**Dupilumab (Dupixent®) Abbreviated New Drug Update (ANDU)**

April 2017

**OVERVIEW**

- **Indications**
  - Dupilumab (Dupixent) is an interleukin-4 receptor (IL-4) \(\alpha\)-antagonist indicated for the treatment of adult patients with moderate to severe atopic dermatitis (AD) whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable. Dupixent can be used with or without topical corticosteroids.

- **Contraindications/Warnings**
  - Contraindicated in patients with known hypersensitivity to dupilumab or any of its excipients.
  - Warnings include the risk of hypersensitivity reactions (e.g., generalized urticaria, serum sickness) and conjunctivitis and keratitis. Also, efficacy and safety have not been established in patients with comorbid asthma or parasitic (helminth) infections.

- **Adverse Reactions**
  - The most common adverse reactions (incidence ≥ 1%) reported in clinical trials were injection site reactions, conjunctivitis, blepharitis, keratitis, eye pruritus, dry eye, and oral and other herpes simplex virus infections.
  - As a therapeutic protein, dupilumab can cause immunogenicity. Approximately 7% of patients treated with dupilumab in clinical trials developed antibodies for dupilumab, and approximately 14% to 30% of these were considered neutralizing antibodies (lower incidence with concurrent topical corticosteroids).

- **Drug Interactions**
  - Live vaccines should be avoided in patients undergoing treatment with dupilumab.
  - Dupilumab can modulate the formation of CYP450 enzymes. Therefore, in patients receiving concomitant drugs that are CYP450 substrates, particularly those with a narrow therapeutic window (e.g., warfarin, cyclosporine), consider monitoring for effect or drug concentration and modify the dose as clinically appropriate.

- **Special Populations**
  - There are no available data on dupilumab use in pregnant women to inform any drug associated risk. As human IgG antibodies can cross the placenta, dupilumab may be transmitted from the mother to the fetus.
  - The safety and effectiveness of dupilumab in pediatric patients have not been established. In patients ages ≥ 65 years, no differences in safety or efficacy were observed in clinical trials.
  - There are no data available on the effect of hepatic or renal impairment on the pharmacokinetics of dupilumab.
• **Availability and Dosage**

- Available as a 300 mg/2 mL single-dose pre-filled syringe for subcutaneous (SC) injection with needle shield.
- Initial dose: 600 mg (given as two 300 mg injections at different injection sites)
  - Dose can be injected subcutaneously into the thigh or abdomen, except for the 2 inches (5 cm) around the navel. The upper arm can also be used if a caregiver administers the injection.
- Maintenance dose: 300 mg given every other week
- Missed doses: administer the injection within 7 days from the missed dose and then resume the original schedule. If > 7 days have elapsed since the missed dose, patient must wait until the next dose as originally scheduled.

• **Clinical Trials**

- Three randomized, double-blind, placebo-controlled trials SOLO 1, SOLO 2, and Trial 3 enrolled a total of 2119 subjects 18 years of age and older whose moderate-to-severe AD was not adequately controlled by 1 or more topical medications. Disease severity was defined by Investigator’s Global Assessment (IGA) score of ≥ 3 in the overall assessment of AD lesions (scale, 0 to 4), an Eczema Area andSeverity Index (EASI) score ≥ 16 (scale, 0 to 72), and a minimum body surface area (BSA) involvement of ≥ 10%. In all three trials, subjects in the dupilumab group received subcutaneous injections of 600 mg at week 0, followed by 300 mg every other week (Q2W). In the monotherapy trials (SOLO 1 and 2), subjects received either dupilumab or placebo for 16 weeks. In the concomitant therapy trial (Trial 3), subjects received dupilumab or placebo with concomitant topical corticosteroids (TCS) and as needed topical calcineurin inhibitors for problem areas only, such as the face, neck, intertriginous and genital areas for 52 weeks.
- Primary endpoint: The primary endpoint was the 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 endpoints included the proportion of subjects with EASI-75 (improvement of at least 75% in EASI score from baseline), and reduction in itch as defined by at least a 4-point improvement in the peak pruritus Numeric Rating Scale (NRS; scale, 0 to 10) from baseline to week 16.
- Baseline characteristics: At enrollment, 59% of subjects were male, 67% were white, 52% of subjects had a baseline IGA score of 3 (moderate AD), and 48% of subjects had a baseline IGA of 4 (severe AD). The baseline mean EASI score was 33 and the baseline weekly averaged peak pruritus NRS was 7.
- Results: In SOLO 1, the primary outcome occurred 38% of patients who received dupilumab every other week compared with 10% who received placebo (p<0.001). In SOLO 2, the primary outcome occurred in 36% of patients who received dupilumab every other week as compared with 8% who received placebo (p<0.001). In addition, in the 2 SOLO trials, an improvement from baseline to week 16 of at least 75% on the EASI was reported in significantly more patients who received each regimen of dupilumab compared to patients who received placebo (p<0.001).
- In Trial 3, the primary endpoint occurred in 39% of patients receiving dupilumab compared to 12% of patients receiving placebo (p-value not available). In addition, an improvement
from baseline to 16 weeks of ≥ 75% on the EASI was also higher in patients receiving dupilumab compared to placebo (69% versus 23%, respectively; p-value not available).

- Clinical Considerations
  - Atopic dermatitis (AD) is a chronic, non-contagious, inflammatory disease of the skin resulting from a combination of genetic and environmental factors affecting approximately 17.8 million Americans and accounting for 10% to 20% of dermatologist visits.³
  - Other immunomodulators approved for the treatment of atopic dermatitis include crisaborole (Eucrisa®), a topical phosphodiesterase-4 inhibitor, and the topical calcineurin inhibitors pimecrolimus (Elidel®) and tacrolimus (Protopic®). Topical corticosteroids are often considered as standard or care for atopic dermatitis, but their use is limited by adverse effects. Other products, such as various emollients, are also routinely involved in therapy to assist in hydration and maintenance of the skin barrier. Nonpharmacologic therapy, such as phototherapy, may be a treatment option for select patients.
    - Treatment guidelines have not addressed newer agents within this class.
    - Newer agents within this class have not been addressed in clinical guidelines.
    - The 2012 American Academy of Allergy, Asthma, and Immunology (AAAAI) guidelines state that topical calcineurin inhibitors are reasonable treatment options for patients as first-line treatment choices, in addition to hydration (emollients) and topical corticosteroids.⁴
    - The 2014 American Academy of Dermatology (AAD) guidelines from 2014 state that emollients, topical corticosteroids, and topical calcineurin inhibitors are the standard of care for the treatment of AD.⁵

- Dupilumab provides another treatment option for patients with moderate to severe atopic dermatitis, and may be used with or without topical corticosteroids.

### Suggested Utilization Management

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<tr>
<th>Anticipated Therapeutic Class Review (TCR) Placement</th>
<th>Immunomodulators, Atopic Dermatitis</th>
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<tbody>
<tr>
<td>Clinical Edit</td>
<td>Prior authorization will be required if product is determined to be non-preferred.</td>
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<tr>
<td><strong>Initial Criteria:</strong> Patient must:</td>
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<tr>
<td>- Be ≥ 18 years of age; <strong>AND</strong></td>
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<td>- Have a diagnosis of moderate to severe atopic dermatitis with ≥ 1 of the following:</td>
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<td>- Involvement of at least 10% of body surface area (BSA); <strong>OR</strong></td>
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<td>- Scoring Atopic Dermatitis (SCORAD) score of 20 or more; <strong>OR</strong></td>
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<td>- Investigator’s Global Assessment (IGA) with a score ≥ 3; <strong>OR</strong></td>
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<tr>
<td>- Eczema Area and Severity Index (EASI) score of ≥ 16; <strong>OR</strong></td>
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- Incapacitation due to AD lesion location (e.g., head and neck, palms, soles, or genitalia); **AND**
  - Have a prior documented trial and failure (or contraindication) of 1 topical corticosteroids of medium to high potency (e.g., mometasone, fluocinolone) and 1 topical calcineurin inhibitors (tacrolimus or pimecrolimus); **AND**
  - Not have responded adequately (or contraindication) to a 3 month minimum trial of at least 1 immunosuppressive systemic agent (e.g., cyclosporine, azathioprine, methotrexate, mycophenolate mofetil, etc.); **AND**
  - Not have responded adequately (or is not a candidate) to a 3 month minimum trial of phototherapy (e.g., psoralens with UVA light [PUVA], UVB, etc) provided patient has reasonable access to photo treatment; **AND**
  - Is not pregnant; **AND**
  - Is not concurrently receiving a live vaccine

**Renewal Criteria:** Patient must:
- Continue to meet above criteria; **AND**
- Not have documented toxicity from the agent (e.g., hypersensitivity, conjunctivitis, keratitis, immunogenicity); **AND**
- Documented response compared to baseline as measured by measures used to qualify moderate to severe AD at baseline (e.g., pruritus, BSA involvement, EASI, IGA, SCORAD).

**Quantity Limit**
- 2 prefilled syringes for the initial dose, then 1 single-dose syringe every 14 days

**Duration of Approval**
- 6 months

**REFERENCES**

1 Dupixent [package insert]. Tarrytown, NY; Regeneron; March 2017.