Interleukin-4 (IL-4) Inhibitor Prior Authorization with Quantity Limit Program Summary

POLICY REVIEW CYCLE

Effective Date **Date of Origin**
03-01-2024

FDA APPROVED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Dupixent® (dupilumab) Injection for subcutaneous use	Treatment of adult and pediatric patients aged 6 months and older 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. Add-on maintenance treatment of adult and pediatric patients aged 6 years and older with moderate-to-severe asthma characterized by an eosinophilic phenotype or with oral corticosteroid dependent asthma • Limitation of Use: Not indicated for the relief of acute bronchospasm or status asthmaticus Add-on maintenance treatment in adult patients with inadequately controlled chronic rhinosinusitis with nasal polyposis (CRSwNP) Treatment of adult and pediatric patients aged 12 years and older, weighing at least 40 kg, with eosinophilic esophagitis (EoE) Treatment of adult patients with prurigo nodularis (PN)		1

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Atopic Dermatitis	Atopic dermatitis (AD), also known as atopic eczema, is a chronic, pruritic inflammatory dermatosis affecting up to 25% of children and 1-5% of adults. AD follows a relapsing course and is associated with elevated serum immunoglobulin (IgE) levels and a personal or family history of type I allergies, allergic rhinitis, and/or asthma. Onset is most common between 3 and 6 months of age, with approximately 60% of patients developing the eruption in the first year of life and 90% by age 5. While the majority of affected individuals have resolution of disease by adulthood, 10 to 30% do not, and a smaller percentage first develop symptoms as adults. AD has a complex pathogenesis involving genetic, immunologic, and environmental factors, which lead to a dysfunctional skin barrier and dysregulation of the immune system. Clinical findings include erythema, edema, xerosis, erosions/excoriations, oozing and crusting, and lichenification. These clinical findings vary by patient age and chronicity of lesions. Pruritus is a hallmark of the condition that is responsible for much of the disease burden borne by patients and their families. Typical patterns include facial, neck and extensor involvement in infants and children; flexure involvement in any age group, with sparing of groin and axillary regions.(2)

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	Goals of treatment are to reduce symptoms (pruritus and dermatitis), prevent exacerbations, and minimize therapeutics risks.(13) Despite its relapsing and remitting nature, the majority of patients with AD can achieve clinical improvement and disease control with nonpharmacological interventions (e.g., emollient use), conventional topical therapies (including corticosteroids and calcineurin inhibitors) and environmental and occupational modifications, when necessary.(4,5,13) The American Academy of Dermatology (AAD) guidelines suggest application of moisturizers should be an integral part of the treatment of patients with AD as there is strong evidence that their use reduces disease severity and need for pharmacologic intervention. They are an important component of maintenance treatment and prevention of flares.(4) The AAD recommends topical corticosteroids (TCS) for patients who fail to respond to good skin care and regular use of emollients alone. Proactive, intermittent use (1-2 times weekly) of topical corticosteroids as maintenance therapy on areas that commonly flare is recommended to help prevent relapses and is more effective than use of emollients alone. Monitoring by physical exam for cutaneous side effects during long-term, potent steroid use is suggested. Proactive, once to twice weekly application of mid-potency TCS for up to 40 weeks has not demonstrated adverse events (e.g., purpura, telangiectasia, striae, focal hypertrichosis, acneiform/rosacea-like eruptions, skin atrophy) in clinical trials.(4) It is recommended that patients with acute flares use super high or high potency topical corticosteroids for one to two weeks, and then replace these with lower potency preparations until the lesions resolve.(14) AAD notes that mid- to higher potency topical corticosteroids are appropriate for short courses to gain rapid control of symptoms, but long-term management should use the least-potent corticosteroid that is effective.(4) In general, if AD is not responding after 2 weeks of treatment, evaluation to determine other treatment plans is indicated.(3,14) Topical calcineurin inhibitors (TCIs) (e.g., pimecrolimus, tacrolimus) are recommended by the AAD as second-line therapy and are effective for acute and chronic treatment. They are particularly useful in selected clinical situations such as recalcitrance to steroids; for sensitive areas (face, anogenital, skin folds); for steroid-induced atrophy; and when there is long-term uninterrupted topical steroid use. TCIs are recommended for use on actively affected areas as a steroid-sparing agent. Proactive, intermittent use of TCIs as maintenance therapy (2-3 times per week) on areas that commonly flare is recommended to help prevent relapses while reducing need for topical corticosteroids and is more effective than use of emollients alone.(4) Prescribing information for Elidel® (pimecrolimus) cream and Protopic® (tacrolimus) ointment indicate evaluation after 6 weeks if symptoms of AD do not improve for adults and pediatrics.(6,12) Phototherapy is recommended as a treatment for both acute and chronic AD in children and adults, after failure of the mentioned above. Systemic immunomodulator agents are indicated and recommended for the subset of adult and pediatric patients in whom optimized topical regimens using emollients, topical anti-inflammatory therapies, adjunctive methods, and/or phototherapy do not adequately control the signs and symptoms of disease. Phototherapy and systemic immunomodulating agents may also be used in patients whose medical, physical, and/or psychological states are greatly affected by their skin disease. Oral cyclosporine, azathioprine, methotrexate, and mycophenolate mofetil are the most commonly used systemic immunomodulators and most efficacious for treating AD. The AAD recommends that systemic corticosteroids should be avoided if possible and should exclusively be reserved for acute, severe exacerbations and as a short-term bridge to other systemic, steroid sparing therapies.(5,18) There is no clear consensus on how to operationalize a definition of the FDA indication for treatment of patients with "moderate to severe" AD. The severity of AD can vary substantially over time and, from a patient's perspective, can include a complex combination of intensity of itch, location, body surface area (BSA) involvement, and degree of skin impairment. Given the variability of patient phenotype and lack of familiarity among clinicians with scoring systems used in clinical trials, it is advisable to create a broad clinically relevant definition inclusive of multiple specific measures of disease intensity for example:(26)

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	• one of the following:
	  ○ affected BSA greater than or equal to 10%
	  ○ Investigator Global Assessment (IGA) greater than or equal to 3
	  ○ Eczema Area and Severity Index (EASI) greater than or equal to 16
	
	OR
	
	• one of the following:
	  ○ affected BSA greater than or equal to 10%
	  ○ involvement of body sites that are difficult to treat with prolonged topical corticosteroid therapy (e.g., hands, feet, face, neck, scalp, genitals/groin, skin folds)
	  ○ severe itch that has been unresponsive to topical therapies

Asthma	Asthma is a chronic inflammatory disorder of the airways.(9,11) It is characterized by variable and recurring clinical symptoms, airflow obstruction, bronchial hyperresponsiveness, and underlying inflammation.(9) Symptoms of asthma include wheezing, coughing, recurrent difficulty breathing, shortness of breath, and chest tightness. Generally, these symptoms will occur or worsen with exposure to allergens and irritants, infections, exercise, changes in weather, stress, or menstrual cycles. Guidelines recommend the use of detailed medical history, physical examination, and spirometry to make a diagnosis of asthma.(9,11)
	
	The Global Initiative for Asthma (GINA) guidelines recommend a stepwise approach for managing asthma. Long-term goals for asthma management are to achieve good control of symptoms, maintain normal activity level, and to minimize the future risk of exacerbations, fixed airflow limitation, and side-effects.(11) IgE is the antibody responsible for activation of allergic reactions and is important to the pathogenesis of allergic asthma and the development and persistence of inflammation. GINA guidelines define moderate asthma as that which is well controlled with Step 3 or Step 4 treatment (e.g., low- or medium-dose inhaled corticosteroids [ICS] in combination with a long-acting beta agonist [LABA] in either treatment track). Severe asthma is defined as asthma that remains uncontrolled despite optimized treatment with high-dose ICS-LABA, or that requires high-dose ICS-LABA to prevent it from becoming uncontrolled. Severe asthma must be distinguished from asthma that is difficult to treat due to inadequate or inappropriate treatment, or persistent problems with adherence or comorbidities such as chronic rhinosinusitis or obesity, as they need very different treatment compared with if asthma is relatively refractory to high-dose ICS-LABA or even oral corticosteroids (OCS). Early initiation of low dose ICS in patients with asthma has led to greater improvement in lung function than initiation of ICS after symptoms have been present for more than 2 to 4 years. The 2023 GINA guidelines recommend every adult and adolescent with asthma should receive ICS-containing controller medication to reduce the risk of serious exacerbation, even in patients with infrequent symptoms.(11)
	
	2023 GINA STEP recommendations for adults and adolescents (12 years of age and over) are intended to reduce the risk of serious exacerbations and are broken into two tracks based on reliever therapy.
	
	Track 1 is the preferred approach recommended by GINA, because using low dose ICS-formoterol as reliever reduces the risk of exacerbations compared with regimens with short-acting β2-agonist (SABA) as reliever, and is a simpler regimen. Note ICS-formoterol should not be used as the reliever by patients taking any other (non-formoterol) ICS-LABA or ICS-LAMA:(11)
	
	• Step 1:
	  ○ As-needed low dose ICS-formoterol
	• Step 2:
	  ○ As-needed low dose ICS-formoterol
	• Step 3: address and treat modifiable risk factors (e.g., adherence, technique) before considering step up

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	○ Maintenance: low dose ICS-formoterol ○ Reliever: as-needed low dose ICS-formoterol • Step 4: ○ Maintenance: medium dose ICS-formoterol ○ Reliever: as-needed low dose ICS-formoterol • Step 5: patients with uncontrolled symptoms and/or exacerbations despite Step 4 treatment should be assessed for contributory factors, have their treatment optimized, and be referred for expert assessment including severe asthma phenotype, and potential add on treatment ○ Maintenance: consider high dose ICS-formoterol ○ Reliever: as-needed low dose ICS-formoterol ○ Add-on LAMA for patients greater than or equal to 18 years (greater than or equal to 6 years for tiotropium) in separate or combination inhalers ○ Refer for phenotypic assessment +/- biologic therapy ▪ Add-on anti-IgE for severe allergic asthma ▪ SC omalizumab in patients greater than or equal to 6 years ▪ Add-on anti-interleukin (IL)5 or anti-IL5R or anti-IL4R for severe eosinophilic/Type 2 asthma ▪ Anti-IL5: SC mepolizumab for patients greater than or equal to 6 years OR IV reslizumab for patients greater than or equal to 18 years of age ▪ Anti-IL5R: SC benralizumab for patients greater than or equal to 12 years ▪ Anti-IL4R: SC dupilumab for patients greater than or equal to 6 years ○ Add-on anti-thymic stromal lymphopoietin (TSLP) for severe asthma ▪ SC tezepelumab for patients greater than or equal to 12 years ○ Add-on azithromycin three days/week reduces exacerbations, but increases antibiotic resistance ○ Maintenance oral corticosteroids (OCS) should be used only as last resort, because short-term and long-term systemic side-effects are common and serious **Track 2** is an alternative approach if Track 1 is not possible or is not preferred by a patient with no exacerbations on their current therapy. Before considering a regimen with SABA reliever, the clinician should consider whether the patient is likely to be adherent with their controller therapy; if not, they will be exposed to the higher risk of exacerbations with SABA-only treatment:(11) • Step 1: ○ Take ICS whenever SABA taken ○ Reliever: as-needed ICS-SABA or as needed SABA • Step 2: ○ Preferred maintenance: low dose ICS ○ Preferred reliever: as-needed ICS-SABA or as-needed SABA ○ Alternative options with limited indications, or less evidence for efficacy and/or safety: ▪ Low dose ICS whenever SABA taken ▪ Daily LTRA. These are less effective than daily ICS, particularly for preventing exacerbations and there is a US FDA boxed warning about the risk of serious mental health effects with montelukast ○ Daily low-dose ICS-LABA as initial therapy leads to faster improvement in symptoms and FEV1 than ICS alone but is costlier, and the reduction in exacerbations compared with SABA is similar to that with ICS ○ For adults with rhinitis who are allergic to house dust mite and have FEV1 > 70% predicted, consider adding sublingual immunotherapy (SLIT) • Step 3: address and treat modifiable risk factors (e.g., adherence, technique) before considering step up

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	○ Preferred maintenance: low dose ICS-LABA ○ Preferred reliever: as-needed ICS-SABA or as-needed SABA ○ Alternative options: ▪ Medium dose ICS ▪ Low-dose ICS plus LTRA but review US FDA boxed warning ○ For adults with rhinitis who are allergic to house dust mite and have FEV1 > 70% predicted, consider adding SLIT • Step 4: ○ Preferred maintenance: medium/high dose ICS-LABA ○ Preferred reliever: as-needed ICS-SABA or as-needed SABA ○ Alternative options: ▪ Add-on LAMA for patients greater than or equal to 18 years (greater than or equal to 6 years for tiotropium my mist inhaler) ▪ Before considering add-on LAMA for patients with exacerbations, increase ICS dose to at least medium ▪ For adults with rhinitis who are allergic to house dust mite and have FEV1 > 70% predicted, consider adding sublingual immunotherapy (SLIT) • Step 5: patients with uncontrolled symptoms and/or exacerbations despite Step 4 treatment should be assessed for contributory factors, have their treatment optimized, and be referred for expert assessment including severe asthma phenotype, and potential add on treatment ○ Maintenance: medium/high dose ICS-LABA ○ Reliever: as-needed ICS-SABA or as-needed SABA ○ Add-on LAMA for patients greater than or equal to 18 years (greater than or equal to 6 years for tiotropium) in separate or combination inhalers ○ Refer for phenotypic assessment +/- biologic therapy ○ Add-on anti-IgE for severe allergic asthma ▪ SC omalizumab in patients greater than or equal to 6 years ○ Add-on anti-interleukin (IL)5 or anti-IL5R or anti-IL4R for severe eosinophilic/Type 2 asthma ▪ Anti-IL5: SC mepolizumab for patients greater than or equal to 6 years OR IV reslizumab for patients greater than or equal to 18 years of age ▪ Anti-IL5R: SC benralizumab for patients greater than or equal to 12 years ▪ Anti-IL4R: SC dupilumab for patients greater than or equal to 6 years ○ Add-on anti-thymic stromal lymphopoietin (TSLP) for severe asthma ▪ SC tezepelumab for patients greater than or equal to 12 years ○ Add-on azithromycin three days/week reduces exacerbations, but increases antibiotic resistance ○ Maintenance OCS should only be used as last resort, because short-term and long-term systemic side-effects are common and serious 2023 GINA STEP recommendations for children (6 to 11 years of age) are intended to reduce the risk of serious exacerbations:(11) • Step 1: ○ Low dose ICS taken whenever SABA taken ○ Reliever: as needed SABA • Step 2 ○ Preferred: daily low dose ICS ○ Preferred reliever: as needed SABA ○ Alternative options: ▪ Low-dose ICS whenever SABA is taken using separate inhalers ▪ Daily LTRA are less effective for exacerbation reduction. Advise parents about US FDA warning on montelukast • Step 3: after checking inhaler technique and adherence, and treating modifiable risk factors (any of the following):

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	○ Medium-dose ICS maintenance plus as-needed SABA ○ Low-dose ICS-LABA maintenance plus as-needed SABA ○ Maintenance and reliever therapy (MART) with a very low dose of budesonide-formoterol DPI • Step 4: Individual children's responses vary, so each of the Step 3 options may be tried before considering a step-up to Step 4. Refer for expert advice ○ Preferred: medium dose ICS-LABA plus as-needed SABA ○ Preferred: low dose ICS-formoterol MART plus as-needed low-dose ICS-formoterol ○ Alternative options: ▪ Add-on tiotropium ▪ Add-on LTRA • Step 5: ○ Refer for phenotypic assessment with or without higher dose ICS-LABA ○ Reliever: as needed SABA (or ICS-formoterol reliever for MART) ○ Add on therapy with anti-IgE or anti-IL4R, anti-IL5 ○ As a last resort consider add on low dose OCS but consider side effects **Severe Asthma Phenotype and Eosinophilic Asthma Subphenotype** Roughly 3% to 10% of adults with asthma have severe asthma as defined by the GINA 2023 guidelines.(11) The European Respiratory Society (ERS)/American Thoracic Society (ATS) guidelines (2014; updated 2020) and the National Asthma Education and Prevention Program Coordinating Committee Expert Panel Working Group mirror the GINA definition of severe asthma, and defined uncontrolled asthma for adult and pediatric patients 5 years of age and over:(9,25) • Frequent severe exacerbations (i.e., two or more bursts of systemic corticosteroids within the past 12 months) • Serious exacerbations (i.e., at least one hospitalization, intensive care unit stay, or mechanical ventilation in the past 12 months) • Airflow limitation (i.e., FEV1 less than 80% predicted) • Asthma that worsens upon tapering of high-dose ICS or systemic corticosteroids A specialist, preferably in a multidisciplinary severe asthma clinic (if available) performs further assessment, which includes the patient's inflammatory phenotype (i.e., Type 2 or non-Type 2).(11) Type 2 inflammation is characterized by the presence of cytokines such as interleukin (IL)-4, IL-5, and IL-13, which are often produced by the adaptive immune system on recognition of allergens. It is also characterized by eosinophilia or increased fraction of exhaled nitric oxide (FeNO) and may be accompanied by atopy. In many patients with asthma, Type 2 inflammation rapidly improves when ICS are taken regularly and correctly; this is classified as mild or moderate asthma. In severe asthma, Type 2 inflammation may be relatively refractory to high dose ICS. Type 2 inflammation is considered refractory if any of the following are found while the patient is taking high dose ICS or daily OCS:(11) • Blood eosinophils greater than or equal to 150 cells/microliter • FeNO greater than or equal to 20 ppb • Sputum eosinophils greater than or equal to 2% • Asthma is clinically allergen-driven Biologic agents should be considered as add-on therapy for patients with refractory Type 2 inflammation with exacerbations or poor symptom control despite taking at least high dose ICS/LABA, and who have allergic or eosinophilic biomarkers or need maintenance OCS.(11) 2023 GINA recommends the biologics below based on patient eligibility factors:

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	• Anti-IgE (omalizumab):
	  ○ Sensitization on skin prick testing or specific IgE
	  ○ Total serum IgE and weight within dosage range
	  ○ Exacerbations in the last year
	• Anti-IL5/Anti-IL5R (benralizumab, mepolizumab, reslizumab):
	  ○ Exacerbations in the last year
	  ○ Blood eosinophils greater than or equal to 150 cells/microliter (for benralizumab and mepolizumab) or greater than or equal to 300 cells/microliter (for reslizumab)
	• Anti-IL4R (dupilumab):
	  ○ Exacerbations in the last year
	  ○ Blood eosinophil greater than or equal to 150 cells/microliter but less than or equal to 1500 cells/microliter, or FeNO greater than or equal to 25 ppb, or taking maintenance OCS
	• Anti-TSLP (tezepelumab):
	  ○ Exacerbations in the last year
	
	Patient response should be evaluated 4 months after initiating therapy and follow up should occur every 3 to 6 months thereafter. 2023 GINA recommends the following step-down therapy process in patients responding well to targeted biologic therapy:(11)
	
	• Reevaluate the need for each asthma medication every 3 to 6 months, but inhaled therapy should not be completely stopped
	• Oral treatments: gradually decreased starting with OCS due to significant adverse effects.
	• Inhaled treatments: consider reducing ICS dose after 3 to 6 months, but do not completely stop inhaled therapy. Continue at least medium dose ICS and remind patients of the importance of continued inhaled controller therapy
	• Biologic treatments: trial withdrawal after 12 months of treatment and only if patient's asthma remains well controlled on medium dose ICS, and for allergic asthma, there is no further exposure to a previous allergic trigger

Chronic Rhinosinusitis with Nasal Polyposis	Chronic rhinosinusitis with nasal polyposis (CRSwNP) is an inflammatory condition affecting the paranasal sinuses. The International Consensus Statement on allergy and rhinology: Rhinosinusitis indicates that the diagnostic criteria for chronic rhinosinusitis (CRS) consist of ALL the following:(24)
	
	• Symptoms greater than or equal to 12 weeks
	• Two of the following symptoms:
	  ○ Nasal discharge (rhinorrhea or post-nasal drainage)
	  ○ Nasal obstruction or congestion
	  ○ Hyposmia (loss or decreased sense of smell)
	  ○ Facial pressure or pain
	• One or more of the following findings:
	  ○ Evidence of inflammation on nasal endoscopy or computed tomography
	  ○ Evidence of purulence coming from paranasal sinuses or ostiomeatal complex
	
	Sinus computed tomography (CT) and/or nasal endoscopy are needed to determine the presence of sinonasal inflammation and nasal polyps. The exact cause of CRSwNP is unknown, but biopsies of nasal polyps have shown elevated levels of eosinophils.(15)
	
	First line therapy for CRSwNP consists of nasal saline irrigation in combination with intranasal corticosteroids.(15-17) The American Academy of Family Physicians notes that no one intranasal corticosteroid is superior to another or that increased dosing provides greater effectiveness. The American Academy of Otolaryngology recommends a short course of oral corticosteroids if no response is seen with intranasal

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	corticosteroids after 3-months of appropriate use.(17) Short courses of oral corticosteroids (up to three weeks) can improve sinonasal symptoms and endoscopic findings. Surgical intervention may be required in patients in which medical therapy is ineffective.(15,16)
Eosinophilic Esophagitis	Eosinophilic Esophagitis (EoE) is an allergen/immune-mediated disease characterized by symptoms of esophageal dysfunction and marked eosinophilic inflammation of the esophageal mucosa in the absence of secondary causes. EoE has dramatically increased in prevalence over the years. EoE is characterized by symptoms related to esophageal dysfunction and histologically with eosinophil-predominant inflammation (a peak count of greater than or equal to 15 eosinophils per high-power field on esophageal biopsy). Atopic and allergic inflammatory conditions commonly occur concomitantly with EoE.(19) The symptoms of EoE are age dependent. Young children may refuse to eat, have decreased appetite, recurring abdominal pain, trouble swallowing, and vomiting. Young adults and adults have the same symptoms, but often struggle to swallow dry or dense, solid foods due to inflammation. Food impaction is a common cause for emergency room visits in patients with EoE. Patients may also have concurrent gastroesophageal reflux disease (GERD). EoE is a progressive disease if left untreated. The chronic inflammation can lead to tissue fibrosis and strictures in the esophagus that require esophageal dilation.(20) The diagnosis of EoE is suspected on the basis of chronic symptoms such as dysphagia, food impaction, food refusal, failure to progress with food introduction, heartburn, regurgitation, vomiting, chest pain, odynophagia, abdominal pain, and malnutrition. Due to the wide range of chronic symptoms, the diagnosis should be highly considered in the presence of concomitant atopic conditions and if there are endoscopic findings. Endoscopic findings associated with EoE include esophageal rings, longitudinal furrows, exudates, edema, strictures, or narrow caliber esophagus. Assessment of non-EoE disorders and esophageal biopsy are required to confirm the diagnosis of EoE, with at least 15 eosinophils (eos)/ high-power field (hpf) present on esophageal biopsy.(21) The American Gastroenterology Association (AGA) and the Joint Task Force on Allergy-Immunology Practice Parameters (JTF) guideline for the management of EoE strongly recommend the use of topical corticosteroids for the treatment of EoE. Studies showed that topical budesonide or topical fluticasone induced histological remission significantly better than placebo and had similar adverse events to placebo. The AGA/JTF conditionally recommend continuing topical corticosteroids for maintenance therapy once remission is achieved. Dilation is only conditionally recommended for patients with dysphagia associated with strictures due to EoE, noting that the dilation does not address the underlying inflammation.(22)
Prurigo Nodularis	Prurigo nodularis (PN) is a skin disorder that is defined by the presence of chronic pruritus and multiple elevated, firm, and nodular lesions. PN is more common in older adults but can occur in children. The underlying cause of PN is unknown, but it appears neural and immunologic processes both play a role in its development. The nodules form in a subset of patients that have chronic pruritus, with the nodules forming in areas with continuous scratching over prolonged periods of time. There is significant disease burden associated with PN including sleep disruption, anxiety, and depression. The nodules are typically firm, dome-shaped, and itchy and range in size from millimeters to several centimeters. The nodules can range in color from flesh tones to brown/black and can range in number from a few to hundreds. The pruritis associated with PN can range from sporadic to continuous and generally the underlying cause is unknown. There are a number of conditions, both dermatologic and other diseases, that are associated with PN, such as atopic dermatitis, kidney disease, diabetes, and HIV.(23) The diagnosis of PN is generally one of exclusion. The American Academy of Dermatology (AAD) indicates that the diagnostic workup should include a clinical examination with a complete review of systems and assessment of PN severity, which

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	should include both disease burden (e.g., quality of life, sleep disturbances) and pruritis intensity. The ADD notes three core features associated with PN:(23) • Presence of firm, nodular lesions • Pruritus that lasts for at least 6 weeks • History and/or signs of repeated scratching, picking, or rubbing Management requires a multifaceted approach with a focus on controlling the underlying pruritis. Topical therapies are initial therapy for limited disease. Topical therapies include topical and intralesional corticosteroids. Topical calcineurin inhibitors and topical calcipotriol have been used but have not been adequately studied. Phototherapy is used in patients with more widespread and refractory PN. Systemic therapies include cyclosporine and methotrexate and are generally used in patients with widespread, refractory disease that does not respond to phototherapy.(23)
Efficacy	**Atopic Dermatitis(1,7,8)** Dupilumab was FDA approved through two randomized, double-blind, placebo-controlled phase 3 trials (SOLO 1 and SOLO 2). All patients in both trials were at least 18 years old, had chronic AD (according to American Academy of Dermatology Consensus Criteria Eichenfield 2014) that had been present for at least 3 years, and had greater than or equal to 10% body surface area (BSA) involvement at the screening and baseline visits. Additionally, all patients had a documented recent history (within 6 months before the screening visit) of inadequate response to treatment with topical medications (defined as failure to achieve and maintain remission or a low disease activity state despite treatment with a daily regimen of topical corticosteroids of medium to higher potency applied for greater than or equal to 28 days or for the maximum duration recommended by the product prescribing information [e.g., 14 days for super-potent topical corticosteroids], whichever is shorter), or whom topical treatments are otherwise medically inadvisable. The primary outcome measure in both trails was proportion of patients with both IGA (Investigator Global Assessment) 0 to 1 (on a 5-point scale) and a reduction from baseline of greater than or equal to 2 points at week 16. There were several secondary endpoints included. Some examples include: proportion of patients with Eczema Area and Severity Index (EASI) -75 (greater than or equal to 75% improvement from baseline) at week 16, percent change from baseline to week 16 in pruritus numerical rating scale (NRS), change from baseline to week 16 in % BSA, and changes in quality of life, anxiety, and depression. The manufacturer reports the following results from SOLO 1 and SOLO 2. In SOLO 1, the primary outcome (an IGA of 0-1 and a reduction of greater than or equal to 2 points from baseline at week 16) occurred in 85 patients (38%) who received dupilumab every other week and in 83 (37%) who received dupilumab weekly, as compared with 23 (10%) who received placebo (P less than 0.001 for both comparisons with placebo). The results were similar in SOLO 2, with the primary outcome occurring in 84 patients (36%) who received dupilumab every other week and in 87 (36%) who received dupilumab weekly, as compared with 20 (8%) who received placebo (P less than 0.001 for both comparisons). In addition, in the two trials, an 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 less than 0.001 for all comparisons). Dupilumab was also associated with improvement in other clinical end points, including reduction in pruritus and symptoms of anxiety or depression and improvement in quality of life. The efficacy and safety of Dupixent monotherapy in adolescent subjects was evaluated in a multicenter, randomized, double-blind, placebo-controlled trial in 251 adolescent subjects 12 to 17 years of age, with moderate-to-severe AD and a minimum BSA involvement of greater than or equal to 10%. Eligible subjects enrolled into this trial had previous inadequate response to topical medication. Subjects in the Dupixent group with baseline weight of less than 60 kg received an initial dose of 400 mg at Week 0, followed by 200 mg every 2 weeks for 16 weeks.

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	Subjects with baseline weight of greater than or equal to 60 kg received an initial dose of 600 mg at Week 0, followed by 300 mg every 2 weeks for 16 weeks. Subjects were permitted to receive rescue treatment at the discretion of the investigator. Subjects who received rescue treatment were considered non-responders. The primary endpoint was the proportion of subjects with an IGA 0 (clear) or 1 (almost clear) and at least a 2-point improvement from baseline to Week 16. Other evaluated outcomes included the proportion of subjects with EASI-75 or EASI-90 (improvement of at least 75% or 90% in EASI from baseline, respectively), and reduction in itch as measured by the Peak Pruritus NRS (greater than or equal to 4-point improvement). The efficacy results at Week 16 were as follows: • IGA 0 or 1: 24% for Dupixent and 2% for placebo • EASI-75: 42% for Dupixent and 8% for placebo • EASI-90: 23% for Dupixent and 2% for placebo • Peak Pruritus NRS (greater than or equal to 4-point improvement): 37% for Dupixent and 5% for placebo **Asthma(1)** The asthma development program included three randomized, double-blind, placebo controlled, parallel-group, multi-center trials (AS Trials 1, 2, and 3) of 24 to 52 weeks in treatment duration which enrolled a total of 2888 subjects (12 years of age and older). Subjects enrolled in AS Trials 1 and 2 were required to have a history of 1 or more asthma exacerbations that required treatment with systemic corticosteroids or emergency department visit or hospitalization for the treatment of asthma in the year prior to trial entry. Subjects enrolled in AS Trial 3 required dependence on daily oral corticosteroids in addition to regular use of high-dose inhaled corticosteroids plus an additional controller(s). In all 3 trials, subjects were enrolled without requiring a minimum baseline blood eosinophil count. In AS Trials 2 and 3 subjects with screening blood eosinophil level of greater than 1500 cells/mcL (less than 1.3%) were excluded. Dupixent was administered as add-on to background asthma treatment. Subjects continued background asthma therapy throughout the duration of the studies, except in AS Trial 3 in which OCS dose was tapered as described below. AS Trial 1 was a 24-week dose-ranging study which included 776 subjects (18 years of age and older). Dupixent compared with placebo was evaluated in adult subjects with moderate to severe asthma on a medium or high-dose inhaled corticosteroid and a long acting beta agonist. Subjects were randomized to receive either 200 mg (N equal to 150) or 300 mg (N equal to 157) Dupixent every other week (Q2W) or 200 mg (N equal to 154) or 300 mg (N equal to 157) Dupixent every 4 weeks following an initial dose of 400 mg, 600 mg or placebo (N equal to 158), respectively. The primary endpoint was mean change from baseline to Week 12 in FEV1 (L) in subjects with baseline blood eosinophils greater than or equal to 300 cells/mcL. Other endpoints included percent change from baseline in FEV1 and annualized rate of severe asthma exacerbation events during the 24-week placebo controlled treatment period. Results were evaluated in the overall population and subgroups based on baseline blood eosinophil count (greater than or equal to 300 cells/mcL and less than 300 cells/mcL. Additional secondary endpoints included responder rates in the patient reported Asthma Control Questionnaire (ACQ-5) and Asthma Quality of Life Questionnaire, Standardized Version (AQLQ(S)) scores. AS Trial 2 was a 52-week study which included 1902 subjects (12 years of age and older). Dupixent compared with placebo was evaluated in 107 adolescents and 1795 adult subjects with moderate-to-severe asthma on a medium or high-dose inhaled corticosteroid (ICS) and a minimum of one and up to two additional controller medications. Subjects were randomized to receive either 200 mg (N=631) or 300 mg (N=633) Dupixent Q2W (or matching placebo for either 200 mg [N equal to 317] or 300 mg [N equal to 321] Q2W) following an initial dose of 400 mg, 600 mg or placebo respectively. The primary endpoints were the annualized rate of severe exacerbation

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	events during the 52-week placebo controlled period and change from baseline in pre-bronchodilator FEV1 at Week 12 in the overall population (unrestricted by minimum baseline blood eosinophils count). Additional secondary endpoints included annualized severe exacerbation rates and FEV1 in patients with different baseline levels of blood eosinophils as well as responder rates in the ACQ-5 and AQLQ(S) scores. AS Trial 3 was a 24-week oral corticosteroid-reduction study in 210 subjects with asthma who required daily oral corticosteroids in addition to regular use of high dose inhaled corticosteroids plus an additional controller. After optimizing the OCS dose during the screening period, subjects received 300 mg Dupixent (N=103) or placebo (N=107) once Q2W for 24 weeks following an initial dose of 600 mg or placebo. Subjects continued to receive their existing asthma medicine during the study; however, their OCS dose was reduced every 4 weeks during the OCS reduction phase (Week 4-20), as long as asthma control was maintained. The primary endpoint was the percent reduction of oral corticosteroid dose at Weeks 20 to 24 compared with the baseline dose, while maintaining asthma control in the overall population (unrestricted by minimum baseline blood eosinophils count). Additional secondary endpoints included the annualized rate of severe exacerbation events during treatment period and responder rate in the ACQ-5 and AQLQ(S) scores. AS Trials 1 and 2 evaluated the frequency of severe asthma exacerbations defined as deterioration of asthma requiring the use of systemic corticosteroids for at least 3 days or hospitalization or emergency room visit due to asthma that required systemic corticosteroids. In the primary analysis population (subjects with baseline blood eosinophil count of greater than or equal to 300 cells/mcL in AS Trial 1 and the overall population in AS Trial 2), subjects receiving either Dupixent 200 mg or 300 mg Q2W had significant reductions in the rate of asthma exacerbations compared to placebo. In the overall population in AS Trial 2, the rate of severe exacerbations was 0.46 and 0.52 for Dupixent 200 mg Q2W and 300 mg Q2W, respectively, compared to matched placebo rates of 0.87 and 0.97. The rate ratio of severe exacerbations compared to placebo was 0.52 (95% CI: 0.41, 0.66) and 0.54 (95% CI: 0.43, 0.68) for Dupixent 200 mg Q2W and 300 mg Q2W, respectively. Prespecified subgroup analyses of AS Trials 1 and 2 demonstrated that there were greater reductions in severe exacerbations in subjects with higher baseline blood eosinophil levels. In AS Trial 2, reductions in exacerbations were significant in the subgroup of subjects with baseline blood eosinophils greater than or equal to 150 cells/mcL. In subjects with baseline blood eosinophil count less than 150 cells/mcL, similar severe exacerbation rates were observed between Dupixent and placebo. Significant increases in pre-bronchodilator FEV1 were observed at Week 12 for AS Trials 1 and 2 in the primary analysis populations (subjects with baseline blood eosinophil count of greater than or equal to 300 cells/mcL in AS Trial 1 and the overall population in AS Trial 2). In the overall population in AS Trial 2, the FEV1 LS mean change from baseline was 0.32 L (21%) and 0.34 L (23%) for Dupixent 200 mg Q2W and 300 mg Q2W, respectively, compared to matched placebo means of 0.18 L (12%) and 0.21 L (14%). The mean treatment difference versus placebo was 0.14 L (95% CI: 0.08, 0.19) and 0.13 L (95% CI: 0.08, 0.18) for Dupixent 200 mg Q2W and 300 mg Q2W, respectively. Subgroup analysis of AS Trials 1 and 2 demonstrated greater improvement in subjects with higher baseline blood eosinophils. **CSNP(1)** Two randomized, double-blind, parallel-group, multicenter, placebo-controlled studies (CSNP Trial 1 and CSNP Trial 2) evaluated Dupixent in CRSwNP. There were 724 subjects aged 18 years and older on background intranasal corticosteroids (INCS) included in the trials. These studies included subjects with CRSwNP despite prior sinonasal surgery or treatment with, or who were ineligible to receive or were intolerant to, systemic corticosteroids in the past 2 years. Patients with chronic rhinosinusitis without nasal polyposis were not included in these trials. Rescue with systemic corticosteroids or surgery was allowed during the studies at the investigator's discretion. In CSNP Trial 1, a total of 276 subjects were randomized to receive either

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	300 mg Dupixent (N=143) or placebo (N=133) every other week for 24 weeks. In CSNP Trial 2, 448 subjects were randomized to receive either 300 mg Dupixent (N=150) every other week for 52 weeks, 300 mg Dupixent (N=145) every other week until week 24 followed by 300 mg Dupixent every 4 weeks until week 52, or placebo (N=153). All subjects had evidence of sinus opacification on the Lund Mackay (LMK) sinus CT scan and 73% to 90% of subjects had opacification of all sinuses. Subjects were stratified based on their histories of prior surgery and co-morbid asthma/nonsteroidal anti-inflammatory drug exacerbated respiratory disease (NSAID-ERD). A total of 63% of subjects reported previous sinus surgery, with a mean number of 2.0 prior surgeries, 74% used systemic corticosteroids in the previous 2 years with a mean number of 1.6 systemic corticosteroid courses in the previous 2 years, 59% had co-morbid asthma, and 28% had NSAID-ERD. The co-primary efficacy endpoints were change from baseline to Week 24 in bilateral endoscopic nasal polyps score (NPS; 0-8 scale) as graded by central blinded readers and change from baseline to Week 24 in nasal congestion/obstruction score averaged over 28 days (NC; 0-3 scale), as determined by subjects using a daily diary. In both studies, key secondary end-points at Week 24 included change from baseline in: LMK sinus CT scan score, daily loss of smell, and 22-item sinonasal outcome test (SNOT-22). In the pooled efficacy results, the reduction in the proportion of subjects rescued with systemic corticosteroids and/or sinonasal surgery (up to Week 52) were evaluated. Statistically significant efficacy was observed in CSNP Trial 2 with regard to improvement in bilateral endoscopic NPS score at week 24 and week 52. Similar results were seen in CSNP Trial 1 at Week 24. In the post-treatment period when subjects were off Dupixent, the treatment effect diminished over time. In both studies, significant improvements in nasal congestion were observed as early as the first assessment at Week 4. A significant decrease in the LMK sinus CT scan score was observed. Dupilumab significantly improved the loss of smell compared to placebo. In both studies, significant improvements in daily loss of smell severity were observed as early as the first assessment at Week 4. Dupilumab significantly decreased sinonasal symptoms as measured by SNOT-22 compared to placebo. In the pre-specified multiplicity-adjusted pooled analysis of two studies, treatment with Dupixent resulted in significant reduction of systemic corticosteroid use and need for sinonasal surgery versus placebo (HR of 0.24; 95% CI: 0.17, 0.35). The proportion of subjects who required systemic corticosteroids was reduced by 74% (HR of 0.26; 95% CI: 0.18, 0.38). The total number of systemic corticosteroid courses per year was reduced by 75% (RR of 0.25; 95% CI: 0.17, 0.37). The proportion of subjects who required surgery was reduced by 83% (HR of 0.17; 95% CI: 0.07, 0.46). The effects of Dupixent on the primary endpoints of NPS and nasal congestion and the key secondary endpoint of LMK sinus CT scan score were consistent in patients with prior surgery and without prior surgery. **EoE(1)** A single randomized, double-blind, parallel-group, multicenter, placebo-controlled trial, including two 24-week treatment periods (Parts A and B), was conducted in adult and pediatric subjects 12 to 17 years of age, weighing at least 40 kg, with EoE (NCT03633617). In both parts, subjects were randomized to receive 300 mg Dupixent every week or placebo. Eligible subjects had greater than or equal to 15 intraepithelial eosinophils per high-power field (eos/hpf) following a treatment course of a proton pump inhibitor (PPI) either prior to or during the screening period and symptoms of dysphagia as measured by the Dysphagia Symptom Questionnaire (DSQ). At baseline, 43% of subjects in Part A and 37% of subjects in Part B had a history of prior esophageal dilations. The coprimary efficacy endpoints in Parts A and B were the (1) proportion of subjects achieving histological remission defined as peak esophageal intraepithelial eosinophil

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	count of less than or equal to 6 eos/hpf at week 24; and (2) the absolute change in the subject reported DSQ score from baseline to week 24. In Parts A and B, a greater proportion of subjects randomized to Dupixent achieved histological remission (peak esophageal intraepithelial eosinophil count less than or equal to 6 eos/hpf) compared to placebo (Part A: 25% vs 2%; Part B: 47% vs 5%). Treatment with Dupixent also resulted in a significant improvement in LS mean change in DSQ score compared to placebo at week 24 (Part A: -21.9 vs -9.6; Part B -23.8 vs -13.9). The results of the anchor-based analyses that incorporated the subjects' perspectives indicated that the observed improvement in dysphagia from Parts A and B is representative of a clinically meaningful within-subject improvement. **PN(1)** The prurigo nodularis (PN) development program included two 24-week randomized, double-blind, placebo-controlled, multicenter, parallel-group trials (PRIME [NCT04183335] and PRIME 2 [NCT04202679]) in 311 adult subjects 18 years of age and older with pruritus (WINRS greater than or equal to 7 on a scale of 0 to 10) and greater than or equal to 20 nodular lesions. PRIME and PRIME 2 assessed the effect of Dupixent on pruritus improvement as well as its effect on PN lesions. In these two trials, subjects received either subcutaneous Dupixent 600 mg (two 300 mg injections) on day 1, followed by 300 mg once every other week (Q2W) for 24 weeks, or matching placebo. At baseline, the mean Worst Itch-Numeric Rating Scale (WI-NRS) was 8.5, 66% had 20 to 100 nodules (moderate), and 34% had greater than 100 nodules (severe). Patients were required to have failed at least a 2-week trial of a medium to super potent topical corticosteroid or topical corticosteroids were not medically advised. The WI-NRS is comprised of a single item, rated on a scale from 0 (no itch) to 10 (worst imaginable itch). Subjects were asked to rate the intensity of their worst pruritus (itch) over the past 24 hours using this scale. The Investigator's Global Assessment for Prurigo Nodularis-Stage (IGA PN-S) is a scale that measures the approximate number of nodules using a 5-point scale from 0 (clear) to 4 (severe). Efficacy was assessed with the proportion of subjects with improvement (reduction) in WI-NRS by greater than or equal to 4 points, the proportion of subjects with IGA PN-S 0 or 1 (the equivalent of 0-5 nodules), and the proportion of subjects who achieved a response in both WI-NRS and IGA PN-S per the criteria described above. Overall, patients treated with Dupixent saw improvement in all endpoints over placebo.
Safety	Dupilumab is contraindicated in patients who have a known hypersensitivity to dupilumab or any excipients of Dupixent.(1)

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POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
Dupixent	dupilumab subcutaneous soln pen-injector ; dupilumab subcutaneous soln prefilled syringe	100 MG/0.67ML ; 200 MG/1.14ML ; 300 MG/2ML	M ; N ; O ; Y	N		

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
Dupixent	Dupilumab Subcutaneous Soln Pen-injector	200 MG/1.14 ML	2	Pens	28	DAYS			
Dupixent	Dupilumab Subcutaneous Soln Pen-injector 300 MG/2ML	300 MG/2ML	4	Pens	28	DAYS			
Dupixent	Dupilumab Subcutaneous Soln Prefilled Syringe	100 MG/0.67 ML	2	Syringes	28	DAYS			
Dupixent	Dupilumab Subcutaneous Soln Prefilled Syringe 200 MG/1.14ML	200 MG/1.14 ML	2	Syringes	28	DAYS			
Dupixent	Dupilumab Subcutaneous Soln Prefilled Syringe 300 MG/2ML	300 MG/2ML	4	Syringes	28	DAYS			

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Dupixent	dupilumab subcutaneous soln pen-injector ; dupilumab subcutaneous soln prefilled syringe	100 MG/0.67ML ; 200 MG/1.14ML ; 300 MG/2ML	Commercial ; HIM ; ResultsRx

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Dupixent	Dupilumab Subcutaneous Soln Pen-injector	200 MG/1.14ML	Commercial ; HIM ; ResultsRx
Dupixent	Dupilumab Subcutaneous Soln Pen-injector 300 MG/2ML	300 MG/2ML	Commercial ; HIM ; ResultsRx
Dupixent	Dupilumab Subcutaneous Soln Prefilled Syringe	100 MG/0.67ML	Commercial ; HIM ; ResultsRx
Dupixent	Dupilumab Subcutaneous Soln Prefilled Syringe 200 MG/1.14ML	200 MG/1.14ML	Commercial ; HIM ; ResultsRx
Dupixent	Dupilumab Subcutaneous Soln Prefilled Syringe 300 MG/2ML	300 MG/2ML	Commercial ; HIM ; ResultsRx

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PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Initial Evaluation **Target Agent(s)** will be approved when ALL of the following are met: 1. ONE of the following: A. The requested agent is eligible for continuation of therapy AND ONE of the following: **Agents Eligible for Continuation of Therapy** All target agents are eligible for continuation of therapy 1. Information has been provided that indicates the patient has been treated with the requested agent (starting on samples is not approvable) within the past 90 days **OR** 2. The prescriber states the patient has been treated with the requested agent (starting on samples is not approvable) within the past 90 days AND is at risk if therapy is changed **OR** B. The patient has a diagnosis of moderate-to-severe atopic dermatitis (AD) AND ALL of the following: 1. ONE of the following: A. The patient has at least 10% body surface area involvement **OR** B. The patient has involvement of body sites that are difficult to treat with prolonged topical corticosteroid therapy (e.g., hands, feet, face, neck, scalp, genitals/groin, skin folds) **OR** C. The patient has an Eczema Area and Severity Index (EASI) score of greater than or equal to 16 **OR** D. The patient has an Investigator Global Assessment (IGA) score of greater than or equal to 3 **AND** 2. ONE of the following: A. The patient has tried and had an inadequate response after a minimum of 3 months with an oral systemic immunosuppressant (e.g., methotrexate, azathioprine, mycophenolate mofetil, cyclosporine) for the treatment of AD **OR** B. The patient has an intolerance or hypersensitivity to an oral systemic immunosuppressant **OR** C. BOTH of the following: 1. ONE of the following: A. The patient has tried and had an inadequate response to at least a mid-potency topical steroid used for a minimum of 4 weeks **OR** B. The patient has an intolerance or hypersensitivity to at least a mid-potency topical steroid **AND** 2. ONE of the following: A. The patient has tried and had an inadequate response to a topical calcineurin inhibitor (e.g., Elidel/pimecrolimus, Protopic/tacrolimus) used for a minimum of 6 weeks **OR** B. The patient has an intolerance or hypersensitivity to a topical calcineurin inhibitor **OR** D. The patient has an FDA labeled contraindication to ALL oral systemic immunosuppressants, mid-, high-, and super-potency topical steroids, AND topical calcineurin inhibitors **AND** 3. The prescriber has assessed the patient's baseline (prior to therapy with the requested agent) pruritus and other symptom severity (e.g., erythema, edema, xerosis, erosions/excoriations, oozing and crusting, and/or lichenification) **AND**

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Module	Clinical Criteria for Approval
	4. The patient will be using standard maintenance therapy (e.g., topical emollients, good skin care practices) in combination with the requested agent **OR** C. The patient has a diagnosis of moderate to severe asthma AND BOTH of the following: 1. ONE of the following: A. The patient has eosinophilic type asthma AND ONE of the following: 1. The patient has a baseline (prior to therapy with the requested agent) blood eosinophilic count of 150 cells/microliter or higher while on high-dose inhaled corticosteroids or daily oral corticosteroids **OR** 2. The patient has sputum eosinophils 2% or higher while on high-dose inhaled corticosteroids or daily oral corticosteroids **OR** B. The patient has oral corticosteroid dependent type asthma **AND** 2. The patient has a history of uncontrolled asthma while on asthma control therapy as demonstrated by ONE of the following: A. Frequent severe asthma exacerbations requiring two or more courses of systemic corticosteroids (steroid burst) within the past 12 months **OR** B. Serious asthma exacerbations requiring hospitalization, mechanical ventilation, or visit to the emergency room or urgent care within the past 12 months **OR** C. Controlled asthma that worsens when the doses of inhaled and/or systemic corticosteroids are tapered **OR** D. The patient has baseline (prior to therapy with the requested agent) Forced Expiratory Volume (FEV1) that is less than 80% of predicted **OR** D. The patient has a diagnosis of chronic rhinosinusitis with nasal polyposis (CRSwNP) AND ALL of the following: 1. The patient has at least TWO of the following symptoms consistent with chronic rhinosinusitis (CRS): A. Nasal discharge (rhinorrhea or post-nasal drainage) B. Nasal obstruction or congestion C. Loss or decreased sense of smell (hyposmia) D. Facial pressure or pain **AND** 2. The patient has had symptoms consistent with chronic rhinosinusitis (CRS) for at least 12 consecutive weeks **AND** 3. There is information indicating the patient's diagnosis was confirmed by ONE of the following: A. Anterior rhinoscopy or endoscopy **OR** B. Computed tomography (CT) of the sinuses **AND** 4. ONE of the following: A. ONE of the following: 1. The patient had an inadequate response to sinonasal surgery **OR** 2. The patient is NOT a candidate for sinonasal surgery **OR** B. ONE of the following: 1. The patient has tried and had an inadequate response to oral systemic corticosteroids **OR** 2. The patient has an intolerance or hypersensitivity to therapy with oral systemic corticosteroids **OR** 3. The patient has an FDA labeled contraindication to ALL oral systemic corticosteroids **AND** 5. ONE of the following: A. The patient has tried and had an inadequate response to intranasal corticosteroids (e.g., fluticasone, Sinuva) used for at least a 3-month trial **OR** B. The patient has an intolerance or hypersensitivity to therapy with intranasal corticosteroids (e.g., fluticasone, Sinuva) **OR**

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Module	Clinical Criteria for Approval
	C. The patient has an FDA labeled contraindication to ALL intranasal corticosteroids **OR** E. The patient has a diagnosis of eosinophilic esophagitis (EoE) AND BOTH of the following: 1. The patient's diagnosis was confirmed by ALL of the following: A. Chronic symptoms of esophageal dysfunction B. Greater than or equal to 15 eosinophils per high-power field on esophageal biopsy C. Other causes that may be responsible for or contributing to symptoms and esophageal eosinophilia have been ruled out **AND** 2. ONE of the following: A. The patient has tried and had an inadequate response to ONE standard corticosteroid therapy for EoE (i.e., budesonide suspension, fluticasone MDI swallowed) **OR** B. The patient has an intolerance or hypersensitivity to standard corticosteroid therapy for EoE **OR** C. The patient has an FDA labeled contraindication to standard corticosteroid therapy for EoE **OR** D. The patient has tried and had an inadequate response to ONE proton pump inhibitor (PPI) used in the treatment of EoE **OR** E. The patient has an intolerance or hypersensitivity to PPI therapy used in the treatment of EoE **OR** F. The patient has an FDA labeled contraindication to ALL PPI therapy used in the treatment of EoE **OR** F. The patient has a diagnosis of prurigo nodularis (PN) and BOTH of the following: 1. The patient has ALL of the following features associated with PN: A. Presence of firm, nodular lesions B. Pruritus that has lasted for at least 6 weeks C. History and/or signs of repeated scratching, picking, or rubbing **AND** 2. ONE of the following: A. The patient has tried and had an inadequate response to at least a mid-potency topical steroid used for a minimum of 2 weeks **OR** B. The patient has an intolerance or hypersensitivity to therapy with at least a mid-potency topical steroid **OR** C. The patient has an FDA labeled contraindication to ALL mid-, high-, and super-potency topical steroids **OR** G. The patient has another FDA approved indication for the requested agent and route of administration **OR** H. The patient has another indication that is supported in compendia for the requested agent and route of administration **AND** 2. If the patient has a diagnosis of chronic rhinosinusitis with nasal polyposis (CRSwNP) BOTH of the following: A. The patient is currently treated with standard nasal polyp maintenance therapy (e.g., nasal saline irrigation, intranasal corticosteroids) **AND** B. The patient will continue standard nasal polyp maintenance therapy (e.g., nasal saline irrigation, intranasal corticosteroids) in combination with the requested agent **OR** 3. If the patient has a diagnosis of moderate to severe asthma, ALL of the following: A. ONE of the following: 1. The patient is NOT currently being treated with the requested agent AND is currently treated with a maximally tolerated inhaled corticosteroid for at least 3 months **OR** 2. The patient is currently being treated with the requested agent AND ONE of the following: A. Is currently treated with an inhaled corticosteroid for at least 3 months that is adequately dosed to control symptoms **OR** B. Is currently treated with a maximally tolerated inhaled corticosteroid for at least 3 months **OR** 3. The patient has an intolerance or hypersensitivity to inhaled corticosteroid therapy **OR**

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Module	Clinical Criteria for Approval
	4. The patient has an FDA labeled contraindication to ALL inhaled corticosteroids **AND** B. ONE of the following: 1. The patient is currently being treated for at least 3 months with ONE of the following: A. A long-acting beta-2 agonist (LABA) **OR** B. Long-acting muscarinic antagonist (LAMA) **OR** C. A leukotriene receptor antagonist (LTRA) **OR** D. Theophylline **OR** 2. The patient has an intolerance or hypersensitivity to therapy with long-acting beta-2 agonists (LABA), long-acting muscarinic antagonists (LAMA), leukotriene receptor antagonist (LTRA), or theophylline **OR** 3. The patient has an FDA labeled contraindication to ALL long-acting beta-2 agonists LABA) AND long-acting muscarinic antagonists (LAMA) **AND** C. The patient will continue asthma control therapy (e.g., ICS, ICS/LABA, LTRA, LAMA, theophylline) in combination with the requested agent **AND** 4. If the patient has an FDA approved indication, then ONE of the following: A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR** B. The prescriber has provided information in support of using the requested agent for the patient's age for the requested indication **AND** 5. The prescriber is a specialist in the area of the patient's diagnosis (e.g., atopic dermatitis -dermatologist, allergist, immunologist; asthma -allergist, immunologist, pulmonologist; CRSwNP -otolaryngologist, allergist, pulmonologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 6. ONE of the following (Please refer to "Agents NOT to be used Concomitantly" table): A. The patient will NOT be using the requested agent in combination with another immunomodulatory agent (e.g., TNF inhibitors, JAK inhibitors, IL-4 inhibitors) **OR** B. The patient will be using the requested agent in combination with another immunomodulatory agent AND BOTH of the following: 1. The prescribing information for the requested agent does NOT limit the use with another immunomodulatory agent **AND** 2. The prescriber has provided information in support of combination therapy (submitted copy required, e.g., clinical trials, phase III studies, guidelines required) **AND** 7. The patient does NOT have any FDA labeled contraindications to the requested agent **Compendia Allowed:** AHFS, DrugDex 1 or 2a level of evidence, or NCCN 1 or 2a recommended use **Length of Approval:** 6 months NOTE: Please approve initial loading dose for asthma, atopic dermatitis, and prurigo nodularis only • 300 mg strength requested: 600 mg (two 300 mg injections) followed by maintenance dose • 200 mg strength requested: 400 mg (two 200 mg injections) followed by maintenance dose NOTE: Quantity Limit applies, please refer to Quantity Limit criteria section below. **Renewal Evaluation** **Target Agent(s)** will be approved when ALL of the following are met: 1. The patient has been previously approved for the requested agent through the plan's Prior Authorization process **AND**

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Module	Clinical Criteria for Approval
	2. ONE of the following: A. The patient has a diagnosis of moderate-to-severe atopic dermatitis (AD) AND BOTH of the following: 1. The patient has had a reduction or stabilization from baseline (prior to therapy with the requested agent) of ONE of the following: A. Affected body surface area **OR** B. Flares **OR** C. Pruritus, erythema, edema, xerosis, erosions/excoriations, oozing and crusting, and/or lichenification **OR** D. A decrease in the Eczema Area and Severity Index (EASI) score **OR** E. A decrease in the Investigator Global Assessment (IGA) score **AND** 2. The patient will continue standard maintenance therapies (e.g., topical emollients, good skin care practices) in combination with the requested agent **OR** B. The patient has a diagnosis of moderate to severe asthma AND BOTH of the following: 1. The patient has had improvements or stabilization with the requested agent from baseline (prior to therapy with the requested agent) as indicated by ONE of the following: A. The patient has had an increase in percent predicted Forced Expiratory Volume (FEV1) **OR** B. The patient has had a decrease in the dose of inhaled corticosteroids required to control the patient's asthma **OR** C. The patient has had a decrease in need for treatment with systemic corticosteroids due to exacerbations of asthma **OR** D. The patient has had a decrease in number of hospitalizations, need for mechanical ventilation, or visits to urgent care or emergency room due to exacerbations of asthma **AND** 2. The patient is currently treated and is compliant with asthma control therapy [e.g., inhaled corticosteroids, ICS/long-acting beta-2 agonist (LABA), leukotriene receptor antagonist (LTRA), long-acting muscarinic antagonist (LAMA), theophylline] **OR** C. The patient has a diagnosis of chronic rhinosinusitis with nasal polyposis (CRSwNP) AND BOTH of the following: 1. The patient has had clinical benefit with the requested agent **AND** 2. The patient will continue standard nasal polyp maintenance therapy (e.g., nasal saline irrigation, intranasal corticosteroids) in combination with the requested agent **OR** D. The patient has a diagnosis other than moderate-to-severe atopic dermatitis (AD), moderate to severe asthma, or chronic rhinosinusitis with nasal polyposis (CRSwNP) AND has had clinical benefit with the requested agent **AND** 3. The prescriber is a specialist in the area of the patient's diagnosis (e.g., atopic dermatitis -dermatologist, allergist, immunologist; asthma -allergist, immunologist, pulmonologist; CRSwNP -otolaryngologist, allergist, pulmonologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 4. ONE of the following (Please refer to "Agents NOT to be used Concomitantly" table): A. The patient will NOT be using the requested agent in combination with another immunomodulatory agent (e.g., TNF inhibitors, JAK inhibitors, IL-4 inhibitors) **OR** B. The patient will be using the requested agent in combination with another immunomodulatory agent AND BOTH of the following: 1. The prescribing information for the requested agent does NOT limit the use with another immunomodulatory agent **AND** 2. The prescriber has provided information in support of combination therapy (submitted copy required, e.g., clinical trials, phase III studies, guidelines required) **AND** 5. The patient does NOT have an FDA labeled contraindications to the requested agent **Compendia Allowed:** AHFS, DrugDex 1 or 2a level of evidence, or NCCN 1 or 2a recommended use

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Module	Clinical Criteria for Approval
	Length of Approval: 12 months NOTE: Quantity Limit applies, please refer to Quantity Limit criteria section below.

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Quantity Limits for the Target Agent(s) will be approved when ONE of the following is met: 1. The requested quantity (dose) does NOT exceed the program quantity limit **OR** 2. ALL of the following: A. The requested quantity (dose) exceeds the program quantity limit **AND** B. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose, or the compendia supported dose, for the requested indication **AND** C. The requested quantity (dose) cannot be achieved with a lower quantity of a higher strength that does not exceed the program quantity limit **Compendia Allowed:** AHFS, DrugDex 1 or 2a level of evidence, or NCCN 1 or 2a recommended use **Length of Approval**: 6 months for Initial; 12 months for Renewal

CONTRAINDICATION AGENTS

Contraindicated as Concomitant Therapy
Agents NOT to be used Concomitantly Abrilada (adalimumab-afzb) Actemra (tocilizumab) Adalimumab Adbry (tralokinumab-ldrm) Amjevita (adalimumab-atto) Arcalyst (rilonacept) Avsola (infliximab-axxq) Benlysta (belimumab) Bimzelx (bimekizumab-bkzx) Cibinqo (abrocitinib) Cimzia (certolizumab) Cinqair (reslizumab) Cosentyx (secukinumab)

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Contraindicated as Concomitant Therapy
Cyltezo (adalimumab-adbm)
Dupixent (dupilumab)
Enbrel (etanercept)
Entyvio (vedolizumab)
Fasenra (benralizumab)
Hadlima (adalimumab-bwwd)
Hulio (adalimumab-fkjp)
Humira (adalimumab)
Hyrimoz (adalimumab-adaz)
Idacio (adalimumab-aacf)
Ilaris (canakinumab)
Ilumya (tildrakizumab-asmn)
Inflectra (infliximab-dyyb)
Infliximab
Kevzara (sarilumab)
Kineret (anakinra)
Litfulo (ritlecitinib)
Nucala (mepolizumab)
Olumiant (baricitinib)
Omvoh (mirikizumab-mrkz)
Opzelura (ruxolitinib)
Orencia (abatacept)
Otezla (apremilast)
Remicade (infliximab)
Renflexis (infliximab-abda)
Riabni (rituximab-arrx)
Rinvoq (upadacitinib)

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Contraindicated as Concomitant Therapy
Rituxan (rituximab)
Rituxan Hycela (rituximab/hyaluronidase human)
Ruxience (rituximab-pvvr)
Siliq (brodalumab)
Simponi (golimumab)
Simponi ARIA (golimumab)
Skyrizi (risankizumab-rzaa)
Sotyktu (deucravacitinib)
Stelara (ustekinumab)
Taltz (ixekizumab)
Tezspire (tezepelumab-ekko)
Tremfya (guselkumab)
Truxima (rituximab-abbs)
Tysabri (natalizumab)
Velsipity (etrasimod)
Wezlana (ustekinumab-auub)
Xeljanz (tofacitinib)
Xeljanz XR (tofacitinib extended release)
Xolair (omalizumab)
Yuflyma (adalimumab-aaty)
Yusimry (adalimumab-aqvh)
Zeposia (ozanimod)
Zymfentra (infliximab-dyyb)

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