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CLINICAL RESPIRATORY REVIEW

Practical and evidence-based guidance for yellow zone medication escalation in adult asthma action plans: A clinical respiratory review

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ABSTRACT

Asthma action plans (AAPs) are a cornerstone of asthma self-management support and are consistently associated with reduced exacerbations, improved quality of life and decreased health-care utilization in adults. However, their real-world uptake remains limited, with clinicians frequently citing uncertainty about how to operationalize appropriate medication escalation during acute loss of asthma control (the "yellow zone"). Since the original publication of the Canadian Thoracic Society-endorsed tool for yellow zone dose escalation, several new inhaler formulations, devices and combination therapies have entered the market. In addition, updated international guidelines and randomized controlled trial findings now converge on a strong recommendation to quadruple inhaled corticosteroid (ICS) doses as a strategy to prevent progression to severe exacerbation. This Clinical Respiratory Review synthesizes the evidence informing yellow zone instructions within AAPs and describes how we updated the point-of-care tool to accommodate new device types and therapeutic combinations. We briefly outline our approach to identifying relevant evidence, then summarize updated yellow zone escalation guidance for monotherapy ICS, ICS/long-acting beta-agonist (LABA), and ICS/LABA/long-acting muscarinic antagonist (LAMA) regimens across Canada, the United States and Europe, describing key pharmacologic principles and practical considerations such as dose-equivalence across devices, regulatory limits and safety data supporting short-term ICS escalation. Finally, we provide actionable advice for clinical practice and highlight priorities for future research.

RÉSUMÉ

Les plans d'action pour l'asthme constituent une pierre angulaire du soutien à l'autogestion de l'asthme et sont systématiquement associés, chez les adultes, à une réduction des exacerbations, à une amélioration de la qualité de vie et à une diminution du recours aux soins de santé. Toutefois, leur adoption en contexte réel demeure limitée, les cliniciens évoquant fréquemment une incertitude quant à la façon de mettre en œuvre une intensification appropriée du traitement médicamenteux lors d'une perte aiguë de la maîtrise de l'asthme (la « zone jaune »). Depuis la publication initiale de l'outil avalisé par la Société canadienne de thoracologie pour l'intensification posologique en zone jaune, plusieurs nouvelles formulations d'inhalateurs, de nouveaux dispositifs et de nouvelles associations thérapeutiques ont été commercialisés. En outre, les lignes directrices internationales mises à jour et les résultats des essais contrôlés randomisés convergent maintenant vers une forte recommandation de quadrupler les doses de corticostéroïdes inhalés (CSI) comme stratégie visant à prévenir la progression vers une exacerbation sévère. Cette revue clinique respiratoire synthétise les données probantes qui sous-tendent les instructions relatives à la zone jaune dans les plans d'action pour l'asthme et décrit la façon dont nous avons mis à jour l'outil destiné au point de service afin de tenir compte des nouveaux types de dispositifs et des nouvelles associations thérapeutiques. Nous présentons brièvement notre démarche de recension des données probantes pertinentes, puis résumons les recommandations actualisées concernant l'intensification du traitement en zone jaune pour les schémas par CSI en monothérapie, CSI/BALA (bêta-agoniste à longue durée d'action) et CSI/BALA/AMLA (antagoniste muscarinique à longue durée d'action) au Canada, aux États-Unis et en Europe. Nous décrivons également les grands principes pharmacologiques et les considérations pratiques, notamment l'équivalence des doses entre les dispositifs, les limites réglementaires et les données d'innocuité appuyant l'intensification des CSI à court terme. Enfin, nous formulons des conseils applicables en pratique clinique et mettons en évidence les priorités de recherche future.

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Introduction

Asthma action plans (AAPs) are personalized written plans provided by healthcare professionals to patients with asthma that contain guidance for treatment escalation during periods of acute loss of asthma control, in order to prevent progression to an asthma exacerbation. Acute loss of asthma control represents a period when asthma symptoms rapidly deteriorate over hours to days and is distinct from the broader concept of overall asthma control assessed over weeks to months, and managed with stepwise escalation/de-escalation of controller therapies and addressing modifiable risk factors for poor control, rather than an AAP.[1] When coupled with education and regular clinical review, AAPs reduce asthma symptoms and healthcare utilization and improve quality of life.[2,3] Despite their proven benefit and endorsement from all major international asthma guidelines in patients with a history of asthma exacerbation, AAP use in practice remains poor.[4,5] Provider-level barriers to AAP use include lack of time, knowledge, experience and confidence, particularly when determining advice for therapeutic escalation of controller therapy in the "yellow zone" (acute loss of asthma control zone) of the AAP.[6,7] To address these barriers, we previously developed an evidence-based tool to facilitate provision of AAPs at the point-of-care to adult patients with asthma.[8] The tool provides practical guidance on how to escalate inhaled controller therapy in response to yellow zone asthma symptoms, based on common baseline controller therapy regimens (the "green zone"). Since its original publication in 2017[8] along with a Practice Guide published in 2019,[9] it has been accessed in full text format > 15,000 times, was endorsed by the Canadian Thoracic Society (CTS), and is referenced in the (latest) CTS 2021 Guideline update: Diagnosis and management of asthma in preschoolers, children and adults.[1] It has also been successfully incorporated into a widely used computerized clinical decision support system (eAMS – electronic Asthma Management System) (www.easthma.ca) that significantly improves AAP delivery, assessment of asthma control and guideline-concordant medication adjustments.[10]

Statement of clinical question

Since publication of the original asthma action plan tool in 2017, the therapeutic landscape for adult asthma has expanded considerably. Multiple new inhaler devices, updated formulations and novel drug combinations have been introduced, and use of triple therapy with an inhaled corticosteroid (ICS), long-acting beta-agonist (LABA) and long-acting muscarinic antagonist (LAMA) has become more common. These developments have created new challenges for clinicians attempting to translate guideline recommendations into precise yet practical yellow zone instructions for patients. The central clinical question guiding this review was therefore whether current evidence supports updating the asthma action plan tool to accommodate these newer therapies and devices, to ensure that the tool remains a relevant, accurate and useful resource for healthcare practitioners striving to deliver guideline-based asthma care.

Methods

To update the previous guidance, we reviewed the most recent iterations of the international asthma guidelines and guidance documents that informed our original guidance, including the Global Initiative for Asthma (GINA) Global Strategy for Asthma Management and Prevention 2025 update,[11] the Canadian Thoracic Society 2021 guideline update on the diagnosis and management of asthma in preschoolers, children and adults[1] and the National Institute for Health and Care Excellence/British Thoracic Society/Scottish Intercollegiate Guidelines Network (NICE/BTS/SIGN) 2024 asthma guideline.[12] We also performed narrative literature reviews for systematic reviews and individual studies pertaining to therapeutic escalation in asthma action plans. Finally, we searched MEDLINE from January 2022 to January 2025 (this date range was chosen to complement the search results of the most recent Cochrane review of AAPs[13]) using the same search terms detailed in the original publication.[8]

Alongside guideline and literature review, we undertook a detailed evaluation of new inhaler products released since 2017. This included reviewing product monographs, dose-equivalency studies, pharmacokinetic data, and safety information for emerging ICS monotherapies, ICS/LABA combinations, and triple therapy inhalers. For Canadian medications, we searched the Government of Canada Drug Product Database, for the US the Food and Drug Administration Drugs@FDA database, and for Europe the European Medicines Agency database. Because device-specific evidence for yellow zone adjustments is largely absent from clinical trials and product monographs, we applied the same evidence-informed and pragmatically grounded framework used in the original publications (see Online Supplemental Appendix Tables A1 and A2 for complete details).[8,9] When high-quality data were available (for example for quadrupling ICS doses) we adhered closely to these findings. When evidence was limited or absent, we synthesized pharmacologic principles, regulatory constraints, and real-world considerations to develop optional yellow zone guidance that would be safe, feasible and clinically meaningful. Final decisions were achieved through consensus discussion among all authors.

Results

Guideline review

In contrast to our review of asthma guidelines in 2017, there is now a much clearer consensus among GINA, NICE/BTS/SIGN, and CTS asthma guidelines regarding the effectiveness of quadrupling the ICS component of baseline asthma therapy as part of the AAP yellow zone strategy for adults.[1,11,12] A total of 2 of the 3 documents referenced the pragmatic randomized controlled trial by McKeever et al. published in 2018 that reported a 19% reduction in the incidence of severe asthma exacerbations over 1 year with use of an AAP that included a quadrupling in the dose of ICS versus 1 without a dose increase, during periods of acute loss of asthma control in patients with a history of at least 1 exacerbation requiring systemic corticosteroid in previous 12 months.[14] There is also

Table 1. Asthma action plan formulation table (for use in age 18+ years): Canada.

REGION: Canada		
ICS monotherapy		
Medications	Green Zone	Change in Yellow Zone (all changes are for 7-14 days)
Flovent HFA (Fluticasone propionate) *(or generic equivalents)*	125 mcg 1 puff bid	Increase to 4 puffs bid
	125 mcg 2 puffs bid	Increase to 4 puffs qid
	250 mcg 1 puff bid	Increase to 4 puffs bid
	250 mcg 2 puffs bid	Increase to 4 puffs bid
Flovent Diskus (Fluticasone propionate) *(or generic equivalents)*	100 mcg 1 puff bid	Increase to 4 puffs bid
	250 mcg 1 puff bid	Increase to 4 puffs bid
	500 mcg 1 puff bid	Increase to 2 puffs bid
Arnuity Ellipta (Fluticasone furoate)	100 mcg 1 puff daily	Option 1: Increase to 4 puffs daily (off-label)[a] Option 2: Prednisone 30-50 mg daily[b]
	200 mcg 1 puff daily	Option 1: Increase to 4 puffs daily (off-label)[a] Option 2: Prednisone 30-50 mg daily[b]
Pulmicort Turbuhaler (Budesonide)	100 mcg 1 puff bid	Increase to 4 puffs bid
	200 mcg 1 puff bid	Increase to 4 puffs bid
	400 mcg 1 puff bid	Increase to 3 puffs bid
QVAR MDI (Beclomethasone)	50 mcg 1 puff bid	Increase to 4 puffs bid
	100 mcg 1 puff bid	Increase to 4 puffs bid
	100 mcg 2 puffs bid	Prednisone 30–50 mg daily[b]
Alvesco MDI (Ciclesonide)	100 mcg 1 puff daily	Increase to 4 puffs daily
	200 mcg 1 puff daily	Increase to 4 puffs daily
	200 mcg 2 puffs daily	Increase to 4 puffs bid
Asmanex Twisthaler (Mometasone)	200 mcg 1 puff daily	Increase to 4 puffs daily
	400 mcg 1 puff daily	Option 1: Increase to 4 puffs daily (off-label)[a] Option 2: Prednisone 30-50 mg daily[b]
ICS/LABA Combination Therapy		
Medications	Green Zone	Change in Yellow Zone (all changes are for 7-14 days)
Advair Diskus (Fluticasone propionate/Salmeterol)	100/50 mcg 1 puff bid	Add Flovent Diskus 100 mcg 3 puffs bid
	250/50 mcg 1 puff bid	Add Flovent Diskus 250 mcg 3 puffs bid
	500/50 mcg 1 puff bid	Add Flovent Diskus 500 mcg 1 puffs bid
Advair HFA (Fluticasone propionate/Salmeterol)	125/25 mcg 2 puff bid	Add Flovent HFA 250 mcg 3 puffs bid
	250/25 mcg 2 puffs bid	Add Flovent HFA 250 mcg 2 puffs bid
Symbicort Turbuhaler (Budesonide/Formoterol) with a non ICS-containing reliever (e.g. Salbutamol)	100/6 mcg 1 puff bid	Increase to 4 puffs bid
	200/6 mcg 1 puff bid	Increase to 4 puffs bid
	200/6 mcg 2 puffs bid	Add Pulmicort Turbuhaler 400 mcg 2 puffs bid
Symbicort Turbuhaler (Budesonide/Formoterol) used as MART *(updated since 2017 table)*	200/6 mcg 1 puff bid + as needed	Option 1: Increase as needed to a maximum of 8 puffs per day Option 2: Increase to 4 puffs bid (no further "as needed" puffs permitted)
	200/6 mcg 2 puff bid + as needed	Option 1: Increase as needed to a maximum of 8 puffs per day Option 2: Prednisone 30-50 mg daily[b]
Symbicort Turbuhaler (Budesonide/Formoterol) used as needed only (no maintenance inhaler) *(updated since 2017 table)*	200/6 mcg 1 puff as needed	Increase Symbicort as needed to a maximum of 8 puffs per day
Zenhale MDI (Mometasone Furoate/Formoterol)	100/5 mcg 2 puffs bid	Option 1: Change to Zenhale MDI 200/5 mcg 4 puffs bid (off-label)[a] Option 2: Prednisone 30-50 mg daily[b]
	200/5 mcg 2 puffs bid	Prednisone 30-50 mg daily[b]
Breo Ellipta (Fluticasone furoate/Vilanterol) *(updated since 2017 table)*	100/25 mcg 1 puff daily	Option 1: add Arnuity Ellipta 100 mcg 3 puffs daily (off-label)[a] Option 2: Prednisone 30-50 mg daily[b]
	200/25 mcg 1 puff daily	Option 1: add Arnuity Ellipta 200 mcg 3 puffs daily (off-label)[a] Option 2: Prednisone 30-50 mg daily[b]
Wixela Inhub (Fluticasone propionate/Salmeterol) *(new since 2017 table)*	100/50 mcg 1 puff bid	Add Flovent Diskus 100 mcg 3 puffs bid
	250/50 mcg 1 puff bid	Add Flovent Diskus 250 mcg 3 puffs bid
	500/50 mcg 1 puff bid	Add Flovent Diskus 500 mcg 1 puff bid
Atectura Breezhaler (Indacaterol/Mometasone) *(new since 2017 table)*	150/80 mcg 1 puff daily	Option 1: Increase to 4 puffs daily (off-label)[a] Option 2: Prednisone 30-50 mg daily[b]
	150/160 mcg 1 puff daily	Option 1: Increase to 4 puffs daily (off-label)[a] Option 2: Prednisone 30-50 mg daily[b]
	150/320 mcg 1 puff daily	Prednisone 30-50 mg daily[b]

(*Continued*)

Table 1. Continued.

ICS/LABA/LAMA Combination Therapy		
Medications	Green Zone	Change in Yellow Zone (all changes are for 7-14 days)
Trelegy Ellipta (Fluticasone furoate/Umeclidinium/Vilanterol) *(new since 2017 table)*	100/62.5/25 mcg 1 puff daily	Option 1: add Arnuity Ellipta100 mcg 3 puffs daily (off-label)[a] Option 2: prednisone 30-50mg daily for 5-7 days[b]
	200/62.5/25 mcg 1 puff daily	Option 1: add Arnuity Ellipta 200 mcg 3 puffs daily (off-label)[a] Option 2: prednisone 30-50 mg daily for 5-7 days[b]
Enerzair Breezhaler (Indacaterol/Glycopyrronium/Mometasone) *(new since 2017 table)*	150/50/160 mcg 1 puff daily	Prednisone 30-50 mg daily[b]
Special Considerations		
In patients with a history of sudden and severe exacerbations, and/or presenting with PEF or FEV1 ≤ personal best/predicted		Prednisone 30-50 mg daily for 5-7 days as first line therapy[b]
If patient fails to improve clinically within 2–3 days of increase in inhaled medication, and/or has a rapid clinical deterioration, and/or has a peak expiratory flow or FEV1 that falls to ≤60% of their personal best value		Prednisone 30-50 mg daily for 5-7 days as rescue (second line) therapy[b]

Abbreviations: ICS, inhaled corticosteroid; LABA, long-acting beta-agonist; MART, maintenance and reliever therapy; LAMA, long-acting muscarinic antagonist; PEF, peak expiratory flow; FEV1, forced expiratory volume in 1 second.

[a]This dose exceeds product monograph total daily dose limits intended for chronic daily use. A short-term dose increase beyond these limits has not been specifically studied, but the evidence for asthma action plans supports its potential to reduce the need for oral corticosteroid. Given the known risks of oral corticosteroid use, we favor this approach (expert opinion). However, the decision to pursue this approach should be based on individual patient and clinician comfort, and critically, clinicians must ensure that patients return to their usual maintenance dose after 7-14 days.

[b]Ask patients to contact the health care provider to consider a prednisone prescription and/or provide a standing prescription for prednisone/prednisolone 30-50 mg daily for 5-7 days. Ensure that patients are appropriately counseled about the risks of short-term prednisone use.

Reference: Kouri A, Jackson L, Kaplan A, Gupta S. Practical and evidence-based guidance for yellow zone medication escalation in adult asthma action plans: A clinical respiratory review. CJRCCSM. 2025.[24]

now more general discussion in each document regarding how different baseline inhaler regimens can be adjusted to achieve this recommended increase but gaps remain. However, apart from the CTS guideline, which links to the original AAP yellow zone completion tool, specific practical guidance on how to operationalize these 4-fold ICS dose increases across different available inhaler formulations is still mostly absent. For example, there is no guidance on how to make yellow zone adjustments when faced with jurisdictional daily dose limits, on when a combination inhaler should be increased to achieve a 4-fold ICS increase versus adding a separate ICS-containing inhaler, or on whether different inhaler device types should be used to add ICS when the same device type is not available. Additionally, there is no discussion of how triple inhaler therapy with ICS/LABA/LAMA should be practically adjusted as part of an AAP.

Narrative review

Our narrative review identified 7 studies relevant to the therapeutic dose escalations proposed in AAP yellow zone.[15–21] These studies report on the safety, efficacy and/or dose-equivalency/comparability in different inhaler devices of fluticasone propionate/furoate, salmeterol, indacaterol, mometasone furoate and glycopyrronium, and they were used to arrive at evidence-based consensus suggestions for yellow zone therapeutic escalations (more detail is provided in the Discussion section).

Literature review

Our literature review revealed 1 Cochrane systematic review of AAP use in children and adults by Kew et al,[13] which did not include any adult AAP studies not already reviewed in our previous publications. The authors of this review referenced the McKeever at al[14] study but did not include it in their analysis due to lack of blinding. However, they assert that these types of pragmatic trials are likely more reflective of real-life clinical settings.[14] Finally, our MEDLINE search did not reveal any new studies evaluating different yellow zone escalation studies other than the previously noted McKeever trial (which confirms the therapeutic approach in the original tool).[14]

Discussion and recommendations

While no substantial new guidance on the practical operationalization of dose escalations in the AAP yellow zone has been offered in the literature, the therapeutic landscape of asthma inhalers has become increasingly complex. Since publication of the original tool, multiple new devices now deliver regimens previously included, and entirely new therapeutic combinations have emerged. These new options introduce new complexities when attempting to apply the ICS quadrupling principle, discussed in detail in the following section. We present updated comprehensive yellow zone suggestions in jurisdiction-specific tables for Canada, the United States, and Europe, in Tables 1-3, optimized for printing for use at the point-of-care.

New inhaler devices containing previously included medications

The first category of updates we addressed were new inhaler devices in the 3 jurisdictions containing medication regimens already included in the initial tool. These include Wixela® Inhub® in Canada and the United States, the Fluticasone Propionate and Salmeterol Inhalation Powder

Table 2. Asthma action plan formulation table (for use in age 18+ years): United States.

REGION: USA		
ICS monothreapy		
Medications	Green Zone	Change in Yellow Zone (all changes are for 7-14 days)
Generic MDI Fluticasone propionate	110 mcg 1 puff bid	Increase to 4 puffs bid
	110 mcg 2 puffs bid	Increase to 4 puffs qid
	220 mcg 1 puff bid	Increase to 4 puffs bid
	220 mcg 2 puffs bid	Increase to 4 puffs bid
Generic Diskus Fluticasone propionate	100 mcg 1 puff bid	Increase to 4 puffs bid
	250 mcg 1 puff bid	Increase to 4 puffs bid
	500 mcg 1 puff bid	Increase to 2 puffs bid
Arnuity Ellipta (Fluticasone furoate)	100 mcg 1 puff daily	Option 1: Increase to 4 puffs daily (off-label)[a] Option 2: Prednisone 30-50 mg daily[b]
	200 mcg 1 puff daily	Option 1: Increase to 4 puffs daily (off-label)[a] Option 2: Prednisone 30-50 mg daily[b]
Pulmicort Flexhaler (Budesonide)	90 mcg 1 puff bid	Increase to 4 puffs bid
	180 mcg 1 puff bid	Increase to 4 puffs bid
	360 mcg 1 puff bid	Increase to 3 puffs bid
QVAR Redihaler (Beclomethasone)	40 mcg 1 puff bid	Increase to 4 puffs bid
	80 mcg 1 puff bid	Increase to 4 puffs bid
	80 mcg 2 puffs bid	Prednisone 30-50 mg daily[b]
Alvesco MDI (Ciclesonide)	80 mcg 1 puff daily	Increase to 4 puffs daily
	160 mcg 1 puff daily	Increase to 4 puffs daily
	160 mcg 2 puffs daily	Increase to 4 puffs bid
Asmanex HFA (Mometasone)	100 mcg 2 puffs bid	Option 1: Add Asmanex HFA 200 mcg 3 puffs bid (off-label)[a] Option 2: Prednisone 30-50 mg daily[b]
	200 mcg 2 puffs bid	Prednisone 30-50 mg daily[b]
Asmanex Twisthaler (Mometasone)	220 mcg 1 puff daily	Increase to 4 puffs daily
	220 mcg 2 puff daily	Prednisone 30-50 mg daily[b]
ICS/LABA Combination Therapy		
Medications	Green Zone	Change in Yellow Zone (all changes are for 7-14 days)
Advair Diskus (Fluticasone propionate/Salmeterol) *(or generic equivalents)*	100/50 mcg 1 puff bid	Add fluticasone propionate Diskus 100 mcg 3 puffs bid
	250/50 mcg 1 puff bid	Add fluticasone propionate Diskus 250 mcg 3 puffs bid
	500/50 mcg 1 puff bid	Add fluticasone propionate Diskus 500 mcg 1 puffs bid
Advair HFA (Fluticasone propionate/Salmeterol) *(or generic equivalents)*	115/21 mcg 2 puff bid	Add fluticasone propionate HFA 110 mcg 3 puffs bid
	230/21 mcg 2 puffs bid	Add fluticasone propionate HFA 220 mcg 2 puffs bid
Wixela Inhub (Fluticasone propionate/ Salmeterol) *(new since 2017 table)*	100/50 mcg 1 puff bid	Add fluticasone propionate Diskus 100 mcg 3 puffs bid
	250/50 mcg 1 puff bid	Add fluticasone propionate Diskus 250 mcg 3 puffs bid
	500/50 mcg 1 puff bid	Add fluticasone propionate Diskus 500 mcg 1 puff bid
Fluticasone Propionate and Salmeterol Inhalation Powder (Multidose Dry Powder Inhaler) (generic version of AirDuo Respiclick) *(new since 2017 table)*	55/14 mcg 1 puff bid	Add fluticasone propionate Diskus 100 mcg 1 puff bid[c]
	113/14 mcg 1 puffs bid	Add fluticasone propionate Diskus 100 mcg 3 puffs bid[c]
	232/14 mcg 1 puff bid	Add fluticasone propionate Diskus 250 mcg 3 puffs bid[c]
Breo Ellipta (Fluticasone furoate/Vilanterol) *(or generic equivalents)*	100/25 mcg 1 puff daily	Option 1: add Arnuity Ellipta 100 mcg 3 puffs daily (off-label)[a] Option 2: Prednisone 30-50 mg daily[b]
	200/25 mcg 1 puff daily	Option 1: add Arnuity Ellipta 200 mcg 3 puffs daily (off-label)[a] Option 2: Prednisone 30-50 mg daily[b]
Symbicort pMDI (Budesonide/Formoterol)	80/4.5 mcg 1 puff bid	Option 1: Increase to 4 puffs bid (off-label)[a] Option 2: Prednisone 30-50 mg daily[b]
	160/4.5 mcg 1 puff bid	Option 1: Increase to 4 puffs bid (off-label)[a] Option 2: Prednisone 30-50 mg daily[b]
	160/4.5 mcg 2 puffs bid	Prednisone 30-50 mg daily[b]

(*Continued*)

Table 2. Continued.

Dulera MDI(Mometasone/Formoterol)	100/5 mcg 2 puffs bid	Option 1: Change to Dulera MDI 200/5 mcg 4 puffs bid (off-label)[a] Option 2: Prednisone 30-50 mg daily[b]
	200/5 mcg 2 puffs bid	Prednisone 30-50 mg daily[b]
Airsupra inhalation aerosol (Albuterol/Budesonide) as needed only (no maintenance inhaler) *(new since 2017 table)*	90/80 mcg 2 puffs as needed	Increase as needed to a maximum of 12 puffs per day
ICS/LABA/LAMA Combination Therapy		
Medications	Green Zone	Change in Yellow Zone (all changes are for 7-14 days)
Trelegy Ellipta (Fluticasone furoate/Umeclidinium/Vilanterol) *(new since 2017 table)*	100/62.5/25 mcg 1 puff daily	Option 1: add Arnuity Ellipta 100 mcg 3 puffs daily (off-label)[a] Option 2: prednisone 30-50 mg daily for 5-7 days[b]
	200/62.5/25 mcg 1 puff daily	Option 1: add Arnuity Ellipta 200 mcg 3 puffs daily (off-label)[a] Option 2: prednisone 30-50 mg daily for 5-7 days[b]
Special Considerations		
In patients with a history of sudden and severe exacerbations, and/or presenting with PEF or FEV1 ≤ personal best/predicted		Prednisone 30-50 mg daily for 5-7 days as first line therapy[b]
If patient fails to improve clinically within 2-3 days of increase in inhaled medication, and/or has a rapid clinical deterioration, and/or has a peak expiratory flow or FEV1 that falls to ≤60% of their personal best value		Prednisone 30-50 mg daily for 5-7 days as rescue (second line) therapy[b]

Abbreviations: ICS, inhaled corticosteroid; LABA, long-acting beta-agonist; LAMA, long-acting muscarinic antagonist; PEF, peak expiratory flow; FEV1, forced expiratory volume in 1 second.

[a]This dose exceeds product monograph total daily dose limits intended for chronic daily use. A short-term dose increase beyond these limits has not been specifically studied, but the evidence for asthma action plans supports its potential to reduce the need for oral corticosteroid. Given the known risks of oral corticosteroid use, we favor this approach (expert opinion). However, the decision to pursue this approach should be based on individual patient and clinician comfort, and critically, clinicians must ensure that patients return to their usual maintenance dose after 7–14 days.

[b]Ask patients to contact the health care provider to consider a prednisone prescription and/or provide a standing prescription for prednisone/prednisolone 30–50 mg daily for 5–7 days. Ensure that patients are appropriately counseled about the risks of short-term prednisone use.

[c]As there is no ICS-only version of this inhaler, we have recommended adding a different dry powder inhaler to achieve the 4-fold increase in ICS. Be sure patient is counseled on correct inhaler technique.

Reference: Kouri A, Jackson L, Kaplan A, Gupta S. Updating the point-of-care tool to guide completion of asthma action plans. 2025.

(Multidose Dry Powder Inhaler in the United States, and various budesonide/formoterol containing devices in the EU (DuoResp® Spiromax, BiResp® Spiromax and GoResp® Digihaler. In these cases, our yellow zone suggestions focusing on quadrupling the ICS component of therapy mirrored those in the original tool for these medications (see Online Supplemental Table A1).[8] For the fluticasone propionate monotherapy regimens, we advise increasing the frequency of maintenance inhaler puffs to quadruple the ICS component. For regimens where this increase would surpass the recommended daily dose limit of fluticasone propionate, we advise increasing the frequency of puffs to target a total daily dose of 2000 mcg, which has been shown to have similar efficacy to a short course of oral corticosteroid.[8] For fluticasone propionate/salmeterol combination regimens, we advise continuing the baseline inhaler frequency and adding fluticasone propionate using the same device type to quadruple the ICS component without surpassing the regulatory dose limit for salmeterol. Once again, where regulatory limits for fluticasone propionate would be surpassed with quadrupling, we targeted a total dose of 2000 mcg. For Wixela Inhub, as there is no fluticasone propionate Inhub monotherapy device, we advise using fluticasone propionate in a Diskus® device, as the mechanism of actuation and inhalation are nearly identical.[16] For the fluticasone propionate/salmeterol Respiclick (the generic version of AirDuo) available in the United States, there is no longer a fluticasone propionate alone option available (ArmonAir Respiclick has been discontinued), so we also advise using fluticasone propionate in a Diskus® device in the yellow zone. For inhalers containing budesonide/formoterol (DuoResp® Spiromax, BiResp® Spiromax and GoResp® Digihaler), we also followed our previous guidance (see Online Supplemental Table A1), advising quadrupling the ICS component. In regimens where this increase would surpass the recommended daily dose limit of budesonide, we advise increasing the frequency of puffs to target a total daily dose of 2400 mcg, which has been shown to be non-inferior to a short course of oral corticosteroid in 2 trials.[22,23]

New inhaler devices containing medication regimens not previously included

The second category of updates was for new devices containing combinations of medications not addressed in the initial tool. These included Atectura® and Enerzair® Breezhaler ® (indacaterol/mometasone and indacaterol/glycopyrronium/mometasone, respectively) and Trelegy® Ellipta® (fluticasone furoate/umeclidinium/vilanterol). Once again, our guiding principle was to quadruple the ICS component of therapy while keeping changes as simple as possible to reduce the chance of patient confusion and error. For Atectura Breezhaler, we advise quadrupling the dose to 4 inhalations daily (quadrupling both the mometasone and indacaterol components) for the low and medium dose products (a preferred option to adding a new inhaler in the yellow zone,

Table 3. Asthma action plan formulation table (for use in age 18+ years): European Union.

REGION: EU		
ICS monotherapy		
Medications	Green Zone	Change in Yellow Zone (all changes are for 7-14 days)
Flixotide Evohaler (Fluticasone propionate)	125 mcg 1 puff bid 125 mcg 2 puffs bid 250 mcg 1 puff bid 250 mcg 2 puffs bid	Increase to 4 puffs bid Increase to 4 puffs qid Increase to 4 puffs bid Increase to 4 puffs bid
Flixotide Accuhaler (Fluticasone propionate)	100 mcg 1 puff bid 250 mcg 1 puff bid 500 mcg 1 puff bid	Increase to 4 puffs bid Increase to 4 puffs bid Increase to 2 puffs bid
Pulmicort Turbohaler (Budesonide)	100 mcg 1 puff bid 200 mcg 1 puff bid 400 mcg 1 puff bid	Increase to 4 puffs bid Increase to 4 puffs bid Increase to 3 puffs bid
Easyhaler Budesonide (Budesonide)	100 mcg 1 puff bid 200 mcg 1 puff bid 400 mcg 1 puff bid	Increase to 4 puffs bid Increase to 4 puffs bid Increase to 3 puffs bid
QVAR MDI / QVAR Easi-Breathe / QVAR Autohaler (Beclomethasone)	50 mcg 1 puff bid 100 mcg 1 puff bid 100 mcg 2 puffs bid	Increase to 4 puffs bid Increase to 4 puffs bid Prednisolone 30-50 mg daily[(b)]
Alvesco Inhaler (Ciclesonide)	80 mcg 1 puff daily 160 mcg 1 puff daily 160 mcg 2 puffs daily	Increase to 4 puffs daily Increase to 4 puffs daily Increase to 4 puffs bid
Asmabec Clickhaler (Beclomethasone)	100 mcg 1 puff bid 250 mcg 1 puff bid	Increase to 4 puffs bid Option 1: Increase to 4 puffs bid (off-label)[(a)] Option 2: Prednisolone 30-50 mg daily[(2)]
Asmanex Twisthaler (Mometasone)	200 mcg 1 puff daily 400 mcg 1 puff daily	Increase to 4 puffs daily Option 1: Increase to 4 puffs daily (off-label)[(1)] Option 2: Prednisolone 30-50 mg daily[(2)]
ICS/LABA Combination Therapy		
Medications	Green Zone	Change in Yellow Zone (all changes are for 7-14 days)
Seretide Accuhaler (Fluticasone propionate/Salmeterol)	100/50 mcg 1 puff bid 250/50 mcg 1 puff bid 500/50 mcg 1 puff bid	Add Flixotide Accuhaler 100 mcg 3 puffs bid Add Flixotide Accuhaler 250 mcg 3 puffs bid Add Flixotide Accuhaler 500 mcg 1 puffs bid
Seretide Evohaler (Fluticasone propionate/Salmeterol)	125/25 mcg 2 puff bid 250/25 mcg 2 puffs bid	Add Flixodide Evohaler 250 mcg 3 puffs bid Add Flixodide Evohaler 250 mcg 2 puffs bid
Seffalair Spiromax (Salmeterol/Fluticasone Propionate) *(new since 2017 table)*	12.75/100 mcg 1 puff bid 12.75/202 mcg 1 puff bid	Prednisolone 30-50 mg daily[(2)(c)] Prednisolone 30-50 mg daily[(2)(3)]
Symbicort Turbohaler (Budesonide/Formoterol) with a non-ICS-containing reliever (e.g. Salbutamol)	100/6 mcg 1 puff bid 200/6 mcg 1 puff bid 200/6 mcg 2 puffs bid	Increase to 4 puffs bid Increase to 4 puffs bid Add Pulmicort Turbohaler 400 mcg 2 puffs bid
Symbicort Turbohaler (Budesonide/Formoterol) used as MART *(updated since 2017 table)*	200/6 mcg 1 puff bid + as needed 200/6 mcg 2 puff bid + as needed	Option 1: Increase as needed to a maximum of 12 puffs per day Option 2: Increase to 4 puffs bid (only 4 further "as needed" puffs permitted/day) Option 1: Increase as needed to a maximum of 12 puffs per day Option 2: Prednisolone 30-50 mg daily[(2)]
Symbicort Turbohaler (Budesonide/Formoterol) used as needed only (no maintenance inhaler) *(updated since 2017 table)*	200/6 mcg 1 puff as needed	Increase as needed to a maximum of 12 puffs per day
DuoResp Spiromax/BiResp Spiromax/GoResp Digihaler (Budesonide/Formoterol) with a non ICS-containing reliever (e.g. Salbutamol) *(new since 2017 table)*	160/4.5 mcg 1 puff bid 160/4.5 mcg 2 puffs bid 320/9 mcg 1 puff bid	Increase to 4 puffs bid Add budesonide DPI 400 mcg 2 puffs bid Add budesonide DPI 400 mcg 2 puffs bid
DuoResp Spiromax/BiResp Spiromax (Budesonide/Formoterol) used as maintenance and reliever therapy (MART) *(new since 2017 table)*	160/4.5 mcg 1 puff bid 160/4.5 mcg 2 puffs bid	Option 1: Increase as needed to a maximum of 12 puffs per day Option 2: Increase to 4 puffs bid (only 4 further "as needed" puffs permitted/day) Option 1: Increase as needed to a maximum of 12 puffs per day Option 2: Prednisolone 30-50 mg daily[(2)]
DuoResp Spiromax/BiResp Spiromax (Budesonide/Formoterol) used as needed only (no maintenance inhaler) *(new since 2017 table)*	160/4.5 mcg 1 puff as needed	Increase as needed to a maximum of 12 puffs per day
Relvar Ellipta (Fluticasone furoate/Vilanterol)	92/22 mcg 1 puff daily 184/22 mcg 1 puff daily	Prednisolone 30-50 mg daily[(2)(3)] Prednisolone 30-50 mg daily[(2)(3)]
Fostair MDI (Beclomethasone/Formoterol)	100/6 mcg 1 puff bid 200/6 mcg 1 puff bid	Increase to 4 puffs bid Option 1: Increase to 4 puffs bid (off-label)[(1)] Option 2: Prednisolone 30-50 mg daily[(2)]

(*Continued*)

Table 3. Continued.

Fostair Nexthaler (Beclomethasone/Formoterol)	100/6 mcg 1 puff bid 200/6 mcg 1 puff bid	Increase to 4 puffs bid Option 1: Increase to 4 puffs bid (off-label)[1] Option 2: Prednisolone 30-50 mg daily[2]
Flutiform MDI (Fluticasone propionate/Formoterol)	50/5 mcg 1 puff bid 125/5 mcg 1 puff bid 250/10 mcg 1 puff bid	Increase to 4 puffs bid Increase to 4 puffs bid Increase to 4 puffs bid
Atectura/Bemrist Breezhaler (Indacaterol/Mometasone)	125/62.5 mcg 1 puff daily 125/127.5 mcg 1 puff daily 125/260 mcg 1 puff daily	Option 1: Increase to 4 puffs daily (off-label)[1] Option 2: Prednisone 30-50 mg daily[2] Option 1: Increase to 4 puffs daily (off-label)[1] Option 2: Prednisone 30-50 mg daily[2] Prednisone 30-50 mg daily[2]
ICS/LABA/LAMA Combination Therapy		
Medications	Green Zone	Change in Yellow Zone (all changes are for 7-14 days)
Trelegy Ellipta (Fluticasone furoate/ Umeclidinium/Vilanterol) (approved for use in asthma in Canada/USA and often used off-label in Europe) *(new since 2017 table)*	100/62.5/25 mcg 1 puff daily 200/62.5/25 mcg 1 puff daily	Prednisolone 30-50 mg daily for 5-7 days[2][3] Prednisolone 30-50 mg daily for 5-7 days[2][3]
Enerzair Breezhaler (Indacaterol/ Glycopyrronium/ Mometasone) *(new since 2017 table)*	114/46/136 mcg 1 puff daily	Prednisolone 30-50 mg daily[2]
Special Considerations		
In patients with a history of sudden and severe exacerbations, and/or presenting with PEF or FEV1 ≤ personal best/predicted		Prednisolone 30-50 mg daily for 5-7 days as first line therapy[2]
If patient fails to improve clinically within 2–3 days of increase in inhaled medication, and/or has a rapid clinical deterioration, and/or has a peak expiratory flow or FEV1 that falls to ≤60% of their personal best value		Prednisolone 30-50 mg daily for 5-7 days as rescue (second line) therapy[2]

Abbreviations: ICS, inhaled corticosteroid; LABA, long-acting beta-agonist; MART, maintenance and reliever therapy; LAMA, long-acting muscarinic antagonist; PEF, peak expiratory flow; FEV1, forced expiratory volume in 1 second.

[a]This dose exceeds product monograph total daily dose limits intended for chronic daily use. A short-term dose increase beyond these limits has not been specifically studied, but the evidence for asthma action plans supports its potential to reduce the need for oral corticosteroid. Given the known risks of oral corticosteroid use, we favor this approach (expert opinion). However, the decision to pursue this approach should be based on individual patient and clinician comfort, and critically, clinicians must ensure that patients return to their usual maintenance dose after 7–14 days.

[b]Ask patients to contact the health care provider to consider a prednisolone prescription and/or provide a standing prescription for prednisolone 30–50 mg daily for 5–7 days. Ensure that patients are appropriately counseled about the risks of short-term prednisone use.

[c]For these ICS/LABA inhalers using either the Spiromax or Ellipta devices, increasing the number of puffs of the controller to quadruple the ICS component was not possible without also exceeding the regulatory and safety limits of LABA, and there are also no ICS-alone versions of these devices that would permit only increasing the ICS component. In these cases, we elected to recommend a course of prednisolone.

Reference: Kouri A, Jackson L, Kaplan A, Gupta S. Updating the point-of-care tool to guide completion of asthma action plans. 2025.

which may increase patient errors and costs).[8] This indacaterol increase exceeds the recommended daily limit (150 mcg), but we found sufficient evidence for safety of daily doses up to 600 mcg of indacaterol.[17] For low-dose Atectura Breezhaler (150/80 mcg), quadrupling results in a mometasone dose comparable to the manufacturer's recommended maximum daily dose (800 mcg). For the medium-dose Atectura Breezhaler (150/160 mcg), the increased mometasone dose (1600 mcg/day) exceeds the manufacturer's limit (based on the dose comparability between mometasone delivered in the Breezhaler versus Twisthaler devices).[18] We found sufficient evidence for the safety and efficacy of the mometasone 1600 mcg dose,[19] and we reasoned as we have with other similar situations, that a short-term ICS dose increase beyond recommended daily limits was unlikely to result in significant safety risks, particularly when the alternative is a course of oral corticosteroids.[8] However, understanding that not all clinicians would be comfortable exceeding recommended daily limits even temporarily, we also provided an alternative option for a short course of oral corticosteroid in these situations.[8] For high-dose Atectura Breezhaler (150/320), we advise adding prednisone, as a 4-fold increase in the 150/320 mcg strength would far exceed the 1600 mcg Twisthaler-comparable mometasone dose and we could not find evidence for the clinical safety of doses in this range. For Enerzair Breezhaler, we could not advise simply quadrupling the baseline inhaler given concerns about anticholinergic effects of surpassing the recommended maximum daily dose of glycopyrronium.[20] Additionally, given that the baseline dose of mometasone (160 mcg) in Enerzair is comparable to 800 mcg of mometasone delivered via Twisthaler (the daily recommended maximum dose), we were also unable to safely offer an option to quadruple the mometasone dose, and so we advise adding prednisone directly. For Trelegy Ellipta, we were not able to find sufficient evidence for the safety of quadrupling the doses of either umeclidinium or vilanterol, so we advise adding Arnuity Ellipta (fluticasone furoate) to quadruple the fluticasone furoate component alone. The safety of short-term fluticasone furoate use has been studied in doses up to 800 mcg/day.[21] Accordingly, we also revised our previous guidance for Breo® Ellipta (fluticasone furoate/vilanterol),[6] to add Arnuity Ellipta rather than quadrupling Breo. Given that these increases exceed the recommended daily dose for fluticasone furoate (200 mcg), we again included an alternative oral corticosteroid option. Finally, for Airsupra® inhalation aerosol (albuterol/budesonide) used as needed, we advise increasing the number of inhalations as needed up to the maximum recommended daily dose (12 inhalations) rather than adhering to a pre-specified 4-fold ICS increase.

Conclusion

As asthma therapies continue to evolve, decision-support tools must also advance to ensure that guideline recommendations are translated effectively at the point-of-care. There also remains a clear need for clinical trials that evaluate inhaler-based yellow-zone strategies across a wider range of regimens, particularly within triple therapy, and for real-world studies examining how patients understand and implement complex escalation instructions during periods of asthma deterioration. Concurrently, growing interest in digital and electronic health record (EHR)-embedded asthma action plan tools highlights an important opportunity to integrate evidence-based recommendations more seamlessly into clinical workflows, enhance adherence to best practices and support patients in navigating increasingly diverse inhaler platforms. Up-to-date, practical yellow-zone guidance is essential to the success of asthma action plans, and the updated tool presented here incorporates contemporary guideline direction, new therapeutic options and real-world pharmacologic considerations to help clinicians provide safe and effective advice for self-management of acute loss of control. As clinical practice continues to shift toward digital integration and personalized self-management support, such tools will play an increasingly important role in ensuring that asthma action plans remain accessible, actionable, and aligned with the evolving needs of both patients and providers.

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