



## A Visual Approach to Simplifying Respiratory Drug Regimens

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### Inhaled Respiratory Drugs

#### 3 Main Categories

##### Beta 2 Agonists

- Binds to beta-2 receptors
- Relaxation of smooth muscles in the lung
- Dilation and opening of airways

##### Muscarinic Antagonists

- Inhibits acetylcholine in bronchial smooth muscle
- Bronchodilation

##### Corticosteroids

- Inhibits the inflammatory response

Can be mixed and matched in various combinations



## Adverse Effects of Inhaled Medications

Drug Category	Adverse Effects
<b>Beta 2 agonists</b>	Tachycardia (up to 200 beats/minute), arrhythmias, nervousness, headache, tremor, dry mouth, palpitation, nausea, dizziness, sleeplessness, hypertension or hypotension
<b>Muscarinic antagonists</b>	Dizziness, headache, dry mouth, dyspepsia, nausea, UTI, urinary retention, constipation
<b>Corticosteroids</b>	Increase risk of upper respiratory tract infections, headache, pharyngitis



## Dosage Forms

- Handheld Inhaler
    - Metered dose inhaler (MDI)
    - Dry powder inhaler (DPI)
    - Aerolizers
    - HandiHaler
    - Twisthaler
    - Flexhaler
- Handheld inhalers

  - Require adequate inhalation force
  - Require coordination to use
  - Are generally more expensive compared to the nebulized solution
- Nebulized solution
  - Oral tablet (Albuterol tablet, corticosteroid: prednisone)
  - Beta 2 agonists and muscarinic antagonists
    - Short-acting and long-acting formulations



## Respiratory Medications NOT in Combination

<p><b>Corticosteroids</b> <span style="float: right; border: 1px solid black; padding: 2px;">End in -sone or -nide</span></p> <ul style="list-style-type: none"> <li>• Handheld Inhaler             <ul style="list-style-type: none"> <li>- Beclomethasone (Qvar)</li> <li>- Budesonide (Pulmicort Flexhaler)</li> <li>- Ciclesonide (Alvesco)</li> <li>- Fluticasone (Flovent HFA/Diskus)</li> <li>- Mometasone (Asmanex Twisthaler)</li> </ul> </li> <li>• Nebulized solution             <ul style="list-style-type: none"> <li>- Budesonide (Pulmicort Respules)</li> </ul> </li> <li>• Oral – Prednisone</li> </ul>	<p><b>Beta 2 Agonists</b> <span style="float: right; border: 1px solid black; padding: 2px;">End in -terol</span></p> <ul style="list-style-type: none"> <li>• Handheld Inhaler             <ul style="list-style-type: none"> <li>- Short Acting                 <ul style="list-style-type: none"> <li>• Albuterol HFA (Ventolin HFA, Proair HFA, Proventil HFA)</li> <li>• Levalbuterol HFA (Xopenex HFA)</li> </ul> </li> <li>- Long acting                 <ul style="list-style-type: none"> <li>• Formoterol (Foradil Aerolizer)</li> <li>• Indacaterol (Arcapta Neohaler)</li> <li>• Olodaterol (Striverdi Respimat)</li> <li>• Salmeterol (Serevent Diskus)</li> </ul> </li> </ul> </li> <li>• Nebulized solution             <ul style="list-style-type: none"> <li>- Short Acting                 <ul style="list-style-type: none"> <li>• Albuterol (AccuNeb)</li> <li>• Levalbuterol (Xopenex)</li> </ul> </li> <li>- Long Acting                 <ul style="list-style-type: none"> <li>• Arformoterol (Brovana)</li> <li>• Formoterol (Perforomist)</li> </ul> </li> </ul> </li> <li>• Oral - Albuterol</li> </ul>
<p><b>Muscarinic Antagonists</b> <span style="float: right; border: 1px solid black; padding: 2px;">End in -ium</span></p> <ul style="list-style-type: none"> <li>• Handheld Inhaler             <ul style="list-style-type: none"> <li>- Short Acting                 <ul style="list-style-type: none"> <li>• Ipratropium HFA (Atrovent HFA)</li> </ul> </li> <li>- Long Acting                 <ul style="list-style-type: none"> <li>• Aclidinium (Turorza Pressair)</li> <li>• Tiotropium (Spiriva Handihaler/Respimat)</li> <li>• Umeclidinium (Incruse Ellipta)</li> </ul> </li> </ul> </li> <li>• Nebulized solution - Ipratropium</li> </ul>	



## Respiratory Medications NOT in Combination

	Corticosteroids	Beta 2 agonists		Muscarinic antagonists	
		Short acting	Long acting	Short acting	Long acting
Handheld Inhaler (MDI or DPI)	<b>Beclomethasone</b> (Qvar)	<b>Albuterol HFA</b> <small>(Ventolin HFA, Proair HFA, Proventil HFA)</small>	<b>Formoterol</b> <small>(Foradil Aerolizer)</small>	<b>Ipratropium HFA</b> <small>(Atrovent HFA)</small>	<b>Aclidinium</b> <small>(Turorza Pressair)</small>
	<b>Budesonide</b> <small>(Pulmicort Flexhaler)</small>		<b>Indacaterol</b> <small>(Arcapta Neohaler)</small>		
	<b>Ciclesonide</b> <small>(Alvesco)</small>	<b>Levalbuterol HFA</b> <small>(Xopenex HFA)</small>	<b>Olodaterol</b> <small>(Striverdi Respimat)</small>		<b>Tiotropium</b> <small>(Spiriva Handihaler, Spiriva Respimat)</small>
	<b>Fluticasone</b> (Flovent HFA, Flovent Diskus)		<b>Salmeterol</b> <small>(Serevent Diskus)</small>		
	<b>Mometasone</b> <small>(Asmanex Twisthaler)</small>				
Nebulized Solution	<b>Budesonide</b> <small>(Pulmicort Respules)</small>	<b>Albuterol</b> <small>(AccuNeb)</small>	<b>Arformoterol</b> <small>(Brovana)</small>	<b>Ipratropium</b>	
		<b>Levalbuterol</b> <small>(Xopenex)</small>	<b>Formoterol</b> <small>(Perforomist)</small>		
Oral	<b>Prednisone</b>	<b>Albuterol</b>			



## Respiratory Medications in Combination

**Beta 2 Agonist** + **Muscarinic Antagonists**

- **Short Acting – PRN or Routine Use**
  - Handheld Inhaler – Albuterol/Ipratropium (Combivent Respimat)
  - Nebulized solution – Albuterol/Ipratropium (DuoNeb)
  
- **Long acting – Routine Use Only**
  - Vilanterol/Umeclidinium (Anoro Ellipta)
  - Olodaterol/Tiotropium (Stiolto Respimat)

**Corticosteroid** + **Beta 2 Agonist**

- **Long acting – Routine Use Only**
  - Budesonide/formoterol (Symbicort)
  - Fluticasone/salmeterol (Advair HFA, Advair Diskus)
  - Fluticasone/vilanterol (Breo Ellipta)
  - Mometasone/formoterol (Dulera)

All long-acting inhalers are handheld inhalers



## Respiratory Medications in Combination

	Corticosteroids	Beta 2 Agonist	Muscarinic Antagonists
<b>Short-Acting – PRN or Routine Use</b>			
<b>Handheld Inhaler (MDI)</b>		<b>Albuterol / Ipratropium</b> (Combivent Respimat)	
<b>Nebulized Solution</b>		<b>Albuterol / Ipratropium</b> (Duoneb)	
<b>Long-Acting – Routine Use Only</b>			
<b>Handheld Device (MDI or DPI)</b>		<b>Vilanterol / Umeclidinium</b> (Anoro Ellipta)	
		<b>Olodaterol / Tiotropium</b> (Stiolto Respimat)	
	<b>Budesonide / Formoterol</b> (Symbicort)		
	<b>Fluticasone / Salmeterol</b> (Advair HFA, Advair Diskus)		
	<b>Fluticasone / Vilanterol</b> (Breo Ellipta)		
	<b>Mometasone / Formoterol</b> (Dulera)		



## Approach to a Patient's Inhaled Medications

- 1) Separate the **PRN** orders from **Routine** orders
  - a) **For PRN therapy**, the patient should only be on a regimen that contains one beta 2 agonist and/or one muscarinic antagonist.

Corticosteroids and long acting beta 2 agonists and muscarinic antagonists should **NOT** be used on a PRN basis.

- b) **For Routine therapy**, the patient does not have to have something from all 3 categories, but if they are on something, they should only have one of that type of medication on board.
- 2) See if there are any duplicate therapies
- 3) Discontinue any duplicate therapies
- 4) Are there any medications you can consolidate?



## Patient Case #1

- Terminal Diagnosis – COPD
- Medication List
  - Proair HFA (albuterol) – 2 puffs q4-6 hours PRN
  - Combivent Respimat (albuterol/ipratropium) – 1 puff q4 hours PRN
  - Spiriva Handihaler (tiotropium) – 1 cap inhaled once daily
  - Xopenex (levalbuterol) – 3mL vial via neb four times a day
  - Advair (fluticasone/salmeterol) – 1 inhalation BID
  - Duoneb (albuterol/ipratropium) – 3mL vial via neb four times a day
  - Prednisone 10mg PO daily
  - Duoneb (albuterol/ipratropium) – 3mL vial via neb q4-6 hours PRN



## Patient Case #1 – Step 1

Separate **PRN** orders from **Routine** orders

- Proair HFA (albuterol) – 2 puffs q4-6 hours PRN
- Combivent Respimat (albuterol/ipratropium) – 1 puff q4 hours PRN
- Spiriva Handihaler (tiotropium) – 1 cap inhaled once daily
- Xopenex (levalbuterol) – 3mL vial via neb four times a day
- Advair (fluticasone/salmeterol) – 1 inhalation BID
- Duoneb (albuterol/ipratropium) – 3mL vial via neb four times a day
- Prednisone 10mg PO daily
- Duoneb (albuterol/ipratropium) – 3mL vial via neb q4-6 hours PRN



## Patient Case #1 – Step 1

Separate **PRN** orders from **Routine** orders

### **PRN orders**

- Proair HFA (albuterol) – 2 puffs q4-6 hours PRN
- Combivent Respimat (albuterol/ipratropium) – 1 puff q4 hours PRN
- Duoneb (albuterol/ipratropium) – 3mL vial via neb q4-6 hours PRN

### **Routine orders**

- Spiriva Handihaler (tiotropium) – 1 cap inhaled once daily
- Xopenex (levalbuterol) – 3mL vial via neb four times a day
- Advair (fluticasone/salmeterol) – 1 inhalation BID
- Duoneb (albuterol/ipratropium) – 3mL vial via neb four times a day
- Prednisone 10mg PO daily



# Patient Case #1 – Step 2

See if there are any duplicate therapies

**PRN orders**

- Proair HFA (albuterol) – 2 puffs q4-6 hours PRN
- Combivent Respimat (albuterol/ipratropium) – 1 puff q4 hours PRN
- Duoneb (albuterol/ipratropium) – 3mL vial via neb q4-6 hours PRN

**Routine orders**

- Spiriva Handihaler (tiotropium) – 1 cap inhaled once daily
- Xopenex (levalbuterol) – 3mL vial via neb four times a day
- Advair (fluticasone/salmeterol) – 1 inhalation BID
- Duoneb (albuterol/ipratropium) – 3mL vial via neb four times a day
- Prednisone 10mg PO daily



## Duplicate Inhaled Therapy Template

	Dosage Form	Corticosteroids	Beta 2 Agonists	Muscarinic Antagonists
<b>PRN</b>	Handheld Inhaler			
	Nebulizer			
<b>Routine</b>	Handheld Inhaler			
	Nebulizer			
	Oral			



### Patient Case #1 – Step 2

	Dosage Form	Corticosteroids	Beta 2 Agonists	Muscarinic Antagonists
<b>PRN</b>	Handheld Inhaler			
	Nebulizer			
<b>Routine</b>	Handheld Inhaler			
	Nebulizer			
	Oral			

**PRN**

Albuterol HFA (Proair)

Albuterol / Ipratropium  
(Combivent Respimat)

Albuterol / Ipratropium  
(Duoneb)



### Patient Case #1 – Step 2

	Dosage Form	Corticosteroids	Beta 2 Agonists	Muscarinic Antagonists
<b>PRN</b>	Handheld Inhaler		Albuterol HFA (Proair)	
	Nebulizer		Albuterol / Ipratropium (Combivent Respimat) Albuterol / Ipratropium (DuoNeb)	
<b>Routine</b>	Handheld Inhaler			
	Nebulizer			
	Oral			

**Routine**

Tiotropium (Spiriva)

Levalbuterol neb  
(Xopenex)

Prednisone

Fluticasone / Salmeterol  
(Advair)

Albuterol / Ipratropium  
(Duoneb)





### Patient Case #1 – Step 2

	Dosage Form	Corticosteroids	Beta 2 Agonists	Muscarinic Antagonists
<b>PRN</b>	Handheld Inhaler		Albuterol HFA (Proair)	
	Nebulizer		Albuterol / Ipratropium (Combivent Respimat)	
<b>Routine</b>	Handheld Inhaler		Levalbuterol neb (Xopenex)	Tiotropium (Spiriva)
	Nebulizer	Fluticasone / Salmeterol (Advair)		
	Oral	Prednisone	Albuterol / Ipratropium (DuoNeb)	



### Patient Case #1 – Step 2

	Dosage Form	Corticosteroids	Beta 2 Agonists	Muscarinic Antagonists
<b>PRN</b>	Handheld Inhaler		Albuterol HFA (Proair)	
	Nebulizer		Albuterol / Ipratropium (Combivent Respimat)	
<b>Routine</b>	Handheld Inhaler		Levalbuterol neb (Xopenex)	Tiotropium (Spiriva)
	Nebulizer	Fluticasone / Salmeterol (Advair)		
	Oral	Prednisone	Albuterol / Ipratropium (DuoNeb)	

Do you see the duplicate therapies?



## Patient Case #1 - Step 3

### Discontinue any duplicate therapies

- Determine the severity of the patient's COPD or lung condition.
- If they are taking nebulized inhaled medications, they most likely do not have enough positive inhalation force to use handheld inhalers.
- Consider keeping the nebulized solutions and D/C the handheld inhalers.

Hospice patients with a terminal diagnosis of COPD or lung cancer generally do not have enough positive inhalation force to use handheld devices and should be on nebulized therapy.



### Step 3 Discontinue any duplicate therapies

	Dosage Form	Corticosteroids	Beta 2 Agonists	Muscarinic Antagonists
PRN	Handheld Inhaler		Albuterol HFA (Proair)	
	Nebulizer		Albuterol / Ipratropium (DuoNeb)	Albuterol / Ipratropium (Combivent Respimat)
Routine	Handheld Inhaler		Levalbuterol neb (Xopenex)	Tiotropium (Spiriva)
		Fluticasone / Salmeterol (Advair)		
	Nebulizer		Albuterol / Ipratropium (DuoNeb)	
	Oral	Prednisone		

Which medications would you discontinue?



### Step 3 Discontinue any duplicate therapies

	Dosage Form	Corticosteroids	Beta 2 Agonists	Muscarinic Antagonists
PRN	Handheld Inhaler		Albuterol HFA (Proair)	
	Nebulizer		Albuterol / Ipratropium (DuoNeb)	
Routine	Handheld Inhaler			Tiotropium (Spiriva)
			Levalbuterol neb (Xopenex)	
		Fluticasone / Salmeterol (Advair)		
	Nebulizer		Albuterol / Ipratropium (DuoNeb)	
	Oral	Prednisone		

The combination therapy of using DuoNeb routinely and PRN, plus prednisone (if a steroid medication is needed) is the most cost-effective therapy for hospice patients with a terminal diagnosis of COPD or lung cancer.



### Step 4 Consolidating Medications

	Dosage Form	Corticosteroids	Beta 2 Agonists	Muscarinic Antagonists
PRN	Nebulizer		Albuterol / Ipratropium (DuoNeb)	
Routine	Nebulizer		Albuterol / Ipratropium (DuoNeb)	
	Oral	Prednisone		

Are there any medications you can consolidate?



## Patient Case #2

- Terminal diagnosis – CHF and COPD
- Medications
  - Ventolin HFA (albuterol) – 2 puffs q4-6 hours PRN
  - Lasix (furosemide) – 20mg tab BID
  - Potassium chloride – 20mEq tab BID
  - Advair (fluticasone/salmeterol) – 1 inhalation BID
  - Levothyroxine – 75mcg tab daily
  - Ipratropium neb – 1 vial via neb four times a day
  - Lisinopril – 10mg tab daily
  - Lorazepam – 1mg q4 hours PRN
  - Duoneb (albuterol/ipratropium) – 3mL vial via neb q4-6 hours PRN
  - Haloperidol – 1mg BID



## Patient Case #2 – Step 1

Separate **PRN** orders from **Routine** orders

- Ventolin HFA (albuterol) – 2 puffs q4-6 hours PRN
- Advair (fluticasone/salmeterol) – 1 inhalation BID
- Ipratropium neb – 1 vial via neb four times a day
- Duoneb (albuterol/ipratropium) – 3mL vial via neb q4-6 hours PRN



## Patient Case #2 – Step 1

Separate **PRN** orders from **Routine** orders

- **PRN**

- Ventolin HFA (albuterol) – 2 puffs q4-6 hours PRN
- Duoneb (albuterol/ipratropium) – 3mL vial via neb q4-6 hours PRN

- **Routine**

- Ipratropium neb – 1 vial via neb four times a day
- Advair (fluticasone/salmeterol) – 1 inhalation BID



## Patient Case #2 – Step 2

See if there are any duplicate therapies

- **PRN**

- Ventolin HFA (albuterol) – 2 puffs q4-6 hours PRN
- Duoneb (albuterol/ipratropium) – 3mL vial via neb q4-6 hours PRN

- **Routine**

- Ipratropium neb – 1 vial via neb four times a day
- Advair (fluticasone/salmeterol) – 1 inhalation BID



**Patient Case #2 – Step 2**

	Dosage Form	Corticosteroids	Beta 2 Agonists	Muscarinic Antagonists
<b>PRN</b>	Handheld Inhaler			
	Nebulizer			

<b>PRN</b>	Albuterol HFA (Ventolin)	Albuterol / Ipratropium (Duoneb)
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**Patient Case #2 – Step 2**

	Dosage Form	Corticosteroids	Beta 2 Agonists	Muscarinic Antagonists
<b>PRN</b>	Handheld Inhaler		Albuterol HFA (Ventolin)	
	Nebulizer		Albuterol / Ipratropium (DuoNeb)	
<b>Routine</b>	Handheld Inhaler			
	Nebulizer			
	Oral			

<b>Routine</b>	Ipratropium neb	Fluticasone / Salmeterol (Advair)
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**Patient Case #2 – Step 2**

	Dosage Form	Corticosteroids	Beta 2 Agonists	Muscarinic Antagonists
<b>PRN</b>	Handheld Inhaler		Albuterol HFA (Proair)	
	Nebulizer		Albuterol / Ipratropium (DuoNeb)	
<b>Routine</b>	Handheld Inhaler	Fluticasone / Salmeterol (Advair)		
	Nebulizer			Ipratropium neb

Do you see the duplicate therapies?



**Patient Case #2 – Step 3**

	Dosage Form	Corticosteroids	Beta 2 Agonists	Muscarinic Antagonists
<b>PRN</b>	Handheld Inhaler		Albuterol HFA (Proair)	
	Nebulizer		Albuterol / Ipratropium (DuoNeb)	
<b>Routine</b>	Handheld Inhaler	Fluticasone / Salmeterol (Advair)		
	Nebulizer			Ipratropium neb

Discontinue any duplicate therapies



**Patient Case #2 – Step 3**

	Dosage Form	Corticosteroids	Beta 2 Agonists	Muscarinic Antagonists
<b>PRN</b>	Handheld Inhaler		Albuterol HFA (Proair)	
	Nebulizer		Albuterol / Ipratropium (DuoNeb)	
<b>Routine</b>	Handheld Inhaler	Fluticasone / Salmeterol (Advair)		
	Nebulizer			Ipratropium neb

Discontinue any duplicate therapies



**Patient Case #2 – Step 4**

	Dosage Form	Corticosteroids	Beta 2 Agonists	Muscarinic Antagonists
<b>PRN</b>	Nebulizer		Albuterol / Ipratropium (DuoNeb)	
<b>Routine</b>	Handheld Inhaler	Fluticasone / Salmeterol (Advair)		
	Nebulizer			Ipratropium neb

Is there any medications you can consolidate?





## Patient Case #2 – Step 4

	Dosage Form	Corticosteroids	Beta 2 Agonists	Muscarinic Antagonists
PRN	Nebulizer		Albuterol / Ipratropium (DuoNeb)	
Routine	Handheld Inhaler	Fluticasone / Salmeterol (Advair)		
	Nebulizer			Ipratropium neb

- Patients with end stage COPD generally do not have enough positive inhalation force to use handheld inhalers.
- The patient is already on nebulized solutions.
- Plan
  - D/C Advair and Ipratropium neb
  - Use Duoneb routinely and PRN
  - Add oral Prednisone, if a steroid is necessary



## Note regarding inhaled corticosteroids use in COPD

- The use of inhaled corticosteroids (ICS) in COPD is controversial.
- Routine use of ICS has been associated with an increased risk of pneumonia, thrush, dysphonia and reduction in bone density.
- ICS are also expensive medications that has been shown to have a minimal impact on COPD exacerbations.
- In a **Cochrane Database Systematic Review**, *the risk of COPD exacerbations have only been reduced by one exacerbation per patient every four years for patients who were taking an ICS compared to salmeterol alone.*

Nannini, Laserson, Poole. Combined corticosteroid and long-acting beta-2 agonists for chronic obstructive pulmonary disease. Cochrane Database Syst Rev 2012;(9):CD006829.



## Note regarding inhaled corticosteroids use in COPD

- In the **WISDOM** (Withdrawal of Inhaled Glucocorticoids and Exacerbations of COPD) trial, published in the NEJM 2014, ICS were withdrawn from patients who were receiving both a long-acting beta agonists and a long-acting muscarinic antagonists over a period of 12 weeks.
- *These patients did not experience an increase in exacerbation or worsening of their condition over the 52 week study period with the withdrawal of ICS.*

The study authors recommended discontinuation of ICS for patients with severe or very severe COPD.

Magnussen, Disse, Rodriguea-Roisin, et al. Withdrawal of inhaled glucocorticoids and exacerbations of COPD. N. Engl. J. Med. 2014;371:1285-4.



## Note regarding inhaled corticosteroids use in COPD

- The **REDUCE** study, published in JAMA 2013, demonstrated that a short 5-day course of oral prednisone 40mg to manage acute COPD exacerbations was noninferior to a 14 day course.
- *Time to next COPD exacerbation in patients with very severe COPD (GOLD stage IV disease)*
  - *5 day steroid group = 43.5 days*
  - *14 day steroid group = 29 days*

Therefore, a short 5-day course of oral prednisone 40mg/day would be appropriate for acute COPD exacerbations.

Leuppi JD, Schuetz P, Bingisser R, et al. Short-term vs conventional glucocorticoid therapy in acute exacerbations of chronic obstructive pulmonary disease: the REDUCE randomized clinical trial. JAMA. 2013;309:2223-2231.



## Summary

- Approach to a patient's inhaled medications
  - 1) Separate **PRN** orders from **Routine** orders
  - 2) See if there are any duplicate therapies
  - 3) Discontinue any duplicate therapies
- ***Duoneb (routinely and prn), plus Prednisone*** (if a steroid medication is needed) is the most cost-effective therapy for hospice patients with a terminal diagnosis of COPD or lung cancer.
- ***Inhaled corticosteroids*** should be ***discontinued*** in patients with severe or very severe COPD.
- A short ***5-day*** course of ***oral Prednisone 40mg/day*** would be appropriate ***for acute COPD exacerbations***.



## Conclusion

- By identifying and discontinuing duplicate inhaled respiratory therapies, patients would be able to avoid potential toxicity and adverse effects.
- This also helps hospices reduce costs towards more cost-effective medications



## Questions?

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