

Clinical Policy: Inhaled Agents for Asthma and COPD

Reference Number: CP.PMN.259

Effective Date: 03.01.21

Last Review Date: 02.25

Line of Business: Medicaid

[Coding Implications](#)

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

Description

The following are inhaled agents for asthma and/or chronic obstructive pulmonary disease (COPD) requiring prior authorization:

- Short acting beta-2 agonist (SABA): albuterol (ProAir[®] Digihaler[®])
- Inhaled corticosteroid (ICS): budesonide (Pulmicort Respules^{®*}, Pulmicort Flexhaler[™]), ciclesonide (Alvesco[®]), fluticasone (ArmonAir[®] Digihaler[™], Flovent[®] HFA, Flovent[®] Diskus[®]), mometasone (Asmanex[®] Twisthaler[®])
- Long acting beta-2 agonist (LABA): arformoterol (Brovana[®]), formoterol (Perforomist), indacaterol (Arcapta[®] Neohaler[®]), olodaterol (Striverdi[®] Respimat[®])
- Long acting muscarinic antagonist (LAMA): glycopyrrolate (Seebri[™] Neohaler[®], Lonhala[®] Magnair[®]), tiotropium bromide monohydrate (Spiriva[®] Respimat[®]), revefenacin (Yupelri[®])
- Combination ICS/LABA: budesonide/formoterol (Symbicort[®], Symbicort Aerosphere^{®*}), fluticasone/vilanterol (Breo Ellipta[®]), fluticasone/salmeterol (Advair Diskus^{®*}, Advair HFA[®], AirDuo[®] Digihaler[™], AirDuo[®] RespiClick[®]), mometasone/formoterol (Dulera[®])
- Combination LABA/LAMA: aclidinium/formoterol (Duaklir[®] Pressair[®]), glycopyrrolate/formoterol (Bevespi Aerosphere[™]), indacaterol/glycopyrrolate (Utibron[™] Neohaler[®]), tiotropium/olodaterol (Stiolto[®] Respimat[®]), umeclidinium/vilanterol (Anoro[®] Ellipta[®])
- Combination ICS/LAMA/LABA: fluticasone/umeclidinium/vilanterol (Trelegy[™] Ellipta[®]), budesonide/glycopyrrolate/formoterol (Breztri Aerosphere[™])
- Phosphodiesterase 3 (PDE3) inhibitor and phosphodiesterase 4 (PDE4) inhibitor: ensifentrine (Ohtuvayre[™])

**Generic agents do not require prior authorization.*

FDA Approved Indication(s)

ProAir Digihaler is indicated for the:

- Treatment or prevention of bronchospasm in patients 4 years of age and older with reversible obstructive airway disease
- Prevention of exercise-induced bronchospasm (EIB) in patients 4 years of age and older

The other inhaled agents are indicated as follows:

Drug Name	Asthma	COPD
ICS		
Alvesco	X (Age ≥ 12 years)	
ArmonAir Digihaler	X (Age ≥ 4 years)	
Asmanex Twisthaler	X (Age ≥ 4 years)	

Drug Name	Asthma	COPD
Flovent Diskus, Flovent HFA	X (Age ≥ 4 years)	
Pulmicort Flexhaler	X (Age ≥ 6 years)	
Pulmicort Respules	X (Age 1-8 years)	
LABA		
Arcapta Neohaler		X
Brovana		X
Perforomist		X
Striverdi Respimat		X
LAMA		
Lonhala Magnair		X
Seebri Neohaler		X
Spiriva Respimat	X (Age ≥ 6 years)	X
Yupelri		X
ICS/LABA		
Advair Diskus	X (Age ≥ 4 years)	X
Advair HFA	X (Age ≥ 12 years)	
AirDuo Digihaler	X (Age ≥ 12 years)	
AirDuo RespiClick	X (Age ≥ 12 years)	
Breo Ellipta	X (Age ≥ 5 years)	X
Dulera	X (Age ≥ 5 years)	
Symbicort	X (Age ≥ 6 years)	X
Symbicort Aerosphere		X
LABA/LAMA		
Anoro Ellipta		X
Bevespi Aerosphere		X
Duaklir Pressair		X
Stiolto Respimat		X
Utibron Neohaler		X
ICS/LABA/LAMA		
Breztri Aerosphere		X
Trelegy Ellipta	X (Age ≥ 18 years)	X
PDE3/PDE4 Inhibitor		
Ohtuvayre		X

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation[®] that inhaled agents for asthma and COPD are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

- A. Inhaled Agents for Asthma or Chronic Obstructive Pulmonary Disease** (must meet all):

1. Diagnosis of asthma or COPD as FDA-approved for the requested agent (*see FDA Approved Indications section*);
2. Age is one of the following (a or b):
 - a. Asthma (i or ii):
 - i. For Flovent HFA: ≤ 12 years;
 - ii. For all other agents: Appropriate age limit per the prescribing information for the requested agent (*see FDA Approved Indications section*);
 - b. COPD: ≥ 18 years;
3. Failure of the following formulary agent(s) at up to maximally indicated doses, unless clinically significant adverse effects are experienced or all are contraindicated:

Requested Agent	Required Step Through Agent(s)
ProAir Digihaler	Two generic albuterol sulfate HFA products, each from a different manufacturer
Brand Pulmicort Respules	Medical justification supports inability to use generic Pulmicort Respules (e.g., contraindications to excipients) <i>AND</i> either age is between 1 to 8 years or documentation supports inability to use inhaler devices
Flovent HFA	Fluticasone propionate HFA (Flovent HFA authorized generic)
Flovent Diskus	Fluticasone propionate diskus (Flovent Diskus authorized generic)
<u>All other ICS</u> : Alvesco, ArmonAir Digihaler, Asmanex Twisthaler, Pulmicort Flexhaler	Qvar [®] RediHaler [™] , Arnuity [®] Ellipta [®] , fluticasone propionate diskus (Flovent Diskus authorized generic), <i>AND</i> Asmanex [®] HFA
<u>LABA</u> : Arcapta Neohaler, Brovana, Perforomist, Striverdi Respimat	Serevent [®] Diskus [®] , unless request is for a nebulized LABA and documentation supports inability to use inhaler devices
<u>LAMA</u> : Lonhala Magnair, Seebri Neohaler, Spiriva Respimat, Yupelri	Incruse [®] Ellipta [®] , Tudorza [®] Pressair [®] , <i>AND</i> generic Spiriva [®] Handihaler, unless request is for a nebulized LAMA and documentation supports inability to use inhaler devices
Brand Advair Diskus, Advair HFA	Medical justification supports inability to use generic fluticasone/salmeterol products (generic Advair Diskus, Wixela [™] Inhub [™]) (e.g., contraindications to excipients)
Brand Symbicort, Symbicort Aerosphere	Medical justification supports inability to use generic Symbicort (e.g., contraindications to excipients)
Breo Ellipta	<ul style="list-style-type: none"> • For age ≥ 6 years: fluticasone/salmeterol (generic Advair Diskus or Wixela Inhub) <i>AND</i> budesonide/formoterol (generic Symbicort) • For age < 6 years: fluticasone/salmeterol (generic Advair Diskus or Wixela Inhub)

Requested Agent	Required Step Through Agent(s)
<u>All other ICS/LABA:</u> AirDuo Digihaler, AirDuo RespiClick, Dulera	Fluticasone/salmeterol (generic Advair Diskus or Wixela Inhub) <i>AND</i> budesonide/formoterol (generic Symbicort)
<u>LABA/LAMA:</u> Anoro Ellipta, Bevespi Aerosphere, Duaklir Pressair, Stiolto Respimat, Utibron Neohaler	One LABA (e.g., Serevent Diskus) in combination with one LAMA (e.g., Incruse Ellipta)
<u>ICS/LABA/LAMA:</u> Breztri Aerosphere, Trelegy Ellipta	<ul style="list-style-type: none"> • For COPD only: one LABA (e.g., Serevent Diskus) in combination with one LAMA (e.g., Incruse Ellipta) • For asthma only: fluticasone/salmeterol (generic Advair Diskus or Wixela Inhub) <i>OR</i> budesonide/formoterol (generic Symbicort)
Ohtuvayre	<ul style="list-style-type: none"> • One LABA (e.g., Serevent Diskus) in combination with one LAMA (e.g., Incruse Ellipta) <p><i>AND</i></p> <ul style="list-style-type: none"> • For members with blood eosinophil count ≥ 100 cells/mcL: Breztri Aerosphere <i>OR</i> Trelegy Ellipta <p><i>Note: Prior failure of triple therapy (ICS/LABA/LAMA) satisfies the requirement for failure of dual therapy (LABA/LAMA).</i></p>

4. For requests for an agent with a digital component (e.g., Digihaler products): Medical justification supports necessity of the digital component (i.e., rationale why inhaler usage cannot be tracked manually);
5. For requests for Ohtuvayre, both of the following (a and b):
 - a. Member has moderate-to-severe COPD as evidenced by one of the following (i or ii):
 - i. Pre- and post-albuterol forced expiratory volume (FEV₁)/forced vital capacity (FVC) ratio of < 0.70 ;
 - ii. Post-albuterol FEV₁ ≥ 30 % and ≤ 70 % of predicted normal;
 - b. Ohtuvayre is not prescribed in combination with Daliresp[®];
6. Request does not exceed one of the following (a or b):
 - a. The health plan quantity limit;
 - b. The FDA-approved maximum dose for the relevant indication (see *Section V*).

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2):

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):

- a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.PMN.255 for Medicaid; or
 - b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Inhaled Agents for Asthma or Chronic Obstructive Pulmonary Disease (must meet all):

1. Member meets one of the following (a or b):
 - a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
 - b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B*);
2. Member is responding positively to therapy;
3. If request is for a dose increase, request does not exceed one of the following (a or b):
 - a. The health plan quantity limit;
 - b. The FDA-approved maximum dose for the relevant indication (see *Section V*).

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2):

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
 - a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.PMN.255 for Medicaid; or
 - b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

- A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

COPD: chronic obstructive pulmonary disease
 EIB: exercise-induced bronchospasm
 FDA: Food and Drug Administration
 FEV₁: forced expiratory volume
 FVC: forced vital capacity
 ICS: inhaled corticosteroid
 GINA: Global Initiative for Asthma

GOLD: Global Initiative for Chronic Obstructive Lung Disease
 LABA: long acting beta-2 agonist
 LAMA: long acting muscarinic antagonist
 PDE: phosphodiesterase
 SABA: short acting beta-2 agonist

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
albuterol (Proventil HFA [®] , Ventolin HFA [®])	<i>Metered-dose inhaler (MDI): 2 puffs every 4 to 6 hours as needed</i> <i>Nebulization solution: 2.5 mg via oral inhalation every 6 to 8 hours as needed</i>	<i>MDI: 12 puffs/day</i> <i>Nebulization solution: 4 doses/day or 10 mg/day</i> Higher maximum dosages for inhalation products have been recommended in National Asthma Education and Prevention Program guidelines for acute exacerbations of asthma.
Arnuity Ellipta (fluticasone furoate)	Asthma: ≥ 12 years: 100-200 mcg inhaled QD 5-11 years: 50 mcg inhaled QD	Asthma: ≥ 12 years: 200 mcg/day 5-11 years: 50 mcg/day
budesonide/formoterol (Symbicort)	Asthma: 2 inhalations BID COPD: 2 inhalations (160/4.5 mcg) BID	Asthma/COPD: 160/4.5 mcg BID
fluticasone/salmeterol (Advair Diskus, Wixela Inhub)	Asthma: 1 inhalation BID (starting dosage is based on asthma severity) COPD: 1 inhalation of 250/50 mcg BID	Asthma: 500/50 mcg BID COPD: 250/50 mcg BID

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Incruse Ellipta (umeclidinium)	COPD: 1 inhalation (62.5 mcg) QD	COPD: 62.5 mcg/day
Qvar RediHaler (beclomethasone)	Asthma: ≥ 12 years: 40 mcg, 80 mcg, 160 mcg, or 320 mcg inhaled BID 4-11 years: 40 mcg or 80 mcg inhaled BID	Asthma: ≥ 12 years: 640 mcg/day 4-11 years: 160 mcg/day
Serevent (salmeterol)	Asthma/COPD: 1 inhalation (50 mcg) BID	Asthma/COPD: 100 mcg/day
Tudorza Pressair (aclidinium)	COPD: 1 inhalation (400 mcg) BID	COPD: 800 mcg/day
Asmanex HFA	Asthma: 2 inhalations BID (starting dosage is based on age and asthma severity)	800 mcg/day
tiotropium bromide monohydrate (Spiriva Handihaler)	COPD: Two inhalations (18 mcg) QD	18 mcg/day

Therapeutic alternatives are listed as Brand name[®] (generic) when the drug is available by brand name only and generic (Brand name[®]) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
 - All agents: hypersensitivity to any component of the requested agent or the following as additionally specified:
 - Advair Diskus, AirDuo Digihaler/RespiClick, Anoro Ellipta, ArmonAir Digihaler, Asmanex Twisthaler, Breo Ellipta, Flovent Diskus, Flovent HFA, Pulmicort Flexhaler, Trelegy Ellipta: milk proteins
 - Brovana: racemic formoterol
 - Advair HFA/Diskus, AirDuo Digihaler/RespiClick, Alvesco, ArmonAir Digihaler, Asmanex Twisthaler, Breo Ellipta, Dulera, Flovent Diskus, Flovent HFA, Pulmicort Flexhaler/Respules, Trelegy Ellipta: primary treatment of status asthmaticus or acute episodes of asthma or COPD requiring intensive measures
 - Anoro Ellipta, Arcapta Neohaler, Bevespi Aerosphere, Brovana, Duaklir Pressair, Stiolto Respimat, Striverdi Respimat, Perforomist, Utibron Neohaler: use of a LABA without an ICS in patients with asthma
- Boxed warning(s): none reported

Appendix D: General Information

- Although inhaler devices with a digital component may offer increased convenience with tracking of inhaler usage, there is currently no evidence that this leads to improved clinical outcomes, including safety and effectiveness.
- Per the Global Initiative for Chronic Obstructive Lung Disease (GOLD) COPD guidelines, combination therapy (LAMA + LABA or ICS + LAMA + LABA) is recommended for Group B and E patients (i.e., those who are very symptomatic or are at

high risk of exacerbation). Selection of which combination to use depends on the individual patient:

- For those with more severe symptoms, LAMA + LABA may be used.
- For those who are inadequately controlled by dual therapy or with blood eosinophil counts at least 300 cells/uL, triple therapy with ICS + LAMA + LABA may be used.
- As of the 2023 guideline update, use of LABA + ICS in COPD is no longer encouraged. If there is an indication for an ICS, then LABA + LAMA + ICS has been shown to be superior to LABA + ICS and is therefore the preferred choice.
- Ohtuvayre may be considered in patients experiencing dyspnea despite LABA + LAMA therapy. For patients experiencing exacerbations despite LABA + LAMA therapy, triple therapy with ICS + LAMA + LABA is instead recommended. This is because while Ohtuvayre improves lung function, its effect on exacerbations has not been evaluated in patients at increased exacerbation risk; conversely, ICS + LAMA + LABA has been shown to reduce exacerbations and may also confer mortality benefit.
- Historical management of asthma has involved an as-needed short-acting beta agonist for reliever therapy, with stepwise approach to add on controller maintenance therapies such as inhaled corticosteroids and long-acting beta agonists. In 2019, the Global Initiative for Asthma (GINA) guidelines for asthma management and prevention began recommending that inhaled corticosteroids be initiated as soon as possible after diagnosis of asthma, including use as reliever therapy (to be administered as-needed alongside a short-acting beta agonist). The National Asthma Education and Prevention Program from the National Heart, Lung, and Blood Institute followed suit with their recommendations in 2020.
- Alvesco: Use in pediatric patients < 12 years of age: Two identically designed randomized, double-blind, parallel, placebo-controlled clinical trials of 12-weeks treatment duration were conducted in 1,018 patients aged 4 to 11 years with asthma but efficacy was not established. In addition, one randomized, double-blind, parallel, placebo-controlled clinical trial did not establish efficacy in 992 patients aged 2 to 6 years with asthma.
- Trelegy Ellipta: In its pivotal trial for asthma, all patients enrolled were inadequately controlled on their current treatments of combination therapy (ICS + LABA). In addition, per the GINA guidelines, the addition of a LAMA to combination medium/high dose ICS + LABA can be considered as an alternative controller option at steps 4/5, following use of /medium/high dose ICS + LABA.

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Advair Diskus	Asthma	1 inhalation BID (starting dosage is based on asthma severity)	500/50 mcg BID
	COPD	1 inhalation of 250/50 mcg BID	250/50 mcg BID
Advair HFA	Asthma	2 inhalations BID (starting dosage is based on asthma severity)	2 inhalations of 230/21 mcg BID
AirDuo Digihaler	Asthma	1 inhalation BID (starting dosage is based on asthma severity)	232/14 mcg BID
AirDuo RespiClick	Asthma	1 inhalation BID (starting dosage is based on asthma severity)	232/14 mcg BID

Drug Name	Indication	Dosing Regimen	Maximum Dose
Alvesco	Asthma	Starting dose for patients who received bronchodilators alone: 80 mcg inhaled BID	320 mcg/day
		Starting dose for patients who received inhaled corticosteroids: 80 mcg inhaled BID	640 mcg/day
		Starting dose for patients who received oral corticosteroids: 320 mcg inhaled BID	640 mcg/day
Anoro Ellipta	COPD	One inhalation by mouth QD	1 inhalation/day
Arcapta Neohaler	COPD	75 mcg inhaled orally QD	75 mcg/day
ArmonAir Digihaler	Asthma	1 inhalation BID (starting dosage is based on asthma severity and age)	232 mcg BID
Asmanex Twisthaler	Asthma	Dose varies based on previous therapy and age: 1 inhalation QD-BID	880 mcg/day
Bevespi Aerosphere	COPD	2 inhalations BID	4 inhalations/day
Breo Ellipta	Asthma	Age ≥ 18 years: 1 inhalation of 100/25 or 200/25 mcg QD Age 12-17 years: 1 inhalation of 100/25 mcg QD Age 5-11 years: 1 inhalation of 50/25 mcg QD	200/25 mcg/day
	COPD	1 inhalation of 100/25 mcg QD	100/25 mcg/day
Breztri Aerosphere	COPD	2 inhalations by mouth BID	4 inhalations/day
Brovana	COPD	One 15 mcg/2 mL vial inhaled via nebulizer every 12 hours	30 mcg/day
Duaklir Pressair	COPD	One inhalation by mouth BID	2 inhalations/day
Dulera	Asthma	Age 5 to 11 years: 2 inhalations of 50/5 mcg BID	200/5 mcg/day
		Age ≥ 12 years: 2 inhalations of 100/5 mcg or 200/5 mcg BID (starting dosage is based on asthma severity)	800/20 mcg/day
Flovent Diskus	Asthma	1 inhalation BID (starting dosage is based on asthma severity)	2,000 mcg/day
Flovent HFA	Asthma	Patients aged 12 years and older: 88 mcg twice daily up to a maximum dosage of 880 mcg twice daily.	880 mcg BID

Drug Name	Indication	Dosing Regimen	Maximum Dose
		Pediatric patients aged 4 to 11 years: 88 mcg twice daily	
Lonhala Magnair	COPD	One 25 mcg vial inhaled via nebulizer BID	50 mcg/day
Ohtuvayre	COPD	3 mg (one ampule) inhaled via nebulizer BID	6 mg/day
Perforomist	COPD	One 20 mcg/2 mL vial inhaled via nebulizer every 12 hours	40 mcg/day
ProAir Digihaler	Treatment or prevention of bronchospasm	2 inhalations every 4 to 6 hours	12 inhalations/day
	Prevention of EIB	2 inhalations 15 to 30 minutes before exercise	2 inhalations before exercise
Pulmicort Flexhaler	Asthma	Starting dose of 180-360 mcg inhaled BID	720 mcg BID
Pulmicort Respules	Asthma	Starting dose for patients who received bronchodilators alone or inhaled corticosteroids: 0.5 mg inhaled per day (0.5 mg QD or 0.25 mg BID; for inhaled corticosteroids, may go up to 0.5 mg BID) Starting dose for patients who received oral corticosteroids: 1 mg inhaled per day (1 mg QD or 0.5 mg BID)	Bronchodilator alone: 0.5 mg/day Inhaled or oral corticosteroid: 1 mg/day
Seebri Neohaler	COPD	One inhalation (15.6 mcg) BID	2 inhalations/day
Spiriva Respimat	Asthma	Two inhalations (1.25 mcg) QD	2.5 mcg/day
	COPD	Two inhalations (2.5 mcg) QD	5 mcg/day
Stiolto Respimat	COPD	Two inhalations by mouth QD at the same time of day	2 inhalations/day
Striverdi Respimat	COPD	Two inhalations QD	5 mcg/day
Symbicort	Asthma	2 inhalations BID (starting dosage is based on asthma severity)	320/9 mcg BID
	COPD	2 inhalations (160/4.5 mcg) BID	320/9 mcg BID
Symbicort Aerosphere	COPD	2 inhalations (160/4.8 mcg) BID	320/9.6 mcg BID
Trelegy Ellipta	COPD	1 inhalation (100/62.5/26 mcg) by mouth QD	1 inhalation/day
	Asthma	1 inhalation (100/62.5/26 mcg or 200/62.5/26 mcg) by mouth QD	1 inhalation/day

Drug Name	Indication	Dosing Regimen	Maximum Dose
Utibron Neohaler	COPD	Inhalation of the contents of one capsule BID	2 capsules/day
Yupelri	COPD	One 175 mcg mcg vial inhaled via nebulizer QD	175 mcg/day

VI. Product Availability

Drug Name	Availability
Advair Diskus	Inhalation powder containing fluticasone/salmeterol: 100/50 mcg, 250/50 mcg, 500/50 mcg
Advair HFA	Inhalation aerosol containing fluticasone/salmeterol: 45/21 mcg, 115/21 mcg, 230/21 mcg
AirDuo Digihaler	Inhalation powder: In each actuation: 55/14 mcg contains 55 mcg of fluticasone propionate and 14 mcg of salmeterol; 113/14 mcg contains 113 mcg of fluticasone propionate and 14 mcg of salmeterol; 232/14 mcg contains 232 mcg of fluticasone propionate and 14 mcg of salmeterol. AirDuo Digihaler contains a built-in electronic module
AirDuo RespiClick	Inhalation powder: In each actuation: 55 mcg/14 mcg contains 55 mcg of fluticasone propionate and 14 mcg of salmeterol; 113 mcg/14 mcg contains 113 mcg of fluticasone propionate and 14 mcg of salmeterol; 232 mcg/14 mcg contains 232 mcg of fluticasone propionate and 14 mcg of salmeterol
Alvesco	Inhalation aerosol: 80 mcg/actuation, 160 mcg/actuation
Anoro Ellipta	Inhalation powder: 62.5 mcg umeclidinium and 25 mcg vilanterol (62.5/25 mcg) per actuation
Arcapta Neohaler	Inhalation powder hard capsules: 75 mcg
ArmonAir Digihaler	Inhalation powder containing 30 mcg, 55 mcg, 113 mcg, or 232 mcg of fluticasone propionate per actuation. ArmonAir Digihaler contains a built-in electronic module
Asmanex Twisthaler	Inhalation device: 110 mcg (delivers 100 mcg/actuation), 220 mcg (delivers 200 mcg/actuation)
Besvespi Aerosphere	Inhalation aerosol: pressurized metered dose inhaler containing a combination of glycopyrrolate (9 mcg) and formoterol fumarate (4.8 mcg) per inhalation; two inhalations equal one dose
Breo Ellipta	Foil blister strips with inhalation powder containing fluticasone/vilanterol: 50/25 mcg, 100/25 mcg, 200/25 mcg
Breztri Aerosphere	Inhalation aerosol: pressurized metered dose inhaler containing a combination of budesonide (160 mcg), glycopyrrolate (9 mcg), and formoterol fumarate (4.8 mcg) per inhalation
Brovana	Inhalation solution (unit-dose vial for nebulization): 15 mcg/2 mL
Duaklir Pressair	Inhalation powder: 30 and 60 metered dose dry powder inhaler metering 400 mcg aclidinium bromide and 12 mcg formoterol fumarate per actuation

Drug Name	Availability
Dulera	Inhalation aerosol containing mometasone/formoterol: 50/5 mcg, 100/5 mcg, 200/5 mcg per actuation
Flovent Diskus	Inhalation powder: Inhaler containing fluticasone propionate (50, 100, or 250 mcg) as a powder formulation for oral inhalation
Flovent HFA	Inhalation aerosol: 44 mcg, 110 mcg, 220 mcg per actuation
Lonhala Magnair	Sterile solution for inhalation in a unit-dose vial: 25 mcg/mL
Ohtuvayre	Inhalation suspension in unit-dose ampule: 3 mg/2.5 mL
Perforomist	Inhalation solution (unit dose vial for nebulization): 20 mcg/2 mL solution
ProAir Digihaler	Inhalation powder: dry powder inhaler 108 mcg of albuterol sulfate (equivalent to 90 mcg of albuterol base) from the mouthpiece per actuation. The inhaler is supplied for 200 inhalation doses. ProAir Digihaler includes a built-in electronic module
Pulmicort Flexhaler	Inhalation device with powder: 90 mcg, 180 mcg
Pulmicort Respules	Inhalation suspension: 0.25 mg/2 mL, 0.5 mg/2 mL, 1 mg/2 mL
Seebri Neohaler	Inhalation powder in capsules: 15.6 mcg of glycopyrrolate inhalation powder for use with the Neohaler device
Spiriva Respimat	Inhalation spray: 1.25 mcg or 2.5 mcg tiotropium per actuation; two actuations equal one dose (2.5 mcg or 5 mcg)
Stiolto Respimat	Inhalation spray: 2.5 mcg tiotropium (equivalent to 3.124 mcg tiotropium bromide monohydrate), and 2.5 mcg olodaterol (equivalent to 2.736 mcg olodaterol hydrochloride) per actuation; two actuations equal one dose
Striverdi Respimat	Inhalation spray: Each actuation from the mouthpiece contains 2.7 mcg olodaterol hydrochloride, equivalent to 2.5 mcg olodaterol. Two actuations equal one dose
Symbicort	Metered-dose inhaler: budesonide (80 or 160 mcg) and formoterol (4.5 mcg) as an inhalation aerosol
Symbicort Aerosphere	Metered-dose inhaler: budesonide (160 mcg) and formoterol (4.8 mcg) as an inhalation aerosol
Trelegy Ellipta	Inhalation powder: disposable inhaler containing 2 foil strips of 30 blisters each: one strip with fluticasone furoate (100 mcg or 200 mcg per blister), and the other strip with a blend of umeclidinium and vilanterol (62.5 mcg and 25 mcg per blister, respectively)
Utibron Neohaler	Inhalation powder in capsule, for use with the Neohaler device: 27.5 mcg of indacaterol and 15.6 mcg glycopyrrolate
Yupelri	Inhalation solution (unit-dose vial for nebulization): 175 mcg/3 mL

VII. References

SABA

1. ProAir Digihaler Prescribing Information. Parsippany, NJ: Teva Pharmaceuticals USA, Inc; September 2020. Available at: https://www.digihaler.com/globalassets/proair_digihaler/proair_digihaler_pi.pdf. Accessed October 28, 2024.

2. Nelson HS, Bensch G, Pleskow WW, et al. Improved bronchodilation with levalbuterol compared with racemic albuterol in patients with asthma. *J Allergy Clin Immunol.* 1998; 102: 943-952.
3. Gawchik SM, Consuelo SL, Noonan M, et al. The safety and efficacy of nebulized levalbuterol compared with racemic albuterol and placebo in the treatment of asthma in pediatric patients. *J Allergy Clin Immunol.* 1999; 103: 615-21

ICS

4. Alvesco Prescribing Information. Marlborough, MA: Sunovion Pharmaceuticals Inc.; February 2023. Available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/021658s011lbl.pdf Accessed October 28, 2024.
5. ArmonAir Digihaler Prescribing Information. Parsippany, NJ: Teva Pharmaceuticals USA, Inc; April 2022. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/208798s013lbl.pdf. Accessed October 28, 2024.
6. Asmanex HFA Prescribing Information. Jersey City, NJ: Organon & Co.; June 2021. Available at: https://www.organon.com/product/usa/pi_circulars/a/asmanex/asmanex_hfa_pi.pdf. Accessed October 28, 2024.
7. Asmanex Twisthaler Prescribing Information. Jersey City, NJ: Organon & Co; June 2021. Available at: https://www.organon.com/product/usa/pi_circulars/a/asmanex/asmanex_pi.pdf. Accessed October 28, 2024.
8. Flovent Diskus Prescribing Information. Research Triangle Park, NC: GlaxoSmithKline; August 2023. Available at: https://gskpro.com/content/dam/global/hcpportal/en_US/Prescribing_Information/Flovent_Diskus/pdf/FLOVENT-DISKUS-PI-PIL-IFU.PDF. Accessed October 28, 2024.
9. Flovent HFA Prescribing Information. Research Triangle Park, NC: GlaxoSmithKline; September 2023. Available at: https://gskpro.com/content/dam/global/hcpportal/en_US/Prescribing_Information/Flovent_HFA/pdf/FLOVENT-HFA-PI-PIL-IFU.PDF. Accessed October 28, 2024.
10. Pulmicort Flexhaler Prescribing Information. Wilmington, DE: AstraZeneca; October 2019. Available at: <https://medicalinformation.astrazeneca-us.com/home/prescribing-information/pulmicort-flexhaler.html>. Accessed October 28, 2024.
11. Pulmicort Respules Prescribing Information. Wilmington, DE: AstraZeneca; October 2019. Available at <https://medicalinformation.astrazeneca-us.com/home/prescribing-information/pulmicort-respules.html>. Accessed October 28, 2024.

LABA

12. Arcapta Neohaler Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; July 2021. Available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/022383s009s010lbl.pdf. Accessed October 28, 2024.
13. Brovana Prescribing Information. Marlborough, MA: Sunovion Pharmaceuticals Inc.; May 2019. Available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/021912s032lbl.pdf. Accessed October 28, 2024.

14. Perforomist Prescribing Information. Morgantown, WV: Mylan Specialty L.P.; May 2019. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/022007s015lbl.pdf. Accessed October 28, 2024.
15. Striverdi Respimat Prescribing Information. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; November 2021. Available at: <https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=5d9a5433-857e-44ea-b3d6-2a400ca0cef5>. Accessed October 28, 2024.

LAMA

16. Lonhala Magnair Prescribing Information. Marlborough, MA: Sunovion Pharmaceuticals Inc; August 2020. Available at: <https://www.drugs.com/pro/lonhala-magnair.html>. Accessed October 28, 2024.
17. Seebri Neohaler Prescribing Information. East Hanover, New Jersey: Novartis Pharmaceuticals Corporation; July 2021. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/207923s005lbl.pdf. Accessed October 28, 2024.
18. Spiriva Handihaler Prescribing Information. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; November 2021. Available at: <https://content.boehringer-ingelheim.com/DAM/7e63d875-6ffb-407d-a561-af1e012045e5/spiriva%20handihaler-us-pi.pdf>. Accessed October 28, 2024.
19. Spiriva Respimat Prescribing Information. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; November 2021. Available at: <https://content.boehringer-ingelheim.com/DAM/68a8a6b5-4e9a-4508-85d3-af1e01205009/spiriva%20respimat-us-pi.pdf>. Accessed October 28, 2024.
20. Yupelri Prescribing Information. Morgantown, WV: Mylan Specialty L.P.; May 2022. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/210598s003lbl.pdf. Accessed October 28, 2024.

ICS/LABA

21. Advair Diskus Prescribing Information. Research Triangle Park, NC: GlaxoSmithKline; June 2023. Available at https://gskpro.com/content/dam/global/hcpportal/en_US/Prescribing_Information/Advair_Diskus/pdf/ADVAIR-DISKUS-PI-PIL-IFU.PDF. Accessed October 28, 2024.
22. Advair HFA Prescribing Information. Research Triangle Park, NC: GlaxoSmithKline; May 2024. Available at: https://gskpro.com/content/dam/global/hcpportal/en_US/Prescribing_Information/Advair_HFA/pdf/ADVAIR-HFA-PI-PIL-IFU.PDF. Accessed October 28, 2024.
23. AirDuo Digihaler Prescribing Information. Frazer, PA: Teva Respiratory, LLC; July 2021. Available at: https://www.digihaler.com/globalassets/airduo_digihaler/airduo_digihaler_pi.pdf. Accessed October 28, 2024.
24. AirDuo RespiClick Prescribing Information. Parsippany, NJ: Teva Pharmaceuticals USA, Inc; July 2021. Available at: <https://www.myairduo.com/globalassets/myairduo/pdf/pi.pdf>. Accessed October 28, 2024.
25. Breo Ellipta Prescribing Information. Research Triangle Park, NC: GlaxoSmithKline; November 2024. Available at https://gskpro.com/content/dam/global/hcpportal/en_US/Prescribing_Information/Breo_Ellipta/pdf/BREO-ELLIPTA-PI-PIL-IFU.PDF. Accessed November 14, 2024.

26. Dulera Prescribing Information. Jersey City, NJ: Organon & Co.; June 2021. Available at https://www.organon.com/product/usa/pi_circulars/d/dulera/dulera_pi.pdf. Accessed October 28, 2024.
27. Symbicort Prescribing Information. Wilmington, DE: AstraZeneca Pharmaceuticals; July 2019. Available at: https://den8dhaj6zs0e.cloudfront.net/50fd68b9-106b-4550-b5d0-12b045f8b184/a4b62ab8-1314-4583-91b4-294ec239f790/a4b62ab8-1314-4583-91b4-294ec239f790_viewable_rendition__v.pdf. Accessed October 28, 2024.
28. Symbicort Aerosphere Prescribing Information. Wilmington, DE: AstraZeneca Pharmaceuticals; April 2023. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/216579s000lbl.pdf. Accessed October 28, 2024.

LABA/LAMA

29. Anoro Ellipta Prescribing Information. Research Triangle Park, NC: GlaxoSmithKline; June 2023. Available at https://gskpro.com/content/dam/global/hcpportal/en_US/Prescribing_Information/Anoro_Ellipta/pdf/ANORO-ELLIPTA-PI-PIL-IFU.PDF. Accessed October 28, 2024.
30. Bevespi Aerosphere Prescribing Information. Wilmington, DE: AstraZeneca Pharmaceuticals; March 2023. Available at: https://den8dhaj6zs0e.cloudfront.net/50fd68b9-106b-4550-b5d0-12b045f8b184/fe60bf8d-1354-42c8-8f3c-5b4ea85ed161/fe60bf8d-1354-42c8-8f3c-5b4ea85ed161_viewable_rendition__v.pdf. Accessed October 28, 2024.
31. Duaklir Pressair Prescribing Information. Morrisville, NC: Circassia Pharmaceuticals Inc.; March 2019. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/210595lbl.pdf. Accessed October 28, 2024.
32. Stiolto Respimat Prescribing Information. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc.; November 2021. Available at <https://content.boehringer-ingelheim.com/DAM/7fe8a4a7-9ed3-41ef-a565-af1e0120af14/stiolto%20respimat-us-pi.pdf>. Accessed October 28, 2024.
33. Utibron Neohaler Prescribing Information. East Hanover, NJ: Novartis Pharmaceuticals Corporation; July 2021. Available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/207930s005s006lbl.pdf. Accessed October 28, 2024.

ICS/LABA/LAMA

34. Breztri Aerosphere Prescribing Information. Wilmington, DE: AstraZeneca Pharmaceuticals LP; January 2022. Available at: <https://medicalinformation.astrazeneca-us.com/home/prescribing-information/breztri.html>. Accessed November 14, 2024.
35. Trelegy Ellipta Prescribing Information. Research Triangle Park, NC: GlaxoSmithKline; June 2023. Available at: https://gskpro.com/content/dam/global/hcpportal/en_US/Prescribing_Information/Trelegy_Ellipta/pdf/TRELEGY-ELLIPTA-PI-PIL-IFU.PDF. Accessed November 14, 2024.

PDE3/PDE4 Inhibitor

36. Ohtuvayre Prescribing Information. Raleigh, NC: Verona Pharma, Inc; June 2024. Available at: www.ohtuvayrehcp.com. Accessed October 28, 2024.

37. Anzueto A et al. Enfisentrine, a novel phosphodiesterase 3 and 4 inhibitor for the treatment of chronic obstructive pulmonary disease: Randomized, double-blind, placebo-controlled, multicenter phase III trials (the ENHANCE trials). *Am J Respir Crit Care Med.* 2023; 208(4): 406-416. doi:10.1164/rccm.202306-0944OC.

Guidelines

- 38. National Heart, Lung, and Blood Institute. Expert panel report 3: guidelines for the diagnosis and management of asthma. National Asthma Education and Prevention Program. Published August 28, 2007. Available from: <http://www.nhlbi.nih.gov/health-pro/guidelines/current/asthma-guidelines/full-report/>. Accessed November 14, 2024.
- 39. Cloutler MM, Dixon AE, Krishnan JA, et al. Managing asthma in adolescents and adults 2020: asthma guideline update from the National Asthma Education and Prevention Program. *JAMA.* 2020; 324: 2301-2317.
- 40. Global Initiative for Asthma. Global strategy for asthma management and prevention (2024 report). Available from: www.ginasthma.org. Accessed November 14, 2024.
- 41. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease (2025 report). Available at: <http://www.goldcopd.org>. Accessed November 26, 2024.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J7601	Enfisentrine, inhalation suspension, fda approved final product, non-compounded, administered through dme, unit dose form, 3 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created: adapted from previously approved individual drug policies - CP.PMN.07 Xopenex HFA/Inhalation Solution, CP.PMN.31 Advair Diskus/HFA, CP.PMN.146 Trelegy Ellipta, CP.PMN.147 Utibron Neohaler, CP.PMN.148 Anoro Ellipta, CP.PMN.200 Duaklir Pressair, CP.PMN.201 Brovana, CP.PMN.203 Arcapta Neohaler, CP.PMN.204 Striverdi Respimat, CP.PMN.229 Breo Ellipta, and CP.PMN.230 Dulera (all to be retired); added additional agents and revised criteria to reflect SDC CY2021 strategy/prior clinical guidance; added requirement for medical justification for requests for agents with digital component.	10.29.20	02.21
Added option for request to not exceed the health plan quantity limit.	04.23.21	
1Q 2022 annual review: per November SDC removed Asmanex HFA as product requiring prior authorization and revised required step through agents for all other ICS products from "Qvar RediHaler AND Arnuity Ellipta" to "Qvar RediHaler, Arnuity Ellipta, AND	11.30.21	02.22

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Asmanex HFA"; added 12 month initial approval authorization for Xopenex for legacy WellCare (WCG.CP.PMN.07 to be retired); references reviewed and updated.		
RT4: updated ArmonAir Digihaler per prescribing information for pediatric extension down to 4 years of age and older, added new 30 mcg strength; references reviewed and updated.	05.16.22	
Per August SDC and prior clinical guidance, added Flovent HFA to policy requiring step through fluticasone propionate HFA (Flovent HFA authorized generic), added maximum age limit of 12 years for Flovent HFA per SDC and Centene core Medicaid formulary status. Template changes applied to other diagnoses/indications and continued therapy section.	08.23.22	11.22
1Q 2023 annual review: for LABA/LAMA and ICS/LABA/LAMA, revised step through requirement for use of ICS/LABA to apply only to asthma and not COPD per updated 2023 GOLD guidelines; for Xopenex, consolidated legacy WellCare initial approval duration from 12 month to 6 months, consistent with standard Medicaid approval duration; updated Appendix D with latest GOLD guideline recommendations; references reviewed and updated.	01.11.23	02.23
Per April SDC, removed Xopenex from policy.	04.20.23	
RT4: added newly approved dosage form Symbicort Aerosphere to policy with redirection to generic Symbicort per SDC and prior clinical guidance; updated Breo Ellipta per prescribing information for pediatric extension down to 5 years of age and older, clarified applicable redirections based on age, and added new 50/25 mcg/actuation strength form. Corrected maximum dose for Bevespi Aerosphere from 2 inhalations/day to 4 inhalations/day per dosing regimen (2 inhalations BID).	05.26.23	
1Q 2024 annual review: no significant changes; references reviewed and updated. Per December SDC, removed Spiriva Handihaler from policy; added Tudorza Pressair and Spiriva Handihaler as additional redirection requirements (in addition to Incruse Ellipta) for LAMA requests.	10.09.23	02.24
Per March SDC, for "All other ICS" requests added additional redirection to fluticasone propionate diskus (Flovent Diskus authorized generic) ; revised Flovent Diskus redirection requirements to fluticasone propionate diskus (Flovent Diskus authorized generic) in a new row.	03.12.24	05.24
RT4: added newly approved agent Ohtuvayre with redirections per SDC.	07.03.24	11.24
HCPCS code added [J7601].	11.07.24	

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q 2025 annual review: no significant changes; updated Appendix D with latest GOLD guideline recommendations on Ohtuvayre; references reviewed and updated. For LABA/LAMAs, removed all “for asthma only” redirections since LABA/LAMAs are indicated only for COPD.	01.15.25	02.25

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members, and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:

For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

©2020 Centene Corporation. All rights reserved. All materials are exclusively owned by Centene Corporation and are protected by United States copyright law and international copyright law. No part of this publication may be reproduced, copied, modified, distributed, displayed, stored in a retrieval system, transmitted in any form or by any means, or otherwise published without the prior written permission of Centene Corporation. You may not alter or remove any trademark, copyright or other notice contained herein. Centene[®] and Centene Corporation[®] are registered trademarks exclusively owned by Centene Corporation.