In adults with asthma, additional treatment with a long-acting beta-agonist (LABA) is recommended when an as-required short-acting bronchodilator and regular use of an inhaled corticosteroid (ICS) do not provide adequate control (Step 3). A combined ICS/long-acting bronchodilator inhaler ensures that the LABA is taken with a steroid and may additionally improve adherence compared with treatment with two inhalers. Maintenance therapy with a combined ICS/LABA inhaler is recommended for patients with stable COPD who remain breathless or have exacerbations despite using short-acting bronchodilators as required and FEV1 (forced expiratory volume in one second) <50 per cent predicted, and for those with FEV1 ≥50 per cent who remain breathless or have exacerbations despite maintenance therapy with a LABA.

Relvar Ellipta

Relvar Ellipta is a new inhaled steroid/long-acting beta-agonist combination taken once daily. In our New products review, Steve Chaplin presents the data relating to its efficacy and adverse events, and Professor Neil Thomson discusses its place in therapy.

Relvar Ellipta is a dry powder inhaler combining the long-acting beta-agonist (LABA) vilanterol trifenatate and the steroid fluticasone furoate. It is licensed for maintenance therapy of asthma at Step 3 in adults and adolescents aged ≥12 years (92/22 and 184/22µg) and in adults with COPD with exacerbations (92/22µg only).

The recommended dose is one inhalation once daily; a month’s treatment costs £27.80 for 92/22µg and £38.87 for 184/22µg.

In clinical trials, Relvar Ellipta improved lung function compared with its component drugs and was as effective and well tolerated as twice-daily inhaled fluticasone propionate/salmeterol (Seretide).

Adverse effects are typical of a combined steroid/LABA inhaler.

Relvar Ellipta is an effective option in patients requiring a combination inhaler in asthma and COPD with the potential to improve adherence to treatment.

Relvar Ellipta is a preloaded dry powder inhaler combining the ICS fluticasone furoate and the LABA vilanterol trifenatate. This is the first formulation for chronic respiratory disease to contain the furoate ester of fluticasone (though it is available as a nasal spray); others contain the propionate. Fluticasone furoate 92µg once daily is equivalent to fluticasone propionate 250µg twice daily in patients with asthma.

Relvar Ellipta is available in two strengths with differing doses of fluticasone (184 and 92µg) and a single dose of vilanterol (22µg) per actuation. Both are licensed as regular treatment of asthma in adults and adolescents aged ≥12 years when the combination is appropriate (patients not adequately controlled with ICS and ‘as needed’ inhaled short-acting beta-agonists). The 92/22µg strength is additionally licensed for the symptomatic treatment of adults with COPD and FEV1 <70 per cent predicted who have an exacerbation history despite regular bronchodilator therapy.

For both indications and both strengths, the recommended dose is one actuation once daily. Patients with asthma should begin treatment with the lower strength if they need a low to mid dose of ICS; those who need a higher dose should use the 184/22µg inhaler. An improvement in lung function occurs after approximately 15 minutes.
No dose adjustment is recommended for people aged >65 or patients with renal impairment. The maximum dose in patients with moderate to severe hepatic impairment is 92/22µg per day.

Clinical trials
Several trials lasting 12–24 weeks have demonstrated that Relvar improves lung function (as measured by FEV₁ and peak expiratory flow rate) more than an ICS alone in the treatment of asthma in patients previously treated with an ICs or an ICs/LABA combined. In these trials, the risk of a severe exacerbation in one year was reduced from 15.9 to 12.8 per cent in patients using Relvar.⁵

One trial (n=806) compared Relvar 92/22µg once daily with inhaled fluticasone/salmeterol (Seretide) 250/50µg twice daily.⁶ About two-thirds of patients had previously been using an ICS/LABA combination. The change in mean 24-hour FEV₁ after 24 weeks (the primary end-point) was not significantly different (341ml with Relvar vs 377ml). Both treatments improved quality of life scores and there were no differences in onset or duration of action; about half of patients in each group achieved a ≥12 per cent and ≥200ml increase from baseline in FEV₁ at 12 and 24 hours at week 24.

In trials comparing Relvar 92/22µg daily with vilanterol 22µg daily in patients with COPD (post-bronchodilator FEV₁ ≤70 per cent, mean 45–48 per cent), the combined inhaler increased trough FEV₁ significantly more than vilanterol alone after 6 or 12 months; there was no significant difference in dyspnoea scores.³⁴ Relvar also significantly reduced the annual rate of moderate to severe exacerbations by 20–34 per cent compared with vilanterol alone.⁴

Three 12-week trials, each of about 500 patients, compared Relvar with fluticasone propionate/salmeterol in patients with COPD. Two found no difference in change in lung function between Relvar 92/22 and fluticasone propionate/salmeterol 250/50 or 500/50; one demonstrated that Relvar increased FEV₁ significantly more than fluticasone propionate/salmeterol 250/50.

There were no consistent differences in secondary end-points such as use of rescue medication.

Adverse effects
The adverse events reported in clinical trials were typical of an ICS/LABA, the most frequent being nasopharyngitis and headache.⁴

References

Declaration of interests
None to declare.

Steve Chaplin is a pharmacist who specialises in writing on therapeutics.
tion over a 24-hour period and reduces the risk of severe exacerbations (asthma) and moderate and severe exacerbations (COPD). The efficacy in improving lung function is similar to twice-daily inhaled fluticasone propionate/salmeterol (250/50µg, asthma; 500/50µg, COPD). There are no published data in either asthma or COPD comparing the efficacy of Relvar with other combination products.

Tolerability/side-effect profile
Relvar is well tolerated and the side-effect profile is similar to that reported with other combination ICS/LABA inhalers. In keeping with previous evidence of a potential risk of pneumonia in people with COPD treated with ICS, Relvar is associated with an increased incidence of pneumonia in COPD and at the higher doses (184/22µg) compared to the lower doses (92/22µg) in asthma.

Potential place in management
Relvar (92/22 and 184/22µg) is an effective option for the regular treatment of adults and adolescents aged 12 years and older with asthma not adequately controlled with ICS and ‘as-needed’ inhaled short-acting beta-agonists (Step 3, British guideline for the management of asthma).

Based on NICE recommendations for the treatment of COPD, Relvar (92/22µg only) is an effective treatment option for patients with stable COPD with a post-bronchodilator FEV1 <70 per cent predicted who are breathless and have exacerbations despite maintenance therapy with a long-acting muscarinic antagonist or despite using short-acting bronchodilators as required if FEV1 <50 per cent predicted or despite maintenance therapy with a LABA if FEV1 ≥50 per cent.

The decision to prescribe Relvar rather than an alternative combination product is likely to be based on the patient’s preference for the inhaler device, their ability to use the dry powder device correctly and the convenience of once-daily dosing frequency as well as comparative costs with other combination products.

Once-daily treatment with Relvar has the potential to improve adherence in asthma or COPD, although to date there are no published data to support improved adherence or effectiveness compared to other ICS/LABA combinations.

References
2. NICE. Chronic obstructive pulmonary disease, CG101 June 2010.

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