



National Prescribing Service Limited

27 June 2008



000001 000
Dr Sam Sample
123 Sample Street
Samletown ABC 1234

Prescribing Practice Review

No. 42 Inhaled corticosteroids and long-acting beta₂ agonists

Dear Dr Sample,

While fixed-dose combinations of inhaled corticosteroid (ICS) and long-acting beta₂ agonist (LABA) are commonly used, each component has a specific place in therapy. This *Prescribing Practice Review* describes when to select and titrate each class of drug. Included are your prescribing data, along with practice points for your review.

Select inhaled corticosteroids and bronchodilators in chronic obstructive pulmonary disease (COPD) and asthma based on the therapeutic effect and a confirmed diagnosis

Use spirometry to assess COPD and asthma symptoms. Appropriate drug choices are distinct in each condition.

In persistent asthma, start with a low-dose inhaled corticosteroid (ICS). Step up or back-titrate to achieve asthma control with the lowest possible dose

Low-dose ICS is highly effective in mild-to-moderate persistent asthma, while increasing doses go hand-in-hand with increasing adverse effects.

In moderate-to-severe COPD, initiate high-dose ICS if bronchodilators alone are insufficient. Discontinue ICS after 4–8 weeks if there is no response

Regularly review medicine use to optimise drug choice, dosing and inhaler technique.

Fixed-dose combinations of an ICS and a long-acting beta₂ agonist (LABA) should not be used for initial therapy in asthma or COPD

Use of budesonide with eformoterol (Symbicort) for maintenance and reliever therapy may suit some people with poorly controlled asthma. Fluticasone with salmeterol (Seretide) is not suitable for acute relief in asthma

An NPS clinical audit *Using inhaled corticosteroids and long-acting beta₂ agonists* will be available in August to help you review your prescribing—an enrolment form is enclosed.

Yours sincerely,

Dr Janette Randall
Chair, National Prescribing Service Limited

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funded by the Australian Government Department of Health and Ageing.

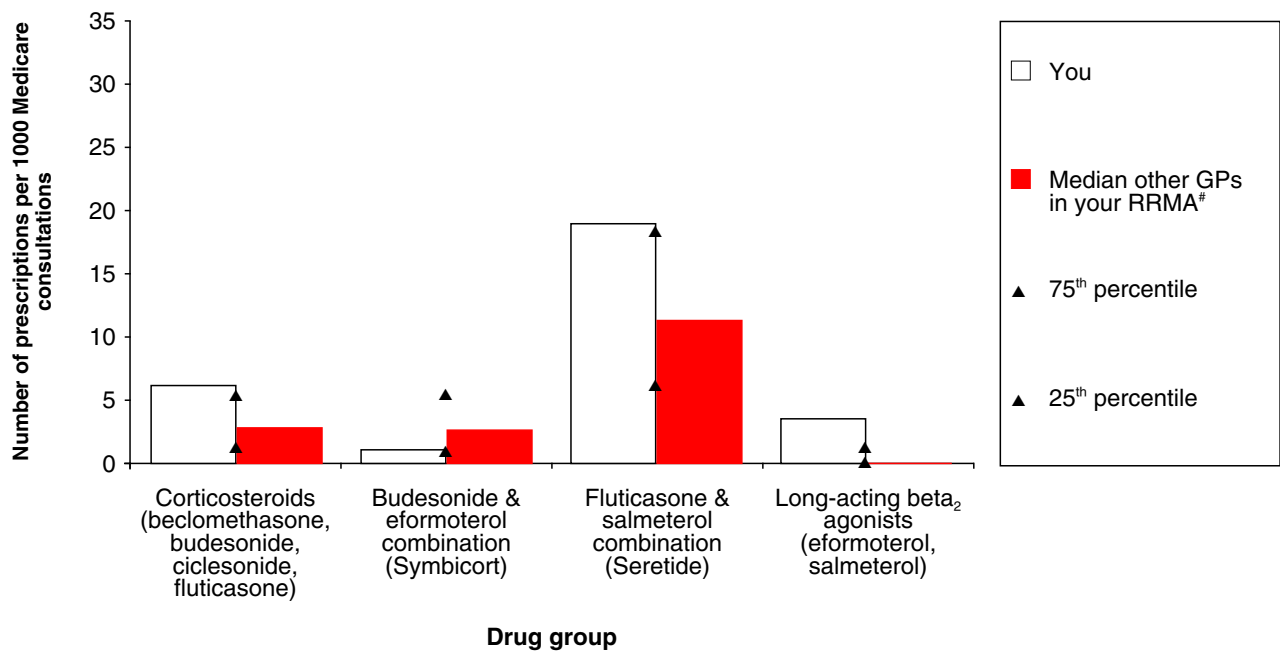
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Your confidential prescribing data

The data shown here from Medicare Australia includes PBS dispensed prescriptions for concession card holders **only** as many lower strength inhaled corticosteroids (ICS) and long-acting beta₂ agonists (LABAs) are below the general patient co-payment.

Data is not included on short-acting beta₂ agonists i.e. salbutamol and terbutaline. Prescribing, regardless of respiratory condition is included (e.g. asthma, chronic obstructive pulmonary disease (COPD) or acute respiratory conditions).

Inhaled corticosteroids and long-acting beta₂ agonists prescribed for concession card holding patients in 2007

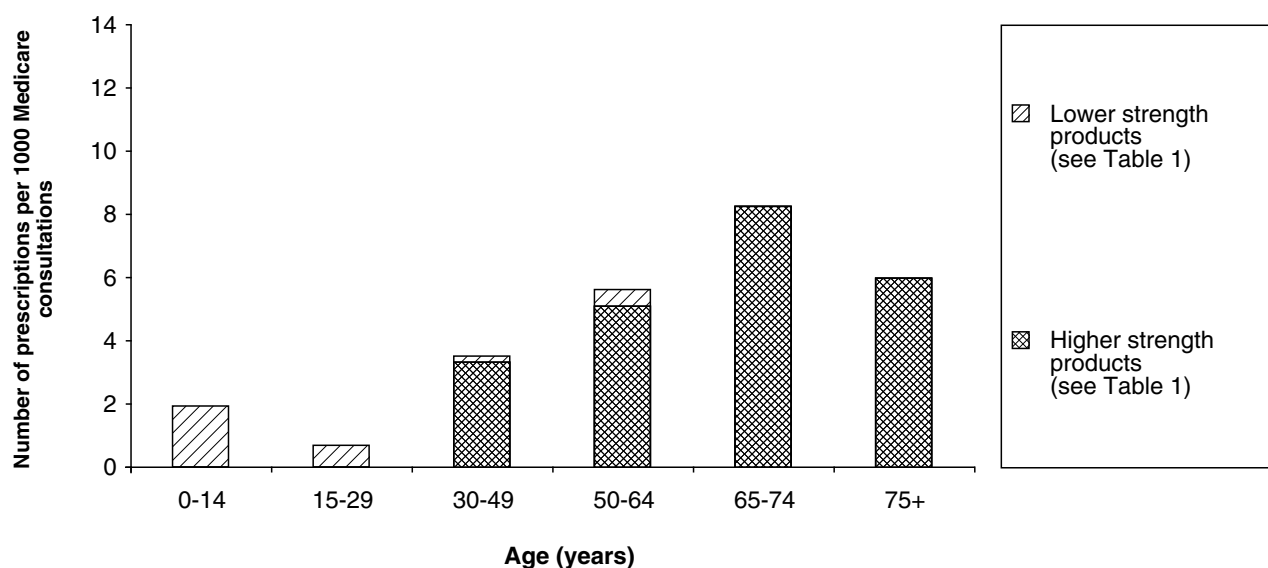


In 2004, two thirds of all inhaled corticosteroids dispensed on the PBS were in a fixed-dose combination with a long-acting beta₂ agonist.¹ In 2007 this had risen to 83% of all inhaled corticosteroid products dispensed.

Practice points

- When choosing a fixed-dose combination product, identify the individual components and assess appropriateness for asthma or COPD because optimal management differs significantly.
- Consider an inhaled corticosteroid:
 - when asthma requires a short-acting beta₂ agonist more than three times per week;
 - in moderate to severe COPD with two or more exacerbations per year.
- The decision to continue inhaled corticosteroids is based on asthma severity and control or COPD responsiveness:
 - in asthma, attempt to back titrate to minimum effective dose during periods of good control (after 6-12 weeks);^{2,3}
 - in COPD, discontinue inhaled corticosteroids if there is no clinically significant response after 4-8 weeks.⁴

Your prescribing of inhaled corticosteroids (in single or fixed-dose combination) for concession card holding patients by age in 2007



Practice points

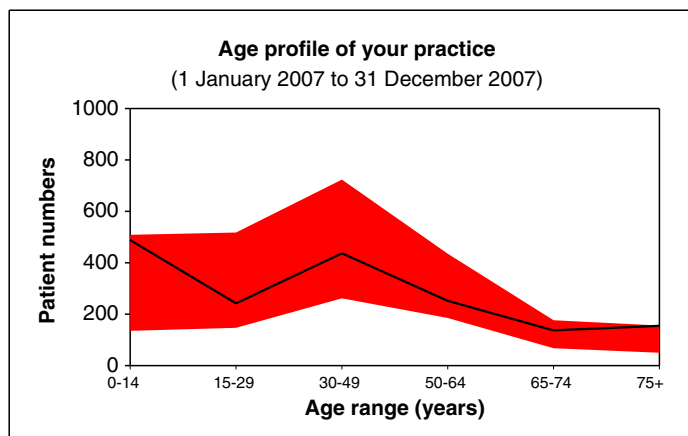
- When prescribing a fixed-dose combination product for maintenance and reliever therapy in asthma, use only lower strengths of budesonide/eformoterol (Symbicort 100/6 microgram and 200/6 microgram). Only eformoterol has an onset of action rapid enough to be effective as a reliever. Do not use the budesonide/eformoterol (Symbicort) 400/12 microgram strength because it can easily lead to overdosing in asthma.
- Only the higher strengths of fluticasone/salmeterol (Seretide 250/25 microgram inhaler and 500/50 microgram accuhaler) are PBS listed for symptomatic treatment of COPD.
- In 2007, most inhaled corticosteroid prescriptions dispensed for concessional patients were for higher strength products (71%). Check if your patients with asthma could be controlled with a lower dose of inhaled corticosteroid.
- In asthma inhaled corticosteroids have a flat dose response. Most of the therapeutic effect is achieved with a total daily dose equivalent to 100–250 micrograms of beclomethasone and the maximum effect with a daily dose of around 500 micrograms.
- Dose equivalence: 100 microgram beclomethasone = 200 microgram budesonide = 80 microgram ciclesonide = 100 microgram fluticasone.

Table 1. Products containing inhaled corticosteroids

Lower strength products		Higher strength products	
single agent products	fixed-dose combination products	single agent products	fixed-dose combination products
Beclomethasone (Qvar) 50-100 microgram/dose	Fluticasone/salmeterol (Seretide) 50-125 microgram/dose	Budesonide (Pulmicort) 400 microgram/dose	Fluticasone/salmeterol (Seretide) 250-500 microgram/dose
Budesonide (Pulmicort) 100-200 microgram/dose	Budesonide/eformoterol (Symbicort) 100-200 microgram/dose	Ciclesonide (Alvesco) 160 microgram/dose	Budesonide/eformoterol (Symbicort) 400 microgram/dose
Ciclesonide (Alvesco) 80 microgram/dose		Fluticasone (Flixotide) 250-500 microgram/dose	
Fluticasone (Flixotide) 50-125 microgram/dose			

Practice profile

Some data shown earlier are presented as prescribing rates (per 1000 Medicare consultations) to adjust for volume of service. Age profile and concession card holding status of patients in your practice are provided to assist you in interpreting your prescribing data.



The black line represents the age profile of patients in your practice. 25% to 75% of other GPs in your RRMA[†] fall within the shaded area.

Medicare patients and concession card holders in your practice

(1 April 2007 to 30 June 2007)

Patients	You	Median other GPs in your RRMA [†]
Total Medicare	711	661
Concession card holders^{**}	174	179

(^{**}includes those reaching Safety Net)

Data from a three month period (1 April 2007 to 30 June 2007) that best represent your patient mix have been provided.

Notes

[®]Data shown are an aggregate for all your provider locations.

[#] The comparator group "other GPs in your RRMA" includes all prescribers who are currently located in a similar geographical region i.e. 1. capital cities, 2. other metropolitan centres, 3. large rural centres, 4. small rural centres, 5. other rural centres, 6. remote centres and 7. other remote centres.

Your RRMA peer group is 1.

[▲] 25% to 75% of all doctors in the comparator group fall in the range shown by the triangular symbols.

Confidentiality

NPS has a contract with Medicare Australia to provide your prescribing feedback data directly to you. NPS does not have access to these data. The data contained in this feedback are not used for any regulatory purposes.

Discrepancies may occur between the data provided and your own prescribing practice. This may be due to either inaccurate recording of your prescriber number in the pharmacy or your prescription pad having been used by another doctor.

If you consider your individual data to be incorrect, have other data queries or general feedback please contact NPS on 02 8217 8700 or by email at info@nps.org.au

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Appropriate use of inhaled corticosteroids and long-acting beta₂ agonists in asthma and COPD

Key Messages

- Select inhaled corticosteroids and bronchodilators in chronic obstructive pulmonary disease (COPD) and asthma based on the therapeutic effect and a confirmed diagnosis
- In persistent asthma, start with a low-dose inhaled corticosteroid (ICS). Step up or back-titrate to achieve asthma control with the lowest possible dose
- In moderate to severe COPD, initiate high-dose ICS if bronchodilators alone are insufficient. Discontinue ICS after 4–8 weeks if there is no response
- Fixed-dose combinations of an ICS and a long-acting beta₂ agonist (LABA) should not be used for initial therapy in asthma or COPD
- Use of budesonide with eformoterol (Symbicort) for maintenance and reliever therapy may suit some people with poorly controlled asthma. Fluticasone with salmeterol (Seretide) is not suitable for acute relief in asthma

While fixed-dose combinations of an inhaled corticosteroid and a LABA are increasingly popular, there is no 'one size fits all' approach to optimal prescribing in asthma and COPD.

Confirm the diagnosis using spirometry

Use spirometry to assess COPD and asthma symptoms

Post-bronchodilator spirometry is needed to confirm irreversible airway obstruction.¹ COPD with a significant bronchodilator response is as common as COPD with no reversibility.²

Diagnosing asthma requires both spirometry and clinical history.³

Spirometry is also recommended for monitoring lung function in both asthma and COPD.^{1,3}

Treat patients with COPD but significant reversibility according to asthma guidelines

For people with clinical features of both asthma and COPD, the reversible (asthma-like) component is more responsive to treatment. Patients who remain hard to manage may benefit from referral for further diagnostic testing.

Consider referring to a respiratory physician to exclude other diagnoses and complications, especially for irreversible obstruction in people younger than 40 years, people with a smoking history of < 10 pack-years*, or people with a rapid decline in FEV₁.¹

* Multiply the number of packs of cigarettes smoked per day by the number of years the person has smoked.

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Select medication according to the diagnosis

Use an inhaled corticosteroid early in persistent asthma and late in moderate to severe COPD

Stepped care starts with a short-acting bronchodilator in COPD and a low-dose inhaled corticosteroid in persistent asthma.^{1,3} Stepped care allows for optimal symptom control with minimal drug therapy, while defining a suitable pathway for managing fluctuating asthma symptoms or progression of COPD.

The mainstay of asthma treatment is the inhaled corticosteroids ('preventers'). International guidelines recommend them as part of initial treatment in persistent asthma, and there is evidence that they improve lung function, improve asthma symptoms and prevent exacerbations.⁴⁻⁷

In COPD, guidelines recommend using a short-acting bronchodilator intermittently as a first step, increasing to regular long-acting treatment (tiotropium [Spiriva] or a LABA) if necessary. Inhaled corticosteroids are only indicated in moderate to severe COPD with repeated exacerbations.*¹

* Inhaled corticosteroids are not approved by the TGA for COPD. They are listed on the PBS general schedule as unrestricted benefits and prescribers may write prescriptions in line with their clinical judgment.

Inhaled corticosteroids have a modest benefit in COPD

A high-dose inhaled corticosteroid (see Table 1 for dose ranges), alone or in combination with a LABA, reduces average exacerbation rates in moderate to severe COPD. In trials, treating 4 people for 1 year prevented 1 exacerbation.⁸ However, it is essential to assess the benefits and harms for each individual (see 'Discontinue inhaled corticosteroids in COPD if there is no response' below).

There is currently no drug treatment that can slow the rate of decline in lung function in COPD.

Table 1. Daily adult inhaled corticosteroid dose equivalents*³

	Low	Medium	High
beclomethasone (CFC-free)	100–200 micrograms	200–400 micrograms	> 400 micrograms
budesonide	200–400 micrograms	400–800 micrograms	> 800 micrograms
ciclesonide	80–160 micrograms	160–320 micrograms	> 320 micrograms
fluticasone	100–200 micrograms	200–400 micrograms	> 400 micrograms

* Doses as labelled: ex-actuator dose for ciclesonide, and ex-valve dose for others.

Tailor the inhaled corticosteroid dose to the condition and the patient

Low-dose inhaled corticosteroid is highly effective in mild to moderate persistent asthma

More than 90% of people with asthma who see a GP have intermittent or mild to moderate persistent asthma, according to Australian survey data.⁹ Low-dose inhaled corticosteroids are highly effective in this population — higher doses add little benefit and increase adverse effects.¹⁰ On the other hand, people with severe asthma may require high-dose inhaled corticosteroid.³

To ensure the lowest exposure to inhaled corticosteroid adverse effects, step up only when necessary and back-titrate when symptoms are stable.

Initiate an inhaled corticosteroid at a high dose in moderate to severe COPD when there are repeated exacerbations

In COPD, all trials of inhaled corticosteroids have used moderate to high doses.⁸ As the adverse effects associated with higher inhaled corticosteroid doses can be serious (including higher rates of pneumonia among COPD patients), inhaled corticosteroids should not be considered for patients with mild COPD.¹ (See the *NPS RADAR* review 'Fluticasone with salmeterol [Seretide] for chronic obstructive pulmonary disease'.)

Do not initiate therapy with a combination inhaler

Use a combination when both components are indicated

Fixed-dose combination inhalers containing an inhaled corticosteroid and a LABA (i.e. Seretide and Symbicort) are an option when guidelines recommend stepping up to a combination (see Table 2).

Table 2. When to start combination therapy with an inhaled corticosteroid and a long-acting bronchodilator in asthma and COPD

Diagnosis	Current therapy	Symptoms	Combination
Asthma	Low-dose inhaled corticosteroid	Inadequately controlled asthma	Low-dose inhaled corticosteroid plus LABA
COPD	Long-acting bronchodilator	FEV ₁ < 50% predicted and repeated exacerbations	High-dose inhaled corticosteroid plus long-acting bronchodilator [†]

[†] Fluticasone with salmeterol (Seretide 250/25 MDI and Seretide 500/50 DPI strengths only) is PBS listed for COPD in people with FEV₁ < 50% predicted who have a history of repeated exacerbations despite regular beta₂ agonist treatment. Budesonide with eformoterol (Symbicort) is neither TGA registered nor PBS listed for COPD.

When starting a fixed-dose combination, take care with the strength

PBS data from 2002–4 show that > 50% of people received prescriptions for inhaled corticosteroids in the highest-strength category (e.g. fluticasone with salmeterol [Seretide] 500/50).¹¹ Starting with a high-strength inhaled corticosteroid may benefit a small proportion of people with severe asthma, but unnecessarily increases the risk of steroid-related adverse effects for those whose symptoms are milder.

Unlike in asthma, a high starting dose of inhaled corticosteroid is recommended in COPD (see Table 3).¹

Table 3. Which combination inhaler is PBS listed for which condition?

Preparation	Strength	Formulation	COPD	Asthma
Fluticasone with salmeterol (Seretide)	50/25	Metered-dose inhaler	✗	✓
	125/25*		✗	✓
	250/25*		✓	✓
	100/50	Dry-powder inhaler	✗	✓
	250/50*		✗	✓
	500/50*		✓	✓
Budesonide with eformoterol (Symbicort)	100/6*	Dry-powder inhaler	✗	✓ [†]
	200/6*		✗	✓ [†]
	400/12 [‡]		✗	✓

* Not recommended for children < 12 years old.

[†] Also suitable for maintenance and reliever regimen (see page 6).

[‡] Not to be used by patients < 18 years old.

Test lung function and check symptoms regularly

Review is important for optimising medicine use

Review asthma patients 6–12 weeks after adjusting therapy.³ Review visits are supported through the Asthma Cycle of Care program (see Box, page 5).

Adults with good asthma control and established medication needs, or children with intermittent asthma, may only require yearly review.³ If asthma symptoms follow a seasonal pattern, a review scheduled before the usual time that they worsen can help ensure appropriate use of maintenance medication.

Review COPD patients 4–8 weeks after changing or stepping up therapy.¹ Lack of response to inhaled therapies in COPD is common and a prompt review allows the best therapy option to be found.

Use spirometry and ask about symptoms

Monitor using both an objective test of lung function (spirometry) and by asking about symptoms. Record functional limits as well as the frequency of symptoms to compare disease severity from visit to visit.

A brief questionnaire or checklist, such as the Asthma Control Questionnaire or the Medical Research Council dyspnoea score is useful for eliciting and grading symptoms and their impact. See *NPS News 58: Inhaled corticosteroids and long-acting beta₂ agonists in asthma and COPD*.

Back-titrate to the lowest dose of inhaled corticosteroid in asthma

Back-titrate when asthma symptoms have been stable for 6–12 weeks

Consider stepping down medication by reducing the inhaled corticosteroid dose by 25% to 50% or, if using combination therapy with the lowest inhaled corticosteroid dose, by stopping the LABA.³

Trials have found that people with stable asthma can step down high-dose inhaled corticosteroid (alone or in combination with a LABA) without worsening symptoms, including exacerbations (over 1 year of follow-up).¹²

Step down the inhaled corticosteroid dose by changing the number of puffs or prescribing a lower-strength inhaler

When using inhaled corticosteroid monotherapy, or combination therapy with separate inhaled corticosteroid and LABA inhalers, the inhaled corticosteroid dose can often be stepped down by reducing the number of puffs used per day.

When necessary, back-titrate the inhaled corticosteroid by switching the patient to a new prescription of an inhaler containing a lower strength. Fixed-dose combination inhalers offer limited flexibility in adjusting the number of puffs per day because the LABA component has only a small recommended dose range (eformoterol 12–48 micrograms daily* and salmeterol 100–200 micrograms daily).^{13,14}

* Up to 72 micrograms when using the SMART regimen (see page 6).

Discontinue inhaled corticosteroids in COPD if there is no response

Many people with COPD show no clinical benefit from inhaled corticosteroids

In view of the risk of serious adverse effects, high-dose inhaled corticosteroids should be stopped if there is no clinical benefit after 4–8 weeks. COPD trials have found an increased risk of pneumonia with these doses^{15,16} but no statistically significant increase in mortality.^{8,16} Rates of inhaled corticosteroid-related candidiasis, dysphonia and bruising were also increased in COPD trials.^{8,15,16}

Check inhaler technique, smoking status and compliance

Ask patients to bring their inhalers with them to review appointments

Ability to use an inhaler can decline within 2 months of first instruction.¹⁷ The most reliable test of inhaler technique is to ask patients to demonstrate it.

Give brief counselling for smoking cessation

Stopping smoking is the single most important intervention in COPD.¹ Smoking also worsens asthma symptoms and accelerates declining lung function.³

Brief counselling by a GP increases quit rates.¹⁸ Offer pharmacotherapy and/or referral if intensive intervention is needed. See *NPS News 45: Managing COPD and preventing progression*.

Ask how many times a week the patient forgets a dose

Few people with asthma or COPD use their maintenance medication every day.¹¹ Educating patients about their disease and the purpose of their medication can help to improve compliance.¹⁹

If a person forgets to use their inhaler regularly, advise on ways to incorporate it into daily activities. For example, suggest using the inhaler immediately before they clean their teeth (this also saves time rinsing excess drug from the mouth and throat).

Asthma cycle of care

The Asthma Cycle of Care (which replaced the Asthma 3+ Visit Plan) provides GPs with incentive payments for ongoing care and regular review of their patients. To be eligible, GPs must plan and complete at least 2 asthma-related consultations within 12 months with a patient who has moderate to severe asthma. Review visits under the Cycle of Care are an opportunity to check lung function, monitor medication use, check inhaler technique and step down medication if well controlled. Details of the requirements are available on the National Asthma Council Australia website (www.nationalasthma.org.au/HTML/management/acc/index.asp).

Budesonide with eformoterol (Symbicort) maintenance and reliever regimen for asthma (SMART)

Consider this alternative dosing regimen only for adults and adolescents with poorly controlled asthma

SMART is only indicated for people with frequent asthma symptoms despite conventional combination therapy or corticosteroids alone. It is not recommended for children under 12 years.¹³

The regimen uses Symbicort for 'single inhaler therapy', that is, for both maintenance dosing and on-demand for acute asthma symptoms. Double-blind trials in people with poorly controlled asthma found this regimen reduced severe asthma exacerbations compared with a conventional regimen.^{20–23}

Unlike in asthma, there is no evidence to support the use of on-demand combination therapy in COPD.

Fluticasone with salmeterol (Seretide) cannot be used on demand

The new regimen uses the Symbicort inhaler instead of a short-acting beta₂ agonist (SABA) 'reliever' (e.g. salbutamol). Eformoterol provides bronchodilation as quickly as a SABA.²⁴

Fluticasone with salmeterol (Seretide) cannot be used in this way because the onset of action for salmeterol is too slow.²⁴

Use this new regimen only in conjunction with a special Asthma Action Plan

Patients need to be taught how to follow the new regimen and associated Asthma Action Plan. Suitable templates are available online (at www.nationalasthma.org.au/html/management/action_plans/ap005.asp).

Assess patients for their ability to monitor asthma symptoms and on-demand inhaler use before selecting them for the maintenance and reliever regimen.

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Citations available online at www.nps.org.au/healthpro

Amended August 2008

The information contained in this material is derived from a critical analysis of a wide range of authoritative evidence. Any treatment decisions based on this information should be made in the context of the clinical circumstances of each patient.



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