# Asthma + Respiratory FOUNDATION NZ

# NZ ADOLESCENT & ADULT ASTHMA GUIDELINES

2020

# Asthma and Respiratory Foundation NZ Adolescent and Adult Asthma Guidelines 2020: a quick reference guide

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#### ABSTRACT

The purpose of the 2020 Asthma and Respiratory Foundation NZ Adolescent and Adult Asthma Guidelines is to provide simple, practical and evidence-based recommendations for the diagnosis, assessment and management of asthma in adolescents and adults (aged 12 and over) in a quick reference format. The intended users are health professionals responsible for delivering asthma care in the community and hospital settings, and those responsible for the training of such health professionals. The main changes in the 2020 update are: 1) combining the recommendations for both adolescents and adults in a single document, 2) the recommendation to avoid SABA-only treatment in the long-term management of asthma, 3) the use of budesonide/formoterol reliever, with or without maintenance budesonide/formoterol, is preferred to SABA reliever, with or without maintenance ICS or ICS/LABA, across the spectrum of asthma severity, 4) introduction of the terminology 'anti-inflammatory reliever (AIR)' therapy to describe the use of budesonide/formoterol as a reliever medication, with or without maintenance budesonide/ formoterol therapy. This approach encompasses and extends the 'Single combination ICS/LABA inhaler Maintenance And Reliever Therapy' (SMART) approach recommended in the previous guideline, 5) the inclusion of two stepwise management algorithms, 6) a clinical allergy section, 7) the role of LAMA therapy in severe asthma, 8) the role of omalizumab in severe allergic asthma and mepolizumab in severe eosinophilic asthma, 9) an appendix detailing educational materials.

#### Abbreviations:

AIR	Anti-inflammatory reliever
COPD	Chronic obstructive pulmonary disease
FeNO	Fraction of expired Nitric Oxide
FEV <sub>1</sub>	Forced expiratory volume in one second
FVC	Forced vital capacity
GINA	Global Initiative for Asthma
ICS	Inhaled corticosteroid
IgE	Immunoglobulin E
LABA	Long-acting beta <sub>2</sub> -agonist
LAMA	Long-acting muscarinic antagonist
pMDI	Pressurised Metered Dose Inhaler
PaO <sub>2</sub> , PaCO <sub>2</sub>	Arterial oxygen and carbon dioxide tension
PEF	Peak expiratory flow
SABA	Short-acting beta <sub>2</sub> -agonist
SMART	Single combination ICS/LABA inhaler Maintenance And Reliever Therapy
SpO <sub>2</sub>	Oxygen saturation measured by pulse oximetry



#### Context<sup>1-7</sup>

Asthma is a major public health problem in New Zealand with up to 20% of children and adults having asthma. The prevalence rates, particularly in Māori and Pacific adults, are among the highest in the world.

Providing health professionals with current best practice guidance sits within the Asthma and Respiratory Foundation New Zealand's work programme as a priority action towards reducing New Zealand's significant respiratory health burden. Three important documents were released by the Foundation in 2015; Te Hā Ora: The National Respiratory Strategy, The Impact of Respiratory Disease in New Zealand: 2014 update and He Māramatanga huangō: Asthma health literacy for Māori children in New Zealand. These place in context the high prevalence and impact of asthma in New Zealand, the inequities suffered by Māori, Pacific peoples and low income families, and the need for a holistic approach when providing asthma care.

#### Guidelines review<sup>8-10</sup>

The Asthma and Respiratory Foundation New Zealand published the Adult Asthma Guidelines in 2016 and the Childhood and Adolescent Asthma Guidelines in 2017. Since their publication, there have been a number of major advances in the treatment of asthma in adolescents and adults. There has also been greater recognition that the investigation and management of asthma in adolescents and adults (aged 12 and over) has a similar evidence base, which warrants the combining of guideline recommendations across these age groups. For this reason, the 2020 update includes recommendations for both adolescents and adults, and incorporates recent advances in knowledge based on high-quality scientific evidence. The major document which has been reviewed to formulate the 2020 update is the Global Initiative for Asthma (GINA) 2019 Update strategy. As previously, a systematic review was not performed; relevant references were reviewed where necessary to formulate this guideline version and referenced as required to support key recommendations. Readers are referred to the GINA 2019 Update strategy for the more comprehensive detail that it provides, accessed at https://ginasthma.org.

#### Grading

No levels of evidence grades are provided because the guidelines are formatted as a Quick Reference Guide. Readers are referred to the GINA 2019 Update strategy and handbooks for the level of evidence for the recommendations on which the guidelines are based.

#### Guideline development group

This group primarily includes members of the Asthma and Respiratory Foundation New Zealand Scientific Advisory Group and comprises representatives from a range of professions and disciplines relevant to the scope of the guidelines. Development of the Adolescent & Adult Asthma Guidelines was funded by the Asthma and Respiratory Foundation New Zealand. No funding was sought or obtained from pharmaceutical companies.

#### Peer review

The draft guidelines were peer-reviewed by a wide range of respiratory health experts and key professional organisations, including representatives from Asthma New Zealand, Can Breathe, New Zealand Nurses Organisation Te Rūnanga o Aotearoa, Nurse Practitioner New Zealand, Comprehensive Care, Hutt Valley DHB, Capital and Coast DHB, Auckland DHB, Ngā Kaitiaki o te Puna Rongoā, PHARMAC, Thoracic Society of Australia and New Zealand, Internal Medicine Society of Australia and New Zealand, University of Auckland, Wellington Free Ambulance Service and the Global Initiative for Asthma Scientific Committee.

#### Presentation

The guidelines are primarily presented through bullet points, key practice points, tables and figures. Key references are provided where necessary to support recommendations that may differ from previous guidelines or current clinical practice. An educational slide set is available on the website. The Asthma and Respiratory Foundation New Zealand encourages the integration of the graphs and figures into local clinical pathways.

#### Dissemination plan

The guidelines will be translated into tools for practical use by health professionals, and used to update Health Pathways and existing consumer resources. The guidelines will be published in the *New Zealand Medical* 



*Journal* and on the Asthma and Respiratory Foundation New Zealand website, and disseminated widely via a range of publications, training opportunities and other communication channels, to health professionals, nursing and medical schools, primary health organisations and district health boards.

#### Implementation

The implementation of the guidelines by organisations will require communication, education and training strategies.

### Expiry date 2024.

Definition<sup>10</sup>

- The GINA consensus definition of asthma is:
  - Asthma is a heterogeneous disease, usually characterised by chronic airway inflammation.

It is defined by the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that vary over time and in intensity, together with variable expiratory airflow limitation.

#### Diagnosis<sup>10-12</sup>

- The diagnosis of asthma starts with the recognition of a characteristic pattern of symptoms and signs, in the absence of an alternative explanation.
- The key to making the diagnosis of asthma is to take a clinical history, undertake a focused physical examination, document variable expiratory airflow limitation and assess response to inhaled bronchodilator and/or ICS treatment (Table 1, Figure 1). There is no reliable single 'gold standard' diagnostic test.

Table 1: Clinical features that increase or decrease the probability of asthma.

#### A. Asthma more likely

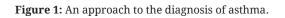
- Two or more of these symptoms:
  - Wheeze (most sensitive and specific symptom of asthma)
  - Breathlessness
  - Chest tightness
  - Cough
- Symptom pattern:
  - Intermittent
  - Typically worse at night or in the early morning
  - Provoked by exercise, cold air, allergen exposure, irritants, viral infections, beta blockers, aspirin or other non-steroidal anti-inflammatory drugs
  - Recurrent or seasonal
  - Began in childhood
- History of atopic disorder or family history of asthma
- Widespread wheeze heard on chest auscultation
- Symptoms rapidly relieved by inhaled SABA or budesonide/formoterol
- Airflow obstruction on spirometry (FEV1/FVC < Lower limit of normal)
- Increase in FEV1 following bronchodilator ≥12%; the greater the increase the greater the probability
- Variability in PEF over time (highest-lowest PEF/mean) ≥15%; the greater the variability the greater the probability

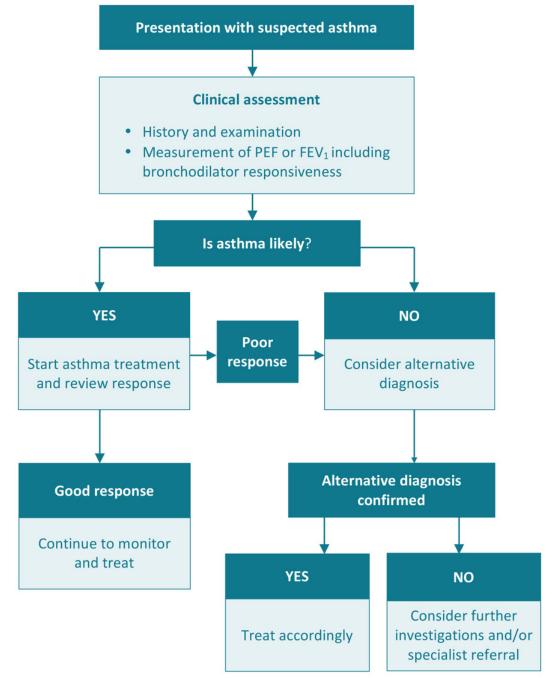
#### B. Asthma less likely

- Chronic productive cough in absence of wheeze or breathlessness
- No wheeze when symptomatic
- Normal spirometry or PEF when symptomatic
- Symptoms beginning later in life, particularly in people who smoke
- Increase in FEV1 following bronchodilator <12%; the lesser the increase the lower the probability
- Variability in PEF over time <15%; the lesser the variability the lower the probability
- No response to trial of asthma treatment
- Clinical features to suggest an alternative diagnosis

Modified from BTS/SIGN asthma guidelines.<sup>11</sup>







Modified from BTS/SIGN asthma guidelines.<sup>11</sup>

#### **Practice points**

 An increase in FEV<sub>1</sub> ≥12% and ≥200ml from baseline after bronchodilator therapy, has traditionally been considered as a diagnostic criterion for asthma. However, most people with asthma will not exhibit this degree of reversibility at one assessment, and normal spirometry does not exclude asthma. There is a substantial overlap in bronchodilator reversibility between individuals with asthma, COPD and those with no respiratory disease, and as a result no clear-cut divisions can be suggested. The greater the magnitude of bronchodilator reversibility the greater the likelihood that there is an asthma component to the disease.



- Alternative methods to identify variable airflow obstruction include repeat measures of spirometry with bronchodilator reversibility, peak flow variability with repeat measures at different times of the day, and other specialist tests such as measures of bronchial challenge testing. Once the diagnosis has been confirmed it is not necessary to routinely undertake bronchodilator reversibility testing.
- In most patients, observing a symptomatic response to treatment may help confirm the diagnosis, however a limited response to bronchodilator or ICS does not rule out asthma. It may be difficult to distinguish between a diagnosis of asthma and COPD, in adults with a smoking history, as they may have clinical features of both disorders. If asthma is believed to be part of the presentation, the management must include an ICS.
- The possibility of an occupational cause should be considered in all cases of adult onset asthma. If occupational asthma is suspected, it needs to be formally investigated and this may require specialist referral.

### Assessing asthma severity, control and future risk<sup>10-14</sup>

Evaluation of asthma severity, the level of control and the risk of future events are all important components of the assessment of individuals with asthma.

Severity of asthma is defined by the treatment needed to maintain good control.

- For symptomatic patients, asthma severity can be determined only after a therapeutic trial of ICS for at least eight weeks. Start the therapeutic trial and book the follow-up appointment for eight weeks later.
- Patients who initially present with frequent symptoms often have mild asthma, which can be well controlled with ICS-based therapy.
- Asthma symptom control is defined by the frequency of symptoms, the degree to which symptoms affect sleep and activity, and the need for reliever medication.

#### **Practice point**

Many patients under-report their asthma symptoms. Different methods for assessing asthma symptom control are available including:

i) Asthma Control Test (ACT)

This test has been widely validated and is recommended with the following cut points:

20–25: well controlled

16–19: partly controlled

5–15: poorly controlled

The latest version of the test can be accessed via http://www.asthmacontrol. co.nz/.

ii) Australian Asthma Handbook

This provides useful alternative questions that might be used to assess control (Table 2).

Assessment of the risk of adverse outcomes including severe exacerbations and mortality (Table 3).

**Table 2:** Definition of levels of recent asthma control in adults and adolescents (regardless of currenttreatment regimen).

Good control	Partial control	Poor control
All of:	One or two of:	Three or more of:
Daytime symptoms ≤2 days	Daytime symptoms >2 days per	Daytime symptoms >2 days per
per week	week	week
Need for SABA reliever ≤2 days	Need for SABA reliever >2 days	Need for SABA reliever >2 days
per week†	per week†	per week†
No limitation of activities	Any limitation of activities	Any limitation of activities
No symptoms during night or	Any symptoms during night or	Any symptoms during night or
on waking	on waking	on waking

† SABA, not including doses taken prophylactically before exercise. (Record this separately and take into account when assessing management.)

Note: Recent asthma symptom control is based on symptoms over the previous four weeks. Modified from the Australian Asthma Handbook.<sup>12</sup>



Table 3: Clinical features associated with increased risk of severe exacerbations and mortality.

#### A. Asthma

- Poor symptom control
- One or more exacerbation requiring oral corticosteroids in the last year
- Hospitalisation or emergency department visit in the last year
- High SABA use (≥3 canisters per year)
- Home nebuliser
- History of sudden asthma attacks
- Impaired lung function (FEV1 <60% predicted)
- Raised blood eosinophil count
- Intensive Care Unit admission or intubation (ever)
- Requirement for long term oral corticosteroids
- B. Comorbidity
- Psychotropic medications
- Major psychosocial problems
- Smoking
- Food allergy/anaphylaxis
- Alcohol and drug abuse
- Aspirin or other non-steroidal anti-inflammatory drug sensitivity
- C. Other factors
- Underuse or poor adherence to ICS treatment
- Discontinuity of medical care
- Socioeconomic disadvantage and poor housing
- Māori and Pacific ethnicity
- Occupational asthma

#### **Practice points**

- 1. High-risk patients can be identified by monitoring healthcare use (such as hospital admissions, emergency and/ or unplanned doctor visits) and medication requirements (such as courses of corticosteroids, frequency of SABA prescriptions, and more prescriptions for SABA than ICS).
- 2. The risk associated with Māori and Pacific ethnicity relates to the wider determinants of severe asthma including damp, cold, mouldy or crowded housing, living in neighbourhoods of high deprivation, discontinuity of medical care, institutional racism, poor health literacy, inadequate income, inadequate treatment and occupational asthma.
- 3. Risk should be assessed at the time of issuing a repeat prescription. Where higher risk is identified a formal asthma review may be required.

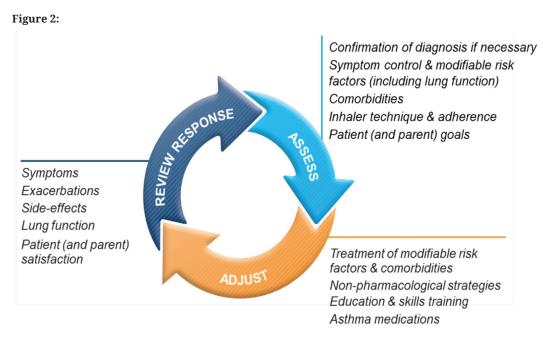
# Identifying management goals in collaboration with the patient<sup>10</sup>

Managing asthma requires a partnership between the patient, their whānau and their healthcare team. This involves agreeing on management goals and a cycle based on repeated assessment, adjustment of treatment and review of responses as outlined in Figure 2 [Box 3–2].

### Inhaler technique and adherence<sup>10,15,16</sup>

The most common reasons for poor asthma control are inadequate inhaler technique and poor compliance/adherence. It is recommended that the patient's inhaler technique is observed at every consultation, with instruction as required. The patient's preference and ability are important considerations in the choice of inhaler device. The lower carbon footprint of dry powder devices (less than 10% of pMDIs) should be considered alongside other factors.





Adapted from GINA Update.<sup>10</sup>

It is recommended that for the regular administration of ICS or ICS/LABA, if a pMDI is used, it is self-administered with a spacer device. There are two methods for inhaling via a spacer: one deep slow inhalation and a 10 second breath-hold; or 5–6 tidal breaths, with one actuation of medication into the spacer at a time.

Adherence can be checked using multiple techniques (questioning, diaries, apps, pharmacy dispensing records). Patients' understanding of the regimen should be confirmed, including their health beliefs, with their regimen tailored accordingly where possible. Fears and misconceptions are common barriers to adherence.

Good inhaler technique and adherence should be confirmed before any increase in treatment is initiated. Practice nurses and pharmacists may be well placed to undertake these checks.

#### **Practice points**

- Check adherence and inhaler technique (and instruct patients using a physical demonstration of correct technique) at every visit.
- Consider alternative inhaler devices if persistent difficulty with technique.

#### Reliever therapy<sup>10,17-23</sup>

- SABA reliever as sole therapy (without ICS or ICS/LABA) is no longer recommended in the long-term management of asthma in adolescents or adults.
- Long-term treatment with ICS/fastonset beta<sub>2</sub>-agonist reliever therapy is superior to SABA reliever in reducing exacerbation risk in adolescents and adults, across the range of asthma severity.
- In New Zealand the only ICS/fast-onset beta,-agonist combination product that is available is budesonide/formoterol and to date this is only approved as reliever therapy using the Turbuhaler device. As a result budesonide/ formoterol Turbuhaler is the preferred reliever treatment for intermittent, mild, moderate and severe asthma. One actuation of budesonide/ formoterol 200/6µg or 100/6µg via Turbuhaler is taken as required to relieve symptoms, rather than the two puffs at a time traditionally used with SABA pMDI reliever inhalers. The budesonide/formoterol 400/12µg formulation should not be used as reliever therapy.

- Repeat administration of budesonide/ formoterol or salbutamol in the ratio of 6µg formoterol to 200µg salbutamol results in a similar short-term bronchodilator response in the treatment of acute asthma.
- Budesonide/formoterol 200/6µg one inhalation as-needed, as sole reliever therapy, reduces the risk of a severe exacerbation by at least 60% compared with SABA sole reliever therapy in adolescents and adults with mild asthma. This regimen is recommended as the preferred initial treatment in patients with intermittent or mild asthma.
- Budesonide/formoterol as reliever therapy reduces the risk of a severe exacerbation by about one-third compared with SABA reliever therapy in adolescents and adults taking maintenance ICS/LABA therapy. As a result budesonide/formoterol maintenance and reliever therapy is preferred to maintenance ICS/LABA and SABA reliever therapy for the treatment of patients with moderate to severe asthma.
- This evidence has led to the term 'Anti-Inflammatory Reliever' (AIR) therapy to describe the use of budesonide/formoterol as a reliever medication, with or without maintenance budesonide/formoterol therapy. This approach encompasses and extends the 'Single inhaler Maintenance and Reliever Therapy' (SMART) approach recommended in previous guidelines (see below).

ICS treatment<sup>10,17-22,24-30</sup>

ICS are the preferred anti-inflammatory 'preventive' therapy. ICS may be administered as:

- A) Budesonide/formoterol 'Anti-Inflammatory Reliever' (AIR) therapy with or without maintenance budesonide/ formoterol
- B) Maintenance ICS together with SABA reliever therapy
- C) Maintenance ICS/LABA with SABA reliever therapy

## Anti-Inflammatory Reliever (AIR) therapy

- AIR therapy (Figure 3) uses the combination budesonide/formoterol inhaler taken as-needed to relieve symptoms. This can be done:
- i) without maintenance ICS: just using the combined budesonide/formoterol inhaler to relieve symptoms in mild asthma.
- ii) with maintenance budesonide/ formoterol: using the combined budesonide/formoterol inhaler taken regularly, with an additional dose taken as-needed to relieve symptoms in moderate and severe asthma. This approach is also known as 'Single combination ICS/LABA inhaler Maintenance and Reliever Therapy' (SMART).
- AIR therapy requires a fast-onset beta-agonist combined with an ICS in a single inhaler for as-needed use to relieve symptoms. At present the only such combination inhaler available in New Zealand is budesonide/formoterol, and it is only approved for use as a reliever therapy with the Turbuhaler device. While there is evidence of efficacy/safety with budesonide/ formoterol pMDI used as a reliever therapy, the pMDI formulation is not licensed for reliever use and therefore this would represent an off-label prescription.
- Other ICS/LABA combinations available in New Zealand that do not contain formoterol, such as fluticasone propionate/salmeterol or fluticasone furoate/vilanterol, should not be used in this way.
- Patients should not be prescribed budesonide/formoterol as a reliever therapy in addition to maintenance fluticasone propionate/salmeterol or fluticasone furoate/vilanterol, as there is no evidence base for the use of two different ICS/LABA products together.
- When using budesonide/formoterol combination inhaler for both regular maintenance use (once or twice daily), and for relief of symptoms (one actuation as required), patients should not be prescribed a SABA reliever inhaler.



#### Maintenance fixed dose ICS plus SABA reliever

- Regularly scheduled ICS may be taken as maintenance therapy together with SABA reliever therapy.
- When taken as regular maintenance therapy, the daily doses of ICS which achieve 80–90% of maximum obtainable efficacy are shown in Table 4. These can be considered 'standard' doses for ICS, rather than 'low' doses. Some patients with severe asthma will require higher doses of ICS.
- It is recommended that when ICS therapy is initiated as a regular maintenance treatment, either as a separate inhaler or in combination with a LABA as an ICS/LABA inhaler, these standard doses are used. There is no greater benefit with initiation of ICS therapy at higher doses.

Maintenance fixed dose ICS/LABA plus SABA reliever therapy

- A combination ICS/LABA inhaler may also be taken as regular maintenance therapy together with SABA reliever therapy. The maintenance ICS/LABA with SABA reliever therapy regimen is less effective than budesonide/ formoterol maintenance and reliever therapy regimen at reducing severe exacerbations in patients with a history of severe exacerbations.
- Fluticasone furoate/vilanterol 100/25µg one inhalation once daily represents an option for patients who may prefer once daily medication use. This regimen does not reduce the risk of severe exacerbations compared with optimised usual care.
- LABA monotherapy is unsafe in patients with asthma and separate

LABA inhalers are a risk if patients are poorly adherent with ICS therapy. LABAs should not be prescribed in a separate inhaler from ICS in patients with asthma.

### Stepwise approach to asthma treatment<sup>22,31</sup>

#### Pharmacological treatment

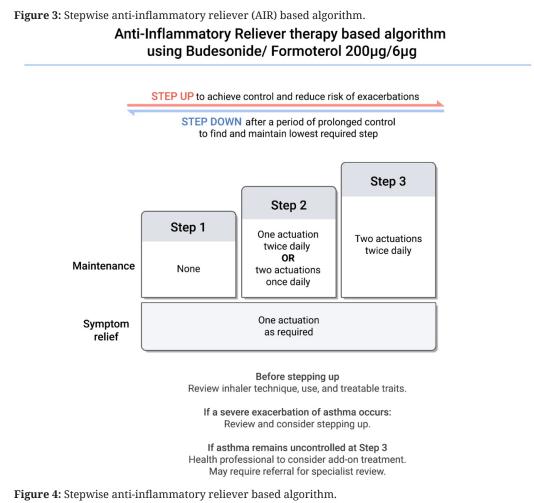
In the stepwise approach to asthma management, patients step up and down as required to achieve and maintain control of their asthma and reduce the risk of exacerbations.

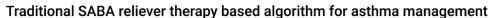
- AIR therapy-based algorithm: This i) is the preferred algorithm, and is based on the use of budesonide/ formoterol as reliever therapy, with or without regular maintenance budesonide/ formoterol therapy. The use of budesonide/formoterol as both maintenance and reliever therapy at steps 2 and 3 is also known as 'Single combination ICS/LABA inhaler Maintenance and Reliever Therapy (SMART)'. The budesonide/ formoterol 200/6µg Turbuhaler formulation is used as the basis for the algorithm as this is the only formulation which has both an evidence base and regulatory approval for AIR therapy with or without regular maintenance budesonide/formoterol therapy. At step 2 the choice of one inhalation twice daily or two inhalations once daily will depend on patient preference.
- ii) SABA reliever therapy-based algorithm: This alternative algorithm is based on the use of a SABA as reliever therapy, in addition to ICS or ICS/LABA maintenance therapy.

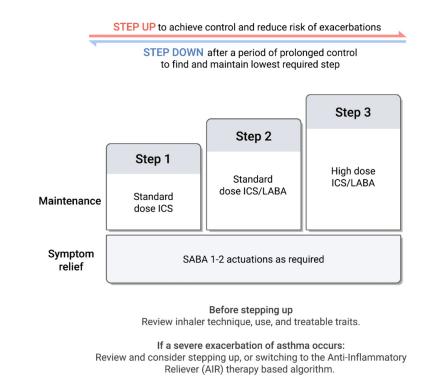
Table 4: The recommended standard daily dose of ICS in adult asthma.

Beclomethasone dipropionate	400–500µg/day
Beclomethasone dipropionate extrafine	200µg/day
Budesonide	400µg/day
Fluticasone propionate	200–250µg/day
Fluticasone furoate	100µg/day









If asthma remains uncontrolled at Step 3 Health professional to consider add-on treatment. May require referral for specialist review.



#### **Practice points**

- Although current evidence indicates that the AIR-based strategy is more effective at preventing exacerbations, the traditional treatment approach may be preferred for individual patients if their asthma is already well controlled on this regimen, or if they have poor technique with the Turbuhaler device.
- Consider stepping up if uncontrolled symptoms, exacerbations or at increased risk, but check diagnosis, adherence, inhaler technique and modifiable risk factors first.
- Consider stepping down if symptoms are controlled for three months and the patient is at low risk for exacerbations.
- At each step check inhaler technique, adherence to treatment, understanding of self-management plan and barriers to self-care.
- Stopping ICS completely is not advised. The minimum level of treatment recommended is as-needed budesonide/formoterol. Treatment with a SABA reliever alone, without maintenance ICS or ICS/LABA therapy is not recommended.
- Consider referral for specialist review and consideration of addition of other treatments if persistent exacerbations or poor control despite step 3 treatment.
- Asthma is common in older people and multi-dimensional assessment may be required to address complicating factors such as comorbidities and frailty.

### Add-on treatments

#### LAMAs<sup>32–34</sup>

Long-acting muscarinic antagonists (LAMAs) have efficacy in severe asthma not well-controlled on ICS/LABA. When added to ICS/LABA treatment they modestly reduce the risk of severe exacerbations, and improve lung function and symptom control. The strongest evidence is with tiotropium 5µg/day delivered via the Respimat device. The addition of tiotropium to maintenance ICS/LABA is a MEDSAFE approved indication, but is not funded in New Zealand for asthma. The alternative approach of prescribing an ICS/LABA/ LAMA 'triple therapy' is neither MEDSAFE approved nor funded in New Zealand. LAMA therapy is funded for patients with COPD with or without co-existent asthma, diagnosed using spirometry, as long as the prescription is endorsed accordingly. As a result it is currently recommended that a LAMA may be considered in asthma patients with features of COPD, who are not controlled at step 3.

#### Biological treatments<sup>35-37</sup>

Monoclonal antibody treatments targeting specific inflammatory pathways now have an established role in severe uncontrolled asthma. They may be effective for patients with severe asthma and elevated serum IgE or markers of Th-2 inflammation (high blood eosinophil counts). Omalizumab (targeting IgE) and both mepolizumab and benralizumab (targeting Interleukin-5) are currently licensed in New Zealand for administration by sub-cutaneous injection. At the time of writing, omalizumab is publically funded in people aged six and above and mepolizumab is funded in people aged 12 and above, meeting specific criteria. The choice of agent is determined by the inflammatory pathway to be targeted and likely to be influenced by the funding guidelines and cost of treatment. There is insufficient evidence regarding comparative efficacy between the different drugs. They should be considered as add-on treatments in patients with severe disease and are likely to remain specialist-only treatments for the foreseeable future.

#### Other medications<sup>10,38</sup>

Alternative therapies such as sodium cromoglycate or nedocromil may be considered in some patients with mild asthma. Montelukast should also be considered as add-on therapy in patients not controlled on standard treatment and in all patients with aspirin-exacerbated respiratory disease. Prescribers should be aware of the risk of neuropsychiatric events associated with montelukast.

Additional high dose ICS, oral corticosteroids, oral theophylline and azithromycin may be considered as other add-on treatments, with specialist review. Both risks and benefits of these treatments should be considered.



The provision of a home nebuliser for administration of bronchodilator medication is discouraged, due to the high dosing and the potential for delay in seeking medical review with its repeated use in a severe exacerbation.

#### Non-pharmacological measures<sup>39,40</sup>

- Key non-pharmacological measures to improve asthma outcomes include smoking cessation (including cannabis, e-cigarettes and vaping), weight loss, asthma education, regular exercise and breathing exercises.
- Avoid triggers that have been identified to provoke attacks in particular attacks associated with features of anaphylaxis. Specifically question about sensitivity to aspirin and non-steroidal anti-inflammatory drugs, and consider aspirin-exacerbated respiratory disease in such patients, especially if there is a history of nasal polyps.
- Currently available house dust mite avoidance measures are not effective.
- Modifications to diet are unlikely to improve asthma control. Food avoidance should not be recommended unless an allergy or sensitivity has been confirmed.
- Exercise should be encouraged. If exercise provokes asthma this is a marker of poor control and should lead to a review of treatment, rather than exercise avoidance. In addition, reliever may be taken pre-exercise.
- Limitation of exposure or removal from the workplace is crucial in the management of occupational asthma. Early removal from exposure may lead to a complete remission.
- Asthma control may be improved by a warm, dry domestic environment. Where a patient is living in poor quality or damp housing, referral to locally available support services such as the healthy homes initiative is appropriate.
- Unflued gas heaters may worsen asthma symptoms; electric heat pumps are recommended.

 As people in low income households have a higher burden of disease and can face barriers to accessing healthcare provision and medications, it is appropriate to check whether patients are accessing their government support entitlements and refer to support services as appropriate.

#### Specific allergy issues<sup>41–48</sup>

A diagnosis of allergy requires a history of reaction to a given allergen, and is confirmed by detection of specific IgE antibodies, either on serum or by skin prick testing. Skin prick testing has a high negative predictive value for allergy to the antigen used and a low risk of systemic allergic reactions, but serum specific IgE may be more appropriate in certain settings, eg, patient unable to stop antihistamine medications, unstable asthma, pregnancy or dermatographism. Aeroallergens such as house dust mite, pollens or pet dander are the most common allergic triggers for asthma.

Allergen immunotherapy can offer clinical improvements in asthma. Confirmation of specific IgE is required prior to starting. Both sublingual and subcutaneous immunotherapy are available but unfunded in New Zealand for aeroallergens; treatment can be expensive and time-consuming. Aspirin desensitisation for patients with aspirin-exacerbated respiratory disease should be done under immunologist/ allergist guidance.

Asthma is the most significant risk factor for fatal food-related anaphylaxis. Failure to recognise and treat anaphylaxis contributes to the risk of fatality.

#### **Practice points**

- Consider testing for allergen-specific IgE to aeroallergens in patients with allergic asthma.
- Allergen immunotherapy may be considered in patients with allergic asthma and allergic rhinitis who have evidence of allergy to house dust mite and/or pollens.
- All patients with food-related anaphylaxis should be referred to an immunologist/allergist.



#### Treatable traits<sup>49–52</sup>

In patients with difficult to treat asthma a key feature of management is the recognition and treatment of overlapping disorders, comorbidities, environmental and behavioural factors for which specific treatment is available, recently referred to as 'treatable traits'. The assessment and management of some of the treatable traits may require specialist referral and consideration of additional interventions. Systematic assessment of treatable traits in the severe asthma clinic is associated with improved outcomes. One schema to consider is as follows:

Table 5: Treatable traits in asthma.

#### **Overlapping disorders**

- COPD
- Bronchiectasis
- Allergic bronchopulmonary aspergillosis
- Dysfunctional breathing including vocal cord dysfunction

#### Comorbidities

- Obesity
- Gastro-oesophageal reflux disease
- Rhinitis
- Chronic rhinosinusitis ± nasal polyps
- Obstructive sleep apnoea
- Depression/anxiety
- Environmental
- Smoking
- Damp, mouldy, cold or crowded housing
- Occupational exposures
- Provoking factors including aeroallergens
- Drugs such as aspirin, other non-steroidal anti-inflammatory drugs and beta blockers
- Insufficient income to access healthcare

#### Behavioural

- Adherence
- Inhaler technique
- Health literacy

#### **Practice point**

The treatable traits approach is particularly important for a patient who has poorly controlled asthma and/or poor respiratory health.

#### Self-management<sup>53-56</sup>

Self-management based on a written, personalised, action plan improves health outcomes and should be offered to and discussed with all people with asthma. Copies should be kept in their medical records. A variety of formats are available for patients and their families, and the most appropriate source of information for the patient should be assessed, whether written, pictorial, electronic, app etc.

#### **Practice points**

- Asthma action plans should be based on symptoms with or without peak flow measurements and comprise either three or four stages depending on patient and health professional preference.
- Asthma and Respiratory Foundation NZ asthma action plans can be downloaded from their website http:// asthmafoundation.org.nz/:
  - Budesonide/formoterol reliever ± maintenance (AIR plan)
  - ICS plus SABA (four-stage plan)
  - ICS or ICS/LABA plus SABA (threestage plan)
- The peak flow level at which patients are guided to recognise worsening asthma is around 80% (of best), severe asthma at 60–70% of best and an asthma emergency at around 50% of best.
- The four-stage plan has been shown to be effective in the management of asthma. In this plan there is an extra step giving patients the option of increasing the dose of ICS, up to four-fold, through increasing the frequency of use, and/or the dose at each use, in response to worsening asthma symptoms or deteriorating peak flow. Patients should be advised to return to their normal ICS dose once asthma symptoms and peak flows have improved.
- The recommended action plans can be modified as required depending on patient and practitioner preference.
- The standard regimen for a course of prednisone in the situation of severe asthma is 40mg daily for five days. An alternative regimen is 40mg daily until definite improvement, and then 20mg daily for the same number of days. These regimens may need to be adjusted according to clinical factors



such as weight, comorbidities and interactions with other medications.

- Adherence to treatment should be routinely assessed and encouragement provided as part of the self-management education. For example, encourage patients to link their inhaler use with some other activity such as cleaning their teeth (and then rinsing their mouth).
- Inhaler technique should be routinely assessed at consultations and training provided as part of self-management education. If using a pMDI, it is preferable to administer via a spacer.
- A four-step adult asthma consultation, which includes guidance for writing an asthma action plan, is provided in the Appendix.

#### AIR asthma action plan with budesonide/formoterol reliever ± maintenance therapy

FC	Sthma espiratory NANDATION NZ *Anti-Inflammatory Reliever Therapy Know your asthma symptoms	Name: Date of plan: Know when and how	v to take y	ourm	edicine	Doctor: Doctor phone:
Feeling good	<ul> <li>Your asthma is under control when</li> <li>You don't have asthma symptoms most days (wheeze, tight chest, a cough or feeling breathless)</li> <li>You have no cough or wheeze at night</li> <li>You can do all your usual activities and exercise freely</li> <li>Most days you do not need extra Symbicort actuations</li> <li>Your peak flow reading is above:</li> </ul>	Symbicort: actuation(s) every night		Symbicort is a 2-in-1 treatment used for both prevention and relief of symptoms. Carry this at all times. You do not need an extra inhaler as a reliever. <b>Other Medication</b>		
Severe	<ul> <li>Your asthma is getting severe when</li> <li>Your asthma symptoms are getting severe (wheeze, tight chest, a cough or feeling breathless)</li> <li>OR your Symbicort is only helping for 2-3 hours</li> <li>OR you are using more than 8 actuations a day in total (regular + reliever use)</li> <li>OR you feel you need to see your doctor</li> </ul>	Let's take action • You need to see your do • Continue any regular Sym Symbicort when needed • Start prednisone if you ha Prednisone	nbicort PLUS to relieve sy ave it:			Other instructions:
	Your peak flow reading is below:	and then	mg	for	days	
Emergency	It is an emergency when  Vour symptoms are getting more severe quickly  OR you are finding it hard to speak or breathe  OR your Symbicort is not helping much  OR you are using your Symbicort every 1-2 hours  Your peak flow reading is below:	<ul> <li>Let's keep calm</li> <li>Dial 111 for ambulance</li> <li>Keep using your Symbicort as often as needed</li> <li>Even if you seem to get better seek medical help right away</li> <li>If you haven't started taking your prednisone, start now</li> </ul>			Best peak flow: Plan prepared by: Next review date: Signature:	



#### Maintenance ICS & SABA reliever four-stage asthma action plan

+ R	Sthma espiratory NUNDATION NZ ACTION PLAN	Name: Date of plan:			Doctor: Doctor phone:
Feeling good	Know your asthma symptoms Your asthma is under control when • you don't have asthma symptoms most days (wheeze, tight chest, a cough or feeling breathless) • you have no cough or wheeze at night • you can do all your usual activities and exercise freely • most days you don't need a reliever Your peak flow reading is above	Know when and how to ta       Preventer       [name]       Reliever       [name]	actuation(s) actuation(s) actuation(s)	every morning	Carry your reliever at all times Other Medication
Getting worse	Caution- your asthma is getting worse when       Let's get prepared       Other instructions:         . you have symptoms most days (wheeze, tight chest, a cough of feeling breathless)       . Step up your preventer medicine:       . Step up your preventer medicine:         . you are waking at night with symptoms       . Jour peak flow reading is below       . Use your reliever as often as needed – through a spacer, if one can be used with your reliever inhaler       Other instructions:			Other instructions:	
Severe	<ul> <li>Caution- your asthma is getting severe when</li> <li>Your symptoms are getting severe (wheeze, tight chest, a cough or feeling breathless)</li> <li>OR your reliever is only helping for 2-3 hours</li> <li>OR you are using more than 12 actuations a day</li> <li>OR you feel you need to see your doctor</li> <li>Your peak flow reading is below</li> </ul>	Let's take action • You need to see your doctor too • Continue your medicine for "gettii • Start prednisone if you have it: Prednisone n and then n	ng worse"	days days	Other instructions:
Emergency	Emergency       Let's keep calm         • Your symptoms are getting more severe quickly       • Dial 111 for ambulance         • OR you are finding it hard to speak or breathe       • Dial vour reliever is not helping much         • OR you are using your reliever every 1-2 hours       • Keep using your reliever as often as needed - through a spacer, if one can be used with your reliever inhaler         • Your peak flow reading is below       • If you haven't started taking your prednisone, start now			aler o right away	Best peak flow: Plan prepared by: Next review date: Signature:

# Maintenance ICS/LABA & SABA reliever three-stage asthma action plan or maintenance ICS & SABA reliever three-stage asthma action plan

+Respiratory YOUR ASTHMA		Name: Doctor:				
FC	ACTION PLAN	Date of plan: Doctor phone:				
Know your asthma symptoms		Know when and ho	w to take	your m	edicine	
Feeling good	<ul> <li>Your asthma is under control when</li> <li>you don't have asthma symptoms most days (wheeze, tight chest, a cough or feeling breathless)</li> <li>you have no cough or wheeze at night</li> <li>you can do all your usual activities and exercise freely</li> <li>most days you don't need a reliever</li> <li>Your peak flow reading is above</li> </ul>	Preventer [name] Reliever [name]	actu	ation(s) ation(s) ation(s)	every morning every night when you need it to relieve your asthma symptoms	Carry your reliever at all times Other Medication
Severe	<ul> <li>Caution- your asthma is getting severe when</li> <li>Your asthma symptoms are getting severe (wheeze, tight chest, a cough or feeling breathless)</li> <li>OR your reliever is only helping for 2-3 hours</li> <li>OR you are using more than 12 actuations in a day</li> <li>OR you feel you need to see your doctor</li> </ul>	Let's take action  You need to see your doc Continue your regular prevoften as needed to relieve Start prednisone if you have Prednisone and then	venter AND symptoms ve it: mg	use your for for	r reliever as days days	Other instructions:
	Your peak flow reading is below					
Emergency	Emergency • Your symptoms are getting more severe quickly • OR you are finding it hard to speak or breathe • OR your reliever is not helping much • OR you are using your reliever every 1-2 hours Your peak flow reading is below	Let's keep calm Dial 111 for ambulance Keep using your reliever as often as needed – through a spacer, if one can be used with your reliever inhaler Even if you seem to get better seek medical help right away If you haven't started taking your prednisone, start now			Best peak flow: Plan prepared by: Next review date: Signature:	



#### Adolescents<sup>57–59</sup>

The recommendations in this guideline apply to people aged 12 and above. Adolescence is a period of increased risk taking and decreased adherence, which may be due to forgetfulness, lack of routines, denial, beliefs about asthma or medication, difficulty using inhalers, fear of side effects and embarrassment in front of peers. They may be taking on risky activities such as smoking, e-cigarettes, vaping or drug taking. Parents/ caregivers/whānau may play a key role in reminding and otherwise encouraging adolescents to take their medication.

Adolescents require an approach that enables them to take increasing responsibility while feeling empowered and confident to do so. Many adolescents report difficulties in communicating with their healthcare professional. Ensure that adolescents have a developmentally appropriate understanding of their asthma and treatment. If they have had asthma for a long time, it will be necessary to transition from the childhood to adult-centric approach to care.

#### **Practice points**

- Prioritise the relationship, offer continuity of care, and emphasise confidentiality. It is important to establish trust and explore barriers to access.
- Attempt to instil a sense of control, that adherence will improve the adolescent's control over their asthma and their lives. Consider if a practice nurse could play a coaching role.
- See adolescents individually first, and then with parents/caregivers as appropriate. Ensure they know that as they transition to adulthood they need to take more responsibility for their own healthcare and can make appointments for themselves.
- Explain risks of sharing inhalers with others (infection, inhaler runs out more quickly).
- Ask about smoking, vaping, and drug taking and advise accordingly.
- Assume that the young person is likely to have other health and social issues and questions. Complete a brief HEADSS (Home & Environment,

Education & Employment, Activities, Drugs, Sexuality, Suicide/Depression) or holistic psychosocial assessment if practicable.

- Consider simple treatment regimens. Ensure that the young person is aware of what to do if symptoms escalate, and has someone to contact if they have concerns.
- Arrange follow-up appointments and ensure the adolescent knows how and when to instigate appointments.

#### Asthma in Māori<sup>60–66</sup>

Māori rights in regard to health, recognised in Te Tiriti of Waitangi and other national and international declarations, promote Māori participation in health-related decision making, as well as equity of health outcomes for all New Zealanders. Currently Māori with asthma are more likely to be hospitalised or die due to asthma than New Zealand European. Despite this, Māori with asthma are less likely to be prescribed ICS, have an action plan or receive adequate education. Major barriers to good asthma management which may affect Māori include access to and cost of care, services and approaches that do not meet their needs, discontinuity and poor quality care, lack of culturally appropriate services and health professionals, failure to provide information that is understandable to the individual, trust and confidence in the health system. Be mindful of institutional/structural racism (barriers) when treating Māori patients. Māori whānau have greater exposure to environmental triggers for asthma, such as smoking and poor housing. It is recommended that for Māori with asthma:

- Asthma providers should undertake clinical audit or other similar quality-improvement activities to monitor and improve asthma care and outcomes for Māori. The asthma action plan system of care, and the anti-inflammatory reliever (AIR) regimen have been shown to improve outcomes in Māori.
- A systematic approach to health-literacy and asthma education for Māori whānau is required. The evidence of the health literacy demands, the barriers and facilitators, and

steps to delivering excellent asthma management with Māori that are described in He maramatanga huango: Asthma health literacy for Maori children in New Zealand apply just as much to adults as they do to children.

- Asthma providers should support staff to develop culturally safe skills for engaging Māori with asthma and their whānau in line with professional requirements. https://www.mcnz.org. nz/our-standards/current-standards/ cultural-safety/
- Māori leadership is required in the development of asthma management programmes that improve access to asthma care and facilitate 'wrap around' services to address the wider determinants (such as housing or financial factors) for Māori with asthma.

#### Asthma in Pacific peoples

Similar considerations as for Māori are likely to apply to asthma in Pacific peoples who also have a disproportionate burden of asthma, including high rates of hospital admission, and should be considered a high-risk group requiring targeted care. Inclusive in this targeted approach is addressing risk factors such as poor housing, over-crowding, health literacy, obesity, smoking and poor access to healthcare services. Be mindful of institutional/structural racism (barriers) when treating Pacific patients.

#### Asthma in pregnancy<sup>10</sup>

- Pregnancy can affect the course of asthma and women should be advised of the importance of maintaining good asthma control during pregnancy to avoid risk to both mother and baby.
- The risks to the baby of poor asthma control and associated exacerbations in pregnancy outweigh any theoretical risks associated with asthma medications.
- ICS, ICS/LABA and SABAs should be used as normal during pregnancy.
- Stopping usual asthma medications during pregnancy is associated with adverse outcomes for both the mother and her baby.

- Oral corticosteroids should be used as normal when indicated for severe asthma exacerbations during pregnancy.
- Acute severe asthma in pregnancy is a medical emergency and should be treated in hospital.
- Consider early referral for specialist review in pregnant patients with poor asthma control or a history of exacerbations.

#### **Practice point**

Treatment as usual for asthma in pregnancy, and early referral if there is poor asthma control or a recent exacerbation.

#### Management of acute severe asthma (Primary care, afterhours or ED)<sup>10,67-73</sup>

- Acute asthma management is based on:
  - objective measurement of severity (Table 6)
  - assessment of the need for referral to hospital and/or hospital admission (Table 7)
  - administering treatment appropriate for the degree of severity, and
  - repeatedly assessing the response to treatment.
- Direct measurement of airflow obstruction is the most objective marker of asthma severity. This can be based on either the measurement of PEF or preferably FEV1, if available at the time of assessment, with both measures expressed as percent of the previous best or predicted reference values.
- The levels of FEV1 or PEF to signify severe and life-threatening asthma in these situations, differ from, and are lower than, those used by patients in action plans in a non-healthcare setting.
- Key priorities include identification of a life-threatening attack requiring urgent admission to an intensive care unit or high dependency unit, and a severe asthma attack requiring hospital admission (Table 7).



Mild/moderate asthma	Increasing symptoms	
exacerbation:	<ul> <li>FEV1 or PEF &gt;50% best or predicted</li> </ul>	
	No features of acute severe asthma	
Acute severe asthma:	Any one of:	
	FEV1 or PEF 30-50% best or predicted	
	• Respiratory rate ≥25/min	
	<ul> <li>Heart rate ≥110/min</li> </ul>	
	Inability to complete sentences in one breath	
	Any one of the following in a patient with severe asthma:	
Life-threatening asthma:	Any one of the following in a patient with severe asthma:	
Life-threatening asthma:	<ul><li>Any one of the following in a patient with severe asthma:</li><li>FEV1 or PEF &lt;30% best or predicted</li></ul>	
Life-threatening asthma:		
Life-threatening asthma:	FEV1 or PEF <30% best or predicted	
Life-threatening asthma:	<ul> <li>FEV1 or PEF &lt;30% best or predicted</li> <li>SpO2 &lt;92% or PaO2 &lt;60mmHg</li> </ul>	
Life-threatening asthma:	<ul> <li>FEV1 or PEF &lt;30% best or predicted</li> <li>SpO2 &lt;92% or PaO2 &lt;60mmHg</li> <li>PaCO2 ≥45mmHg</li> </ul>	
Life-threatening asthma:	<ul> <li>FEV1 or PEF &lt;30% best or predicted</li> <li>SpO2 &lt;92% or PaO2 &lt;60mmHg</li> <li>PaCO2 ≥45mmHg</li> <li>Inability to talk#</li> </ul>	
Life-threatening asthma:	<ul> <li>FEV1 or PEF &lt;30% best or predicted</li> <li>SpO2 &lt;92% or PaO2 &lt;60mmHg</li> <li>PaCO2 ≥45mmHg</li> <li>Inability to talk#</li> <li>Silent chest#</li> </ul>	

**Table 6:** Levels of severity of acute asthma exacerbation.

#These are very late manifestations and reflect a patient at risk of imminent respiratory arrest.

#### **Practice points**

A pragmatic rule is that a lack of response to initial bronchodilator treatment and/or a requirement for repeat doses indicates the likely requirement for referral to hospital and/or admission.

- For most patients initial treatment with a SABA via a spacer and oral corticosteroids is likely to be sufficient. Reserve nebulised bronchodilators for those with severe asthma who do not respond to initial inhaled therapy.
- Nebulisers may increase the risk for aerosolisation of viruses such as SARS-CoV-2 (COVID-19) and influenza. Nebulisers should be avoided, if

possible, in any patient who could be infected. If they are used, appropriate aerosolisation infection precautions should be implemented.

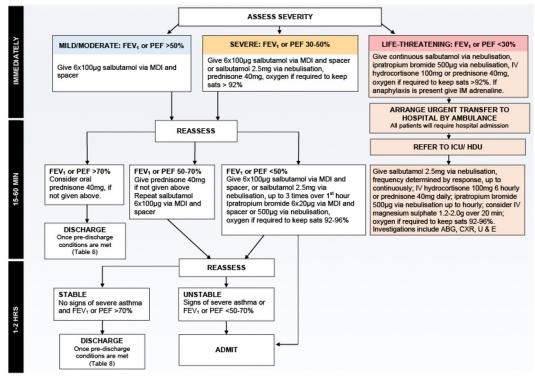
- There is insufficient evidence to guide the use of combination budesonide/ formoterol by health professionals in the setting of acute severe asthma and for this reason a SABA is the preferred agent in this setting.
- Consider and treat anaphylaxis with intramuscular adrenaline (epinephrine) in acute severe asthma. Be vigilant in patients with known food allergy and/or anaphylaxis plans, and recognise that skin signs may be absent.

 Table 7: Criteria for referral to hospital and/or hospital admission.

•	Patients with any feature of lit	fe-threatening asthma
---	----------------------------------	-----------------------

- Patients with any feature of severe attack persisting after initial treatment
- Patients in whom other considerations suggest that admission may be appropriate:
  - Still have significant symptoms after bronchodilator treatment
  - Living alone/socially isolated
  - Psychosocial problems
  - Physical disability or learning difficulties
  - Previous near fatal attack
  - Exacerbation despite adequate dose of oral corticosteroids pre-presentation
  - Presentation at night and especially if no means of communication or transport
  - Pregnancy





#### ALGORITHM FOR THE MANAGEMENT OF ACUTE SEVERE ASTHMA

For practical purposes, the  $FEV_1$  and PEF are considered interchangeable when expressed as % predicted for the purpose of assessment of acute asthma severity.

- There is insufficient evidence to support the use of intramuscular adrenaline in severe asthma without anaphylaxis, and so intramuscular adrenaline is not recommended unless there are signs or clinical suspicion of anaphylaxis.
- Intravenous magnesium sulphate may be administered in life-threatening asthma. There is no role for intravenous beta-2 agonists, unless inhaled treatment cannot be given. Similarly, there is no role for intravenous aminophylline.
- There is insufficient evidence to support the use of non-invasive

ventilation in life-threatening asthma, outside an intensive care unit or high dependency unit setting, and as a result it is not recommended in other settings.

- For patients who are treated in primary care or discharged from the afterhours or ED, long-term management should be reviewed and an early follow-up appointment with their primary healthcare team should be arranged (Table 8).
- All patients not taking ICS should have an ICS dispensed and appropriate technique taught before going home.

#### Table 8: Pre-discharge considerations.

- 1. Most patients presenting with acute exacerbations of asthma should have a course of oral prednisone, 40mg daily for at least five days.
- 2. An acute exacerbation is an opportunity to consider switching patients to AIR therapy with ICS/formoterol as the maintenance and reliever treatment, as the optimal treatment to reduce the risk of future severe exacerbations.
- 3. It is recommended that patients have prednisone and ICS dispensed prior to discharge to ensure there are no barriers to taking medication.
- 4. Consider referral to a specialist respiratory service.
- 5. Before the patient goes home, ensure that the patient:
- Can use their inhalers correctly, and has a supply of their medication (including ICS).
- Has a written self-management plan which includes the treatment prescribed, and when to seek further urgent medical review.
- Knows when to contact emergency medical help if worsens.
- Arranges an early follow-up appointment with their primary healthcare team for review.



### Appendix: the four-step asthma consultation

	2. Consider other relevant clinical issues	3. Decide if increase or decrease in maintenance therapy required	4. Complete the asthma action plan
Complete the Asthma Control Test (ACT) score 20–25: well controlled 16–19: partly controlled 5–15: poorly controlled Review lung function tests Peak flow monitoring and/or Spirometry Review history of severe asthma attacks in last 12 months (requiring urgent medical review, oral corticosteroids or bronchodilator nebuliser use)	Ask & investigate (eg prescribing records) about medication use, including adherence with maintenance treatment Check inhaler technique Enquire about clinical features associated with an increased risk Consider treatable traits Decide whether peak flow monitoring is indicated	Is a step up in the level of treatment required if asthma is not adequately controlled, poor lung function or recent severe exacerbation? Is a change to the AIR regimen required in patients who have had a recent severe exacerbation? Is a step down in the level of treatment possible if there has been a sustained period of good control?	<ul> <li>Decide which plan to use:</li> <li>AIR budesonide/formoterol reliever ± maintenance therapy</li> <li>3-stage maintenance ICS or ICS/LABA + SABA reliever</li> <li>4-stage maintenance ICS + SABA reliever</li> <li>[This includes the instruction to increase dose and frequency of ICS in worsening asthma]</li> <li>For those with peak flow instructions, enter personal best recent peak flow and peak flow at each level in the plan. The recommended cut points of &lt;80% for getting worse, &lt;60 to 70% for severe asthma and &lt;50% for an emergency are a reference guide only and can be adjusted according to clinical judgement depending on the patient.</li> <li>Enter the prednisone regimen. The standard regimen in severe asthma is 40mg daily for five days. An alternative regimen is 40mg daily until there is definite improvement and then 20mg daily for the same number of days.</li> <li>Enter additional instructions in the box provided. This may include avoidance of provoking factors such as aspirin.</li> <li>Save a copy of the plan on the patient record.</li> </ul>

Completing the budesonide/formoterol reliever ± maintenance therapy (AIR) asthma action plan

	Write number of actuations	Ensure that the patient's inhaler technique is checked	Write any additional asthma medications here	Any special ins can be writte
Asthma Respiratory Totubaction M2 *Anti-Inflammatory Reliever Therapy Know your asthma symptoms	Name: Date of plan: Know when and ho	w to take your medicine	Doctor: Doctor phone:	
Your asthma is under control when - You don't have asthma symptoms most days (wheeze, tight chest, a cough or feeling breathless) - You have no cough or wheeze at night - You can do all your usual activities and exercise freely - Most days you do not need extra Symbicort	Regularly scheduled Symbicort:	actuation(s) every morning	Symbicort is a 2-in-1 reatment used f prevention and relief of symptoms. Ca times. You do not newd an extra inhale Other Medication	arry this at all
Most days you do not need extra Symbicort actuations Your peak flow reading is above:	As needed Symbicort to relieve symptoms:	1 actuation when you need it to relieve your asthma symptoms	٥	
Your asthma is getting severe when Your asthma symptoms are getting severe (wheeze, tight chest, a cough or feeling breathless) OR your Symbicart is only helping for 2-3 hours OR you are using more time a actuations a day in total (regular + reliever ise)	Let's take action  You need to see your of Continue any regular Sy Symbicort when needee Start prednisone if you	<b>loctor today</b> mbicort PLUS 1 actuation of your d to relieve symptoms	Other instructions:	/
OR you feel you need to see your doctor Your peak flow reading is below:	Prednisone and then	mg for days mg for days		
It is an emergency when • Your symptoms are getting more severe quickly • OR you are finding it hard to speak or breathe • OR your Symb Kort is not helping much • OR you are using your Symbicort every 1-2 hours Your peak flow reading helow: o		rt as often as needed ttter seek medical help right away ng your prednisone, start now	Best peak flow: Plan prepared by: Next review date: Signature:	
	ire a prescription ided if appropriate	A phamacist may give a patient an of prednisone if this has been pre		a action plans to be signed

Completing the maintenance ICS & SABA reliever four-stage asthma action plan

Write name of reliever e.g. Ventolin e.g. Beclazone	Write number of actuations	Ensure that the patient's inh and spacer technique is che		Write any special instructions here
Asthma + Respiratory roundation N2 Know your asthing a symptoms	Name: Date of plan: Know when any how	to take your medicine	Doctor: Doctor phone:	
Your asthma is under centrol when • you don't have asthma symitoms most days (wheeze; tight chest, a cough or feeling breathless) • you have no cough or wheeze reg night • you can do all your usual activities and exercise freely • most days you don't need a relievel Your peak flow reading is above o	Preventer oname) Reliever oname)	actuation(s) every morning actuation(s) every night actuation(s) when you need it to relieve your asthma symptoms	Orry your reliever at all times Other Medication	
Caution- your asthma is getting worse when • you have symptoms most hays (wheeze, tight chest, a cough or feeling treathless) • you are waking at night with symptoms • you are getting a cold Your peak flow reading is pelowe	Let's get prepared • Step up your preventer med Take actuations four Use your reliever as often as one can be used with your re	icine: times each day needed – through a spacer, if	Other instructions:	~
Caution- your asthna is getting severe when • Your symptoms are getting severe (wheeze, tight chest, a cough or f feling threathless) • OR your reliever if only helping for 2-3 hours • OR you are using more plan 12 actuations a day • OR you feel you need to see your doctor Your peak flow reading ispelow o	Let's take action • You need to see your doctor Continue your medicine for S tart prednisone if you have Prednisone and then	or today 'getting worse''	Other instructions:	
Emergency           • Your symptoms are getting more severe quickly         • OR you are inding it hardto speak or breatle         • OR your relevent in ot happing much           • OR you are using your relevere every 1-2 hyurs         • OR you are using your relevere every 1-2 hyurs	Let's keep calm • Dial 111 for ambulance • Keep using your reliever as c spacer, if one can be used wi • Even if you seem to get bett • If you haven't started taking	ith your reliever inhaler er seek medical help right away	Best peak flow: Plan prepared by: Next review date: Signature:	
The cut points recommended may be adjusted depending on the patient for prevente			ve a patient an emergency supply s has been previously prescribed	Asthma action plans need to be signed



e name of prevente Seretide, Past Write name of reliever e.g. Ventolin Write number of actuations Ensure that the patient's inhaler and spacer technique is checked Write any additional sthma medications he Write any special instructions here Asthma Respiratory JR ASTHMA ON PLAN Kr d how to take your medicin Your asthma is under co rol wher arry your reliever at all ti you don't have asthma syr Other Medication wheeze, tight chest, a co you have no cough or wi every night you can do all your usual activ freely Poliou when vou need most days you don't need a rel it to reliev your asthma symptoms Your peak flow reading is abov Caution- your asthma is Other instructions ting severe when Let's take action .. You need to see your doctor today or feeling breathless eze, tight chest, a Continue your regular preventer AND use your reliever as often as needed to relieve symptoms • OR your reliever is onl ping for 2-3 hours OR you are using n 12 actuations in a day sone if you have it • OR you feel you ne e vour doctor Prednis mg for davs and then mg for days Your peak flow rea Emergency Let's keep alm... Dial 111 for ambulance ere quickly your reliever as often as needed – through a ne can be used with your reliever inhaler OR you are o speak or breathe Keep usi spacer, if OR your re oing much Even if vo seem to get better seek medical help right away er every 1-2 hou OR you ar n't started taking your prednisone, start no If you h e cut points recommended may djusted depending on the patient Ensure a prescription is provided. Asthma action plans need to be signed A phamacist may give a patient an emergency supply of prednisone if this has been previously prescribed

Completing the maintenance ICS/LABA & SABA reliever or maintenance ICS & SABA reliever three-stage asthma action plan

# Useful documents/resources/IT support/educational tools/audit tools section

#### Health professionals

#### Asthma control

The Asthma Control Test can be used during a consultation/appointment to standardise the review of asthma symptoms: http://www.asthmacontrol.co.nz/.

#### Asthma self-management plans (action plans)

Every person with asthma should have an individualised written asthma plan, which is updated yearly. The plan should be appropriate for level of treatment, asthma severity, health literacy, culture and ability to self-manage. There is a range of plans available:

https://www.nzasthmaguidelines.co.nz/resources

#### **Inhaler technique**

Correct inhaler technique is central for good asthma control. Incorrect use of an inhaler may lead to worsening asthma control due to inadequate drug delivery to the airways. Information and videos on correct inhaler technique can be found here:

https://www.nationalasthma.org.au/living-with-asthma/how-to-videos; https://www.health-navigator.org.nz/medicines/i/inhaler-devices/?tab=10755#Overview

#### **Dispensing records**

Clinicians are encouraged to check pharmacy dispensing records for a patient when assessing concordance with asthma medication. These records may be available through primary care, pharmacy or district health board patient records systems.



#### Audit Tools

Health professionals providing asthma care are encouraged to participate in audit https://bpac.org.nz/Audits/docs/bpac\_audit\_asthma\_management2017.pdf

https://www.thoracic.org.au/researchawards/new-zealand-national-asthma-audit

#### **Resource for school teachers**

The Teachers' Asthma Toolkit is a free online tool that covers information about asthma, how asthma affects education, how asthma is treated, common triggers and what to do in an asthma emergency. The toolbox is interactive, featuring video clips, animations, classroom resources and child-friendly activities.

https://learnaboutlungs.asthmaandrespiratory.org.nz/

#### Resources for those who have asthma and their families

#### Asthma apps

The My Asthma App provides educational information on asthma, signs and symptoms, triggers, treatment, medication, ACT, helpful contacts and resources. It includes the ability to include an individualised asthma action plan. This resource was developed by the Asthma and Respiratory Foundation New Zealand and can be downloaded from: Android: bit.ly/ AsthmaAppAndroid or

Apple: bit.ly/AsthmaAppApple

### Websites providing guidelines, educational information and e-learning course

Online information on asthma is readily available. There are several New Zealand and Australian websites which provide high-quality information and downloadable resources on asthma and other conditions which may impact on asthma management. These include:

Asthma and Respiratory Foundation New Zealand https://www.asthmafoundation.org.nz/

https://www.asthmafoundation.org.nz/health-professionals/copd-asthma-fundamentals

Asthma New Zealand https://www.asthma.org.nz/

Allergy New Zealand http://www.allergy.org.nz/

Severe asthma toolkit https://toolkit.severeasthma.org.au/

National Asthma Council Australia https://www.nationalasthma.org.au/

The New Zealand Formulary has information on drugs in sport http://www.nzf.org.nz

Australian Society of Clinical Immunology and Allergy website has a range of information, action plans, treatment plans, patient handouts and e-learning course for health professionals https://www.allergy.org.au/

National Institute for Clinical Excellence has a useful patient inhaler decision aid https://www.nice.org.uk/guidance/ng80/resources/ inhalers-for-asthma-patient-decision-aid-pdf-6727144573

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#### REFERENCES:

- Asthma and Respiratory Foundation of New Zealand 2015. Te Hā Ora (The Breath of Life): National Respiratory Strategy. Wellington: The Asthma Foundation.
- Jones B, Ingham T. He Māramatanga huangō: Asthma health literacy for Māori children in New Zealand: Report to the Ministry of Health. Wellington: Ministry of Health 2015.
- 3. Telfar Barnard L, et al. The impact of respiratory disease in New Zealand:

2018 update. Wellington: Asthma Foundation 2019.

- 4. Holt S, Beasley R. The Burden of Asthma in New Zealand. Asthma & Respiratory Foundation NZ and Medical Research Institute of New Zealand. Auckland: Adis International Ltd 2002; 48p.
- 5. ISAAC Steering Committee. Worldwide variation in prevalence of symptoms of asthma, allergic rhinoconjunctivitis and atopic eczema: ISAAC. Lancet 1998; 351:1225–32.
- 6. Lai CKW, et al. Global variation in the prevalence and severity of asthma symptoms: Phase Three of the International Study of Asthma and Allergies in Childhood (ISAAC). Thorax 2009; 64:476–83.
- 7. Masoli M, et al. Global Burden of Asthma. Global Initiative for Asthma (GINA) 2004. www.ginasthma.com
- 8. Beasley R, et al. Asthma and Respiratory Foundation NZ adult asthma guidelines: A quick reference guide. NZMJ 2016; 129:83–102.



- 9. Asher I, et al. Asthma and Respiratory Foundation NZ child and adolescent asthma guidelines: A quick reference guide. NZMJ 2016; 130:10–33.
- **10.** Global Strategy for Asthma Management and Prevention. Global Initiative for Asthma (GINA). 2019 Update.
- 11. British Thoracic Society, Scottish Intercollegiate Guidelines Network. QRG 141: British Guideline on the Management of Asthma Quick Reference Guide. October 2014.
- National Asthma Council Australia. Australian Asthma Handbook Quick Reference Guide. Version 2.0, available at: http://www.asthmahandbook.org.au/
- Nathan R, et al. Development of the Asthma Control Test: a survey for assessing asthma control. J Allergy Clin Immunol 2004; 113:59–65.
- Schatz M, et al. Asthma control Test: reliability, validity, and responsiveness in patients not previously followed by asthma specialists. J Allergy Clin Immunol 2006; 117:549–56.
- **15.** Janson C, et al. Carbon footprint impact of the choice of inhalers for asthma and COPD. Thorax 2020; 75:82–4.
- 16. Wilkinson AJK, et al. Costs of switching to low global warming potential inhalers. An economic and carbon footprint analysis of NHS prescription data in England. BMJ Open 2019; 9:e028763. doi: 10.1136/ bmjopen-2018-028763.
- 17. Bateman ED, et al. As-needed budesonide-formoterol versus maintenance budesonide in mild asthma. N Engl J Med 2018; 378:1877–87.

- 18. Hardy J, et al. Budesonide-formoterol reliever therapy versus maintenance budesonide plus terbutaline reliever therapy in adults with mild to moderate asthma (PRACTICAL): a 52-week, open-label, multicentre, superiority, randomised controlled trial. Lancet 2019; 394:919–28.
- 19. O'Byrne PM, et al. Inhaled combined budesonide– formoterol as needed in mild asthma. N Engl J Med 2018; 378:1865–76.
- 20. Beasley R, et al. Controlled trial of budesonide-formoterol as-needed for mild asthma. N Engl J Med 2019; 380:2020–30.
- 21. Sobieraj DM, et al. Association of inhaled corticosteroids and long-acting  $\beta$ -agonists as controller and quick relief therapy with exacerbations and symptom control in persistent asthma a systematic review and meta-analysis. JAMA 2018; 319:1485–96.
- 22. Beasley R, et al. ICS-formoterol reliever therapy stepwise treatment algorithm for adult asthma. Eur Respir J 2020; 55:1901407. doi: 10.1183/13993003.01407-2019.
- 23. Balanag VM, et al. Efficacy and safety of budesonide/ formoterol compared with salbutamol in the treatment of acute asthma. Pulm Pharmacol Ther 2006; 19:139–47.
- 24. Powell H, Gibson P. High dose versus low dose inhaled corticosteroids as initial starting dose for asthma in adults and children. The Cochrane Collaboration. The Cochrane Library 2008, Issue 4.
- **25.** Holt S, et al. Dose-response relation of inhaled fluticasone propionate in adolescents and adults with

asthma: meta-analysis. BMJ 2001; 323:253–6.

- 26. Masoli M, et al. Dose-response relationship of inhaled budesonide in adult asthma: a meta-analysis. Eur Respir J 2004; 23:552–8.
- 27. Pauwels RA, et al. Early intervention with budesonide in mild persistent asthma: a randomised, doubleblind trial. Lancet 2003; 361:1071–6.
- 28. Beasley R, et al. Call for withdrawal of LABA single-therapy inhaler in asthma. Lancet 2010; 376:750–1.
- 29. Woodcock A, et al. Effectiveness of fluticasone furoate plus vilanterol on asthma control in clinical practice: an open-label, parallel group, randomised controlled trial. Lancet 2017; 390:2247–55.
- **30.** Patel M, et al. Efficacy and safety of maintenance and reliever combination budesonide–formoterol inhaler in patients with asthma at risk of severe exacerbations: a randomised controlled trial. Lancet Respir Med 2013; 1:32–42.
- **31.** Gibson PG, et al. Asthma in older adults. Lancet 2010; 376:803–13.
- **32.** Anderson DE, et al. Long-acting muscarinic antagonists (LAMA) added to inhaled corticosteroids (ICS) versus the same dose of ICS alone for adults with asthma. Cochrane Database Syst Rev 2015; 8:CD011397.
- **33.** Sobieraj DM, et al. Association of inhaled corticosteroids and long-acting muscarinic antagonists with asthma control in patients with uncontrolled, persistent asthma: a systematic review and meta-analysis. JAMA 2018; 319:1473–84.

- 34. Virchow JC, et al. Single inhaler extrafine triple therapy in uncontrolled asthma (TRIMARAN and TRIGGER): two doubleblind, parallel-group, randomised, controlled phase 3 trials. Lancet 2019; 394:1737–49.
- **35.** Normansell R, et al. Omalizumab for asthma in adults and children. Cochrane Database Syst Rev 2014; 1:CD003559.
- **36.** Pavord ID, et al. Mepolizumab for severe eosinophilic asthma (DREAM): a multicentre, double-blind, placebo-controlled trial. Lancet 2012; 380:651–9.
- **37.** Peters MC, Wenzel SE. Intersection of biology and therapeutics: type 2 targeted therapeutics for adult asthma. Lancet 2020; 395:371–83.
- 38. Kowalski ML, et al. Diagnosis and management of NSAID-Exacerbated Respiratory Disease (N-ERD)—a EAACI position paper. Allergy 2019; 74:28–39.
- **39.** Gotzsche PC, Johansen HK. House dust mite control measures for asthma. The Cochrane Collaboration 2008.
- 40. Howden-Chapman P, et al. Effect of insulating existing houses on health inequality: cluster randomised study in the community. BMJ 2007; 334:460.
- **41.** Australasian Society of Clinical Immunology and Allergy. Skin prick testing for the diagnosis of allergic disease: a manual for practitioners. ASCIA 2016. http://allergy.org.au/images/ stories/pospapers/ASCIA\_ SPT\_Manual\_March\_2016. pdf . Accessed 17/12/19.
- **42.** Australasian Society of Clinical Immunology and Allergy. Laboratory

tests in the diagnosis of allergic disease. ASCIA. http://allergy.org.au/hp/ papers/tests-in-the-diagnosis-of-allergic-diseases Accessed 17/12/19.

- **43.** Novakova P, et al. Allergen immunotherapy in asthma: current evidence. J Asthma 2019; doi: 10.1080/02770 903.2019.1684517.
- **44.** Agache I, et al. EAACI Guidelines on Allergen Immunotherapy: House dust mite-driven allergic asthma. Allergy 2019; 74:855–73.
- **45.** Dhami S, et al. Allergen immunotherapy for allergic asthma: A systematic review and meta-analysis. Allergy 2017; 72:1825–48.
- **46.** Smith PK, et al. Risk multipliers for severe food anaphylaxis. World Allergy Organ J 2015; 8:30.
- 47. Kool B, et al. Adult food-induced anaphylaxis hospital presentations in New Zealand. Postgrad Med J 2016; 92:640–4.
- **48.** Turner PJ, et al. Fatal Anaphylaxis: Mortality Rate and Risk Factors. J Allergy Clin Immunol Pract 2017; 5:1169–78.
- **49.** Agusti A, et al. Treatable traits: towards precision medicine of chronic airways diseases. Eur Respir J 2016; 47:410–9.
- 50. Agusti A, et al. Precision medicine in airway diseases: moving to clinical practice. Eur Respir J 2017; 50:1701655.
- **51.** Pavord I, et al. After asthma: redefining airways diseases. Lancet 2018; 391:350–400.
- **52.** Clark VL, et al. Multidimensional assessment of severe asthma: A systematic review and meta-analysis. Respirology 2017; 22:1262–75.
- **53.** Holt S, et al. The use of the self-management

plan system of care in adult asthma. Prim Care Resp J 2004; 13:19–27.

- 54. Gibson PG, Powell H. Written action plans for asthma: an evidence-based review of the key components. Thorax 2004; 59:94–9.
- 55. Reddel HK, et al. A summary of the new GINA strategy: a roadmap to asthma control. Eur Respir J 2015; 46:622–39.
- 56. Reddel HK, et al. The GINA asthma strategy report: what's new for primary care? NPJ Primary Care Respiratory Med 2015; 25;150–6.
- 57. Sadof M, Kaslovsky R. Adolescent asthma: a developmental approach. Curr Opin Pediatr 2011; 23:373–8.
- 58. Buston KM, Wood SF. Non-compliance amongst adolescents with asthma: listening to what they tell us about self-management, Family Practice 2000; 17:134–8.
- **59.** Holley S, et al. Barriers and facilitators to asthma self-management in adolescents: A systematic review of qualitative and quantitative studies. Pediatr Pulmonol 2017:52:430-42.
- **60.** Hobbs M, et al. Reducing health inequity for Maori people in New Zealand. Lancet 2019; 394:1613–4.
- 61. Gillies TD, et al. Ethnic disparities in asthma treatment and outcomes in children aged under 15 years in New Zealand: analysis of national databases. Prim Care Respir J 2013; 22:312–8.
- 62. Metcalfe S, et al. Variation in the use of medicines by ethnicity during 2006/07 in New Zealand: a preliminary analysis. NZMJ 2013; 126:14–41.
- **63.** Harris RB, et al. The relationship between

socially-assigned ethnicity, health and experience of racial discrimination for Maori: analysis of the 2006/07 New Zealand Health Survey. BMC Public Health 2013; 13:844.

- 64. Robson B, Harris R. Hauora: Màori Standards of Health IV. A study of the years 2000–2005. 2007.
- 65. Tatau Kahukura: Māori Health Chart Book 2015, 3rd edition. Accessed 17/12/19. http://www. health.govt.nz/publication/ tatau-kahukura-maori-health-chart-book-2015-3rd-edition.
- **66.** Pilcher J, et al. Combination budesonide/formoterol inhaler as maintenance and reliever therapy in

Māori with asthma. Respirology 2014; 19:842–51.

- **67.** Aldington S, Beasley R. Asthma exacerbations. 5: Assessment and management of severe asthma in adult in hospital. Thorax 2007; 62:447–58.
- **68.** Rowe BH, et al. Corticosteroids for preventing relapse following acute exacerbations of asthma. Cochrane Database Syst Rev 2007; (3):CD000195.
- **69.** Bowler SD, et al. Corticosteroids in acute severe asthma: effectiveness of low doses. Thorax 1992; 47:584–7.
- 70. Camargo CA Jr, et al. Continuous versus intermittent beta-agonists in the

treatment of acute asthma. Cochrane Database Syst Rev 2003; (4):CD001115.

- 71. Cates CJ, et al. Holding chambers (spacers) versus nebulisers for beta-agonist treatment of acute asthma. Cochrane Database Syst Rev 2013; (9):CD000052.
- 72. Emerman CL, et al. Comparison of 2.5 vs 7.5 mg of inhaled Albuterol in the treatment of acute asthma. Chest 1999; 115:92–6.
- 73. Rodrigo GJ, Castro-Rodriguez JA. Anticholinergics in the treatment of children and adults with acute asthma: a systematic review with meta-analysis. Thorax 2005; 60:740–6.

Notes

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