BlueCross BlueShield of Arizona
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**PHARMACY COVERAGE GUIDELINES**
**SECTION: DRUGS**

**ORIGINAL EFFECTIVE DATE: 4/1/19**
**LAST REVIEW DATE: 2/21/19**
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**ARCHIVE DATE:**

# DUPIXENT® (dupilumab) subcutaneous injection

**Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Pharmacy Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.**

**This Pharmacy Coverage Guideline provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.**

**The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.**

**The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.**

**State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.**

**Pharmacy Coverage Guidelines are subject to change as new information becomes available.**

**For purposes of this Pharmacy Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.**



This Pharmacy Coverage Guideline does not apply to FEP or other states' Blues Plans.

Information about medications that require precertification is available at www.azblue.com/pharmacy.

Some large (100+) benefit plan groups may customize certain benefits, including adding or deleting precertification requirements.

All applicable benefit plan provisions apply, e.g., waiting periods, limitations, exclusions, waivers and benefit maximums.

Precertification for medication(s) or product(s) indicated in this guideline requires completion of the request form in its entirety with the chart notes as documentation. All requested data must be provided. Once completed the form must be signed by the prescribing provider and faxed back to BCBSAZ Pharmacy Management at (602) 864-3126 or emailed to Pharmacyprecert@azblue.com. **Incomplete forms or forms without the chart notes will be returned.**

## DUPIXENT® (dupilumab) subcutaneous injection (cont.)

**Criteria:**

- **Criteria for initial therapy:** Dupixent (dupilumab) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Prescriber is a physician specializing in or is in consultation with an Allergist, Immunologist, Pulmonologist, or Dermatologist

  2. A confirmed diagnosis of **ONE** of the following
     - Individual 18 years of age or older with moderate-to-severe atopic dermatitis involving at least 10% of BSA or lesions that have moderate to severe features involving areas of the face, head, neck, hands, feet, groin, or intertriginous areas

     - Individual is 12 years of age or older with moderate-to-severe asthma, with uncontrolled symptoms, with an eosinophilic phenotype or corticosteroid dependent asthma to be used as add-on maintenance treatment

  3. Individual has failed, or is intolerant to, or has a contraindication such that the individual is unable to use **ONE** the following:
     - **For moderate-to-severe atopic dermatitis**:
       - At least a 2 month trial of **each** of the following: medium to very high potency corticosteroid **AND** a calcineurin inhibitor **AND** a phosphodiesterase 4 inhibitor

     - **For moderate-to-severe asthma, with uncontrolled symptoms:**
       - At least a 3 month trial of maximally-dosed inhaled corticosteroids **AND** long-acting inhaled beta-agonists **AND** another asthma controlling medication (such as LTRA, LAMA, or theophylline) with or without daily oral corticosteroid

  4. **ALL** of the following baseline tests have been completed before initiation of treatment with continued monitoring as clinically appropriate:
     - **For moderate-to severe eosinophilic asthma**: Blood eosinophil count is $\geq$ 300 cells/microliter

  5. There is no concurrent use with Cinqair (reslizumab), Fasenra (benralizumab), Nucala (mepolizumab), Xolair (omalizumab), or any other biologic therapy [e.g., Rituxan (rituximab), Remicade/Inflectra (infliximab), Enbrel (etanercept)]

  6. Dupixent is not being used concurrently with live vaccines

  **Initial approval duration**: 4 months

- **Criteria for continuation of coverage (renewal request):** Dupixent (dupilumab) is considered ***medically necessary*** and will be approved when **ALL** of the following criteria are met:

  1. Prescriber is a physician specializing in or is in consultation with an Allergist, Immunologist, Pulmonologist, or Dermatologist

## DUPIXENT® (dupilumab) subcutaneous injection (cont.)

2. Individual's condition responded or has worsened while on therapy [this can be modified or changed depending on drug or condition]
    - Response is defined as:
        - **For atopic dermatitis**, achieved and maintains **BOTH** of the following:
            - 20% reduction in percent BSA involved over baseline
            - Reduction in severity of pruritus, cracking, and if initially present, oozing/bleeding of affected skin
        - **For asthma**, achieved and maintains **TWO** of the following:
            - Decreased incidence of asthma exacerbation
            - Decreased need for use of rescue medications
            - Decrease need for systemic corticosteroids
            - Decrease in hospitalizations/emergency room visits
            - Improvement in FEV1 from baseline
        - No evidence of disease progression

3. Individual has been adherent with the medication

4. Dupixent is not being used concurrently with live vaccines

5. There is no concurrent use with Cinqair (reslizumab), Fasenra (benralizumab), Nucala (mepolizumab), Xolair (omalizumab), or any other biologic therapy for atopic dermatitis [e.g., Rituxan (rituximab), Remicade/Inflectra (infliximab), Enbrel (etanercept)]

6. Individual has not developed any significant level 4 adverse drug effects that may exclude continued use
    - Significant adverse effect such as:
        - Hypersensitivity reaction to Dupixent or other ingredients of the product
        - Severe/serious systemic eosinophilia, eosinophilic pneumonia, or eosinophilic granulomatosis with polyangiitis

**Renewal duration**: 12 months

- Dupixent (dupilumab) for all other indications not previously listed or if above criteria not met is considered ***experimental or investigational*** based upon:

1. Lack of final approval from the Food and Drug Administration, and
2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
3. Insufficient evidence to support improvement of the net health outcome, and
4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives, and
5. Insufficient evidence to support improvement outside the investigational setting.

These indications include, *but are not limited to:*
- Treatment with dosing or frequency outside the FDA-approved dosing and frequency

## DUPIXENT® (dupilumab) subcutaneous injection (cont.)

**Description:**

Dupixent (dupilumab) is a monoclonal antibody used for the treatment of adults with moderate-to-severe atopic dermatitis not adequately controlled with topical prescription therapies or when those therapies are not advisable. It can be used with or without topical corticosteroids. Dupixent (dupilumab) is also indicated for add-on maintenance treatment of moderate-to-severe asthma with an eosinophilic phenotype or with corticosteroid dependent asthma in patients 12 years of age and older. Dupixent is not indicated for the relief of acute bronchospasm or status asthmaticus.

Treatment of atopic dermatitis initially involves use of topical prescription therapies such as corticosteroids, calcineurin inhibitors (tacrolimus ointment, pimecrolimus cream) and topical phosphodiesterase 4 (PDE-4) inhibitors (crisaborole ointment). Topical corticosteroids are considered the standard of care; strength and formulation of the preparation is selected based on severity, duration of treatment, location of exacerbation, and age of individual. Topical calcineurin and topical PDE-4 inhibitors should be reserved for problem areas only, such as the face, neck, intertriginous and genital areas.

Asthma is a complex disorder characterized by variable and recurring clinical symptoms, airflow obstruction, bronchial hyper-responsiveness, and underlying inflammation.

Inflammation is an important component in the pathogenesis of asthma. Multiple cell types (e.g., mast cells, eosinophils, neutrophils, macrophages, and lymphocytes) and mediators (e.g., histamine, eicosanoids, leukotrienes, and cytokines) are involved in inflammation.

Asthma can be divided into subtypes, which are associated with airway inflammation with eosinophils. It is estimated that about half of individuals with severe asthma exhibit the eosinophilic phenotype with elevated eosinophil levels (a marker of inflammation) in both the blood and airways. Activated eosinophils can increase airway smooth muscle contraction and mucous secretion. Interleukin-5 (IL-5) is an important cellular signal in eosinophilic inflammation.

About 10% of asthma patients have severe asthma that may be uncontrolled despite high doses of standard-of-care asthma controller medicines and can require the use of chronic oral corticosteroids (OCS). Severe, uncontrolled asthma is debilitating and potentially fatal with patients experiencing frequent exacerbations and significant limitations on lung function and quality of life.

Inhaled corticosteroids are the most effective long-term therapy for control and management of asthma. Asthma is said to be well controlled when asthma symptoms are twice a week or less; rescue bronchodilator medication use is twice a week or less; there is no nocturnal or early morning awaking due to asthma symptoms; there are no limitations of work, school, or exercise; and the Forced Expiratory Volume (FEV1) is normal or the patient's personal best. On the other hand, indicators of asthma that is not adequately controlled include limitation of normal activities, poor lung function with FEV1 of < 80% predicted, at least 2 episodes per year of asthma exacerbations requiring oral systemic corticosteroids. More frequent and intense exacerbations requiring urgent, unscheduled care, hospitalization, or ICU admission point toward worse disease control.

Dupilumab is a human monoclonal IgG4 antibody that inhibits interleukin-4 (IL-4) and interleukin-13 (IL-13) signaling by specifically binding to the interleukin-4 receptor alpha (IL-4Rα) subunit shared by the IL-4 and IL-13 receptor complexes. Dupilumab inhibits IL-4 signaling via the Type I receptor and both IL-4 and IL-13 signaling through the Type II receptor.

## DUPIXENT® (dupilumab) subcutaneous injection (cont.)

Inflammation is an important component in the pathogenesis of asthma and atopic dermatitis. Multiple cell types that express IL-4Rα (mast cells, eosinophils, macrophages, lymphocytes, epithelial cells, goblet cells) and inflammatory mediators (histamine, eicosanoids, leukotrienes, cytokines, chemokines) are involved in inflammation. Blocking IL-4Rα with dupilumab inhibits IL-4 and IL-13 cytokine-induced inflammatory responses, including the release of pro-inflammatory cytokines, chemokines, nitric oxide, and IgE; however, the mechanism of dupilumab action in asthma has not been definitively established.

**Definitions:**

**Adult:** Age 18 years and older

**Severe Asthma:** Asthma that does not respond to repeated courses of treatment with beta 2-agonist medications.

**Recurrent Exacerbations:** 2 or more acute exacerbations in a 12-month period

**Atopic Dermatitis Therapies:**

Topical corticosteroids (TCS):
- Low-potency corticosteroids are recommended for maintenance therapy
- Intermediate and high-potency corticosteroids should be used for the treatment of clinical exacerbation over short periods of time
- Ultra-high-potency corticosteroids should be used only for very short periods (1-2 weeks) and in non-facial non-skinfold areas.
- Do not use potent fluorinated corticosteroids on the face, eyelids, genitalia, and intertriginous areas or in young infants.

Topical calcineurin inhibitors (TCI):
- Tacrolimus ointment (Protopic and generics) is indicated as second-line therapy for moderate to severe atopic dermatitis
- Elidel (pimecrolimus) cream is indicated as second line therapy for mild to moderate atopic dermatitis

Topical phosphodiesterase 4 (PDE-4) inhibitor:
- Eucrisa (crisaborole) ointment is indicated for treatment of mild to moderate atopic dermatitis

## DUPIXENT® (dupilumab) subcutaneous injection (cont.)

**Relative Potency of Selected Topical Corticosteroid Products:**

| Product | Dosage form | Strength |
|---|---|---|
| ***Category I – Very high potency*** | | |
| Augmented betamethasone dipropionate | Gel, ointment | 0.05 |
| Clobetasol propionate | Ointment, gel, cream | 0.05 |
| Fluocinonide | Cream | 0.1 |
| Diflorasone diacetate | Ointment | 0.05 |
| Halobetasol propionate | Ointment, cream | 0.05 |
| ***Category II – High potency*** | | |
| Amcinonide | Ointment, cream, lotion | 0.1 |
| Augmented betamethasone dipropionate | Cream, lotion | 0.05 |
| Betamethasone dipropionate | Ointment, cream | 0.05 |
| Betamethasone valerate | Ointment | 0.1 |
| Desoximetasone | Ointment, cream | 0.25 |
| Desoximetasone | Gel | 0.05 |
| Diflorasone diacetate | Ointment (emollient base), cream | 0.05 |
| Fluocinonide | Ointment, gel, cream | 0.05 |
| Halcinonide | Ointment, cream | 0.1 |

**Asthma Control Classification:**

| | Classification of Asthma Control (12 years of age and older) | | |
|---|---|---|---|
| | Well Controlled | Not Well Controlled | Very Poorly Controlled |
| Symptoms | ≤ 2 days/week | ≥ 2 days/week | Throughout the day |
| Nighttime awakenings | ≤ 2 days/month | 1-3x/week | ≥ 4x/week |
| Interference with normal activities | None | Some limitation | Extremely limited |
| SABA use to control symptoms (not for EIB prevention | ≤ 2 days/week | > 2 days/week | Several times/day |
| FEV1 or peak flow | > 80% predicted or personal best | 60-80% predicted or personal best | < 60% predicted or personal best |
| Asthma Control Test | ≥ 20 | 16-19 | ≤ 15 |

**Asthma control test: a validated set of questions**

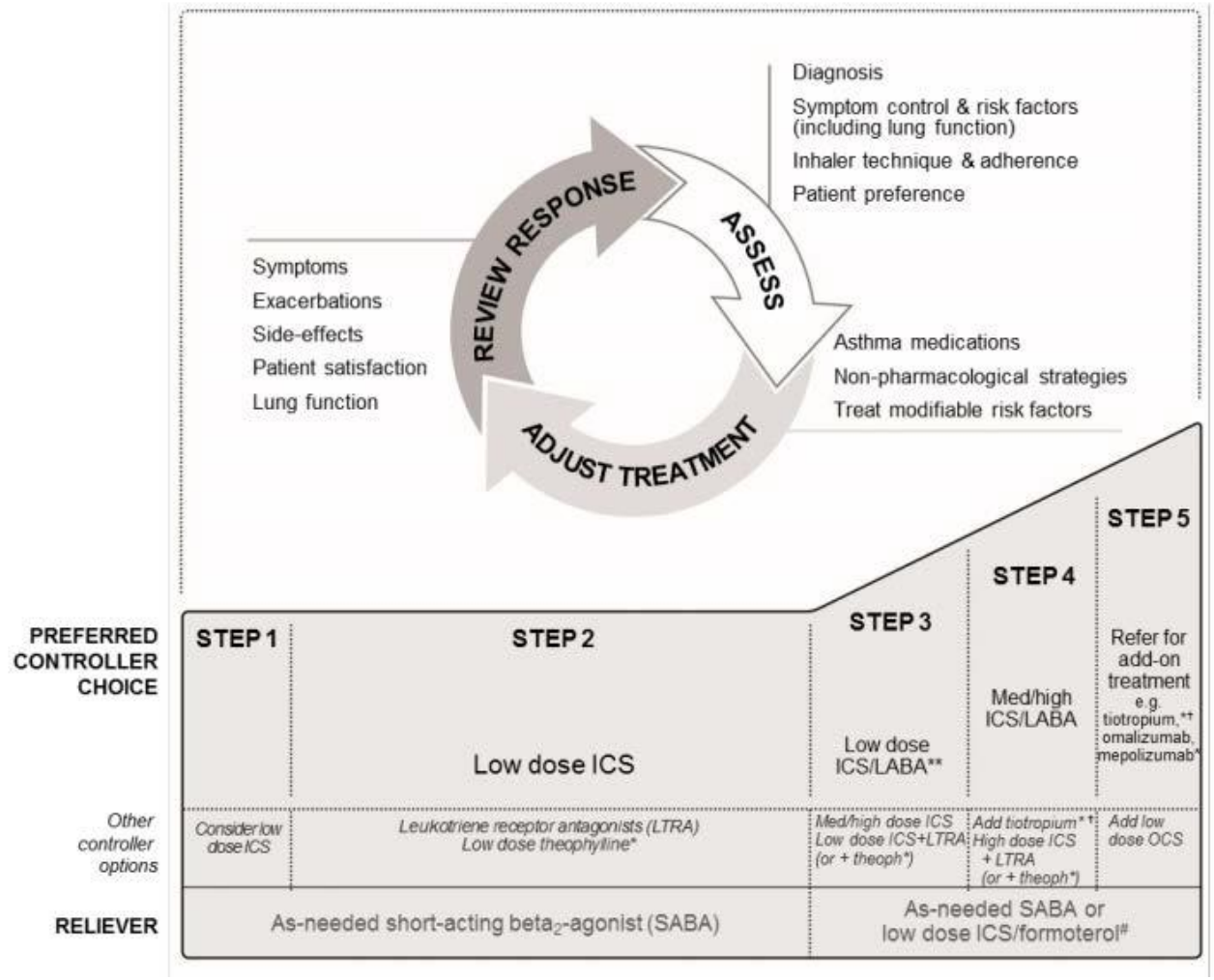
The Asthma Control Test provides a numerical score to help determine if your asthma symptoms are well controlled.
Step 1: Circle the number of each answer in the score box provided [ ].
Step 2: Add up each score in each box [ ] for the total.
Step 3: Take the completed test to your healthcare provider to talk about your score.

## DUPIXENT® (dupilumab) subcutaneous injection (cont.)

| Asthma Control Test | | | | |
|---|---|---|---|---|
| **1. In the past 4 weeks, how much of the time did your asthma keep you from getting as much done at work, school or at home?** | | | | |
| All of the time [1] | Most of the time [2] | Some of the time [3] | A little of the time [4] | None of the time [5] |
| **2. During the past 4 weeks, how often have you had shortness of breath?** | | | | |
| More than once a day [1] | Once a day [2] | 3 to 6 times a week [3] | Once or twice a week [4] | Not at all [5] |
| **3. During the past 4 weeks, how often did your asthma symptoms (wheezing, coughing, shortness of breath, chest tightness or pain) wake you up at night or earlier than usual in the morning?** | | | | |
| 4 or more nights a week [1] | 2 to 3 nights a week [2] | Once a week [3] | Once or twice [4] | Not at all [5] |
| **4. During the past 4 weeks, how often have you used your rescue inhaler or nebulizer medication (such as albuterol)?** | | | | |
| 3 or more times per day [1] | 1 to 2 times per day [2] | 2 or 3 times per week [3] | Once a week or less [4] | Not at all [5] |
| **5. How would you rate your asthma control during the past 4 weeks?** | | | | |
| Not Controlled at all [1] | Poorly controlled [2] | Somewhat controlled [3] | Well controlled [4] | Completely controlled [5] |
| | | | | |
| Total Score: _____ | | | | |
| Interpretation of Total Score:<br>Well controlled: $\geq$ 20<br>Not well controlled: 16-19<br>Very poorly controlled: $\leq$ 15 | | | | |

## DUPIXENT® (dupilumab) subcutaneous injection (cont.)

**2016 GINA Guidelines on Stepwise Approach to Treatment of Asthma**




**Resources:**

Dupixent (dupilumab) product information accessed 12-18-18 at DailyMed: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=595f437d-2729-40bb-9c62-c8ece1f82780

Boguniewicz M, Alexis AF, Beck LA, et al. Expert Perspectives on Management of Moderate-to-Severe Atopic Dermatitis: A Multidisciplinary Consensus Addressing Current and Emerging Therapies. J Allergy Clin Immunol Pract. Nov - Dec 2017; 5 (6):1519-1531

Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention, 2016. Accessed 01/24/2018. Available at www.ginasthma.org.

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**Fax completed prior authorization request form to 602-864-3126** or email to pharmacyprecert@azblue.com.
Call 866-325-1794 to check the status of a request.
All requested data must be provided. **Incomplete forms or forms without the chart notes will be returned.**
Pharmacy Coverage Guidelines are available at www.azblue.com/pharmacy.

# Pharmacy Prior Authorization Request Form

**Do not copy for future use. Forms are updated frequently.**
**REQUIRED: Office notes, labs, and medical testing relevant to the request that show medical justification are required.**

## Member Information

| Member Name (first & last): | Date of Birth: | Gender: | BCBSAZ ID#: |
|---|---|---|---|
| Address: | City: | State: | Zip Code: |

## Prescribing Provider Information

| Provider Name (first & last): | Specialty: | NPI#: | DEA#: |
|---|---|---|---|
| Office Address: | City: | State: | Zip Code: |
| Office Contact: | Office Phone: | Office Fax: | |

## Dispensing Pharmacy Information

| Pharmacy Name: | Pharmacy Phone: | Pharmacy Fax: |
|---|---|---|

## Requested Medication Information

| Medication Name: | Strength: | Dosage Form: |
|---|---|---|
| Directions for Use: | Quantity: / Refills: | Duration of Therapy/Use: |

☐ Check if requesting **brand** only ☐ Check if requesting **generic**

☐ Check if requesting continuation of therapy (prior authorization approved by BCBSAZ expired)

## Turn-Around Time For Review

☐ Standard ☐ Urgent. Sign here: _____ ☐ Exigent (requires prescriber to include a written statement)

## Clinical Information

1. **What is the diagnosis? Please specify below.**

   **ICD-10 Code:** _____ **Diagnosis Description:** _____

2. ☐ Yes ☐ No **Was this medication started on a recent hospital discharge or emergency room visit?**

3. ☐ Yes ☐ No **There is absence of ALL contraindications.**

4. **What medication(s) has the individual tried and failed for this diagnosis? Please specify below.**
Important note: Samples provided by the provider are not accepted as continuation of therapy or as an adequate trial and failure.

| Medication Name, Strength, Frequency | Dates started and stopped or Approximate Duration | Describe response, reason for failure, or allergy |
|---|---|---|
| | | |
| | | |
| | | |
| | | |
| | | |
| | | |

5. **Are there any supporting labs or test results? Please specify below.**

| Date | Test | Value |
|---|---|---|
| | | |
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# Pharmacy Prior Authorization Request Form

**6. Is there any additional information the prescribing provider feels is important to this review? Please specify below.**
For example, explain the negative impact on medical condition, safety issue, reason formulary agent is not suitable to a specific medical condition, expected adverse clinical outcome from use of formulary agent, or reason different dosage form or dose is needed.

**Signature affirms that information given on this form is true and accurate and reflects office notes**

Prescribing Provider's Signature: Date:

**Please note**: Some medications may require completion of a drug-specific request form.

**Incomplete forms or forms without the chart notes will be returned.**

Office notes, labs, and medical testing relevant to the request that show medical justification are required.