

# Texas Vendor Drug Program

## Drug Use Criteria: Aerosolized Agents - Metered-Dose Inhalers (MDIs): Beta<sub>2</sub> Adrenergic Drugs (Short-Acting)

### Publication History

1. Developed January 1995.
2. Revised **April 2023**; April 2021; March 2019; March 2017; May 2016; February 2016; July 2014; October 2012; October 2010; January 2008; March 2003; March 2002; March 2001; March 2000; May 1999; February 1999; February 1998; March 1997; August 1995.

***Medications listed in the tables and non-FDA approved indications that may be included in these retrospective criteria are not indicative of Vendor Drug Program formulary coverage.***

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**TEXAS**  
Health and Human  
Services

Medical and  
Social Services

# 1 Dosage

## 1.1 Adults

Beta<sub>2</sub>-adrenergic drugs, used routinely in asthma management, can be identified as long-acting or short-acting agents. Both short- and long-acting compounds can be used to prevent bronchospasm. However, short-acting compounds are the drugs of choice for acute bronchospasm as these agents act within minutes to cause bronchodilation. Drugs in this category include albuterol and levalbuterol. For acute bronchospasm, treatment is initiated with a short-acting beta<sub>2</sub>-adrenergic agent either as a metered-dose inhaler or a nebulizer solution. Treatment of acute attacks is usually for a finite time period based on the intensity of the attack and/or the need for medical attention either through emergency department management or hospitalization. Usage is individualized based on patient characteristics.<sup>1-9</sup>

Although not FDA-approved, beta<sub>2</sub>-selective adrenergic agents such as albuterol are effective in chronic obstructive pulmonary disease (COPD) maintenance therapy to improve lung function and mucociliary clearance. Albuterol has become one of the mainstays of therapy for acute exacerbations of chronic obstructive pulmonary disease COPD due to rapid onset of action as well as efficacy in producing bronchodilation.<sup>10</sup>

For preventive/ maintenance therapy, albuterol is FDA-approved as preventive therapy for exercise-induced asthma. To manage exercise-induced bronchospasm (EIB) in adults, two 90 mcg albuterol inhalations are administered at least 15 to 30 minutes before exercise on an as-needed basis.<sup>1-6</sup>

Ipratropium/albuterol combination therapy is FDA-approved for use as second-line therapy in adult COPD patients who continue to experience bronchospasm with an aerosol bronchodilator and require a second bronchodilator.<sup>1,11</sup>

Maximum recommended daily doses for available inhalational beta<sub>2</sub>-adrenergic agents as monotherapy and combination therapy are summarized in Tables 1 and 2. Prescribed dosages exceeding these criteria will be reviewed.

**Table 1. Maximum Adult Daily Dose for Inhalational Beta<sub>2</sub>-Adrenergic Agents (Short-Acting) – Monotherapy<sup>1-7</sup>**

Drug Name	Treatment Indication	Dosage Form/ Strength	Maximum Recommended Dosage
albuterol aerosol solution (Proventil HFA®, Ventolin HFA®, generic)	asthma, <b>prevention of exercise-induced bronchospasm</b>	aerosol (90 mcg albuterol base/actuation)	12 actuations/day (total dose = 1080 mcg albuterol base)
albuterol inhalation powder (ProAir RespiClick®, ProAir Digihaler®)	asthma, <b>prevention of exercise-induced bronchospasm</b>	(90 mcg albuterol base/actuation)	12 actuations/day (total dose = 1080 mcg albuterol base)
levalbuterol (Xopenex HFA®, generic)	asthma	aerosol (45 mcg levalbuterol free base/actuation)	12 actuations/day (total dose = 540 mcg levalbuterol free base)

**Table 2. Maximum Adult Daily Dose for Inhalational Beta<sub>2</sub>-Adrenergic Agents (Short-Acting) – Combination Therapy<sup>1,11</sup>**

Drug Name	Treatment Indication	Dosage Form/ Strength	Maximum Recommended Dosage
ipratropium/ albuterol (Combivent Respimat®)	chronic obstructive pulmonary disease	inhalation spray (20 mcg ipratropium/ 100 mcg albuterol/ actuation)	6 actuations/ day (total dose = 120 mcg ipratropium/ 600 mcg albuterol)

## 1.2 Pediatrics

Proventil® HFA, Ventolin® HFA, ProAir RespiClick®, **ProAir Digihaler®, and generic albuterol HFA** are FDA-approved for use in children 4 years of age and older for prevention/treatment of bronchospasm and prevention of exercise-induced bronchospasm.<sup>1-6</sup> Levalbuterol is FDA-approved for use in children 4 years of age and older for prevention/treatment of bronchospasm.<sup>1,7</sup>

To prevent EIB in pediatric patients 4 years of age and older, two albuterol 90 mcg inhalations are administered at least 15 to 30 minutes before exercise on an as-needed basis.<sup>1-6</sup>

Combination therapy with ipratropium and albuterol is not FDA-approved for use in pediatric patients as safety and efficacy in this patient population have not been established.<sup>1,11</sup>

Pediatric dosages for short-acting beta<sub>2</sub>-agonists used to manage acute asthma exacerbations are summarized in Table 3. Dosages exceeding these recommendations will be reviewed.

**Table 3. Maximum Recommended Pediatric Daily Dose for Inhalational Beta<sub>2</sub>-Adrenergic Agents (Short-Acting) – Monotherapy<sup>1-7</sup>**

<b>Drug Name</b>	<b>Treatment Indication</b>	<b>Dosage Form/ Strength</b>	<b>Maximum Recommended Dosage</b>
albuterol (Proventil HFA®, Ventolin HFA®, generics)	asthma, <b>prevention of exercise-induced bronchospasm</b>	aerosol solution (90 mcg albuterol base/actuation)	≥ 4 years of age: 12 actuations/day (total dose = 1080 mcg albuterol base)
albuterol (ProAir RespiClick®, ProAir Digihaler®)	asthma, <b>prevention of exercise-induced bronchospasm</b>	inhalation powder (90 mcg albuterol base/actuation)	≥ 4 years of age: 12 actuations/day (total dose = 1080 mcg albuterol base)
levalbuterol (Xopenex HFA®)	asthma	aerosol (45 mcg levalbuterol free base/actuation)	≥ 4 years of age: 12 actuations/day (total dose = 540 mcg levalbuterol free base)

## 2 Duration of Therapy

Metered-dose inhalers are designed to deliver a set number of inhalations based on the canister size as well as the medication prescribed. Days' supply for inhalational beta<sub>2</sub>-adrenergic agents is summarized in Table 4 and 5, based on the maximum

recommended doses listed in Tables 1-3, and the number of actuations per canister or number of capsules per blister card listed in Tables 4 and 5. Excessive use may be identified based on refill frequency. Inappropriate supply of short-acting beta<sub>2</sub>-adrenergic agents will be monitored by reviewing excessive refills.

**Table 4. Days' Supply for Available Short-Acting Beta<sub>2</sub>-Adrenergic Agent Metered-Dose Inhalers (Adult and Pediatric Patients) – Monotherapy <sup>2-7</sup>**

<b>Drug</b>	<b># of Actuations Per Canister</b>	<b>Days' Supply (based on maximum dose per day)<sup>+</sup></b>
<b>Albuterol (generic) 8.5 g canister</b>	<b>200</b>	<b>~ 16 days</b>
Albuterol (ProAir RespiClick®) 0.65 g inhaler	200	~16 days
Albuterol (ProAir Digihaler®) 0.65 g inhaler	200	~16 days
Albuterol (Proventil HFA®) 6.7 g canister	200	~16 days
Albuterol (Ventolin HFA®) 8 g canister 18 g canister	60 200	5 days ~16 days
Levalbuterol (Xopenex HFA®) 15 g canister	200	~ 16 days

<sup>+</sup>calculated based on canister size and maximum dose allowed per day (summarized in Tables 1 and 2)

**Table 5. Days' Supply for Available Short-Acting Beta<sub>2</sub>-Adrenergic Agent Metered-Dose Inhalers (Adult Patients) – Combination Therapy <sup>11</sup>**

<b>Drug</b>	<b># of Actuations Per Canister</b>	<b>Days Supply (based on maximum dose per day)<sup>+</sup></b>
Ipratropium/albuterol (Combivent® Respimat®) (4 g cartridge)	120	20 days

### 3 Duplicative Therapy

The use of two or more metered-dose inhaler short-acting beta<sub>2</sub>-adrenergic compounds concurrently for prevention and control of asthma symptoms is not justified and will be reviewed. Nebulized short-acting beta<sub>2</sub>-adrenergic therapy is available for pediatric patients who are too ill or too young to obtain medication from an aerosolized metered-dose device. However, adjunctive administration of a short-acting beta<sub>2</sub>-adrenergic agonist metered-dose inhaler with a short-acting beta<sub>2</sub>-agonist nebulized bronchodilator is also not recommended and will be reviewed.

Acute asthma exacerbations require treatment with short-acting beta<sub>2</sub>-adrenergic agents even though maintenance therapy with a long-acting beta<sub>2</sub>-agonist like salmeterol may be prescribed concomitantly. Patients may receive a long- and short-acting beta<sub>2</sub>-adrenergic drug concurrently for short time periods to manage acute attacks. Patient profiles containing excessive prescriptions for a short-acting beta<sub>2</sub>-adrenergic drug (i.e., frequent refill of short-acting beta<sub>2</sub>-adrenergic agonist within a 30-day time period) in conjunction with long-acting beta<sub>2</sub>-agonists will be reviewed.

### 4 Drug-Drug Interactions

Patient profiles will be assessed to identify those drug regimens which may result in clinically significant drug-drug interactions. Drug interactions considered clinically relevant for short-acting beta<sub>2</sub>-adrenergic bronchodilators are summarized in Table 6. Only those drug-drug interactions classified as clinical significance level 1 or those considered life-threatening which have not yet been classified will be reviewed.

**Table 6. Inhaled Short-Acting Beta<sub>2</sub>-Adrenergic Agents Drug-Drug Interactions**

Target Drug	Interacting Drug	Interaction	Recommendation	Clinical Significance Level <sup>+</sup>
beta <sub>2</sub> -agonists	MAOIs (including linezolid)	concurrent administration of MAOIs with beta <sub>2</sub> -agonists may increase risk of tachycardia, hypomania, or agitation due to potentiation of effects on vascular system	administer combination cautiously or within 2 weeks of MAOI discontinuation; observe patients for adverse effects	major (CP)

Target Drug	Interacting Drug	Interaction	Recommendation	Clinical Significance Level <sup>+</sup>
beta <sub>2</sub> -agonists	TCA's	concurrent administration of TCA's with beta <sub>2</sub> -agonists may potentiate effects on cardiovascular system and increase risk of adverse events	cautiously administer TCA's and beta <sub>2</sub> -agonists together, including within 2 weeks of TCA discontinuation; monitor patients and observe for changes in blood pressure, heart rate and ECG	moderate (CP)
beta <sub>2</sub> -agonists	beta blockers	concurrent administration may decrease effectiveness of beta-adrenergic blocker or beta-2 agonists	combination not recommended in asthma/ COPD patients; if adjunctive therapy necessary, utilize cardioselective beta blocker (e.g., atenolol, bisoprolol)	major (CP)
beta <sub>2</sub> -agonists	diuretics	potential for worsening of diuretic-associated hypokalemia and/or ECG changes with beta <sub>2</sub> -agonist concurrent administration, especially with high beta <sub>2</sub> -agonist doses	administer combination cautiously; monitor potassium levels as necessary	moderate (CP)
beta <sub>2</sub> -agonists	atomoxetine	concurrent administration may increase risk of cardiovascular adverse effects (e.g., tachycardia, hypertension); interaction may be less likely with inhaled beta <sub>2</sub> -agonists	monitor patients for increased cardiovascular adverse effects	moderate (CP)

Target Drug	Interacting Drug	Interaction	Recommendation	Clinical Significance Level <sup>+</sup>
beta <sub>2</sub> -agonists	QTc interval-prolonging medications (e.g., class I, III anti-arrhythmic, tricyclic antidepressants, dolasetron)	concurrent administration may increase risk of cardiotoxicity (e.g., life-threatening arrhythmias, cardiac arrest) as arformoterol and formoterol may cause QTc interval prolongation and, rarely, torsades de pointes	administer combination cautiously	moderate (CP)
ipratropium/ albuterol	antimuscarinics	co-administration may produce additive anticholinergic effects and potential for increased adverse effects	cautiously administer ipratropium with other antimuscarinics; monitor for increased adverse effects	moderate (CP)

<sup>+</sup>CP = *Clinical Pharmacology*

COPD = *chronic obstructive pulmonary disease*; ECG = *electrocardiogram*; MAOIs = *monoamine oxidase inhibitors*;

TCAs = *tricyclic antidepressants*

## 5 References

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