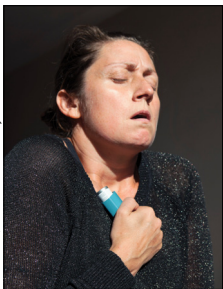


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Strict adherence rules to obtain monoclonal therapy might cost lives



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Asthma drugs targeting so-called T2 pathophysiology are now in use.¹ The first drug, called mepolizumab, an anti-interleukin-5 monoclonal antibody, has been approved by the National Institute for Health and Care Excellence (NICE).² Other anti-interleukin-5 antibodies are being assessed, and monoclonal antibodies targeting interleukin 4, interleukin 13, and interleukin 33 are likely to follow. These drugs widen the treatment options available for patients with severe asthma who remain uncontrolled despite standard high-dose inhaled or oral corticosteroids, or omalizumab (anti-IgE) therapy.

This progress comes at a price. The drugs are expensive and need to be administered parenterally in hospital. Given this high cost, approval by NICE is confined to patients shown to be adherent to standard treatment. In England and Wales, mepolizumab and omalizumab therapy is restricted to patients who attend commissioned regional severe asthma centres, have been assessed by a multi-disciplinary team, and are adherent to more than 80% of doses of inhaled or oral corticosteroids. Adherence is estimated using pharmacy reviews and, if available, fractional exhaled nitric oxide (FeNO) suppression testing.

These stipulations are rational; most patients achieve control with inhaled treatment alone and non-adherence has been linked to a higher risk of asthma exacerbations.^{3,4} Reviews of asthma deaths, including the 2014 UK National Review of Asthma Deaths,⁵ have consistently identified non-adherence to inhaled corticosteroids as an important and modifiable risk factor. The simplest way to

improve asthma outcomes in most patients is to enhance adherence to inhaled corticosteroids,⁶ not use expensive injectable treatments.

Non-adherence covers a range of behaviours including not taking medication, not attending hospital appointments, and self-discharge from hospital before being medically fit. Causes range from concerns about dependence on and the safety of long-term corticosteroids, stigmatisation, cost,⁷ external factors including alcohol or drug abuse, psychosis, and depression. These issues are not easy to modify even within a well organised severe asthma service; and despite psychoeducational nurse-led intervention, the majority of patients who are non-adherent remain persistently non-compliant.⁸ It is this combination of an inability to engage with services despite health-care professionals' best efforts and poor compliance that might leave some patients at substantial risk.

The recent tragic death of a teenager from fatal asthma highlights this issue. The patient was identified as high risk following a previous near fatal asthma attack and had eosinophilic inflammation with treatment non-adherence. Her poor corticosteroid adherence, assessed via prescription collection records and a FeNO suppression test, made her ineligible for treatment with monoclonal therapy under NICE recommendations.

Although possible that even with monoclonal therapy the outcome would have been the same, if a parenteral therapy had been prescribed, the treating clinicians would have been sure that this drug had

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been administered, a technique suggested in a recent editorial.⁹ Subsequently, this therapy might have bought time for another psychosocial intervention to work. A similar approach has been used before with a short course of triamcinolone, an intramuscular steroid.¹⁰

For very high-risk patients, the insistence on adherence before monoclonal therapy is administered should be challenged. In cases of eosinophilic asthma with a previous documented episode of a near-fatal attack (ICU admission or respiratory arrest), temporary monoclonal antibody therapy should be considered even in the face of poor adherence. In this small group of patients, the stakes are high and the ability to deliver appropriate therapy might be curtailed by current guidelines. A treat first, address adherence later approach, might provide more time for other interventions to work. Ultimately, it might save lives.

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A pragmatic approach to simplify inhaler therapy for COPD



Current guidelines for chronic obstructive pulmonary disease (COPD) recommend a stepwise approach to inhaled pharmacotherapy.¹ The assessment of COPD is based on severity of airflow limitation (spirometric grades 1–4), as well as symptom burden and risk of exacerbations (groups A–D). Symptoms and exacerbations are the main factors that drive treatment decisions. The greatest health-care burden is associated with frequent exacerbations of COPD—ie, in patients in groups C and D.

The guidelines are complicated; they suggest escalating treatment from monotherapy with long-acting β agonists (LABA) or long-acting muscarinic receptor antagonists (LAMA), to combination inhaler therapy with LABA and LAMA (LABA/LAMA) or to inhaled corticosteroid (ICS) with LABA (ICS/LABA), followed, finally, by triple therapy (ICS/LABA/LAMA). Currently, triple therapy requires the use of two separate inhalers—ICS/LABA and LAMA—often via different devices, which can be associated with poor long-term compliance. However, single inhalers that administer triple therapy, which are in development,

could soon become available. These inhalers include a once-daily option with fluticasone furoate, vilanterol, and umeclidinium, or twice-daily options with beclomethasone, formoterol, and glycopyrronium or budesonide, formoterol, and glycopyrronium. There are already many different inhaler devices for mono and dual therapy, so prescribers are becoming increasingly confused in selecting a treatment option, especially in primary care.

We therefore propose a less complex and more pragmatic approach to prescribing that is stratified by number of exacerbations and blood eosinophil count, whereby there are only two options for patients with COPD. These options would be single inhalers comprising either LABA/LAMA or ICS/LABA/LAMA (figure). The rationale for this simplified approach is as follows. The use of two long-acting bronchodilators is more effective than the use of one in terms of lung function, symptoms, and number of exacerbations.² Hence, it appears cogent to use a single LABA/LAMA combination inhaler as the first-line treatment for patients with increased severity of symptoms or more



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