New drugs

Umeclidinium bromide

Incruse Ellipta (GlaxoSmithKline)
62.5 microgram as dry powder for inhalation

Umeclidinium bromide with vilanterol

Anoro Ellipta (GlaxoSmithKline)
62.5 microgram/25 microgram as dry powder for inhalation

Approved indication: chronic obstructive pulmonary disease
Australian Medicines Handbook section 19.1

For more than a decade tiotropium bromide was the only long-acting anticholinergic bronchodilator available in Australia. In 2014 glycopyrronium bromide (Aust Prescr 2014;37:64-71), aclidinium bromide (Aust Prescr 2014;37:172-79) and umeclidinium bromide emerged.

Like the other members of its class, umeclidinium bromide is an antagonist at acetylcholine receptors. In the lungs this causes bronchodilation which begins within 15 minutes of an inhalation and lasts for over 24 hours. The bioavailability of an inhaled dose is about 13% with most of the absorbed dose being metabolised and then excreted in the faeces. Although this metabolism includes cytochrome P450 2D6 and umeclidinium is a substrate of P-glycoprotein, there are unlikely to be clinically significant pharmacokinetic drug interactions. No dose adjustments are needed in patients with renal or moderate liver impairment.

The recommended dose of 62.5 microgram once daily refers to the amount of umeclidinium, rather than umeclidinium bromide, in each blister on a foil strip. When the contents are inhaled through a specific device, a dose of 55 microgram umeclidinium is delivered.

A short-term trial compared umeclidinium with placebo in patients with chronic obstructive pulmonary disease (COPD) and a smoking history of at least 10 pack-years. At the start of the study the mean value of the forced expiratory volume in one second, before the next dose (trough FEV_1), was 1.21 L in the placebo group and 1.26 L in the umeclidinium 62.5 microgram group. After 12 weeks this had not risen in the 68 patients given placebo, but trough FEV_1 increased by 120 mL in the 69 patients who inhaled umeclidinium 62.5 microgram.

In a larger study, 418 patients inhaled umeclidinium 62.5 microgram and 280 inhaled placebo for 24 weeks. The mean trough FEV_1 was 1.2 L in both groups at the start of the study. It rose by 115 mL after 24 weeks of umeclidinium, but was unchanged in the placebo group. This study also included 421 patients who inhaled vilanterol 25 microgram (a long-acting $beta_2$ agonist) and 413 who inhaled a combination of umeclidinium 62.5 microgram and vilanterol 25 microgram. The combination increased trough FEV_1 by a further 52 mL compared with umeclidinium alone, and by 95 mL compared to vilanterol alone. All the active treatments reduced dyspnoea, and exacerbations were less frequent than with placebo (7-9% vs 13% of patients).[1]

Common adverse events with umeclidinium were headache, cough and nasopharyngitis, but their frequency was similar in the placebo groups. The longer-term safety of a higher dose (125 microgram) was assessed in 227 patients. They were compared with 109 patients randomised to take a placebo. After 52 weeks adverse events which were more frequent than with placebo included supraventricular tachycardia, sinus tachycardia and supraventricular extrasystoles. These arrhythmias are probably the result of antimuscarinic effects. Caution is therefore needed when prescribing umeclidinium for patients with arrhythmias and those at risk of narrow-angle glaucoma or urinary retention. There are no data about umeclidinium in pregnancy and lactation.

Umeclidinium is suitable as a maintenance treatment for chronic obstructive pulmonary disease and can be combined with a long-acting $beta_2$ agonist for more severe cases. However, there is little information about how this drug compares with similar treatments. One trial in the drug's development included patients who were randomised to take tiotropium 18 microgram once daily, but they were not compared with patients who took umeclidinium alone. Taking a combination of umeclidinium and vilanterol (62.5/25 microgram) for 24 weeks resulted in an average trough FEV_1 value that was 60 mL higher than with tiotropium alone.

Like other bronchodilators, not all patients will have a clinically significant response to umeclidinium. In the 24-week efficacy study only 53% of the patients inhaling umeclidinium had a clinically important difference in dyspnoea, while the response rate to placebo was 41%.[1]

T manufacturer provided the product information for both products

Some of the views expressed in the following notes on newly approved products should be regarded as preliminary, as there may be limited published data at the time of publication, and little experience in Australia of their safety or efficacy. However, the Editorial Executive Committee believes that comments made in good faith at an early stage may still be of value. Before new drugs are prescribed, the Committee believes it is important that more detailed information is obtained from the manufacturer's approved product information, a drug information centre or some other appropriate source.

NEW DRUGS

REFERENCE †

1. Donohue JF, Maleki-Yazdi MR, Kilbride S, Mehta R, Kalberg C, Church A. Efficacy and safety of once-daily umeclidinium/vilanterol 62.5/25 mcg in COPD. Respir Med 2013;107:1538-46.

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The Transparency score (T) is explained in 'New drugs: T-score for transparency', Aust Prescr 2014;37:27.

† At the time the comment was prepared, a scientific discussion about this drug was available on the website of the European Medicines Agency (www.ema.europa.eu)