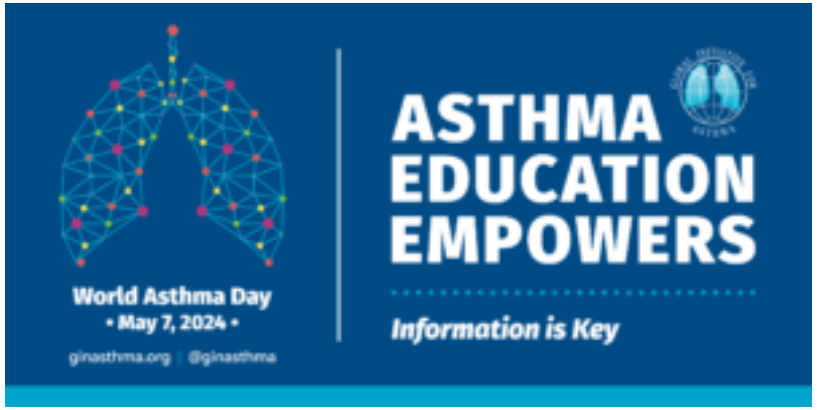

GINA GUIDELINES FOR ASTHMA MANAGEMENT Ages 6-11 years

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Professor, Pediatric Pulmonology and Sleep Medicine

Financial Disclosure

- Planners, Content Reviewers and Speakers for this activity:
  - Did provide disclosure information.
  - Have no relevant financial arrangements or affiliations with commercial interests
  - May discuss commercial products/services and/or non-FDA approved uses of products/providers of services.
- Commercial Support

  This activity receives no commercial support.

Goals of Asthma Treatment

- Few asthma symptoms
- No sleep disturbance
- No exercise limitation
- Maintain normal lung function
- Prevent flares
- Prevent asthma deaths
- Minimize medications side effects

Symptom control (ACT)

Risk Reduction

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Terminology

- **A**nti-**I**nflammatory **R**eliever = **AIR**
  - e.g. ICS-formoterol, ICS-SABA
  - Provides rapid symptom relief, plus a small dose of ICS
  - Reduces the risk of exacerbations, compared with using a SABA reliever

Regimens with ICS-formoterol anti-inflammatory reliever

- As-needed-only ICS-formoterol = **AIR-only**
  - The patient takes low-dose ICS-formoterol whenever needed for symptom relief
- **M**aintenance **A**nd **R**eliever **T**herapy with ICS-formoterol = **MART**
  - A low dose of ICS-formoterol is used as the patient's maintenance treatment, plus whenever needed for symptom relief
- ICS-formoterol can also be used before exercise or allergen exposure

ICS: inhaled corticosteroid: SABA: short-acting beta$_2$-agonist; MART is sometimes also called SMART

Why are we moving away from SABA alone in patients 6 y & older

- Patients with “mild” asthma can have severe life-threatening events or fatal asthma exacerbations. (30% of asthma deaths). This risk is reduced substantially with use of ICS
- SABA only treatment associated with increased risk of exacerbations and lower lung function, and asthma related deaths.
- Regular use of SABA increases allergic responses and airway inflammation, and reduces the bronchodilator response to SABA when its needed
- Over-use of SABA (3 or more canisters in a yr) associated with increased risk of severe exacerbations. 12 or more canisters a year (perhaps less) is associated with increased risk of asthma related death.

Combination as-needed ICS-SABA

- BEST study, combination BDP-albuterol *(Papi et al, NEJMed 2007, n=445, 6 months)*
  - Mean number of exacerbations per patient per year lower with as-needed combination (0.74) and regular BDP (0.71) compared with as-needed albuterol (1.63, P<0.001) and regular combination BDP-albuterol (1.76, P<0.001)

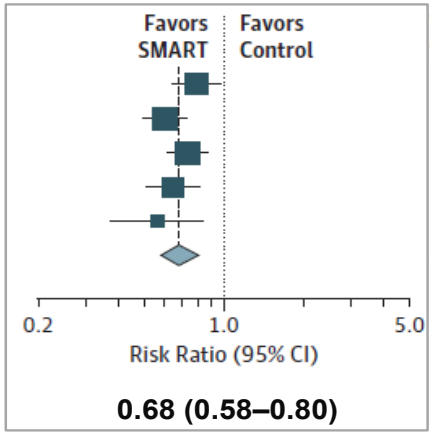
Taking ICS whenever SABA taken with separate inhalers

- TREXA study, BDP and albuterol, children and adolescents *(Martinez et al, Lancet 2011, n=288, 9 months)*
  - Frequency of exacerbations highest with albuterol alone (49%); lower with daily BDP (28%, p=0.03), daily plus as-needed BDP and SABA (31%, p=0.07) and as-needed BDP+SABA (35%, p=0.07)
  - Growth 1.1cm less in daily and combined groups but not as-needed-only group
- BASALT study, BDP and albuterol, adults *(Calhoun et al, JAMA 2012, n=342, 9 months)*
  - Similar exacerbations with as-needed BDP+SABA as with 6-weekly physician-adjusted or FeNO-adjusted ICS
- ASIST study, BDP and albuterol, African-American children and adolescents *(Sumino et al, Annals ATS 2020, n=206, 12 months)*
  - Similar symptoms control and exacerbations compared with physician-adjusted ICS

BDP: beclometasone dipropionate; ICS: inhaled corticosteroids; SABA: short-acting beta2-agonists

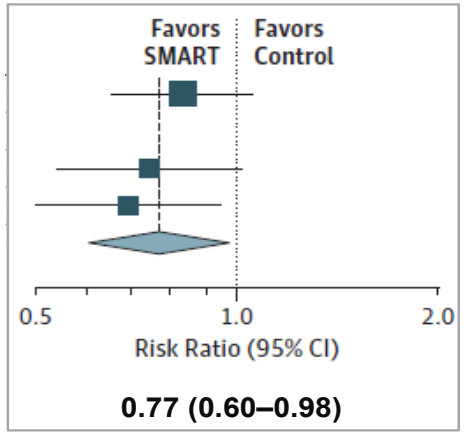
MART- Maintenance and Reliever Therapy

- MART with ICS-formoterol reduces severe exacerbations compared with ICS or ICS-LABA plus SABA reliever, with similar symptom control
  - Confirmed by regulatory studies and pragmatic open-label studies, n~30,000
- Both budesonide and formoterol contribute to the reduction in severe exacerbations

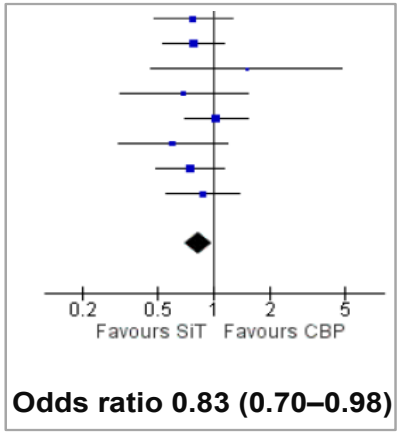


Compared with same dose ICS-LABA +SABA

Sobieraj et al, JAMA 2018 (n=22,748)

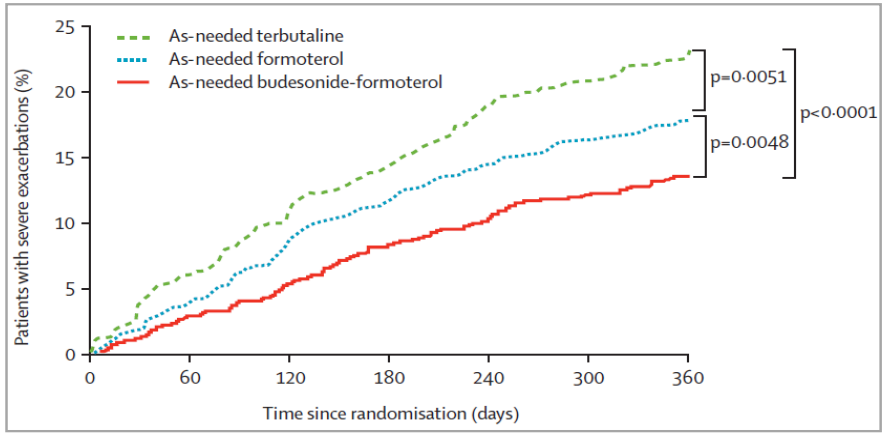


Compared with higher dose ICS-LABA + SABA



Compared with conventional best practice

Cates et al, Cochrane 2013 (n=4,433)



Compared with formoterol or SABA reliever

Rabe, Lancet 2006
N=3,395, all taking maintenance budesonide-formoterol

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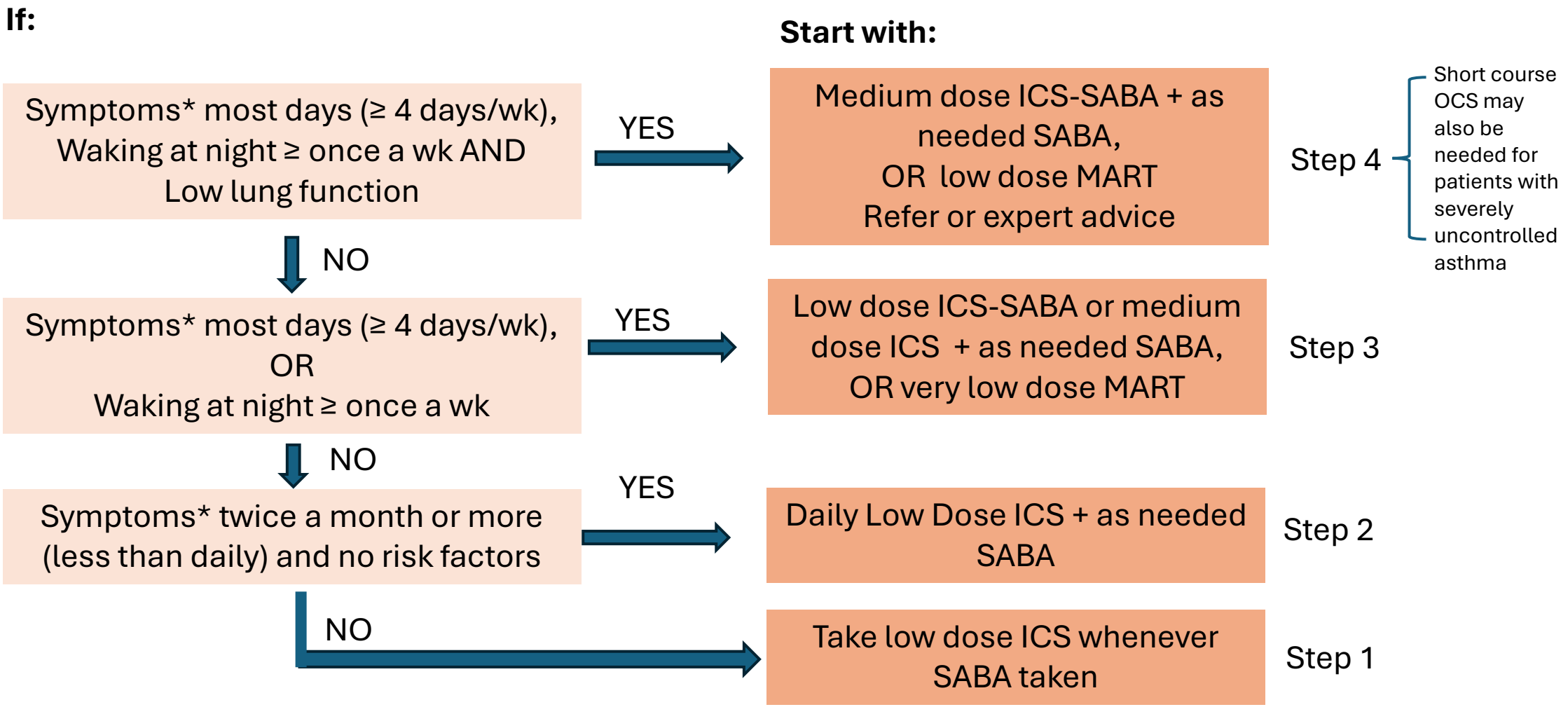
Where to start:



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* or need for reliever

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Step	Age (years)	Medication and device (check patient can use inhaler)	Metered dose (mcg/inhalation)	Delivered dose (mcg/inhalation)	Dosage
Steps 1–2 (AIR-only)	6–11	(No evidence)	-	-	-
	12–17	Budesonide-formoterol DPI	200/6	160/4.5	**1 inhalation whenever needed**
Step 3 MART					PLUS 1 inhalation whenever needed
	12–17	Budesonide-formoterol DPI	200/6	160/4.5	**1 inhalation once or twice daily,**
Step 4 MART					PLUS 1 inhalation whenever needed
	12–17	Budesonide-formoterol DPI	200/6	160/4.5	**2 inhalations twice daily,**
Step 5 MART	12–17	Budesonide-formoterol DPI	200/6	160/4.5	**2 inhalations twice daily,**

DPI: dry powd *mber of puffs*

Follow up after initiating treatment

- Review response to treatment after 2-3 months or earlier depending on clinical urgency
- Adjust treatment accordingly
- Step down once good control has been maintained for 3 months (or more)

Assessing Control: Symptoms

A. Asthma symptom control

In the past 4 weeks, has the patient had:		Well controlled	Partly controlled	Uncontrolled
• Daytime asthma symptoms more than twice/week?	Yes☐ No☐	None of these	1–2 of these	3–4 of these
• Any night waking due to asthma?	Yes☐ No☐			
• SABA* reliever for symptoms more than twice/week?	Yes☐ No☐			
• Any activity limitation due to asthma?	Yes☐ No☐			

Hx of uncontrolled symptoms is an important risk factor for exacerbations

Treatment strategy: ICS containing RX, switch to AIR, action plan, technique review, more freq f/u

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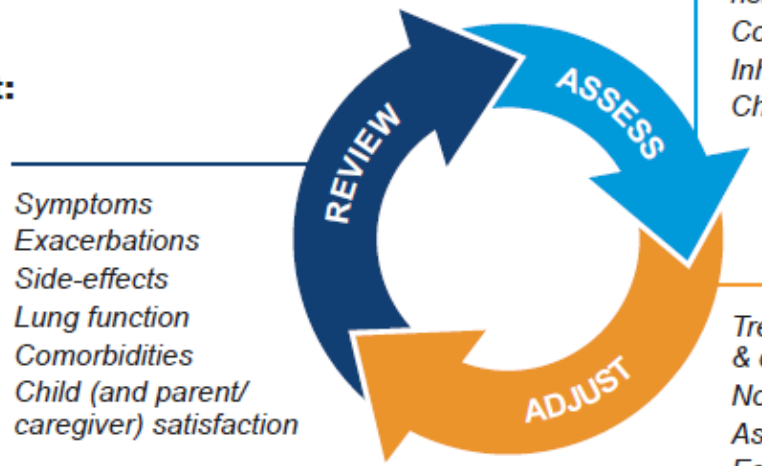
Assessing Control: Risk

Factors that increase the risk of exacerbations even if the patient has a few asthma symptoms

Medications	*High SABA use* (≥3 canisters/year is associated with increased exacerbations, increased mortality, particularly if ≥1 canister/mo *Inadequate ICS;* not prescribed ICS, poor adherence, poor technique
Other medical Conditions	Obesity, chronic rhinosinusitis, GERD, confirmed food allergy, pregnancy
Exposures	Smoking, vaping, allergen exposure if sensitized, air pollution
Psychosocial	Major psychosocial or socioeconomic problems.
Lung function	Lowe FEV-1 (especially ≦60% predicted); high bronchodilator responsiveness
Type 2 inflammatory markers	High blood eosinophils, elevated FeNO (in adults w/allergic asthma taking ICS)
Exacerbation history	Ever intubated or ICU for asthma, ≥1 severe exacerbation in last 12 months

GINA 2023 – Children 6–11 years

Personalized asthma management:
Assess, Adjust, Review



Confirmation of diagnosis if necessary
Symptom control & modifiable risk factors (see Box 2-2)
Comorbidities
Inhaler technique & adherence
Child and parent/caregiver preferences and goals

Symptoms
Exacerbations
Side-effects
Lung function
Comorbidities
Child (and parent/ caregiver) satisfaction

Treatment of modifiable risk factors & comorbidities
Non-pharmacological strategies
Asthma medications (adjust down or up)
Education & skills training

Asthma medication options:
Adjust treatment up and down for individual child's needs

	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5
PREFERRED CONTROLLER to prevent exacerbations and control symptoms	Low dose ICS taken whenever SABA taken*	Daily low dose inhaled corticosteroid (ICS) (see table of ICS dose ranges for children)	Low dose ICS-LABA, OR medium dose ICS, OR very low dose ICS-formoterol maintenance and reliever (MART)	Medium dose ICS-LABA, OR low dose ICS-formoterol maintenance and reliever therapy (MART). Refer for expert advice	Refer for phenotypic assessment ± higher dose ICS-LABA or add-on therapy, e.g. anti-IgE, anti-IL4Rα, anti-IL5
Other controller options (limited indications, or less evidence for efficacy or safety)	*Consider daily low dose ICS*	*Daily leukotriene receptor antagonist (LTRA), or low dose ICS taken whenever SABA taken**	*Low dose ICS + LTRA*	*Add tiotropium or add LTRA*	*As last resort, consider add-on low dose OCS, but consider side-effects*
RELIEVER	As-needed SABA (or ICS-formoterol reliever* in MART in Steps 3 and 4)				

*Anti-inflammatory relievers (AIR)

How to prescribe low-dose ICS-formoterol in GINA Track 1

Example: budesonide-formoterol 200/6 mcg [160/4.5 delivered dose]

- **Steps 1–2**: take 1 inhalation whenever needed for symptoms
- **Step 3**: take 1 inhalation twice a day (or once a day) PLUS 1 inhalation whenever needed for symptoms
- **Steps 4–5**: take 2 inhalations twice a day PLUS 1 inhalation whenever needed for symptoms
- As-needed doses of ICS-formoterol can also be taken before exercise *(Lazarinis et al, Thorax 2014)* or before allergen exposure *(Duong et al, JACI 2007)*

See following slides for medications, doses, and maximum number of inhalations in any day for GINA Track 1

Reliever doses of ICS-formoterol - how much can be taken?

- For ICS-formoterol with 6 mcg (4.5 mcg delivered dose) of formoterol, take **1 inhalation** whenever needed for symptom relief
- Another inhalation can be taken after a few minutes if needed
- Maximum total number of inhalations in any single day (as-needed + maintenance)
  - **Budesonide-formoterol**: maximum 12 inhalations* for adults, 8 inhalations for children, based on extensive safety data *(Tattersfield et al, Lancet 2001; Pauwels et al, ERJ 2003)*
  - **Beclometasone-formoterol**: maximum total 8 inhalations in any day *(Papi et al, Lancet Respir Med 2013)*
- Emphasize that most patients need far fewer doses than this!

- For pMDIs containing 3 mcg formoterol (2.25 mcg delivered dose), take 2 inhalations each time

**For budesonide-formoterol 200/6 [delivered dose 160/4.5 mcg], 12 inhalations gives 72 mcg formoterol (54 mcg delivered dose)*

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Action plan for MART with ICS-formoterol

A Practical Guide to Implementing SMART in Asthma Management

Helen K. Reddel, MB, BS, PhD[a,*], Eric D. Bateman, MB, ChB, MD[b,*], Michael Schatz, MD, MS[c], Jerry A. Krishnan, MD, PhD[d], and Michelle M. Cloutier, MD[e] *Sydney, Australia; Cape Town, South Africa; Chicago, Ill; and Farmington, Conn*

Reddel et al, JACI in Practice 2022; 10: S31-s38

This article includes a writable action plan template
That can be modified for other combination ICS-formoterol inhalers, and for as-needed-only ICS-formoterol

For additional action plans with ICS-formoterol reliever, see National Asthma Council Australia Action plan library
www.nationalasthma.org.au/health-professionals/asthma-action-plans

My Asthma Action Plan

For Single Inhaler Maintenance and Reliever Therapy (SMART)
with budesonide/formoterol

Name: _____ Action plan provided by: _____

Date: _____ Doctor: _____

Usual best PEF: _____ L/min *(if used)* Doctor's phone: _____

Normal mode

My SMART Asthma Treatment is:

☐ budesonide/formoterol 160/4.5 (12 years or older)

☐ budesonide/formoterol 80/4.5 (4-11 years)

My Regular Treatment Every Day:

(Write in or circle the number of doses prescribed for this patient)

Take [1, 2] inhalation(s) in the morning

and [0, 1, 2] inhalation(s) in the evening, every day

Reliever

Use 1 inhalation of budesonide/formoterol whenever needed for relief of my asthma symptoms

I should always carry my budesonide/formoterol inhaler

My asthma is stable if:

- I can take part in normal physical activity without asthma symptoms

AND

- I do not wake up at night or in the morning because of asthma

Other Instructions

_____

_____

Asthma Flare-up

If over a Period of 2-3 Days:

- My asthma symptoms are getting worse **OR NOT** improving

OR

- I am using more than 6 budesonide/formoterol reliever inhalations a day (if aged 12 years or older) or more than 4 inhalations a day (if aged 4-11 years)

I should:

☒ Continue to use my regular everyday treatment **PLUS** 1 inhalation budesonide/formoterol whenever needed to relieve symptoms

☐ Start a course of prednisolone

☐ Contact my doctor

Course of Prednisolone Tablets:

Take _____mg prednisolone tablets

per day for _____days **OR**

_____

_____

If I need more than **12 budesonide/formoterol inhalations (total)** in any day (or more than 8 inhalations for children 4-11 years), I **MUST** see my doctor or go to the hospital the same day.

Asthma Emergency

Signs of an Asthma Emergency:

- Symptoms getting worse quickly
- Extreme difficulty breathing or speaking
- Little or no improvement from my budesonide/formoterol reliever inhalations

If I have any of the above danger signs, I should dial _____ for an ambulance and say I am having a severe asthma attack.

While I am waiting for the ambulance start my asthma first aid plan:

- Sit upright and stay calm.
- Take 1 inhalation of budesonide/formoterol. Wait 1-3 minutes. If there is no improvement, take another inhalation of budesonide/formoterol (up to a maximum of 6 inhalations on a single occasion).
- If only albuterol is available, take 4 puffs as often as needed until help arrives.
- Start a course of prednisolone tablets (as directed) while waiting for the ambulance.
- Even if my symptoms appear to settle quickly, I should see my doctor immediately after a serious attack.

Modified from Australian action plan with permission from National Asthma Council Australia and AstraZeneca Australia