Pharmacy Management Drug Policy

SUBJECT: Interleukin Antagonists for Asthma and Other Conditions: Nucala (mepolizumab), Cinqair (reslizumab), Fasenra (benralizumab), & Dupixent (dupilumab)
POLICY NUMBER: Pharmacy-62
EFFECTIVE DATE: 12/15
LAST REVIEW DATE: 10/18/2019

If the member's subscriber contract excludes coverage for a specific service or prescription drug, it is not covered under that contract. In such cases, medical or drug policy criteria are not applied. Medical or drug policies apply to commercial and Health Care Reform products only when a contract benefit for the specific service exists.

DESCRIPTION:

Asthma is a heterogeneous syndrome that might be better described as a constellation of phenotypes, each with distinct cellular and molecular mechanisms, rather than as a singular disease. One of these phenotypes is eosinophilic asthma. Development of eosinophilic inflammation is dependent on the biological activity of Interleukin-5 (IL-5), an inflammatory cytokine. IL-5 is responsible for growth, differentiation, recruitment, activation, and survival of eosinophils. Nucala (mepolizumab), Cinqair (reslizumab), and Fasenra (benralizumab), IL-5 antagonist monoclonal antibodies, antagonize the IL-5/eosinophil inflammatory pathway. Nucala and Cinqair do so by binding to IL-5, and Fasenra through direct binding to the IL-5 surface receptors on eosinophils.

Dupixent (dupilumab) is a human monoclonal IgG4 antibody that inhibits interleukin-4 (IL-4) and interleukin-13 (IL-13) signaling by specifically binding to the IL-4Rα subunit shared by the IL-4 and IL-13 receptor complexes. These actions decrease interleukin signaling which reduces production and survival of eosinophils, thereby reducing inflammation.

Eosinophilic granulomatosis with polyangiitis (EGPA, also known as Churg-Strauss Syndrome [CSS]) is a systemic small- and medium-vessel necrotizing vasculitis, characterized by extravascular granulomas, eosinophilia, and tissue infiltration by eosinophils. It occurs in people with adult-onset asthma, allergic rhinitis, nasal polyposis, or a combination. Mepolizumab, by inhibiting IL-5 signaling, reduces the production and survival of eosinophils and is thought, therefore, to reduce inflammation. However, the mechanism of mepolizumab action in asthma and EGPA has not been definitively established.

Nucala (mepolizumab) is indicated for add-on maintenance treatment of patients with severe asthma aged ≥ 6 years who have an eosinophilic phenotype. Nucala is also indicated for the treatment of adult patients with eosinophilic granulomatosis with polyangiitis (EGPA).

Cinqair (reslizumab) is indicated for add-on maintenance treatment of patients with severe asthma aged ≥18 years who have an eosinophilic phenotype.

Fasenra (benralizumab) is indicated for add-on maintenance treatment of patients with severe asthma aged ≥ 12 years who have an eosinophilic phenotype.

Dupixent (dupilimumab) is indicated as an add-on maintenance treatment in patients with moderate-to-severe asthma aged 12 years and older with an eosinophilic phenotype or with oral corticosteroid-dependent asthma.

Dupixent (dupilimumab) is indicated for the treatment of patients 12 years and older with moderate-to-severe atopic dermatitis whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable.

Dupixent (dupilimumab) is indicated as an add-on maintenance treatment in adult patients with inadequately controlled chronic rhinosinusitis with nasal polyposis (CRSwNP).

POLICY:

Moderate to Severe Asthma

Based upon our criteria and review of the peer-reviewed literature, treatment with Nucala, Cinqair, Fasenra, or Dupixent administered in accordance with FDA guidelines, has been medically proven to be an effective and well tolerated treatment that reduces the risk of asthma exacerbations in patients with severe eosinophilic asthma. Therefore, it is considered **medically appropriate** if **all** of the following criteria are met:

1. Patient must be at least 12 years of age for Fasenra and Dupixent, or at least 18 years of age for Cinqair **AND**

2. Patient must be at least 12 years of age for Nucala 100 mg **prefilled syringe** or 100 mg **autoinjector** or at least 6 years of age for Nucala **vial for injection** as FDA approved dosing is 40 mg for 6-11 years of age **AND**

3. Patient must be followed by and drug ordered by an allergist/immunologist or pulmonologist **AND**

4. Patient must have moderate to severe persistent asthma **AND**

5. Patient must be a non-smoker. Non-smoker is defined as someone who has not smoked in the preceding 6 months **AND**

6. Patient must have well-documented use of high-dose inhaled corticosteroids (ICS) (see Tables 1 and 2 in policy guidelines section) for **at least 6 months**, be compliant with existing therapy, and have followed GINA guidelines for asthma treatment including an adequate trial of a high-dose inhaled steroid in combination with a long-acting beta agonist
    a. Compliance will be assessed based on pharmacy refill history. If the patient does not have pharmacy benefits through this health plan, a recent pharmacy profile will be requested. Progress notes documenting usage of sample medication may also be requested.
    b. If there is a contraindication to use of a long-acting beta agonist, then an alternative controller drug may be used in combination with a high-dose inhaled steroid such as a leukotriene inhibitor or long-acting muscarinic antagonist.

c. Patient must have documentation of inadequate control despite optimal therapy (above) for a period of at least 6 months **AND**

7. Patient must have a pre-bronchodilator forced expiratory volume in 1 second (FEV_1) of less than 80% of the predicted value (in the case of adults) OR a pre-bronchodilator FEV_1 of less than 90% of the predicted value or a ratio of the FEV_1 to the forced vital capacity (FVC) of less than 0.8 (in the case of adolescents aged 6 to 18 years) **AND**

8. For Nucala: Patient must have a peripheral blood eosinophil count of at least 150 cells per microliter within the **preceding 6 weeks** before Nucala request OR at least 300 cells per microliter at any time within the **preceding year AND (proceed to criterion #8)**
For Cingair: Patient must have a peripheral blood eosinophil count of at least 400 cells per microliter within the **preceding 6 weeks AND (proceed to criterion #8)**
For Fasenra: For non-oral steroid dependent patients - must have a peripheral blood eosinophil count of at least 300 cells per microliter within the **preceding 6 weeks;** for oral corticosteroid dependent patients – must have a peripheral blood eosinophil count of at least 150 cells per microliter within the **preceding 6 weeks AND (proceed to criterion #8)**
For Dupixent: Patient must have a peripheral blood eosinophil count of at least 150 cells per microliter within the **preceding 6 weeks.** *If the patient is oral corticosteroid dependent, then eosinophil count is not required **(proceed to criterion #8).**

*****See links to eosinophil calculators in policy guidelines section below*****

9. Patient must have experienced **3 or more** asthma exacerbations within the **preceding 12 months** that required medical intervention (defined as non-routine doctor visits, urgent care visits, emergency room visits, hospital admissions, or documented need for acute systemic steroids) despite existing therapy as outlined in Criterion #5
10. Additional consideration may be given to patients who are continuously maintained on systemic corticosteroids for the purposes of asthma control but whose exacerbation frequency or FEV_1 may not otherwise meet policy criteria.
11. Initial approval will be for 6 months. Subsequent recertifications after the initial 6-month approval will require an objective assessment of response from the provider (reductions in hospitalizations, ER visits, and rescue medication use) as well as compliance history with the inhaled corticosteroid and controller medication. Recertification will not be granted if the patient starts or re-starts smoking. See recertification statement and approval time period table in policy guidelines section of this policy.

Eosinophilic Granulomatosis with Polyangiitis (EGPA)

Based upon our criteria and review of the peer-reviewed literature, treatment with **Nucala (mepolizumab)** administered in accordance with FDA guidelines, has been medically proven to be an effective and well tolerated treatment for adult patients with eosinophilic granulomatosis with polyangiitis (EGPA, also known as Churg-Strauss Syndrome [CSS]). Therefore, it is considered **medically appropriate** if **all** of the following criteria are met:

1. Patient must be at least 18 years of age

2. Patient must be followed by and drug ordered by an allergist/immunologist, pulmonologist, or neurologist.

3. Patient must have a diagnosis of relapsing or refractory eosinophilic granulomatosis with polyangiitis (EGPA) which has existed for at least the past 6 months.
   a. Patient must have a history of relapse requiring an increase in glucocorticoid dose, initiation or increase in other immunosuppressive therapy, or hospitalization in the previous 2 years while receiving at least 7.5 mg/day prednisone (or equivalent) **OR**
   b. Within the past 6 months, the patient must have had failure to achieve remission following a standard induction regimen administered for at least 3 months OR recurrence of symptoms of EGPA whilst tapering glucocorticoids. Standard treatment regimens may include prednisone [or equivalent] dosed at least 7.5 mg/day in combination with an immunosuppressant such as cyclophosphamide, azathioprine, methotrexate, or mycophenolate mofetil. For refractory disease, if glucocorticoids are used alone, then the dose attempted must be at least 15 mg/day prednisone [or equivalent] **AND**
   c. There must be a history or presence of asthma **AND**
   There must be a blood eosinophil level of at least 10% or an absolute eosinophil count of more than 1000 cells per microliter measured within the past 6 weeks (**See links to eosinophil calculators in policy guidelines section below**) **AND**
   d. There must be presence of two or more of the following clinical findings: confirmation through biopsy, motor deficit or nerve conduction abnormality, pulmonary infiltrates, sinonasal abnormality, cardiomyopathy, glomerulonephritis, alveolar hemorrhage, palpable purpura, or positive test for antineutrophil cytoplasmic antibody (ANCA).

4. Patient must be on a stable dose of oral corticosteroids (equivalent to at least 7.5mg per day of prednisone) for at least 4 weeks immediately preceding start of Nucala therapy.

5. A baseline Birmingham Vasculitis Activity Score (BVAS) from within 4 weeks prior to start of Nucala therapy must be provided.

6. Nucala will not be approved for granulomatosis with polyangiitis (also known as GPA or Wegener's granulomatosis) or microscopic polyangiitis.

7. Recertification after the initial 6-month approval will require documentation of attainment and maintenance of remission while on Nucala. Remission is defined as BVAS equal to 0 (zero) while maintained on an oral corticosteroid dose no greater than 7.5 mg per day prednisone or equivalent. Subsequent recertifications will require documentation of ongoing maintenance of remission while on Nucala. Given the expectation that some benefit may be realized without having achieved BVAS equal to 0 (zero), consideration may be given on recertification when there is additional subjective evidence or statement of medical necessity from provider showing clear improvement in symptoms attributed to the use of Nucala which warrants continued use of the drug.

Atopic Dermatitis

Dupixent will be covered for the treatment of atopic dermatitis when the following criteria have been met:

1. Must be prescribed by or in consultation with an allergist, immunologist, or dermatologist **AND**
2. Must be ≥ 12 years of age **AND**
3. Must have a diagnosis of moderate to severe atopic dermatitis
    a. Must involve at least 10% body surface area **AND**
    b. Must have evidence of functional impact on everyday activities **AND**
4. In the past 6 months, must have had trial and failure or contraindication to:
    a. Medium to higher potency prescription topical corticosteroid therapy
        - Adequate trial is defined as ≥ 28 days or for the maximum duration recommended by the product prescribing information (i.e.; 14 days for super-potent topical corticosteroids), whichever is shorter **AND**
    b. Tacrolimus or pimecrolimus **AND**
    c. Eucrisa
5. QL of 8 ml for the first 28 days of therapy, then 4ml per 28 days thereafter.
6. Initial and subsequent approval duration for atopic dermatitis is 2 years.

Chronic Rhinosinusitis with Nasal Polyps

Dupixent will be covered for the treatment of chronic rhinosinusitis with nasal polyps when the following criteria have been met:

1. Must have a diagnosis of chronic rhinosinusitis with nasal polyps (CRSwNP) made by allergist, immunologist, or otolaryngologist. Chronic is defined as having lasted for at least 12 weeks **AND**
2. Must be ≥ 18 years of age **AND**
3. Must have:
    a. Documented inadequate response despite at least 3 months of compliant use of mometasone nasal spray at a dose of 2 sprays in each nostril twice daily (compliance will be verified through pharmacy claims history) **AND**
    b. Documented inadequate response despite at least 3 months of compliant use of Xhance nasal spray at a dose of 2 sprays in each nostril twice daily (compliance will be verified through pharmacy claims history) **AND**
4. Must have had either:
    a. Prior nasal surgery within the last 2 years **OR**
    b. Prior treatment with systemic corticosteroids within the past 6 months
        - A minimum 15-day course of prednisone at a starting dose of 40 mg per day (or other systemic corticosteroid at comparable dosing) is required **AND**
5. Must be a non-smoker, defined as someone who has not smoked in the preceding 6 months **AND**
6. Must be used in combination with an intranasal corticosteroid
    a. Dupixent as monotherapy for this indication will not be authorized as Dupixent is only FDA approved as an add-on maintenance treatment for this indication
7. Initial approval will be granted for 6 months. Recertification will require documentation of continued use of an intranasal corticosteroid (compliance will be verified through pharmacy claims history) and clinical benefit from Dupixent use. Subsequent approval will be granted for 2 years and will require

documentation of continued use of an intranasal corticosteroid with compliance verified through pharmacy claims history.

POLICY GUIDELINES:

1. Prior-authorization is contract dependent.

2. Cinqair is administered by a healthcare professional and is covered under the medical benefit.

3. Fasenra prefilled syringe is administered by a healthcare professional and is covered under the medical benefit. Fasenra autoinjector (Fasenra PEN) is self-administered and is covered under the pharmacy benefit.

4. Dupixent is self-administered and is covered under the pharmacy benefit.

5. Nucala vial for injection is administered by a healthcare professional for patients 6 years of age and older and is covered under the medical benefit. Nucala prefilled autoinjector and prefilled syringe is self-administered for patients 12 years of age and older and is covered under the pharmacy benefit.

6. Nucala dosing for asthma for adults, adolescents, and children 12 years and older: 100 mg subcutaneously once every 4 weeks. Nucala dosing for asthma for patients aged 6 to 11 years: 40 mg subcutaneously once every 4 weeks. Nucala dosing for EGPA: 300mg subcutaneously once every 4 weeks (as 3 separate 100-mg injections into the upper arm, thigh, or abdomen).

   Cinqair dosing for adults 18 years of age and older: 3 mg/kg intravenously once every 4 weeks.

   Fasenra dosing for adults, adolescents, and children 12 years and older: 30 mg subcutaneously once every 4 weeks for the first 3 doses, then 30 mg subcutaneously once every 8 weeks thereafter (into the upper arm, thigh, or abdomen). Another loading dose will not be granted for patients who have received a loading dose under the pharmacy or medical benefit and request to switch to the other benefit for continued therapy.

   Dupixent is self-administered with indication-dependent dosing as follows:

   - Eosinophilic asthma:
     Initial dosage:
     400 mg subcutaneously (given as two 200 mg injections) or 600 mg subcutaneously (given as two 300 mg injections)

     Maintenance dosage:
     200 mg (following 400 mg initial dose) or 300 mg (following 600 mg initial dose) subcutaneously once every other week

   - Oral corticosteroids-dependent asthma, or patients with co-morbid moderate-to-severe atopic dermatitis for which DUPIXENT is indicated:
     Initial dosage:

600 mg subcutaneously (given as two 300 mg injections)

Maintenance dosage:
300 mg subcutaneously given once every other week

- Atopic dermatitis:
  Adults
  Initial dosage:
  600 mg subcutaneously (given as two 300 mg injections)

  Maintenance dosage:
  300 mg subcutaneously given once every other week

  Adolescents (12-17 years)

Body Weight	Initial Dose	Subsequent Doses (every other week)
less than 60 kg	400 mg (two 200 mg injections)	200 mg
60 kg or more	600 mg (two 300 mg injections)	300 mg

- Chronic rhinosinusitis with nasal polyps:
  300 mg subcutaneously given once every other week

Cinqair will only be authorized when administered by a healthcare professional in the prescriber's office or within a supervised medical treatment facility. Because of the risk of anaphylaxis, patients should be closely observed for an appropriate period of time after administration and health care providers administering Cinqair should be prepared to manage anaphylaxis which can be life-threatening. Patients should also be informed of the signs and symptoms of anaphylaxis and instructed to seek immediate medical care should symptoms occur.

7. Nucala, Cinqair, Fasenra, and Dupixent will not be authorized in the following circumstances:
   a. Concurrent use with omalizumab (Xolair) for asthma
   b. Concurrent use with any other interleukin inhibitor for asthma
   c. Nucala is only approved for subcutaneous injection. Cinqair is only approved for intravenous infusion. Fasenra is only approved for subcutaneous injection. Dupixent is only approved for subcutaneous injection. Administration in any manner other than which drug is FDA-approved will not be authorized.
   d. Diagnoses of any non-FDA approved indication
   e. Relief of acute bronchospasm or status asthmaticus
   f. Any non-FDA approved dosing regimen

8. If Nucala, Cinqair, Fasenra, or Dupixent therapy is initiated with samples and the member does not meet policy criteria for coverage (as outlined above) before the start of therapy, coverage will not be granted upon completion of samples.

9. **Nucala** authorization for asthma treatment will not be granted for patients <6 years of age as Nucala has not been proven safe and effective in this patient population. For the diagnosis of

EGPA, Nucala will not be authorized for patients <18 years of age. **Cinqair** authorization will not be granted for patients <18 years of age as Cinqair has not been proven safe and effective in this patient population. **Fasenra** authorization will not be granted for patients <12 years of age as Fasenra has not been proven safe and effective in this patient population. For both asthma and atopic dermatitis, authorization of **Dupixent** will not be granted for patients <12 years of age as Dupixent has not been proven safe and effective in this patient population.

10. Safety of concurrent use of Nucala, Cinqair, Fasenra, and Dupixent with other monoclonal antibodies used to treat inflammation (TNF-inhibitors, interleukin antagonists, etc.) has not been established.

11. For contracts where Insurance Law § 4903(c-1), and Public Health Law § 4903(3-a) are applicable, if trial of preferred drug(s) is the only criterion that is not met for a given condition, and one of the following circumstances can be substantiated by the requesting provider, then trial of the preferred drug(s) will not be required.
    a. The required prescription drug(s) is (are) contraindicated or will likely cause an adverse reaction or physical or mental harm to the member;
    b. The required prescription drug is expected to be ineffective based on the known clinical history and conditions and concurrent drug regimen;
    c. The required prescription drug(s) was (were) previously tried while under the current or a previous health plan, or another prescription drug or drugs in the same pharmacologic class or with the same mechanism of action was (were) previously tried and such prescription drug(s) was (were) discontinued due to lack of efficacy or effectiveness, diminished effect, or an adverse event;
    d. The required prescription drug(s) is (are) not in the patient's best interest because it will likely cause a significant barrier to adherence to or compliance with the plan of care, will likely worsen a comorbid condition, or will likely decrease the ability to achieve or maintain reasonable functional ability in performing daily activities;
    e. The individual is stable on the requested prescription drug. The medical profile of the individual (age, disease state, comorbidities), along with the rational for deeming stability as it relates to standard medical practice and evidence-based practice protocols for the disease state will be taken into consideration.
    f. The above criteria are not applicable to requests for brand name medications that have an AB rated generic. We can require a trial of an AB-rated generic equivalent prior to providing coverage for the equivalent brand name prescription drug.

12. **Unless otherwise stated above** within the individual drug criteria, approval time periods are listed in the table below.
    a. Continued approval at time of recertification will require documentation that the drug is providing ongoing benefit to the patient in terms of improvement or stability

in disease state or condition. Such documentation may include progress notes, imaging or laboratory findings, and other objective or subjective measures of benefit which support that continued use of the requested product is medically necessary. Also, ongoing use of the requested product must continue to reflect the current policy's preferred formulary. Recertification reviews may result in the requirement to try more cost-effective treatment alternatives as they become available (i.e.; generics, biosimilars, or other guideline-supported treatment options). Requested dosing must continue to be consistent with FDA-approved or off-label/guideline-supported dosing recommendations.

Line of Business	Initial approval	Continued approval
Medicaid Managed Care (MMC) / Child Health Plus (CHP)	6 months	12 months
Commercial / Exchange	Outpatient Hospital – 6 months	Outpatient Hospital – 6 months
	Home Care or Office Based – 6 months	Home Care or Office Based – 2 years
Medicare	Outpatient Hospital – 6 months	Outpatient Hospital – 6 months
	Home Care or Office Based – 6 months	Home Care or Office Based – 2 years

13. Tables 1 and 2. Estimated comparative daily doses for inhaled glucocorticoids in adolescents and adults; Usual doses of combination inhaled glucocorticoids and long-acting beta-agonists for the treatment of asthma in adolescents age 12 and older and adults

Estimated comparative daily doses for inhaled glucocorticoids in adolescents and adults

Drug	Low dose	Medium dose	High dose
Beclomethasone HFA (Qvar and Qvar RediHaler products available in United States)*	80 to 160 mcg	>160 to 320 mcg	>320 mcg
40 mcg per puff	2 to 4 puffs	¶	¶
80 mcg per puff	1 to 2 puffs	3 to 4 puffs	>4 puffs
Beclomethasone HFAΔ (Qvar product available in Canada, Europe, and elsewhere)	100 to 200 mcg	>200 to 400 mcg	>400 mcg
50 mcg per puff	2 to 4 puffs	¶	¶
100 mcg per puff	1 to 2 puffs	3 to 4 puffs	>4 puffs
Budesonide DPI (Pulmicort Flexhaler product available in United States)*	180 to 360 mcg	>360 to 720 mcg	>720 mcg
90 mcg per inhalation	2 to 4 inhalations	¶	¶
180 mcg per inhalation	1 to 2 inhalations	3 to 4 inhalations	>4 inhalations
Budesonide DPIΔ (Pulmicort Turbuhaler product available in Canada, Europe, and elsewhere)	200 to 400 mcg	>400 to 800 mcg	>800 mcg
100 mcg per inhalation	2 to 4 inhalations	¶	¶
200 mcg per inhalation	1 to 2 inhalations	3 to 4 inhalations	¶
400 mcg per inhalation	1 inhalation	2 inhalations	>2 inhalations
Ciclesonide HFA (Alvesco product available in United States, Europe, and elsewhere)*	80 to 160 mcg	>160 to 320 mcg	>320 mcg
80 mcg per puff	1 to 2 puffs	3 to 4 puffs	¶
160 mcg per puff	1 puff	2 puffs	>2 puffs
Ciclesonide HFAΔ (Alvesco product available in Canada)	100 to 200 mcg	>200 to 400 mcg	>400 mcg
100 mcg per puff	1 to 2 puffs	3 to 4 puffs	¶
200 mcg per puff	1 puff	2 puffs	>2 puffs
Flunisolide MDI (Aerospan product available in United States)*	320 mcg	>320 to 640 mcg	Insufficient data
80 mcg per puff	4 puffs	5 to 8 puffs	Insufficient data
Fluticasone propionate HFA (Flovent HFA product available in United States)*	88 to 220 mcg	>220 to 440 mcg	>440 mcg
44 mcg per puff	2 to 5 puffs	¶	¶
110 mcg per puff	1 to 2 puffs	3 to 4 puffs	¶
220 mcg per puff	○	2 puffs	>2 puffs
Fluticasone propionate HFAΔ (Flovent HFA product available in Canada, Europe, and elsewhere)	100 to 250 mcg	>250 to 500 mcg	>500 mcg
50 mcg per puff	2 to 5 puffs	¶	¶
125 mcg per puff	1 to 2 puffs	3 to 4 puffs	¶
250 mcg per puff	○	2 puffs	>2 puffs
Fluticasone propionate DPI (Flovent Diskus product available in United States and Canada)*	100 to 250 mcg	>250 to 500 mcg	>500 mcg
50 mcg per inhalation	2 to 5 inhalations	¶	¶
100 mcg per inhalation	1 to 2 inhalations	3 to 5 inhalations	¶
250 mcg per inhalation	1 inhalation	2 inhalations	>2 inhalations
500 mcg per inhalation (strength not available in United States)	○	1 inhalation	>1 inhalation
Fluticasone propionate DPI (Armonair Respiclick product available in United States)*	100 to 250 mcg	>250 to 500 mcg	>500 mcg
55 mcg per inhalation	2 to 4 inhalations	¶	¶
113 mcg per inhalation	1 to 2 inhalations	3 to 4 inhalations	>4 inhalations
232 mcg per inhalation	1 inhalation	2 inhalation	>2 inhalations
Fluticasone furoate DPI (Arnuity Ellipta product available in United States)* **NOTE:** Inhaled fluticasone furoate has a greater anti-inflammatory potency per microgram than fluticasone propionate inhalers. Thus, fluticasone furoate is administered at a lower daily dose and used only once daily.	50 mcg (by use of pediatric DPI, which is off-label in adolescents and adults)	100 mcg	200 mcg
50 mcg per inhalation	1 inhalation	¶	¶
100 mcg per inhalation	○	1 inhalation	2 inhalations
200 mcg per actuation	○	○	1 inhalation
Mometasone DPI§ (Asmanex DPI product available in United States)*	110 to 220 mcg	>220 to 440 mcg	>440 mcg
110 mcg per inhalation	1 to 2 inhalations	¶	¶
220 mcg per inhalation	1 inhalation	2 inhalations	>2 inhalations
Mometasone HFA§ (Asmanex HFA product available in United States)*	100 to 200 mcg	>200 to 400 mcg	>400 mcg
100 mcg per actuation	1 to 2 inhalations	¶	¶
200 mcg per actuation	1 inhalation	2 inhalations	>2 inhalations
Mometasone DPI§§ (Asmanex Twisthaler product available in Canada, Europe, and elsewhere)	200 mcg	>200 to 400 mcg	>400 mcg
200 mcg per inhalation	1 inhalation	2 inhalations	>2 inhalations
400 mcg per inhalation	○	1 inhalation	>1 inhalation

- **The most important determinant of appropriate dosing is the clinician's judgment of the patient's response to therapy.** The clinician must monitor the patient's response on several clinical parameters and adjust the dose accordingly. The stepwise approach to therapy emphasizes that once control of asthma is achieved, the dose of medication should be carefully titrated to the minimum dose required to maintain control, thus reducing the potential for adverse effects.
- Depending on the specific product, total daily doses are administered once or twice daily.
- Some doses are outside the approved product information recommendations.

DPI: dry powder inhaler; HFA: hydrofluoroalkane propellant metered dose inhaler.
* Doses shown and strengths (ie, mcg per puff or inhalation) are based upon product descriptions approved in the United States which may differ from how strengths are described for products available in other countries. Consult local product information before use.
¶ Select alternate preparation with higher mcg/puff to improve convenience.
Δ Products shaded in light blue color are not available in the United States but are available widely elsewhere.
○ Select preparation with fewer mcg/puff.
§ Approved for once-daily dosing in mild asthma in some countries.

National Heart, Blood, and Lung Institute Expert Panel Report 3 (EPR 3): Guidelines for the Diagnosis and Management of Asthma; 2007. NIH Publication 08-4051 available at http://www.nhlbi.nih.gov/health-pro/guidelines/current/asthma-guidelines/full-report; updated with additional data from Global Initiative for Asthma (GINA); Global Strategy for Asthma Management and Prevention; 2017. Available at www.ginasthma.org

Usual doses of combination inhaled glucocorticoids and long-acting beta-agonists for the treatment of asthma in adolescents age 12 and older and adults

Medication	Low dose	Medium dose	High dose
Budesonide-formoterol HFA (Brand name: Symbicort)			
80 mcg-4.5 mcg	2 puffs twice a day		
160 mcg-4.5 mcg		2 puffs twice a day	
Fluticasone furoate-vilanterol DPI (Brand name: Breo Ellipta)*			
NOTE: Inhaled fluticasone furoate has a greater anti-inflammatory potency per microgram than fluticasone propionate inhalers. Thus, fluticasone furoate is administered at a lower daily dose and used only **once** daily.			
100 mcg-25 mcg		1 inhalation once daily	
200 mcg-25 mcg			1 inhalation once daily
Fluticasone propionate-salmeterol DPI (Brand name: Advair Diskus)			
100 mcg-50 mcg	1 inhalation twice a day		
250 mcg-50 mcg		1 inhalation twice a day	
500 mcg-50 mcg			1 inhalation twice a day
Fluticasone propionate-salmeterol HFA (Brand name: Advair HFA)			
45 mcg-21 mcg	2 puffs twice a day		
115 mcg-21 mcg		2 puffs twice a day	
230 mcg-21 mcg			2 puffs twice a day
Fluticasone propionate-salmeterol DPI (Brand name: AirDuo RespiClick)¶			
55 mcg-14 mcg	1 inhalation twice a day		
113 mcg-14 mcg	1 inhalation twice a day	1 inhalation twice a day	
232 mcg-14 mcg			1 inhalation twice a day
Mometasone-formoterol HFA (Brand name: Dulera)			
100 mcg-5 mcg		2 puffs twice a day	
200 mcg-5 mcg			2 puffs twice a day

Do not exceed the maximum number of inhalations/puffs per day listed in the table due to the risk of toxicity from an excess dose of long acting beta-agonist (ie, salmeterol, formoterol, or vilanterol). Brand names and dose per puff or per inhalation of commercially available fixed dose combinations are according to United States licensed product information. Consult local product information before use.

HFA: metered dose inhaler with hydrofluoroalkane propellant; DPI: dry powder inhaler.
* Not approved for use in patients <18 years old.
¶ In AirDuo inhalers the daily dose of salmeterol is approximately one-fourth of the dose in Advair, and the daily dose of fluticasone is approximately one-half that of the comparable low, medium, and high dose strengths of Advair. AirDuo contains lactose.

UpToDate®

14. The following websites have eosinophil calculators for converting reported units:
    a. http://gsknucala.com/
    b. https://www.fasenrahcp.com/m/fasenra-eosinophil-calculator.html
    c. https://www.omnicalculator.com/health/eosinophil-count
    d. https://www.merckmanuals.com/medical-calculators/AbsEoCount.htm

UPDATES:

Date:	Revision:
10/19	Revision
9/19	Revision
7/19	Revision
6/19	Revision
5/19	Revision
3/19	Revision
2/19	Committee Approval
1/19	Revision
11/18	Revision
9/18	Revision
3/18	Revision
2/18	Revision
12/17	Revision
7/17	Revision
4/16	Revision
3/16	Revision
1/16	Revision
12/15	Created

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