixent)]</td>
</tr>
</tbody>
</table>

### REFERENCES

**Package Insert, FDA, Drug Compendia**


Clinical Trials, Definitions, Peer-Reviewed Publications


Government Agencies, Professional Societies, and Other Authoritative Publications


C. Ring J, Alomar A, Bieber T, et al; European Dermatology Forum (EDF); European Academy of Dermatology and Venereology (EADV); European Federation of Allergy (EFA); European Task Force on Atopic Dermatitis (ETFAD); European Society of Pediatric Dermatology (ESPD); Global Allergy and Asthma European Network (GA2LEN). Guidelines for the treatment of atopic eczema (atopic dermatitis) part 1. J Eur Acad Dermatol Venereol. 2012;26(8):1045-1060.[PubMed 22805051]