In view of the recent promotion of the SMART regimen, (Symbicort single inhaler Maintenance And Reliever Therapy) we thought we should review the use of inhalers containing a combination of a long acting beta agonist (LABA) and inhaled corticosteroid (ICS).

The SMART regimen is the use of budesonide/eformoterol combined (Symbicort) as a single inhaler for both maintenance and reliever therapy.

**KEYPOINTS**

- Using Symbicort for both maintenance and relief of asthma, is gaining acceptance around the world but when it should be introduced is not yet established.

- A combined LABA/ICS inhaler can be considered for maintenance therapy for patients whose asthma is not well controlled on separate LABA and ICS inhalers (Special Authority).

- The combined budesonide/eformoterol inhaler (Symbicort) can be considered for single inhaler maintenance and reliever therapy for adults with poorly controlled asthma characterised by frequent exacerbations while using a conventional regimen.

- The combined fluticasone/salmeterol inhaler (Seretide) should not be used for single inhaler maintenance and reliever therapy, because the LABA salmeterol has a slower onset of action than eformoterol. Salmeterol is not indicated for the immediate relief of acute asthma attacks.

- High dose symbicort inhalers containing budesonide/eformoterol 400/12 are not suitable for single inhaler maintenance and reliever therapy.

- People using SMART should not exceed six inhalations in one hour or twelve inhalations in any 24-hour period.

- SMART is not appropriate for young children, patients who tend to overuse reliever inhalers or patients with “problem asthma” (vocal cord dysfunction, respiratory symptoms due to obesity, anxiety-hyperventilation).

**LABA THERAPY IN ASTHMA**

LABA therapy improves symptom control and lung function and reduces the need for rescue medication in people with asthma which is poorly controlled on ICS. LABA therapy should be considered for people for whom regular use of standard dose ICS has failed to control asthma adequately.

Initial LABA therapy should not be commenced in patients with rapidly deteriorating asthma. It is not appropriate to commence LABA therapy for people not already on ICS.

Side effects of LABA therapy include fine tremor, palpitations, arrhythmias, tachycardia and paradoxical bronchospasm. Other side effects include anxiety, headache, muscle cramps, urticaria, angioedema, hypotension, hypokalaemia in high doses, and sleep and behavioural disturbance in children.
**COMBINATION LABA / ICS INHALERS**

Combination LABA / ICS inhalers are available under a special authority for subsidy when an adult with asthma remains poorly controlled on a dose of at least 800 micrograms per day of beclomethasone or budesonide, or 500 micrograms per day of fluticasone and a LABA, and the prescriber considers the patient would receive additional clinical benefit from switching to a combination product. The specified doses for children are lower than this.

**SINGLE INHALER MAINTENANCE AND RELIEVER THERAPY (SMART)**

**SMART regimen being promoted in New Zealand**

Single inhaler maintenance and reliever therapy (SMART) is being promoted for the management of asthma. The single inhaler (Symbicort) contains both budesonide and eformoterol. The highest dose Symbicort inhaler (400/12) is not included in SMART due to the risk of supra-therapeutic doses.

**Combination inhalers containing salmeterol are not suitable for single inhaler therapy**

Combination inhalers of salmeterol with an ICS, such as Seretide, are not suitable for single inhaler maintenance and reliever therapy. Salmeterol should not be used for the relief of acute asthma symptoms because it has a significantly slower onset of action than either eformoterol, salbutamol or terbutaline.

**Single inhaler therapy available but when to use is not yet resolved**

Using Symbicort for both maintenance and relief of asthma, is gaining acceptance around the world but when it should be introduced is not yet established.

BNF 54 lists single inhaler for maintenance and reliever therapy with Symbicort 100/6 or 200/6 for adults over the age of 18 years but this regimen is not mentioned in its asthma management tables.¹

**Results of trials encouraging**

Clinical trials up until March 2007 demonstrate that by comparison with Seretide plus short acting beta agonist, single inhaler therapy with Symbicort:

- reduces the total number of observed asthma exacerbations
- increases the time elapsed before hospitalisation
- decreases the total amount of oral steroid used
- decreases the inhaled corticosteroid burden ² ³ ⁴

**Fewer Exacerbations**

In the COMPASS trial the SMART regimen resulted in a significant reduction in severe exacerbations of asthma in adults and adolescents (aged 12 years and older) in comparison with either equivalent maintenance dose fluticasone/salmeterol with a short acting beta agonist as required, or a maintenance dose budesonide/eformoterol at twice the SMART dose with a short acting beta agonist as required.⁵

Significant reductions in the number of severe exacerbations, and in the time elapsed before the first severe exacerbation, were also seen using the SMART regimen in the STAY and COSMOS trials.² ³

**Comparable adverse events**

Adverse event profiles were comparable in all of the treatment groups of the trials considered.² ⁴ ⁵

**Decreased corticosteroid burden**

The average total dose of ICS/LABA used in the SMART regimen approximated to 0.75 of the dose administered in the other treatment groups. This corresponds to a lower amount of ICS administered, a lower drug load and a lower glucocorticosteroid burden.

**How should general practitioners respond?**

The dust has not yet settled on the results of these trials. They appear to be signaling a paradigm shift in asthma management. The role of ICS during worsening asthma is
under review. With the new combined single inhaler method, people are receiving additional ICS earlier in the onset of an exacerbation, in combination with a fast acting beta agonist. It is yet to be determined what each of the components contributes to the improved response.

GPs will no doubt respond with their usual pragmatic approach whilst specialist experts scrutinise the evidence and work out how this regimen fits into asthma management guidelines. In the meantime it may be appropriate to use the SMART regimen for adults, who are not under optimal control with a conventional regimen, especially if they are experiencing frequent exacerbations.

Cautions with the use of the symbicort single inhaler maintenance and reliever regimen

If this regimen is used the following cautions need to be observed.

- Search for aggravating factors for asthma such as inhaled allergens, smoking, anxiety etc.
- Doses should not exceed six inhalations at one time or twelve inhalations in any 24-hour period.
- Safety and efficacy has not been established for children under 12 years of age.
- Symbicort 400/12 is not suitable for the SMART regimen.
- Inhaled ICS can cause dose dependent side effects similar to those from non-inhaled ICS.
- Side effects of beta-agonists may include the advent of tolerance, paradoxical bronchoconstriction, or even increased airway inflammation if used to excess.
- The SMART regimen is not suitable for patients who are not sensitive to variations in airway flow, for patients who tend to overuse reliever inhalers or for those patients with “problem asthma” (vocal cord dysfunction, respiratory symptoms due to obesity, anxiety-hyperventilation).

References: