

# Adapting inhaled medication practice in COPD and asthma to avoid funding the tobacco industry.

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## INTRODUCTION

The 2018 Cape Town Declaration identifies the activities of the tobacco industry as incompatible with the human right to health<sup>1</sup>. The Global Burden of Disease Study estimates the annual global death toll from smoking to be 8.71 million<sup>2</sup>. Through the cultivation, production, processing and disposal of its products, the industry creates a substantial burden on the environment, which falls mainly in low and middle-income countries<sup>3</sup>. Tobacco multinationals stand condemned as a major obstacle to the achievement of the UN's sustainable development goals<sup>4</sup>.

Based on its market share of at least 12% of cigarettes sold worldwide, (<https://tobaccotactics.org/wiki/philip-morris-international/>), Philip Morris International (PMI) kills more than a million people per year. PMI's bid to take over Vectura, an inhaler company whose products are used extensively by people with COPD and asthma, conditions caused and aggravated by its products, is therefore a cause for concern. A range of consequences follow from such a takeover. Vectura, its employees, and *anyone continuing to work for or collaborate with* Vectura, become excluded from membership of respiratory professional societies as well as collaboration with academic institutions, on grants and from publication in medical journals<sup>5,6</sup>. The details of these policies vary, but as an example, the European Respiratory Society excludes anyone with tobacco industry links in the last 10 years. Many Vectura scientists will choose to leave rather than face long-term pariah status. Policies that exclude the tobacco industry from interaction with government (Article 5.3 of the WHO's Framework Convention on Tobacco Control) would also apply to Vectura.

Vectura currently receives income from the sale of a range of inhalers currently in widespread use. If a takeover by PMI goes ahead, The European Respiratory Society states that "health professionals will avoid prescribing drugs from any company that enriches the tobacco industry due to the ethical implications"<sup>5</sup>. Patients with lung disease are also likely to be reluctant to use tobacco industry linked devices.

We discuss the ethical issues raised around choice of medication in this context, and present potential alternative medications for clinicians, commissioners and patients considering switching.

## VECTURA INHALERS

The Vectura website states that their "*combination of formulation science, device technology and inhaled development expertise has contributed to the success of 13 inhaled medicines, launched by our partners and licensees. Since launch, they have generated \$11 billion in sales and in 2020 these products were used by 10 million patients worldwide.*"<sup>7</sup> The products are set out in Table 1 and Figure 1, based on the Vectura Group plc Annual Report and Accounts 2020.<sup>8</sup> The Vectura accounts report revenue income in 2020 for Flutiform, royalty and other marketed revenues for the GSK Ellipta, Novartis Breezhaler, Hikma generic

Advair programme, and Sandoz Forspiro.

Data from the NHS Business Services Authority (<https://www.nhsbsa.nhs.uk/statistical-collections/prescription-cost-analysis-england/prescription-cost-analysis-england-202021>) show that in 2020, English primary care spend on inhalers totalled £960.5 million. The Vectura products listed equate to £177 million - almost a fifth of total inhaler expenditure.

Fortunately, over 120 inhaled products are now licensed for the treatment of asthma and COPD in the UK, so there are likely to be several suitable alternatives for patients that healthcare professionals can prescribe, to avoid directing income to the tobacco industry if the takeover goes ahead. Some examples are set out in Table 2.

Inevitably, a change in prescribing policy will require switching some individuals to alternative preparations and different inhaler devices. It may also require a change in the inhaled drug(s) to different ones in the same class. It is important therefore, that proposed changes are performed in collaboration with each patient as a partner, using the principles of shared decision making<sup>9</sup>. Changes in inhaled therapy will require careful discussion with patients about the reasons for such a change, potential available options and their agreement to switch.

In order to ensure that asthma and COPD control is optimised, it is essential that inhaler technique is taught and checked, before an alternative is prescribed. An assessment of each patient’s inspiratory capacity to use either a dry powder inhaler or an aerosol device (pMDI, breath-actuated pMDI or soft mist inhaler) should be made to determine the most appropriate type of device to prescribe.<sup>10</sup>The use of low carbon inhaler devices may be prioritised in patients able to use dry powder or soft mist inhalers, but if not, then pMDIs should be used.

**Table 1.** Current approved inhaled medicines developed in partnership with Vectura

Product	Manufacturer(s) / Partners
Flutiform pMDI	Kyorin (Japan) MundiPharma
Flutiform K-haler	MundiPharma
Ultibro Breezhaler	Novartis
Seebri Breezhaler	Novartis
Energair Breezhaler	Novartis
AirFluSal Forspiro	Sandoz
AirBuFo Forspiro++	Sandoz
Fluticasone Propionate and Salmeterol*	Hikma (US)
Breelib+	Bayer
Incruse Ellipta	GSK
Anoro Ellipta	GSK
Relvar/Breo Ellipta	GSK
Trelegy Ellipta	GSK

Information adapted from Vectura accounts<sup>8</sup>.

\* Hikma Pharmaceuticals plc announced that they had resumed the launch of a generic version of Advair diskus in the US.<sup>11</sup>

+ Breelib is a nebuliser approved for the administration of iloprost (Ventavis®) and generic Iloprost Zentiva nebuliser solution to adult patients with primary pulmonary hypertension.

++ AirBuFo Forspiro is authorised in a number of Member States of the EEA, including Belgium, Denmark, France, Ireland, Italy, Norway, Portugal, Spain, Sweden.<sup>12</sup>

Brand Name	Generic Drugs	Licence	Manufacturer / Partners	Alternative Options
Flutiform pMDI	Fluticasone Propionate / Formoterol	Asthma	Kyorin MundiPharma	No alternatives in same drug combination. Alternatives in pMDI include beclometasone / formoterol (Fostair®), Luforbec®) Fluticasone Propionate / salmeterol (AirFluSal®), Aloflute®, Combisal®, Sereflo®, Seretide®, Sirdupla®) - NB. Not all brands available in low, medium and high dose ICS. Budesonide / formoterol (Symbicort®). NB. Only available in two strengths (low and medium dose), and with HFA 227 propellant with a very high carbon impact.
Flutiform K-haler	Fluticasone Propionate / Formoterol	Asthma	MundiPharma	Flutiform K-haler discontinued in UK April 2021. No ICS/LABA available in breath-actuated pMDI devices. For alternatives in pMDI, see Flutiform pMDI, above.

<b>Brand Name</b>	<b>Generic Drugs</b>	<b>Licence</b>	<b>Manufacturer / Partners</b>	<b>Alternative Options</b>
Ultibro Breezhaler	Indacaterol / glycopyrronium	COPD	Novartis	DPI alternative: Duaklir Genuair (formoterol / aclidinium) Aerosol alternatives: Bevespi Aerosphere pMDI (formoterol / glycopyrronium) Spiolto Respimat (olodaterol / tiotropium)
Seebri Breezhaler	Glycopyrronium	COPD	Novartis	DPI alternative: Eklira Genuair (aclidinium) Tiotropium (Spiriva®) HandiHaler, Braltus® Zonda, Tiogiva® MRX003-R inhaler, Acopair® NeumoHaler) Aerosol alternative: Spiriva Respimat (tiotropium)

<b>Brand Name</b>	<b>Generic Drugs</b>	<b>Licence</b>	<b>Manufacturer / Partners</b>	<b>Alternative Options</b>
Energair Breezhaler	Mometasone / Indacaterol / glycopyrronium	Asthma	Novartis	There are no alternative ICS/LABA/LAMA DPI inhalers licensed for use in asthma. DPI alternatives would require use of a suitable ICS/LABA DPI in combination with Spirva Respimat (the only licensed LAMA for asthma. Aerosol alternative: Trimbow MDI (budesonide / formoterol / glycopyrronium). NB. Trimbow is licensed in asthma as a medium dose ICS, whilst Energair is a high dose ICS, so a switch would represent an ICS dose reduction.

<b>Brand Name</b>	<b>Generic Drugs</b>	<b>Licence</b>	<b>Manufacturer / Partners</b>	<b>Alternative Options</b>
AirFluSal Forspiro	Fluticasone Propionate / Salmeterol	Asthma, COPD	Sandoz	Alternative DPIs include: Fluticasone Propionate / Salmeterol DPIs: Seretide® Accuhaler, Fixkoh® Airmaster, Fusacomb® Easyhaler, Stalpex® G7 inhaler Alternative DPIs for other ICS/LABA drugs include: Budesonide / formoterol: DuoResp® Spiromax, Fobumix® Easyhaler, Symbicort® Turbohaler Beclometasone / formoterol: (Fostair® NEXThaler)

Brand Name	Generic Drugs	Licence	Manufacturer / Partners	Alternative Options
AirBuFo Forspiro	Budesonide / formoterol	Asthma, COPD	Sandoz	Not licensed in the UK. Alternative DPIs include: Budesonide / formoterol: DuoResp® Spiromax, Fobumix® Easyhaler, Symbicort® Turbohaler Alternative DPIs for other ICS/LABA drugs include: Beclometasone / formoterol: (Fostair® NEXThaler) Fluticasone Propionate / Salmeterol DPIs: Seretide® Accuhaler, Fixkoh® Airmaster, Fusacomb® Easyhaler, Stalpex® G7 inhaler
Fluticasone Propionate and Salmeterol*	Fluticasone Propionate / Salmeterol	Asthma, COPD	Hikma	Not licensed in the UK. Alternative DPIs include: Fluticasone Propionate / Salmeterol DPIs: Seretide® Accuhaler, Fixkoh® Airmaster, Fusacomb® Easyhaler, Stalpex® G7 inhaler
Breelib+	Nebuliser for administration of Ventavis (iloprost), or generic Iloprost Zentiva	Pulmonary Hypertension	Bayer	No other licensed iloprost nebuliser solution preparations available

<b>Brand Name</b>	<b>Generic Drugs</b>	<b>Licence</b>	<b>Manufacturer / Partners</b>	<b>Alternative Options</b>
Incruse Ellipta	Umeclidinium	COPD	GSK	DPI alternative: Eklira Genuair (aclidinium) Tiotropium (Spiriva®) HandiHaler, Braltus® Zonda, Tiogiva® MRX003-R inhaler, Acopair® NeumoHaler) Aerosol alternative: Spiriva Respimat (tiotropium)
Anoro Ellipta	Vilanterol / Umeclidinium	COPD	GSK	DPI alternative: Duaklir Genuair (formoterol / aclidinium) Aerosol alternatives: Bevespi Aerosphere pMDI (formoterol / glycopyrronium) Spiolto Respimat (olodaterol / tiotropium)



Brand Name	Generic Drugs	Licence	Manufacturer / Partners	Alternative Options
Relvar/Breo Ellipta	Fluticasone furoate / vilanterol	Asthma, COPD	GSK	No alternatives in same drug combination. DPI alternatives: Fluticasone Propionate / Salmeterol DPIs: Seretide® Accuhaler, Fixkoh® Airmaster, Fusacomb® Easyhaler, Stalpex® G7 inhaler Budesonide / formoterol: DuoResp® Spiromax, Fobumix® Easyhaler, Symbicort® Turbohaler Beclometasone / formoterol: (Fostair® NEXThaler) DPI alternative: Trimbow NEXThaler (budesonide / formoterol / glycopyrronium). Available from September 2021. Aerosol alternatives: Trimbow MDI (budesonide / formoterol / glycopyrronium).
Trelegy Ellipta	Fluticasone furoate / vilanterol / glycopyrronium	COPD	GSK	

**ETHICAL CONSIDERATIONS** Ethical issues in medicine, such as those arising here around avoiding or switching away from inhaled medications whose use benefits the tobacco industry, can be considered in terms of four principles – beneficence, non-maleficence, autonomy and distributive justice.

### Beneficence

Protecting people with lung disease from the moral distress of having to use inhalers that fund the tobacco industry, an industry which is a key cause of the development and progression of lung disease, is an important

benefit of switching. So too is reinforcing the policy that the tobacco industry needs to be excluded from healthcare, based on its long and extensively documented history of dishonesty and diversion around the harms of smoking. It challenges the attempt by the industry to divert attention from the actions that are actually needed to end smoking, achieving the UK's Smokefree 2030 ambition, such as a polluter-pays levy on tobacco industry profits and raising the legal age of sale to 21<sup>13</sup>.

### **Non-maleficence**

The key concern is that individual patients might come to harm from switching inhalers. However, as outlined in the previous section, the diversity of the inhaler market means that a range of alternatives in the same class(es), that are likely to be equally effective, are available. It is worth noting that commissioning bodies have a history of mandating wholesale inhaler switching for populations, often for reasons of economy. It should be acknowledged that there is a degree of idiosyncrasy in response to inhaled medications, even in the same class, as well as variation in the ability to use a particular inhaler device. The objective is to avoid tobacco industry linked devices wherever possible rather than absolutely prohibit their use, to allow for the occasional instance where not using them would genuinely cause a deterioration in an individual patient's condition.

People with lung disease, particularly where it is directly linked to smoking, are likely to want to avoid products that fund the tobacco industry as a matter of moral choice. There is evidence that patients consider environmental impact of treatments to be of importance.<sup>14</sup> As one person with asthma writes; *"2nd hand smoke has put me in ICU... I am not ok with using a device that is associated with a tobacco company"*<sup>15</sup>

Some individuals on tobacco-industry linked inhalers who are well-controlled may wish to remain on their current regime. The reasons for switching should be explained clearly, but they may not be reassured that other inhalers will be as effective. Some may have tried a range of inhalers previously before settling on their present regime. It is important to respect individual choices where possible.

### **Distributive justice**

Distributive justice requires consideration of fairness and the broader population consequences of a choice, in addition to the impact on the individual patient. Although the support needed for the initiation of any inhaler is broadly similar in terms of education and explanation to ensure appropriate technique, there is likely to be some opportunity cost to switching inhalers. It may be sensible to build this into annual reviews rather than attempting to switch a whole population at once. Avoiding the initiation of these products should of course start immediately if the takeover goes ahead.

It's nearly 70 years since Philip Morris vice president George Weissman announced that if the company had any thought or knowledge that in any way they were selling a product harmful to consumers, they would stop business immediately<sup>16</sup>. Rather than do this, the tobacco industry have denied the science, aggressively marketed cigarettes to young people and consistently opposed tobacco control measures. The attempt by the industry to present itself as promoting healthcare while simultaneously profiting massively from cigarettes is obscene. Moreover, although the burden of tobacco production falls most heavily in poorer countries, profits accrue in the rich<sup>3</sup>.

The tobacco industry makes £900 million profit /year on UK sales alone and has a much higher profit margin (50-70%) than other products such as food and household goods (typically 12-20%)<sup>13</sup>. This represents a substantial market failure, as the industry is only profitable because it is able to avoid paying for the external costs of its products - the global societal costs of tobacco are estimated to be more than \$2 Trillion/year<sup>17</sup>. Rather than engaging in expansion into the healthcare sector, the tobacco industry must instead be forced to pay to put right the harm it has caused. The fact that PMI are in a position to takeover Vectura highlights the need for the government to take forward the proposed polluter pays levy on tobacco industry profits<sup>18</sup>.

### **CONCLUSION**

There are a range of alternative inhalers available that people currently using Vectura products could switch to if it this becomes necessary because of a tobacco industry takeover. A consideration based on beneficence, non-maleficence, autonomy, and distributive justice demonstrates strong ethical reasons to support this switch, which can be achieved without any significant risk to patient outcomes.

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NSH and TC conceived this analysis, TC produced the first draft which was then amended by both authors. Both authors approve the final draft. We thank Olivia Fulton for the permission to cite her tweet.

## CONFLICT OF INTERESTS

NSH reports no conflicts of interest related to this work.

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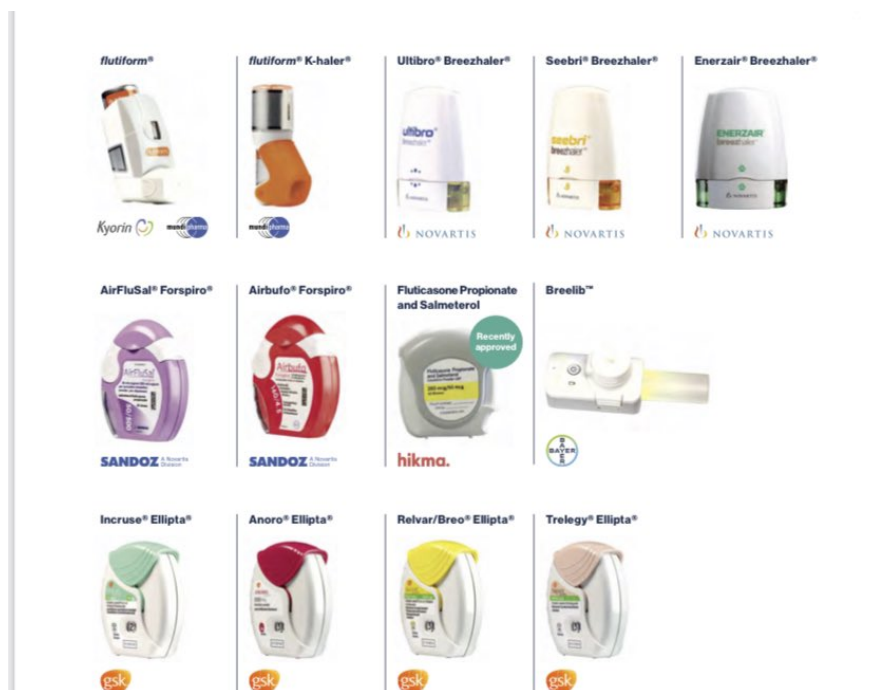
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Figure 1 Inhalers listed in the Vectura accounts as generating revenue, or income from ‘royalty & other marketed revenues’



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