

# What in the inhaler is happening?

AN ASTHMA UPDATE FOR PEDIATRIC HEALTHCARE PROVIDERS

PAUL THILL, PHARM.D, BCPS

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# Disclosure statement

PAUL THILL, PHARM.D - SPEAKER  
HAS DECLARED THAT HE HAS NO COMMERCIAL INTERESTS OR  
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## Learning Objectives

By the end of this presentation, the participant should be able to...

- Characterize the local pediatric asthma outcome data for Saginaw County in terms of hospital admission rates, mortality and short-acting beta-agonist fill rates.
- Summarize the GINA guideline medication recommendations to manage symptoms and risk in pediatric asthma and anticipate upcoming changes based upon newly published research
- Describe and implement maintenance-reliever therapy for step 3 asthma patients and identify patients who might be appropriate for as-needed ICS/LABA therapy
- Investigate appropriateness of step-up and step-down therapy and decide when referral to an asthma specialist for possible biologic therapy is appropriate

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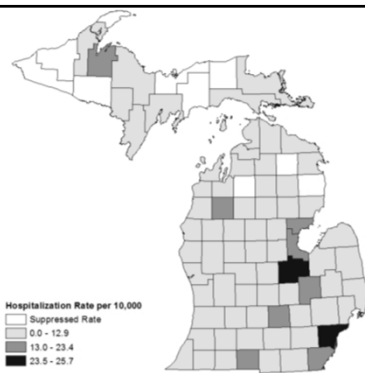
## Epidemiology of Asthma in Saginaw

### Key Findings:

- Asthma burden in Saginaw County is greater than Michigan
- Saginaw County hospitalization rate 74% higher than rate for Michigan
- Saginaw County asthma mortality rate twice as high as rate for Michigan
- Fewer Saginaw peds Medicaid patients had PCP asthma visits
- More Saginaw peds Medicaid patients had ED visits for asthma
- Saginaw Medicaid children with overuse SABAs at a higher rate than Michigan

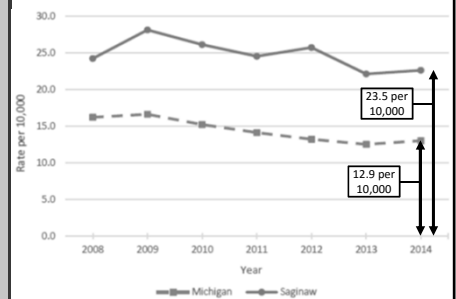
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## Hospitalization Rate by County

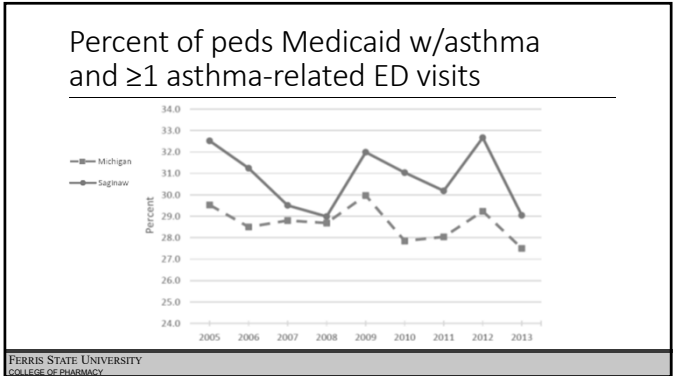
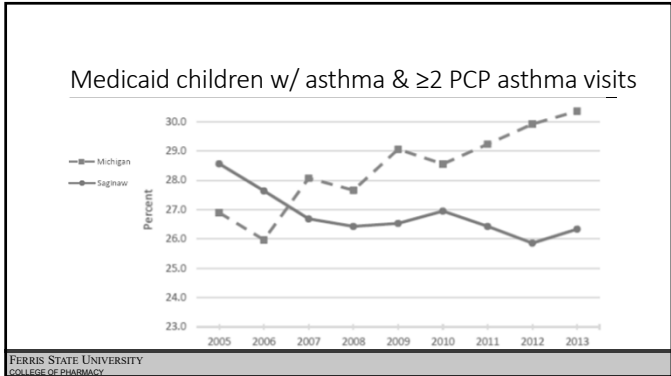
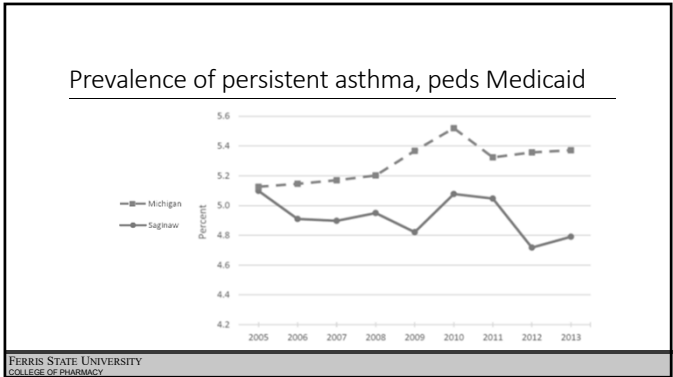
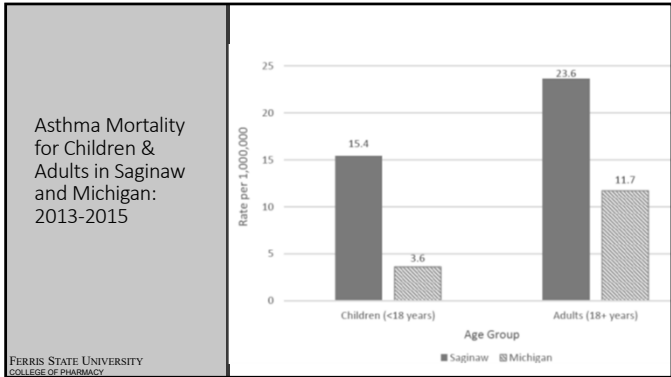
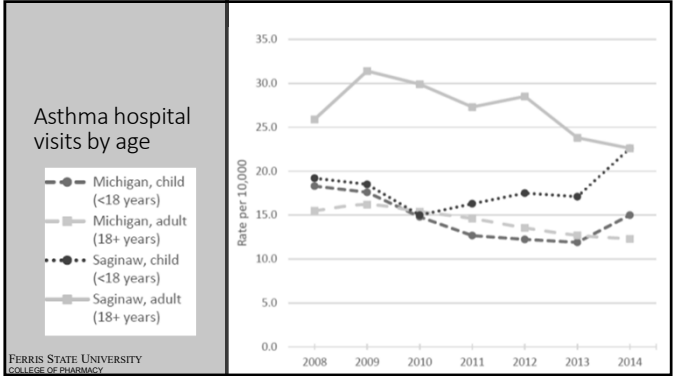
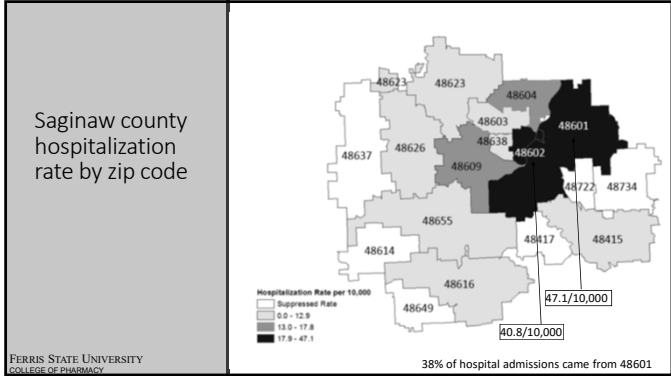


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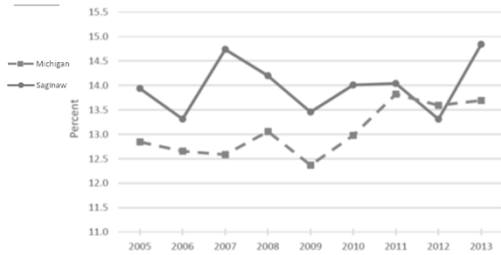
## Saginaw County asthma hospitalization rate



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## Percent Overuse\* of SABAs among Children on Medicaid with Asthma



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\*overuse defined as >7 canisters of albuterol filled/year

## Symptom & Risk reduction strategies

HOW SHOULD WE ADVISE PEDIATRIC PATIENTS AND CAREGIVERS TO MANAGE ASTHMA SYMPTOMS AND RISK?

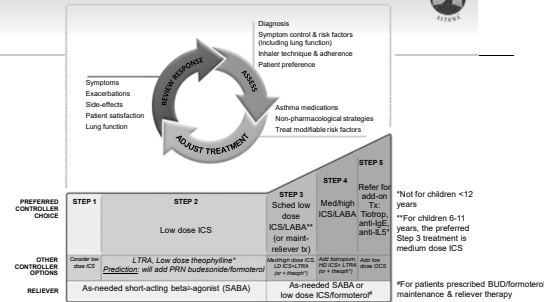
SHOULD WE RECOMMEND SEASONAL USE OF ICS?

SHOULD WE RECOMMEND "YELLOW ZONE" ICS INCREASES?

SHOULD WE RECOMMEND INTERMITTENT ICS/LABA USE?

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## Stepwise management – Age 6 & older



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GINA 2018, Box 3-6



Can I take (or increase) my controller  
...at the change of the seasons?  
...at the first sign of symptoms?  
...when I'm in the Yellow Zone?

## Seasonal use of controllers (ICS)

What do the guidelines say?

- NIH/NHLBI EPR3 (2007)
  - "If daily long-term control therapy is discontinued after the season of increased risk... a clinic contact should be scheduled 2–6 weeks after discontinuation..." (Evidence D).
  - "Consider treating patients who may have seasonal asthma (symptoms only in relation to certain seasonal molds or pollens with few symptoms the rest of the year) as having persistent asthma during the season and as having intermittent asthma the rest of the year." (Evidence D)
- GINA (2018)
  - Maintenance-reliever therapy - ICS/formoterol scheduled & PRN, single inhaler (Evidence A)
  - Recommend low dose ICS for "most patients with asthma" even "infrequent symptoms"
  - Seasonal ICS
    - Evidence level D – "Panel Consensus"; No published trials
    - "start when symptoms commence & continue until 4 wks after relevant pollen season ends"
    - "Insufficient evidence to step down from Step 2 (low dose ICS) to as-needed ICS"

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## Yellow-zone escalation of controller ICS (Flovent)

Design

- Prospective, Randomized
- Double-blind
- 48-week treatment phase
- 254 Children 5-11 yo
- Mild-mod persistent asthma on ICS

Intervention:

- Flovent HFA 44 – 2 puffs 2x/day
- Intervention: 5x dose (220mcg 2p 2x/d)
- Control: no change in yellow zone

Primary outcome: severe exacerb.

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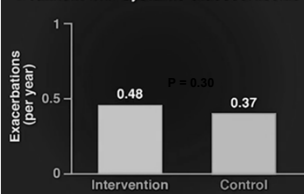
Jackson, N Engl J Med 2018

## Yellow-zone escalation of controller ICS (Flovent)

### Results

- Severe exacerbation rate
  - Numerically higher in "intervention" group
  - Not statistically different
- Side effects (growth rate)
  - 0.23 cm/yr slower
  - 16% higher ICS dosage in intervention group
- Secondary outcomes (no sig difference)
  - Time to first exacerbation
  - Albuterol use
  - Symptom scores
  - Rate of treatment failure

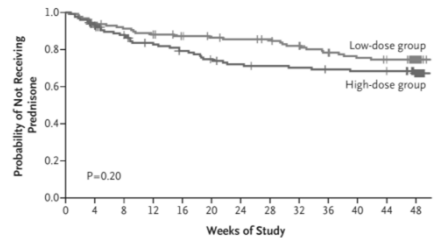
### Rate of Asthma Exacerbations Leading to Treatment with Systemic Glucocorticoids



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## Yellow-zone escalation of controller (Flovent)



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## As-needed ICS/LABA (Symbicort)

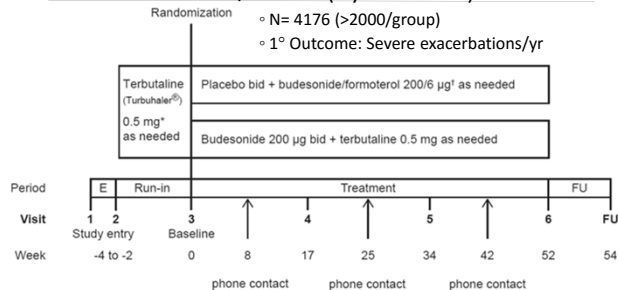
52-wk, R, DB, MC trial – ≥12yo mild asthma eligible for GINA step 2



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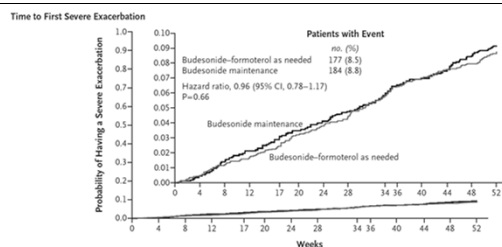
## As-needed ICS/LABA (Symbicort)



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## As-needed ICS/LABA - rate of exacerbation



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## As-needed ICS/LABA - Conclusion

- Budesonide/formoterol prn = budesonide BID for exacerbation prevention
- Symptoms statistically better with scheduled budesonide
  - ACQ-5 statistically better in budesonide; did not reach clinical significance (0.11 out of 6)
  - AQLQ statistically better in budesonide; did not reach clinical significance (0.1 out of 7)
- Exposure to ICS was median 66 vs. 267 mcg/day
- Adherence
  - "Very high" at 63%
  - Led to a lower exacerbation rate
- Simplified regimen, lower ICS exposure
- DPI Symbicort not available; US equivalent Symbicort 80 MDI 1-2 puffs prn

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## Flexible ICS therapy:



- PRN Flovent – NO
- Yellow-zone Flovent increase – NO
- Increase & decrease q2-3 mo – YES



- Maintenance-reliever Symbicort – Step 3 in 12yo+
- As needed for Mild asthma (Step 2) – YES (80 mcg)
- 6-11yo step 3 – prefer med dose ICS

## Referral for biologic therapy

### Who? According to GINA Guidelines

- Patient still uncontrolled after 3-6 mo of med-high dose ICS/LABA
- Adherent to regimen, inhaler technique is observed as correct, asthma diagnosis confirmed (PFT)
- Environmental assessment – smoking, allergens (occupational, NSAIDs, B-blockers)

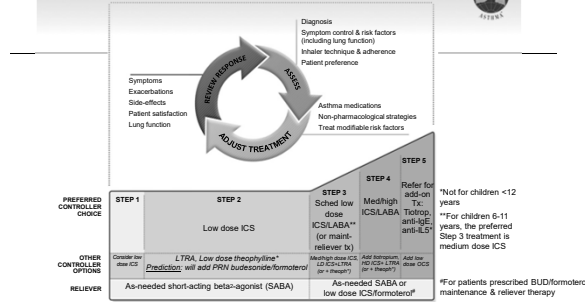
### What?

- IgE-neutralizer (need elevated IgE) – omalizumab (Xolair)
- IL-5-blockers (eosinophilic) – mepolizumab (Nucala), benralizumab (Fasenra), reslizumab (Cinqair)
- IL-4, IL-13-blocker – dupilumab (Dupixent)
- What's next – TSLP-blockers (tezepelumab); CRTH2-blockers (fevipiprant)

### When?

- Should take a year to get there after diagnosis
- Need to be at step 4, adherent, good technique with environment/comorbidities under control

## Stepwise management – Age 6 & older



## Device-specific issues

### Spacer for all(?)

- For 0-3 facemask/spacer – ICS and even albuterol
- For 4-6 – mouthpiece/spacer

### Qvar Redihaler + spacer?

- Flovent HFA
- DPI/self-driven ≥5yo

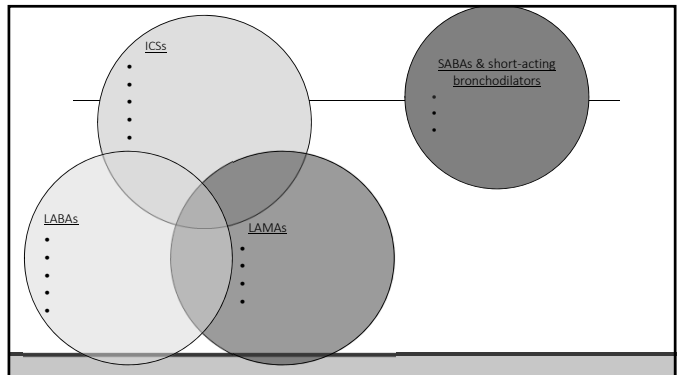
### Generics

- MCS issues
- Advairs gone wild – AirDuo (55, 113, 232/14) – 1 puff, Wixela, Advair (not Advair)
- Albuterol finally(?) – Ventolin HFA, ProAir HFA

### Primatene mist

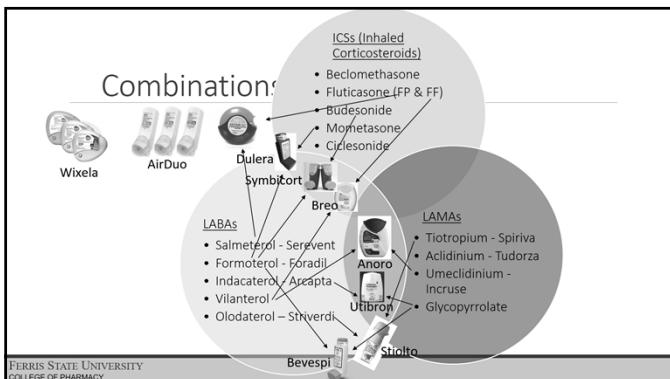
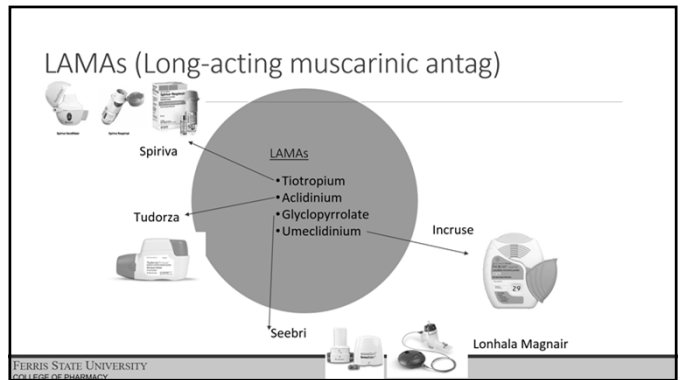
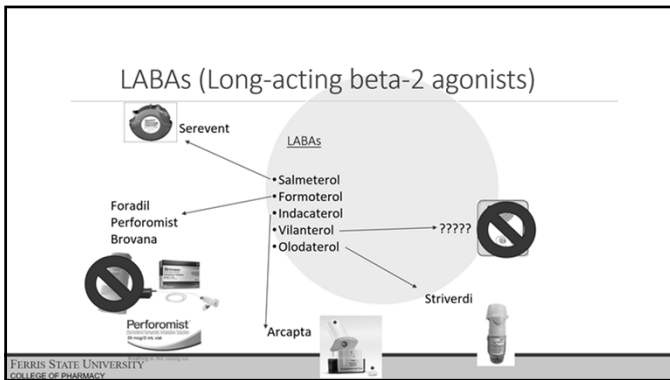
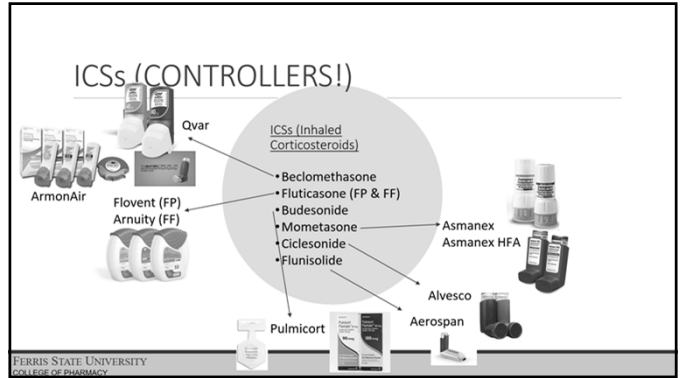
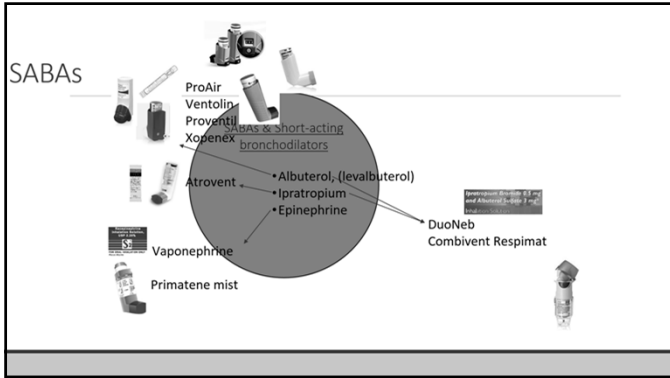
## How do I remember them?

[tinyurl.com/inhaledmedchart](http://tinyurl.com/inhaledmedchart)



### Inhaled Asthma & COPD Medications 2019

SABAs	Albuterol Nebulization	Generic, Accuneb	"Accuneb <sup>®</sup> " - 0.31, 0.63 mg & 1.25 mg/3 mL	Pre-mixed unit dose (3 mL); this lower dose usually not recommended
			Generic - 2.5 mg/3 mL (0.083%)	Pre-mixed unit dose (3 mL); also available as 0.5 ml to add to other agents or NS for nebulization
	Albuterol	ProAir (& <a href="#">Resplick</a> ), Ventolin, generic	90 mcg/puff; Need to select a device with a counter (NOT Proventil, Xopenex)	MDI; should be used with a spacer; shake 5 seconds; 4 primes to start; reprime after 2 wk without use or if dropped; expires 6 mo after opening; ProAir comes in both HFA (MDI) and <a href="#">Resplick<sup>®</sup> DPI</a>
	Levalbuterol	Xopenex HFA & Neb	45 mcg/puff (200); 0.31, 0.63 or 1.25 mg/unit dose	MDI: Shake 5 seconds; 4 primes to start; reprime after 3 days without use; no counter on this device Unit dose for neb; must use as soon as foil wrapper is opened
Inhaled Corticosteroids (ICS)	Beclomethasone	Qvar Redihaler	40 or 80 mcg/actuation (120)	MDI only for use without spacer (no shaking required)
	Budesonide	Pulmicort flexhaler <a href="#">DPI</a>	90 mcg/puff (60); 180 mcg/puff (120)	Counter increments of 10; moves every 5; twist to the right, then left to load; do not tip once loaded
		Pulmicort, generic	0.25, 0.5 or 1 mg/unit dose nebulizer vial	Deliver with mask if <3 yo; older child may use a mouthpiece; expires 2 wks after open
	Fluticasone	<a href="#">Flovent Diskus</a> , ArmonAir	50, 100, 250 mcg, 55, 113, 232/puff (60)	Dry powder inhalers; No priming; do not tip once loaded; avoid humidity & moisture
		Flovent HFA	44, 110 or 220 mcg/puff (124)	MDI; shake for 5 seconds; 4 puff priming; reprime after 7 days w/o use or if dropped
		Arnuity <a href="#">Ellipta</a> DPI	50, 100 or 200 mcg/puff (30)	1 puff <u>daily</u> ; Fluticasone furoate different dosing vs. Flovent above; only for asthma; 50 mcg for 5-11yo
	Mometasone	Asmanex <a href="#">twisthaler</a> DPI; Asmanex HFA	220 mcg (30, 60, 120); 110 mcg/puff (30) for peds 4-11 yo; 100 mcg & 200 mcg HFA (124)	Dose counter; no priming; do not tip once loaded; avoid humidity & moisture; may give once daily in evening; HFA
Ciclesonide	Alvesco HFA	80 or 160 mcg/puff (60)	1 puff 2x/day; shaking not required; 3 puffs to prime; reprime 10d unused; counter moves every 10 puffs	
Flunisolide	Aerospan HFA	80 mcg/puff (120)	Has a built in non-valved, extremely low volume "spacer"; This is the only ICS without a dose counter	
LABAs	Salmeterol	Serevent Diskus DPI	50 mcg/actuation (60)	No priming; do not tip once loaded; avoid humidity; expires 6 wk after open
	Formoterol	Perforomist Neb	20 mcg nebulization	COPD indication only
	Arformoterol	Brovana Neb	15 mcg ampule	COPD indication only
	Olodaterol	Striverdi <a href="#">Respimat</a>	2.5 mcg/puff (60)	2 puffs/dose once daily; 60 dose inhaler; see Combivent respimat for device specifics
	Indacaterol	Arcapta <a href="#">Neohaler</a> DPI	75 mcg inhaled capsule	COPD; once daily; capsule inserted into DPI device
ICS/LABA Combo	Fluticasone propionate/ Salmeterol	Advair Diskus	100/50, 250/50 or 500/50 mcg/puff (60)	Same as Serevent DPI except expires one month after opening; also comes as generic, unbranded version
		Wixela <a href="#">Inhub</a> DPI	100/50, 250/50 or 500/50 mcg/puff (60)	Generic equivalent for Advair DPI (same dosing)
		Advair HFA	45/21, 115/21 or 230/21 mcg/puff (124)	Same as Flovent HFA except reprime @ 4 wk without use or if dropped
		AirDuo Resplick DPI	55/14, 113/14, 232/14 mcg/puff (60)	Dose is 1 puff twice a day; also available cheaper as "unbranded" version covered by Michigan Medicaid
	Flutic furoate/ Vilanterol	Breo Ellipta DPI	100 mcg/25 & 200/25 mcg/puff (30)	1 puff daily; Indicated for COPD (100/25 dose) and asthma (≥18 yr old)
	Budesonide/ Formoterol	Symbicort HFA	80/4.5 or 160/4.5 mcg/puff (120)	MDI; use with spacer; shake 5 seconds; 2 primes to start, reprime after 7d without use; do not use more than BID; expires 90 days after opening
Mometasone/ Formoterol	Dulera HFA	100 mcg/5 mcg, 200 mcg/5 mcg (120)	MDI; use with spacer; shake 5 seconds; 4 primes to start, reprime after 5d without use; do not use more than BID; expires 90 days after opening	
LABA/LAMA	Umeclidinium/ Vilanterol	Anoro Ellipta DPI	62.5 mcg/25 mcg/puff (30)	LAMA/LABA combo for COPD; 1 puff daily; technique same as other Ellipta inhalers
	Tiotropium/ Olodaterol	Stiolto Respimat	2.5 mcg/2.5 mcg/puff (60)	LAMA/LABA combo for COPD; 2 puffs/dose; 1 dose daily; same as other Respimat devices
	Glycopyrrolate/ indicaterol	Utibron Neohaler DPI	15.6 mcg/27.5 mcg/ capsule	LAMA/LAMA combo for COPD; 1 capsule inhaled twice a day via neohaler device; (similar to handihaler)
	Glycopyrrolate/ formoterol	Bevespi MDI	9 mcg/4.8 mcg/puff (120);	2 puffs twice a day – only MDI LAMA/LABA combo for COPD (can be used with a spacer)
	Aclidinium/ formoterol	Duaklir Pressair DPI	400 mcg/12 mcg (60)	
Anticholinergics	Ipratropium	Atrovent MDI/Neb	17 mcg/puff (200); Nebulization 0.5 mg/3ml	SAMA; Prime x2 at first and if unused >3 days; counter goes down every 5 puffs
	Ipratropium/albuterol	Duoneb Neb	0.5 mg/3mg/3 ml nebulization	SAMA/SABA; given via nebulizer; can be used in acute asthma, but mostly for COPD.
	Ipratropium/albuterol	Combivent Respimat	20/100 mcg; (120 puffs)	Typical dose 1 puff q6h prn; if unused for a significant period, reprime; locks when counter reaches "0"
	Tiotropium	Spiriva DPI, Respimat	18 mcg DPI; 2.5 mcg and 1.25 mcg/puff MDI (60)	LAMA; 2 puffs/dose daily for respimat; 1.25mcg is for step 4 in 6yo or older
	Umeclidinium	Incruse Ellipta DPI	62.5 mcg/puff (30 puffs/inhaler)	LAMA; 1 puff daily; Ellipta instructions same as other Ellipta products
	Aclidinium	Tudorza <a href="#">Pressair</a> DPI	400 mcg/puff (60 puffs/inhaler)	LAMA; 1 puff twice a day; Dose window tells user Pressair inhaler is ready and if the dose was given.
	Glycopyrrolate	Seebri Neohaler DPI	15.6 mcg/capsule DPI	LAMA; 1 capsule inhaled twice a day via neohaler device (capsule DPI)
		Lonhala Neb	25 mcg/1mL nebulized	LAMA; 1 ampule nebulized twice a day via dedicated Magnair nebulized compressor
Revefenesin	Yupelri	175 mcg/3 ml nebulization	LAMA; 1 ampule nebulized via standard jet neb/compressor	
3in1	Umecl/Vilant/Flutic Fur	Trelegy Ellipta	62.5 mcg/25 mcg/ 100 mcg	LAMA/LABA/ICS 1 puff daily



### Summary

- Saginaw is one of the worst counties in Michigan for asthma control
- Opportunities for improvement include innovative strategies like single inhaler budesonide/formoterol
- Seasonal controller (ICS) use is likely to be removed from recommendations and should not be recommended for pediatrics
- Adherence, inhaler technique and environmental factors/comorbidities should be considered before stepping up; Step up/down q3 months
- Once adequately trialing & failing step 4+, referral for biologics is appropriate
- Know how to teach the new inhalers; ask your pharmacist to help with selection, insurance coverage and teaching