The recommended treatment option for patients with poorly controlled asthma despite low to moderate doses of inhaled corticosteroid (ICS) and after assessment of adherence, inhaler technique and trigger factors, is the addition of an inhaled long-acting beta-agonist (LABA) bronchodilator in a single combination inhaler.\(^1\)

The British Thoracic Society (BTS)/Scottish Intercollegiate Guidelines Network (SIGN) guideline on the management of asthma does not consider that the efficacy or safety of currently available ICS/LABA combination products – fluticasone/salmeterol (Seretide), budesonide/formoterol (Symbicort) and beclometasone/formoterol (Fostair) – differs when administered regularly in equivalent ICS doses.

The main factors influencing the decision to prescribe a particular combination product are patient preference, inhaler device (and technique), dose frequency and cost. Ideally a new combination product should impact favourably on one or more of these factors.

Flutiform is a pressurised metered-dose inhaler containing fluticasone propionate and formoterol fumarate that is licensed for use as a combination treatment at Step 3 and above of the guideline.

Each inhaler contains 120 puffs (actuations) and has a front-facing dose counter indicating the number of actuations remaining. The AeroChamber Plus spacer device can be used in patients who find it difficult to use inhalers. Assessment by patients of treatment response is similar to other combination devices.

**Clinical trials**

In patients with mild to severe asthma fluticasone/formoterol is more effective than fluticasone alone and is at least as effective as the combination of its components administered as separate inhalers (see Figure 1).\(^2\)\(^3\)

The comparison with fluticasone/salmeterol was a nonblinded trial in 202 adults (mean age 46–48) with mild to severe asthma (mean presalbutamol FEV\(_1\) 67 per
cent predicted, range 41–85 per cent), conducted in 25 centres in five European countries. Participants were randomised to treatment with fluticasone/formoterol 100/10µg or 250/10µg twice daily or fluticasone/salmeterol 100/50µg or 250/50µg twice daily, the dose depending on the baseline steroid requirement of each patient. The primary end-point was the predose FEV₁ after 12 weeks’ treatment; noninferiority was defined as the lower limit of the 95% CI ≥0.2 litre in the per protocol population (n=191).

Fluticasone/formoterol was noninferior to fluticasone/salmeterol. They were also similar for secondary end-points including use of relief medication, symptom scores, sleep disturbance, patient assessment and quality-of-life score. Consistent with the more rapid effect of formoterol compared with salmeterol, fluticasone/formoterol had a faster onset of action than fluticasone/salmeterol throughout the study.

The comparison between fluticasone/formoterol 250/10µg twice daily and budesonide/formoterol 400/12µg twice daily was a double-blind trial in 279 patients aged at least 12 with mild to moderate asthma (presalbutamol FEV₁ 65 per cent predicted, range 50–80 per cent), using the same primary and secondary end-points and non-inferiority threshold as in the previous trial. After 12 weeks’ treatment, fluticasone/formoterol was noninferior to budesonide/formoterol for the primary and secondary end-points.

The efficacy and safety of fluticasone/formoterol has not been compared with beclometasone/formoterol.

The adverse effects of fluticasone/formoterol are similar to that reported with the individual drugs. There are no published data on the use of fluticasone/formoterol in children under 12 years.

Where does it fit in the current treatment scheme?
Fluticasone/formoterol is a combination product for patients not adequately controlled with inhaled ICS and ‘as-required’ inhaled short-acting beta₂-agonist (SABA) or for patients already adequately controlled on both an inhaled ICS and LABA.

The 50/5µg and 125/5µg inhalers are indicated in adults and adolescents aged 12 years and above, and the 250/10µg inhaler in adults only. Fluticasone/formoterol is not licensed for use in children aged below 12 years. As discussed, published data suggest that the efficacy and safety of fluticasone/formoterol is similar to the currently licensed combination products fluticasone/salmeterol and budesonide/formoterol. Fluticasone/formoterol is not licensed for use as a rescue medication so should not be used in place of budesonide/formoterol in the SMART (Symbicort Maintenance
A decision whether to prescribe the fluticasone/formoterol combination inhaler rather than an alternative combination is likely to be based on patient preference for the inhaler device and ability to use the device correctly, as well as the comparative cost with other ICS/LABA combinations.

References


Declaration of interests

Steve Chaplin, none to declare; Professor Thomson has participated in advisory boards and/or received consultancy fees from Chiesi and Respivert; received lecture fees from AstraZenica, Chiesi, GlaxoSmithKline and Novartis; industry-sponsored grant funding from AstraZenica, GlaxoSmithKline, MedImmune and Novartis, and Synairgen for participating in clinical trials.

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