

# Medicines Management Programme

## Inhaled Medicines for Chronic Obstructive Pulmonary Disease (COPD)



Medicines Management  
Programme

Prescribing and Cost Guidance

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## List of Abbreviations

ACOS	Asthma-COPD overlap syndrome
BA	Breath-actuated
BD	Twice daily
CAT	COPD assessment test
COPD	Chronic obstructive pulmonary disease
DPI	Dry powder inhaler
DP	Drugs Payment
FEV <sub>1</sub>	Forced expiratory volume in one second
FVC	Forced vital capacity
GMS	General Medical Services
GOLD	Global Initiative for Chronic Obstructive Lung Disease
HPRA	Health Products Regulatory Authority
HSE	Health Service Executive
ICS	Inhaled corticosteroids
LABA	Long-acting beta <sub>2</sub> -agonist
LAMA	Long-acting muscarinic antagonist
MMP	Medicines Management Programme
mMRC	Modified Medical Research Council
MDI	Metered dose inhaler
NICE	National Institute for Health and Care Excellence
PCRS	Primary Care Reimbursement Service
pMDI	Pressurised metered dose inhaler
SABA	Short-acting beta <sub>2</sub> -agonist
SAMA	Short-acting muscarinic antagonist
SMI	Soft mist inhaler
▼	This medicinal product is subject to additional monitoring.

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## 1. Background

Chronic obstructive pulmonary disease (COPD) is a preventable and treatable condition characterised by chronic, slowly progressive airway obstruction.<sup>1-3</sup> COPD is the preferred term for patients with airways obstruction who were previously diagnosed with chronic bronchitis or emphysema.<sup>4</sup> Other conditions now referred to as COPD are chronic obstructive airways disease and chronic airway flow limitation.<sup>5</sup>

A clinical diagnosis of COPD should be considered for any patient > 35 years with risk factors for COPD and symptoms that include dyspnoea, chronic cough or sputum production.<sup>1,4</sup> The presence of a post-bronchodilator  $FEV_1/FVC < 0.70$  confirms the presence of persistent airflow limitation of COPD.<sup>1,4</sup>

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) classifies patients with COPD into four categories (A-D). GOLD implemented a refinement of its ABCD assessment tool for COPD in 2017. As part of this, spirometric classification of the severity of airflow limitation in COPD was separated from the “ABCD” groups (see Table 1). The ABCD groups and their associated implications for pharmacotherapy recommendations are now exclusively derived from patient symptoms and their history of exacerbations.<sup>1</sup>

There are currently 42 licensed inhalers for the treatment of COPD that are reimbursed by the Health Service Executive (HSE) Primary Care Reimbursement Service (PCRS).<sup>6,7</sup> These drugs and devices represent a considerable cost to the health service. Analysis of 2017 PCRS pharmacy claims data was performed to estimate total expenditure on inhalers used in obstructive airways disease. Patients over the age of 45 years were included in the analysis under the assumption that this age group would largely represent COPD. Between the General Medical Services (GMS) and Drugs Payment (DP) schemes, pharmacy claims for inhalers for COPD amounted to expenditure<sup>i</sup> in excess of €73 million in 2017.<sup>8</sup> Expenditure on inhalers used in

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<sup>i</sup> Expenditure estimates include ingredient cost, pharmacy fee, and tax, where applicable.

obstructive airways disease for all age groups exceeded €91.9 million on the GMS and DP schemes in 2017. Of this, €42.3 million (46%) was spent on inhalers containing a combination of an inhaled corticosteroid (ICS) and a long-acting beta<sub>2</sub>-agonist (LABA).<sup>8</sup>

## 2. Purpose

This document outlines, in general terms, the pharmacological treatment of stable COPD, and provides practice tips and pricing information on licensed, reimbursable inhalers for the treatment of COPD. It is aimed primarily at cost-effective prescribing. It was first published in July 2014, with subsequent updates in January 2015, October 2015, November 2016 and October 2018 to take account of new products, price updates and updated international guidelines.

Prescribers should be cognisant of the costs associated with inhaled therapies for COPD and where possible, should endeavour to prescribe less expensive inhaled therapies for the management of COPD.

## 3. Definitions

For the purposes of this report the associated cost refers to the reimbursed cost of the inhaler preparation as listed on the HSE PCRS website ([www.pcrs.ie](http://www.pcrs.ie)). Only licensed, reimbursable inhalers are included in this review. Where two or more preparations of the same device are listed, the less expensive preparation has been selected for the evaluation. The prices listed do not include mark-up or dispensing fees that private/DP scheme patients may be charged. Costs are correct as of 20 July 2018. For a full list of all reimbursed prices please refer to [www.pcrs.ie](http://www.pcrs.ie) (under list of reimbursable items). Unless otherwise stated, the terms 'actuation' and 'puff' are considered interchangeable.

#### 4. Assessment of COPD using GOLD Classification<sup>1</sup>

In order to determine the appropriate pharmacological treatment for a patient with stable COPD, they must initially be assessed to establish their GOLD patient group.

##### **Step 1: Assess symptoms:** (See Appendix 4)

**COPD Assessment Test (CAT)** is a patient-completed questionnaire that is a comprehensive measure of symptoms and complements existing approaches to assessing COPD. *Determine whether the patient has less symptoms (<10) or more symptoms (>10) using the CAT scale.*

Or

**mMRC (modified-Medical Research Council Questionnaire)** provides an assessment of the impact of dyspnoea. *Determine if the patient has less breathlessness (0-1) or more breathlessness (≥2).*



##### **Step 2: Assess risk of exacerbations:**

- Assess the number of moderate or severe **exacerbations\*** the patient has had within the previous 12 months.
- Determine whether the patient has had one or more **hospitalisation(s)** in the previous year for a COPD exacerbation.



##### **Step 3: Determine GOLD patient group classification** (according to table 1)

- Pharmacological treatment is based on GOLD classification.
- Patients can start in any classification and can migrate between groups, therefore regular assessment is essential.

\*A COPD exacerbation is defined as an acute worsening of respiratory symptoms that result in additional therapy. A moderate exacerbation is one that is treated with a short-acting bronchodilator plus antibiotics and/or oral corticosteroids. A severe exacerbation is one that requires hospitalisation or a visit to a hospital emergency department.

**Table 1: GOLD Classification according to risk of future exacerbations & symptom burden<sup>1</sup>**

Patient group	Exacerbations in the previous 12 months	mMRC <sup>†</sup>	CAT <sup>†</sup>	Exacerbation Risk & Symptoms
A	0-1*	0-1	< 10	Low risk, less symptoms
B	0-1*	≥ 2	≥ 10	Low risk, more symptoms
C	≥ 2 exacerbations* or ≥ 1 exacerbation leading to hospital admission	0-1	< 10	High risk, less symptoms
D	≥ 2 exacerbations* or ≥ 1 exacerbation leading to hospital admission	≥ 2	≥ 10	High risk, more symptoms

<sup>†</sup>Either the mMRC or the CAT should be measured to assess the symptom burden

\* Not leading to hospital admission

## 5. Treatment of COPD

### 5.1 Smoking cessation

Smoking cessation following a diagnosis of COPD is the intervention with the greatest capacity to influence the natural history of the disease.<sup>1,4,9,10</sup> All patients should be actively encouraged to quit smoking and appropriate support should be provided. For more information on smoking cessation support services, visit [www.quit.ie](http://www.quit.ie).

### 5.2 Inhaled therapies for COPD

None of the existing pharmacological agents have been shown to modify the long-term decline in lung function associated with COPD, however appropriate treatment can reduce COPD symptoms, reduce the frequency and severity of exacerbations, and improve health status and exercise tolerance.<sup>1</sup>

Inhalation is the preferred route of administration in stable COPD.<sup>1,11-13</sup>

- Airway smooth muscle relaxation leading to bronchodilation is achieved mainly by beta<sub>2</sub>-agonists and muscarinic antagonists.<sup>14</sup>
- Regular treatment with long-acting inhaled bronchodilators is more effective and convenient than treatment with short-acting bronchodilators.<sup>1,11</sup>
- Combination bronchodilator therapy may increase the degree of bronchodilation with fewer associated side-effects.<sup>1,15-17</sup>
- ICS monotherapy is not recommended in the long-term treatment of COPD.<sup>1</sup>

### 5.3 Inhaler devices

The selection of a suitable inhaler device is crucial in the management of COPD. Currently available inhaler devices for the treatment of COPD are pressurised metered dose inhalers (pMDI), breath-actuated metered dose inhalers (BA MDI), breath-actuated dry powder inhalers (DPI) and soft mist inhalers (SMI).<sup>12</sup>

Poor inhaler technique is a common cause of suboptimal COPD management. Inadequate inhalation technique may be mistaken for a lack of response to a drug.<sup>18</sup> Inhaler technique and adherence to therapy should be assessed before concluding that the current therapy requires modification.<sup>1</sup> Successful use of a given drug/device combination requires that patients are continually instructed on its use and inhaler technique should be assessed regularly.<sup>12</sup> National Institute for Health and Care Excellence (NICE) guidance on the management of COPD recommends that inhalers should only be prescribed after patients have received training in the use of the device and have demonstrated satisfactory technique. This guidance also states that patients should have their ability to use an inhaler device regularly assessed by a competent healthcare professional.<sup>4</sup> Videos to guide patients on appropriate inhaler technique are available on the COPD Support Ireland website [www.copd.ie](http://www.copd.ie).

#### 5.3.1 Pressurised Metered Dose Inhalers (pMDI)

Pressurised Metered Dose Inhalers (pMDIs) consist of a pressurised canister inside a plastic case with a mouthpiece attached (Figure 1). pMDIs use a propellant to push the medication out of the inhaler and the dose is taken by simultaneous inhalation by the individual. Examples include: Ventolin® Evohaler (salbutamol) and Atrovent® CFC-free inhaler (ipratropium). A spacer device, e.g. Volumatic® should be used where coordinating pMDI actuation and inhalation is problematic.<sup>13,18</sup>

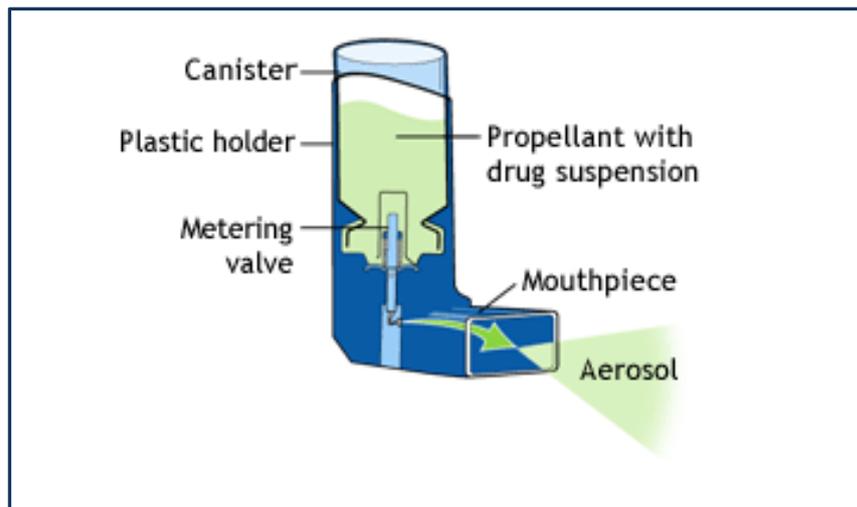


Figure 1: Pressurised Metered Dose Inhaler (pMDI)

### 5.3.2 Breath-Actuated Metered Dose Inhalers (BA MDI)

These inhalers automatically release a spray of medication when the person begins to inhale. They usually look similar to pMDI but do not require coordination of actuating the device and inhaling. An example is: Salamol® Easi-Breathe CFC-free inhaler (salbutamol).

### 5.3.3 Soft Mist Inhalers (SMI)

There are currently three soft mist inhalers (SMI) licensed for use in COPD, Spiriva® Respimat (containing the long-acting muscarinic antagonist (LAMA) tiotropium), Striverdi® Respimat (containing the LABA olodaterol) and Spiolto® Respimat (containing the LAMA tiotropium and the LABA olodaterol). Two actuations once daily are required for all three respimat inhalers.

### 5.3.4 Dry Powder Inhalers (DPI)

There are over 25 DPIs licensed for the treatment of COPD with 11 different device types. The different DPI devices are listed in table 2. DPIs contain ICS, LAMA, LABA and short-acting beta<sub>2</sub>-agonist (SABA) therapies alone and combination therapies of LABA/LAMA, ICS/LABA and ICS/LABA/LAMA. DPIs require a deep and fast inhalation in order to deliver the drug to the lungs; a sufficient inspiratory flow is required by the patient in order to achieve this.<sup>16</sup>

**Table 2: Dry Powder Inhaler (DPI) devices currently on the market for COPD**

Device	Image	Individual product examples	Category	Notes
<b>Aerolizer</b>		Foradil® (formoterol)	LABA	Load the inhaler device each time with capsule prior to inhalation
<b>AirFluSal</b>		Forspiro® (fluticasone propionate/salmeterol)	ICS/LABA	Pre-loaded in foil blister pack Visual screen to view if powder fully inhaled
<b>Breezhaler</b>		Onbrez® (indacaterol) Seebri® (glycopyrronium) Ultibro® (indacaterol/glycopyrronium)	LABA LAMA LABA/LAMA	Load the inhaler device each time with capsule prior to inhalation
<b>Diskus</b>		Serevent® (salmeterol) Flixotide® (fluticasone propionate) Seretide® (fluticasone propionate/salmeterol) Ventolin® (salbutamol)	LABA ICS ICS/LABA SABA	Pre-loaded inhaler device
<b>Easyhaler</b>		Bufomix® (budesonide/formoterol)	ICS/LABA	Pre-loaded inhaler device To be used within four months of opening the laminate bag
<b>Ellipta</b>		Incruse® (umeclidinium ) Anoro® (vilanterol/umeclidinium) Relvar® (fluticasone furoate/vilanterol) Trelegy® (fluticasone furoate/umeclidinium/vilanterol)	LAMA LABA/LAMA ICS/LABA ICS/LAMA/LABA	Pre-loaded inhaler device Device has a six week expiry from date of opening the bag
<b>Genuair</b>		Eklira® (aclidinium ) Brimica® (aclidinium/formoterol)	LAMA LABA/LABA	Pre-loaded inhaler device To be used within 60 (Brimica) or 90 (Eklira) days of opening the pouch
<b>Handihaler</b>		Spiriva® (tiotropium)	LAMA	Load the inhaler device each time with capsule prior to inhalation Visual area to view capsule After first opening of the blister use within the next nine days Discard the inhaler device 12 months after first use

Device	Image	Individual product examples	Category	Notes
<b>Spiromax</b>		DuoResp® (budesonide/formoterol) Aerivio® (fluticasone propionate/salmeterol)	ICS/LABA ICS/LABA	Use within six months of removing from the foil wrapping Use within three months of removing from the foil wrapping
<b>Turbohaler</b>		Bricanyl® (terbutaline) Oxis® (formoterol) Pulmicort® (budesonide) Symbicort® (budesonide/formoterol)	SABA LABA ICS ICS/LABA	Pre-loaded inhaler device
<b>Zonda</b>		Braltus® (tiotropium)	LAMA	Load the inhaler device each time with a capsule prior to inhalation The inhaler device should only be used with the bottle of capsules provided with it Do not reuse the inhaler device for another bottle of capsules Discard capsules 60 days after first opening the bottle

### Practice tip: Inhaler Devices

A patient's ability to use inhalers correctly is crucial when prescribing an inhaler device:

- DPIs may be preferred in COPD as the particle deposition tends to be more central with the fixed airflow limitation and lower inspiratory flow rate in COPD.<sup>19</sup>
- Some COPD patients may have difficulty using a DPI, which often involves loading the dose or priming the device, and a pMDI, breath-actuated MDI or SMI may be considered. A spacer device, e.g. Volumatic®, may be useful where coordinating pMDI actuation and inhalation is problematic.<sup>13,18</sup>

## 5.4 Inhaled Therapies in the Management of Stable COPD

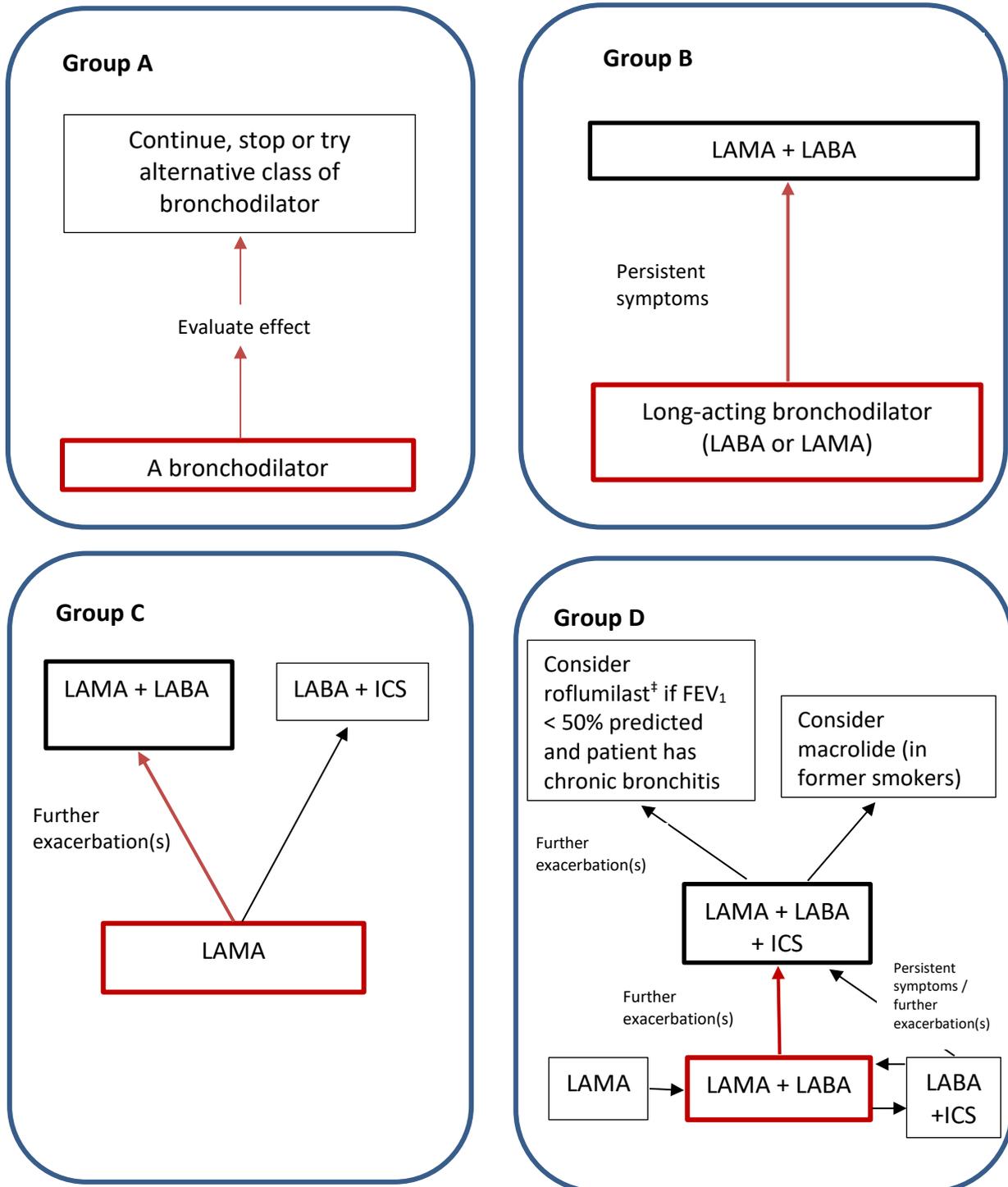
This section outlines the recommended inhaled treatments for COPD according to symptom burden and risk of exacerbations. Many patients with COPD are already on treatment and return with persistent symptoms after initial therapy, or less commonly with resolution of some symptoms that subsequently require less therapy. Therefore, in line with the GOLD guidelines escalation and de-escalation strategies are proposed for each GOLD patient group classification.<sup>1</sup> Figure 2 outlines the pharmacological treatment algorithms for each of the GOLD patient group classifications. The response to any new inhaled therapy that has been added to a patient's regimen should be assessed within **three months** of commencing the new inhaler.

Full pricing information for all currently licensed, reimbursed inhalers for the treatment of COPD is available in section 6 of this Prescribing and Cost Guidance.

### Prescribing Tip: Black Triangle ▼

- Many of the newly available treatments for COPD carry the black triangle symbol.
- These products are subject to additional monitoring and healthcare professionals are asked to report any suspected adverse reactions to the Health Products Regulatory Authority (HPRA).
- Refer to the summary of inhaler costs to see all products subject to this alert (Appendix 3).

The red boxes indicate the preferred option for initiation of treatment within the GOLD patient groups. The red arrows indicate the preferred option for escalation of treatment; the black arrows indicate alternative treatment options.



‡ Roflumilast: This is an oral phosphodiesterase-4 inhibitor. It is not reimbursed by the HSE.

Figure 2: Pharmacological treatment algorithms by GOLD patient group classification<sup>1</sup>

### Group A

- All Group A patients should be offered bronchodilator treatment based on its effect on breathlessness.<sup>1</sup>
- LAMAs and LABAs are preferred over short-acting agents except for patients with dyspnoea only.<sup>1</sup>

### Group B

- Initial therapy in Group B patients should consist of monotherapy with a long-acting bronchodilator (LABA or LAMA).<sup>1</sup>
- For patients with persistent breathlessness on monotherapy, the use of a LABA and a LAMA in combination is recommended.<sup>1</sup>
- For patients with severe breathlessness, initial therapy with a LABA and a LAMA may be considered.<sup>1</sup>

### Group C

- Initial therapy in Group C patients should consist of a LAMA.<sup>1</sup> Treatment with a LAMA has demonstrated a greater effect on exacerbation rates in comparison to LABA treatment.<sup>20,21</sup>
- Patients who experience further exacerbations should have their treatment escalated to a combination of a LABA and a LAMA.<sup>1</sup>

### Group D

- Initial therapy in Group D patients should consist of a combination of a LABA and a LAMA.<sup>1</sup>
- If a single bronchodilator is selected as initial treatment, a LAMA should be chosen due to its greater effect on exacerbation rates in comparison to LABA treatment.<sup>20,21</sup>

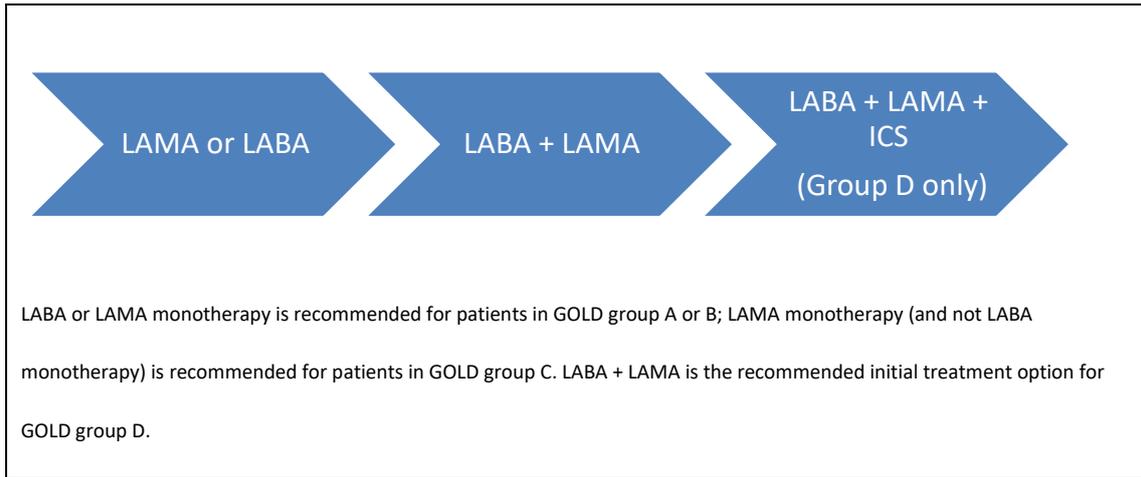
## Group D continued

- A LABA/LAMA combination is superior to an ICS/LABA combination in preventing exacerbations.<sup>22-24</sup>
- Treatment with an ICS, either alone or in combination with a LABA, is associated with an increased risk of non-fatal pneumonia.<sup>1,25</sup>
- Initial therapy with an ICS/LABA combination may be considered:
  - in patients with a history of asthma-COPD overlap syndrome (ACOS)<sup>1,26</sup>
  - in patients with a high blood eosinophil count.<sup>1,27-29</sup>
- If patients develop further exacerbations while on a LABA/LAMA combination there are two options:<sup>1</sup>
  - escalate treatment to ICS/LABA/LAMA (preferred option); or
  - switch to an ICS/LABA combination. If this does not positively impact on exacerbations or symptoms, a LAMA can be added.
- If patients treated with ICS/LABA/LAMA still have exacerbations consider stopping the ICS due to the increased risk of adverse effects (including non-fatal pneumonia) and evidence showing no significant harm from withdrawal.<sup>1,30,31</sup>
- Macrolide: Azithromycin (250 mg daily or 500 mg three times weekly) or erythromycin (500 mg twice daily) for one year in patients prone to exacerbations reduced the risk of exacerbations compared to usual care. Azithromycin use was associated with an increased incidence of bacterial resistance, impaired hearing tests and cardiac arrhythmias. It has been suggested that less benefit is seen in active smokers. There is no data available on the efficacy or safety of chronic azithromycin treatment to prevent COPD exacerbations beyond one-year of treatment.<sup>1</sup> The macrolides reimbursed by the PCRS **are not licensed for this indication** in Ireland.<sup>6,7</sup>

### Prescribing Tips

- Prescribe all inhaled medicines by BRAND to ensure the correct device is dispensed.
- Stop any additional inhaler therapy that does not lead to any benefit after three months despite appropriate inhaler technique.
- The patient's inhaler technique, compliance with administration instructions and adherence to therapy should be assessed before concluding that the current therapy requires modification.
- If patient compliance / technique is good with a particular inhaler device, use the same type of device if possible for any additional inhaler therapy that is required.
- When prescribing a new inhaler do not add it to the patient's repeat prescription until effectiveness has been assessed and established.
- Review patients on ICS. Where appropriate, consider a stepwise reduction in the ICS dose whilst maintaining treatment with a bronchodilator or a combination of bronchodilators i.e. LABA and/or LAMA. Ensure regular review of patients when stepping down. (see Section 7 - Deprescribing)

Figure 3 provides a summary of the recommended escalation strategies for the treatment of stable COPD as outlined in the GOLD guidelines.



**Figure 3: Summary of GOLD Pharmacological Treatment Algorithms Escalation Strategies**

In order to promote compliance and to attempt to limit the number of different inhaler devices that a patient has to use at any one time, the MMP has developed four different treatment pathways for inhaled medicines for stable COPD (Figures 4 – 7). These treatment pathways are based on inhaler devices, and they facilitate the use of the same type of device if modifications to a patient’s treatment are required. The treatment pathways represent the preferred inhalers for initiation and escalation of treatment of stable COPD according to the GOLD guidelines.<sup>1</sup>

**The MMP recommends the ELLIPTA pathway as the preferred option for patients with COPD** due to the cost-effectiveness of this pathway in comparison to the other options. The ability of the patient to successfully administer the dose of the inhaled medicine is the primary objective; the treatment pathway which facilitates this should be chosen.

Where patients are being reviewed for potential medication change due to a change in symptoms or exacerbations, consideration should be given to switching them to the ELLIPTA pathway.

**Table 3: Cost Price of Inhalers within Treatment Pathways<sup>7</sup>**

Treatment Pathway	LABA (€)	LAMA (€)	LABA + LAMA (€)	ICS + LABA + LAMA (€)
Ellipta	20.11	31.34	43.15	59.35
Respimat	28.20	32.14	44.82	72.18
Genuair	20.11	33.22	45.36	64.08
Breezhaler	31.24	33.29	47.31	77.09

ELLIPTA pathway (for LAMA, LABA/LAMA and LABA/LAMA/ICS) plus TURBOHALER

(for LABA)

Inspiratory Flow Rate Required: Ellipta and Turbohaler – Medium/High

**INCRUSE® ELLIPTA (LAMA)**  
(Umeclidinium)

**OR**

**OXIS® TURBOHALER (LABA)**  
(Formoterol)



One actuation daily



Two actuations once or twice daily

**ANORO® ELLIPTA (LABA/LAMA)** (Vilanterol + Umeclidinium)



One actuation daily

**TRELEGY® ELLIPTA (LABA/LAMA/ICS)**  
(Vilanterol + Umeclidinium + Fluticasone)



One actuation daily

Figure 4: Ellipta Pathway

**RESPIMAT pathway (for LABA, LAMA and LABA/LAMA) plus EVOHALER (for ICS)**

**Inspiratory Flow Rate Required: Evohaler and RespiMat – Low**

**SPIRIVA® RESPIMAT (LAMA)**  
(Tiotropium)

**OR**

**STRIVERDI® RESPIMAT (LABA)**  
(Olodaterol)



Two actuations daily



Two actuations daily

**SPIOLTO® RESPIMAT (LABA/LAMA)**  
(Olodaterol + Tiotropium)



Two actuations daily

**SPIOLTO® RESPIMAT (LABA/LAMA)**  
(Olodaterol + Tiotropium)

**PLUS**

**FLIXOTIDE® EVOHALER 250 mcg (ICS)**  
(Fluticasone)



Two actuations daily

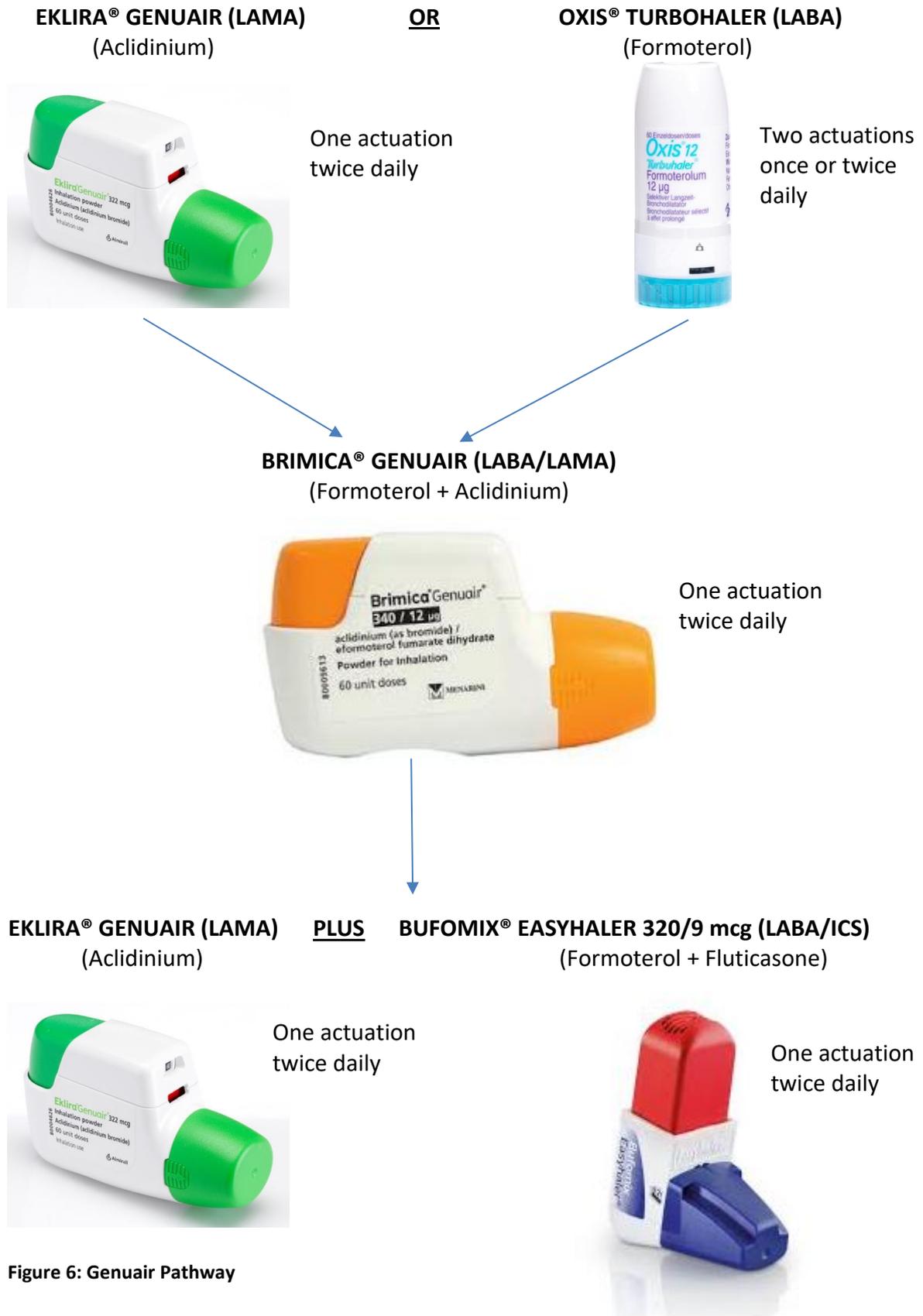


Two actuations twice daily

Figure 5: RespiMat Pathway

**GENUAIR pathway (for LAMA and LABA/LAMA) plus EASYHALER (for ICS/LABA) plus Turbohaler (for LABA)**

**Inspiratory Flow Rate Required: Easyhaler, Genuair and Turbohaler – Medium/High**



**Figure 6: Genuair Pathway**

**BREEZHALER pathway (for LABA, LAMA and LABA/LAMA) plus DISKUS (for ICS/LABA)**

**Inspiratory Flow Rate Required:** Breezhaler and Diskus – Medium/High

**SEEBRI® BREEZHALER (LAMA)**  
(Glycopyrronium)

**OR**

**ONBREZ® BREEZHALER (LABA)**  
(Indacaterol)



One actuation daily



One actuation daily

**ULTIBRO® BREEZHALER (LABA/LAMA)**  
(Indacaterol + Glycopyrronium)



One actuation daily

**ULTIBRO® BREEZHALER (LABA/LAMA)**  
(Indacaterol + Glycopyrronium)

**PLUS FLIXOTIDE® DISKUS 500mcg (ICS)**  
(Fluticasone)



One actuation daily



One actuation twice daily

Figure 7: Breezhaler Pathway

## 6. Licensed & Reimbursable Inhalers

### 6.1 Short-acting beta<sub>2</sub>-agonists (SABA)

Table 4 details the costs associated with salbutamol and terbutaline inhaler preparations for COPD. Typical usage would be eight actuations per day for salbutamol and four actuations per day for terbutaline.<sup>18,32,33</sup> They should be used as required to relieve intermittent or worsening symptoms.<sup>11</sup>

**Table 4: Inhaled short-acting beta<sub>2</sub>-agonists (SABA)**

Drug and device	Device type	Strength mcg	Doses per device	Cost per device €	Cost per actuation €
<b>Salbutamol</b>					
Salamol <sup>®</sup> CFC-free inhaler	pMDI	100	200	2.96	0.01
Salbutamol <sup>®</sup> CFC-free inhaler	pMDI	100	200	3.00	0.02
Ventamol <sup>®</sup> CFC-free inhaler	pMDI	100	200	2.95	0.01
Salbul <sup>®</sup> Inhalation Suspension	pMDI	100	200	3.01	0.02
Ventolin <sup>®</sup> Evohaler	pMDI	100	200	2.72	0.01
Salamol <sup>®</sup> Easi-Breathe CFC-free inhaler	BA MDI	100	200	7.95	0.04
Novolizer <sup>®</sup> Salbutamol	BA MDI	100	200	8.90	0.04
Ventolin <sup>®</sup> Diskus	DPI	200	60	4.48	0.07
<b>Terbutaline</b>					
Bricanyl <sup>®</sup> Turbohaler	DPI	500	100	5.79	0.06

### 6.2 Short-acting muscarinic antagonists (SAMA)

Table 5 details the costs associated with the only available ipratropium inhaler for COPD, Atrovent<sup>®</sup>. Typical usage would be approximately eight actuations per day.<sup>18,34</sup> It should be used as required to relieve intermittent or worsening symptoms.<sup>11</sup>

**Table 5: Inhaled short-acting muscarinic antagonists (SAMA)**

Drug and device	Device type	Strength mcg	Doses per device	Cost per device €	Cost per actuation €
<b>Ipratropium</b>					
Atrovent <sup>®</sup> CFC-free inhaler	pMDI	20	200	2.67	0.01

### 6.3 Long-acting muscarinic antagonists (LAMA)

Table 6 details the costs associated with acclidinium, glycopyrronium, tiotropium and umeclidinium inhaler devices for COPD. Typical usage is one actuation twice daily for Eklira® Genuair (aclidinium), one actuation per day for Seebri® Breezhaler (glycopyrronium), Spiriva® Handihaler (tiotropium), Braltus® (tiotropium) and Incruse® Ellipta (umeclidinium), and two actuations once daily for Spiriva® Respimat (tiotropium).<sup>18,35-40</sup>. Concurrent use of a LAMA and a SAMA is not recommended; patients therefore should be informed to discontinue any inhalers containing a SAMA if they are commenced on a LAMA.<sup>35-41</sup>

**Table 6: Inhaled long-acting muscarinic antagonists (LAMA)**

Drug and device	Device type	Labelled Strength mcg (dose delivered)	Doses per device	Cost per device €	Cost per actuation €
<b>Aclidinium bromide</b>					
Eklira® Genuair ▼	DPI	322	60	33.22	0.55 (1.11 per day)
<b>Glycopyrronium</b>					
Seebri® ▼ Breezhaler	DPI	44	30	33.29	1.11 (per day)
<b>Tiotropium</b>					
Spiriva® Handihaler	DPI	10	30	33.40	1.11 (per day)
Spiriva® Respimat	SMI	2.5	60	32.14	0.54 (1.07 per day)
Braltus®	DPI	10	30	31.24	1.04 (per day)
<b>Umeclidinium</b>					
Incruse® Ellipta ▼	DPI	55	30	31.34	1.04 (per day)

### 6.4 Long-acting beta<sub>2</sub>-agonists (LABA)

Table 7 details the costs associated with the LABAs formoterol, indacaterol, olodaterol and salmeterol for COPD. Cost per actuation is listed and is not indicative of cost per day as products may require one or two actuations per day or up to four actuations per day depending on the drug and device (refer to individual SmPCs for licensed doses and frequencies). Typical usage may be two - four actuations per day for formoterol and salmeterol (depending on the device strength), two actuations from the Respimat inhaler once daily for olodaterol and one actuation per day for indacaterol.<sup>18,42-49</sup>

**Table 7: Inhaled long-acting beta<sub>2</sub>-agonists (LABA)**

Drug and device	Device type	Strength mcg	Doses per device	Cost per device €	Cost per actuation €
<b>Formoterol</b>					
Foradil® Aerolizer	DPI	12	60	22.42	0.37
Oxis® Turbohaler	DPI	12	60	20.11	0.34
Oxis® Turbohaler	DPI	6	60	16.55	0.28
<b>Indacaterol</b>					
Onbrez® Breezhaler	DPI	150	30	31.53	1.05
Onbrez® Breezhaler	DPI	300	30	31.24	1.04
<b>Olodaterol</b>					
Striverdi Respimat® ▼	SMI	2.5	60	28.20	0.47
<b>Salmeterol</b>					
Salmeterol Neolab®	pMDI	25	120	26.37	0.22
Serevent® Evohaler	pMDI	25	120	23.91	0.20
Serevent® Diskus	DPI	50	60	24.03	0.40

### 6.5 Combined long-acting beta<sub>2</sub>-agonist and long-acting muscarinic antagonist (LABA/LAMA)

Table 8 outlines the cost associated with combination LABA/LAMA inhalers. Ultibro® Breezhaler contains a combination of indacaterol and glycopyrronium, and Anoro® Ellipta contains a combination of vilanterol and umeclidinium. Both of these are administered once daily.<sup>18,50,51</sup> Brimica® Genuair contains a combination of acclidinium and formoterol, and one actuation is administered twice daily.<sup>52</sup> Spiolto® Respimat contains a combination of tiotropium and olodaterol, and is administered as two actuations once daily at the same time each day.<sup>53</sup>

#### Prescribing Tip

Dual therapy with a LABA and a LAMA is recommended as the preferred initial treatment choice for patients in GOLD classification group D, and as the preferred step-up treatment choice for group B and C patients.

**Table 8: Combination inhaler devices containing LABA/LAMA**

Drugs and device	Device type	Strength mcg	Doses per device	Cost per device €	Cost per actuation €
<b>Indacaterol/Glycopyrronium</b>					
Ultibro® Breezhaler ▼	DPI	85/43	30	47.31	1.58 (per day)
<b>Vilanterol/Umeclidinium</b>					
Anoro® Ellipta ▼	DPI	55/22	30	43.15	1.44 (per day)
<b>Acclidinium/formoterol</b>					
Brimica® Genuair ▼	DPI	340/12	60	45.36	0.76 (1.51 per day)
<b>Tiotropium/olodaterol</b>					
Spiolto® Respimat	SMI	2.5/2.5	60	44.82	0.75 (1.49 per day)

### Prescribing Tip

If a patient requires both a LAMA and a LABA as inhaled therapy for symptom control, prescribe a combination treatment which may assist

in:

- promoting compliance (due to less inhaled treatments required)
- reducing cost of dual therapy
- reducing confusion in use of different devices.

When prescribing a LABA/LAMA combination for COPD,

think....

**ANORO® Ellipta 55/22 mcg (vilanterol/umeclidinium)**

## 6.6 Inhaled corticosteroids (ICS)

Table 9 outlines the cost associated with ICS. Cost per actuation is listed and is not indicative of cost per day as doses vary between products (refer to individual SmPCs for licensed doses and frequencies). Typical usage can be 2 - 4 actuations per day, depending on the inhaler device and strength.<sup>18,54-56</sup>

**Table 9: Inhaled corticosteroids**

Drug and device	Device type	Strength mcg	Doses per device	Cost per device €	Cost per actuation €
<b>Budesonide</b>					
Pulmicort® Turbohaler	DPI	400	50	12.84	0.26
<b>Fluticasone propionate</b>					
Flixotide® Diskus	DPI	500	60	29.78	0.50
Flixotide® Evohaler	pMDI	250	120	27.36	0.23

### Practice tip

- ICS monotherapy is not indicated in the long-term management of COPD.
- Long-term treatment with ICS may be considered in combination with LABAs for GOLD classification Group C and D patients with a history of exacerbations despite appropriate treatment with long-acting bronchodilators, in line with treatment algorithms. A combination inhaler containing an ICS and LABA is preferred (e.g. Bufomix® 320/9 mcg).
- Regular ICS therapy does not modify the long-term decline in FEV<sub>1</sub> or mortality in patients with COPD.<sup>1</sup>
- Treatment with ICS, alone or in combination with a LABA, is associated with an increased risk of non-fatal pneumonia.<sup>1,25</sup>

### 6.7 Combined inhaled corticosteroids and long-acting beta<sub>2</sub>-agonist (ICS/LABA)

An inhaler containing a combination of ICS and LABA may be considered for GOLD classification Group C and D patients with a history of exacerbations despite appropriate treatment with long-acting bronchodilators, in line with treatment algorithms.<sup>1</sup> Table 10 details the available combination inhalers and their associated costs.<sup>18,57-65</sup> Typical usage is twice daily but Relvar® is once daily dosing.

Notably, Seretide® Evohaler and Relvar® Ellipta 184/22 mcg strength are **not licensed for the treatment of COPD**.<sup>66,67</sup>

Table 10: Combination inhaler devices containing ICS/LABA

	Drugs and device	Device type	Strength mcg	Doses per device	Cost per device €	Cost per actuation €	Cost per day €‡
<b>Budesonide/Formoterol</b>							
EQUIVALENT DOSES	Bufomix® Easyhaler*	DPI	160/4.5	120	31.86	0.27	1.06
	DuoResp® Spiromax	BA MDI	160/4.5	120	37.58	0.31	1.25
	Symbicort® Turbohaler*	DPI	200/6	120	38.62	0.32	1.29
EQUIVALENT DOSES	Bufomix® Easyhaler*	DPI	320/9	60	31.86	0.53	1.06
	DuoResp® Spiromax	BA MDI	320/9	60	36.85	0.61	1.23
	Symbicort® Turbohaler*	DPI	400/12	60	36.67	0.61	1.22
<b>Fluticasone propionate/Salmeterol</b>							
EQUIVALENT DOSES	Aerivio® Spiromax	DPI	500/50	60	33.85	0.56	1.13
	AirFluSal® Forspiro	DPI	500/50	60	41.41	0.69	1.38
	Seretide® Diskus	DPI	500/50	60	38.23	0.64	1.28
<b>Fluticasone furoate/Vilanterol</b>							
	Relvar® Ellipta ▼	DPI	92/22	30	32.59	1.09	1.09

\* Bufomix® Easyhaler and Symbicort® Turbohaler (fixed-dose combination of budesonide and formoterol) have been shown to be bioequivalent with regard to total systemic exposure and exposure via the lungs.<sup>57,60</sup>

‡ Cost per day for standard daily doses i.e. “one inhalation twice daily” for devices with 60 doses, “one inhalation once daily” for devices with 30 doses and “two inhalations twice daily” for devices with 120 doses. Where there are two strengths of the same brand of inhaler, the strength which provides the correct dose in the least number of inhalations should be chosen.



### Practice tip

- The quantity of **LABA** per actuation differs between Seretide® Evohaler and Seretide® Diskus.
- Seretide® Evohaler is not licensed for the treatment of COPD.
- **One puff per dose only of Seretide® Diskus should be prescribed.** More than one puff per dose of Seretide® Diskus is not licensed.
- Prescribing Seretide® 50/500 mcg Diskus two puffs twice daily, rather than the recommended one puff twice daily, leads to excessive dosing, an increased risk of adverse effects, and drug wastage.

## Practice Point

ICS/LABA combination products cost the state over €42 million per year.

New therapies with equivalent efficacy offer the opportunity to save money for both patients and the state without compromising on safety and efficacy.

**Bufomix® Easyhaler 320/9 mcg** is dose equivalent to **Symbicort® Turbohaler 400/12 mcg** but is **13%** less expensive.

**Aerivio® Spiromax 50/500 mcg** is dose equivalent to **Seretide® Diskus 50/500 mcg** but is **11%** less expensive.

## Prescribing Tip

When prescribing an ICS/LABA combination for COPD, think....

***BUFOMIX® Easyhaler 320/9 mcg (budesonide/formoterol)***  
***twice daily***

## 6.8 Combined inhaled triple therapy (ICS/LAMA/LABA)

There is only one inhaler containing a fixed-dose combination of a LAMA, a LABA and an ICS marketed and reimbursed by the PCRS in Ireland – Trelegy® Ellipta. One actuation daily is the licensed dose.<sup>68</sup> The usage of these three agents together in the treatment of COPD is commonly referred to as triple therapy.<sup>69</sup> Table 11 outlines the costs associated with this product.

**Table 11: Combination inhaler device containing ICS/LAMA/LABA**

Drug and device	Device type	Strength mcg	Doses per device	Cost per device €	Cost per actuation €
<b>Fluticasone furoate/Umeclidinium/Vilanterol</b>					
Trelegy® Ellipta	DPI	92/55/22	30	59.35	1.98

## 7. Deprescribing

The GOLD 2018 report includes information on de-escalation of treatment where the introduction of additional inhaled therapy has not improved symptoms. De-escalation is proposed in situations where it is felt that treatment was ineffective, or when patients are over-treated.<sup>1</sup>

The response to any new inhaled therapy that has been added to a patient's regimen should be assessed within **three months** of commencing the new inhaler. This should include an assessment of symptoms and how daily activities of life have changed since the inhaler was started. If the new inhaler does not lead to any benefit after three months of treatment despite appropriate inhaler technique, then it should be stopped.<sup>26,70,71</sup>

### 7.1 Deprescribing Inhaled Corticosteroids

When reviewing COPD inhaler therapy, particularly in the context of this guidance, there may be patients in whom ICS are no longer indicated. Patients may currently be using an ICS in combination with a LABA, or in combination with a LABA and a LAMA. Approximately €42.3 million was spent on combination ICS/LABA inhalers on the GMS and DP schemes in 2017.<sup>8</sup>

The GOLD 2018 report recommends ICS are used in the treatment of stable COPD in the following circumstances only:<sup>1</sup>

- in combination with a LABA as a second-line treatment escalation option in Group C and D patients (with LABA and LAMA recommended as first-line treatment)
- in combination with a LABA and a LAMA (triple therapy) as the preferred treatment escalation option in Group D patients, if the patient develops further exacerbations on initial LABA/LAMA combination therapy.

The long-term use of ICS is associated with increased risk of adverse events, including non-fatal pneumonia, mycobacterial infections, diabetes onset and progression, and fractures.<sup>1,25,72-75</sup>

### Practice Point

Identify patients prescribed an ICS (as dual or triple therapy) for the treatment of stable COPD.

**Where appropriate, consider a stepwise reduction of the ICS dose whilst maintaining treatment with a long-acting bronchodilator, or a combination of long-acting bronchodilators i.e. LABA + LAMA.**

When reviewing patients in GOLD Group C and D on an ICS/LABA combination, it may be appropriate for them to change to a LABA/LAMA combination and to commence deprescribing of their ICS in a stepwise manner. Similarly, if a patient in GOLD Group D continues to develop further exacerbations while on an ICS/LABA combination, it may be more appropriate for them to step treatment across to a LABA/LAMA combination rather than escalating to triple therapy.<sup>1</sup>

**If the patient is on a high-dose ICS it is not advisable to stop this suddenly as there is a risk of adrenal suppression.**<sup>54-46,60-65</sup> Suitable step-down regimens are outlined in figure 4 in order to facilitate withdrawal of ICS.

Evidence from a randomised controlled trial has shown that in patients with severe but stable COPD who were receiving triple therapy, the stepwise withdrawal of ICS was non-inferior to the continuation of such therapy, with respect to the risk of moderate or severe exacerbations.<sup>30</sup> The withdrawal of ICS in patients on long-term triple therapy with no more than one exacerbation in the previous year was found to result in no significant difference in the rates of COPD exacerbations when compared to patients who remained on triple therapy.<sup>31</sup>

Withdrawal of ICS in patients on triple therapy with a blood eosinophil count of 300 cells per  $\mu\text{l}$  or more led to an increase rate of exacerbations in this cohort.<sup>31,76</sup> Deprescribing of ICS in patients on triple therapy is therefore not recommended in these patients.

## 7.2 Components of Stepdown Withdrawal of Inhaled Corticosteroids

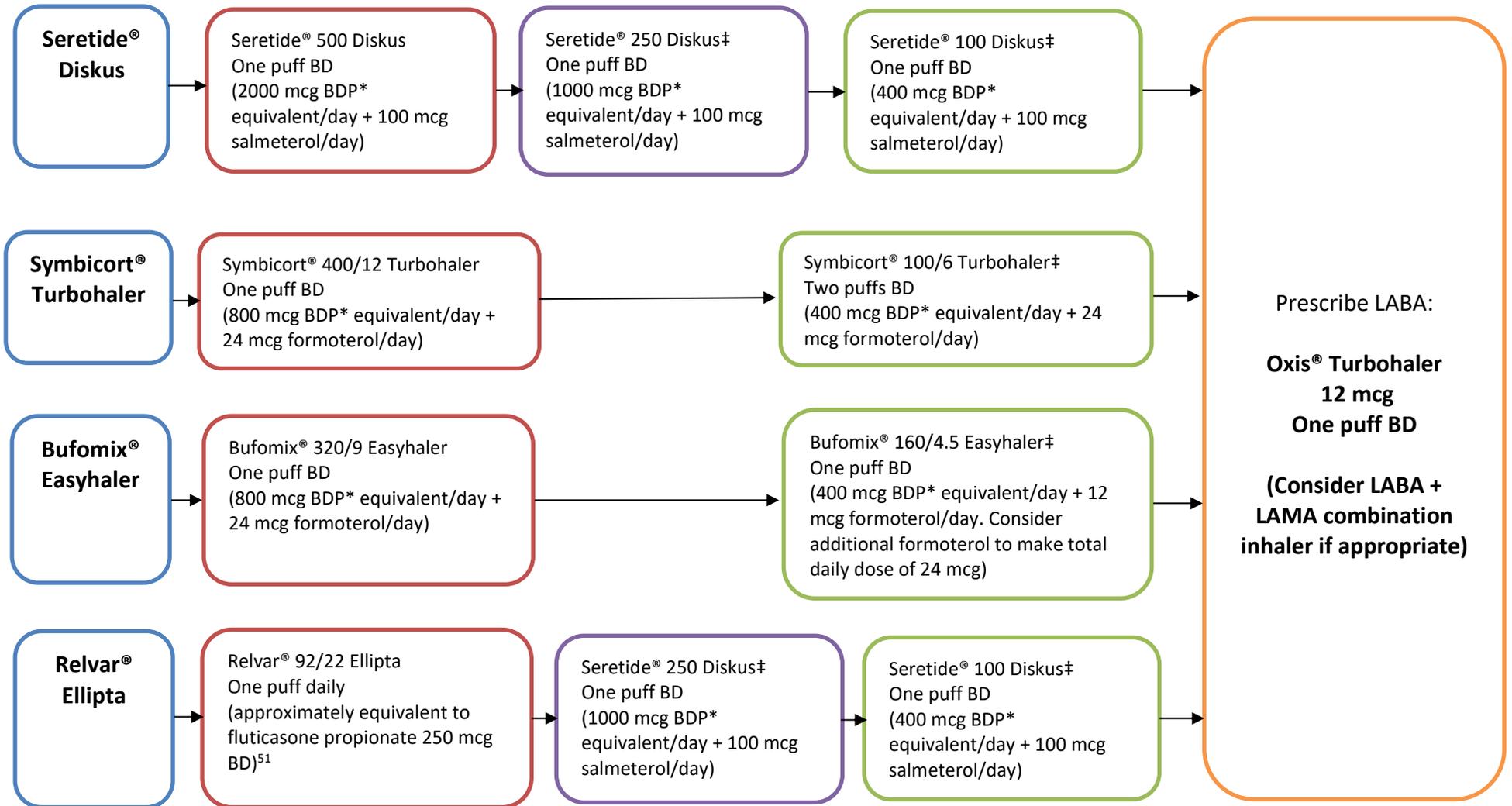
*(adapted from “Reducing the use of inhaled corticosteroids in mild-moderate COPD – Clinical Guidance” – Clinical Effectiveness Group, Centre of Primary Care & Public Health, Queen Mary University of London<sup>77</sup>)*

Figure 8 provides examples of ICS withdrawal regimens. The following points should be considered when withdrawing ICS in patients with COPD:

- Discuss the balance of risks and benefits of ICS with the patient. Provide written information and a management plan for a phased reduction of ICS using a series of inhalers reducing in steroid potency.
- Initially step down to the next lowest potency inhaler.
- Step down should occur no more frequently than every six weeks after a face-to-face review and assessment of symptoms.
- Patients who have been stepped down need to be followed up two weeks after step down, or sooner if symptoms necessitate, and periodically thereafter as clinically needed.
  - Consider face-to-face or telephone reviews during the withdrawal phase.
- Maintain or increase dose of bronchodilators (LAMA/LABA), or commence additional bronchodilator if required.
- Ensure good inhaler technique.
- Encourage uptake of influenza and pneumococcal vaccination, smoking cessation and pulmonary rehabilitation.
- Advise on the identification and early self-management of exacerbations; provide rescue medication (antibiotics and oral corticosteroids) if appropriate.

These regimens should be used as a guide. Step down should be individualised for each patient. It is important to ensure that the dose of the long-acting bronchodilator is maintained and not stepped down at the same time.

Step down treatment every six weeks and follow up after two weeks



\*Total daily dose of ICS in terms of beclomethasone dipropionate (BDP) equivalent (standard particle size)<sup>78</sup>

‡Medicinal product not licensed for use in COPD  
BD: Twice daily

Figure 8: Examples of ICS Withdrawal Regimens

## 8. Nebulised therapy

The preferred route of drug administration in COPD is by inhaler. However, in some instances, e.g. physical disability, the use of a nebuliser may be appropriate.<sup>79</sup> Nonetheless, nebuliser loading and operation requires manipulative skill, and if lack of such skill is responsible for inadequate technique with inhaler devices, it is likely that this may also be the case with a nebuliser.<sup>4</sup> One of the primary advantages of nebulisers in COPD is the minimal coordination and effort required during inhalation compared to pMDIs and DPIs.<sup>79</sup> A further advantage of using nebulisers is their ability to aerosolise high doses of drugs that are not readily attainable using DPIs or pMDIs.<sup>80</sup>

During an exacerbation of COPD, bronchodilator therapy can also be administered via a nebuliser if necessary and oxygen given if appropriate. Short-acting bronchodilators available in solutions for nebulisation are salbutamol (SABA) and ipratropium (SAMA); a solution containing these two drugs in combination is also available.<sup>6</sup> Regular use of high dose bronchodilator therapy via a nebuliser may cause significant side-effects, e.g. tachycardia, tremor.<sup>79</sup>

The role of nebulised or inhaled corticosteroids for the treatment of chronic COPD and during an exacerbation is less clear. Use is associated with an increased risk of non-fatal pneumonia and prescribers should be mindful of this risk and exercise due caution.<sup>1,4,25</sup>

## 9. Summary

The treatment of COPD requires careful evaluation of the individual patient. The choice of inhaled therapy should be made according to a number of criteria, including symptom burden of COPD, risk of exacerbation, cost and patient preference.

Inhalers for COPD represent the largest proportion of inhaler expenditure, accounting for approximately €73 million of an overall expenditure of €91.9 million in 2017 (GMS and DP schemes). Approximately 46% (€42.3 million) of this overall expenditure was on devices containing a combination of ICS and LABA, corresponding to an average of approximately 65,700 prescriptions and over €3.5 million in expenditure per month.

In order to promote compliance and to attempt to limit the number of different inhaler devices that a patient has to use at any one time, the MMP has developed four different treatment pathways for inhaled medicines for stable COPD (Figures 4 – 7). These treatment pathways are based on inhaler devices, and they facilitate the use of the same type of device if modifications to a patient’s treatment is required. **The MMP recommends the ELLIPTA pathway as the preferred option for patients with COPD** due to the cost-effectiveness of this pathway in comparison to the other options.

Where patients are being reviewed for potential medication change due to a change in symptoms or exacerbations, **consideration should be given to switching them to the ELLIPTA pathway.** The ability of the patient to successfully administer the dose of the inhaled medicine is the primary objective; the treatment pathway which facilitates this should be chosen.

In light of current treatment guidelines and emerging evidence the MMP recommends that prescribers should review all patients with COPD using an ICS and consider withdrawal in a stepwise manner where appropriate.

If a patient continues to require an ICS/LABA combination, there are now a number of combination inhalers available that offer a cost saving to both patients and the state and the MMP recommends consideration of these when prescribing in this category.

**Bufomix® 320/9 mcg is dose equivalent to Symbicort® 400/12 mcg but is 13% less expensive. Aerivio® Spiromax 50/500 mcg is dose equivalent to Seretide® Diskus 50/500 mcg but is 11% less expensive.**

There is significant variation between individual inhaled drugs and inhaler devices for the treatment of COPD in terms of cost, with reimbursement costs ranging from €0.11 to €1.98 per day. For private/DPS patients on inhaled therapies for COPD, these costs may be significantly higher. Prescribers should be mindful of variations in cost when prescribing inhaled therapies for the treatment of COPD and should endeavour to

prescribe the most cost-effective treatment that is appropriate for a particular patient, in line with international best practice.

Prescribers should pay close attention to the dosing recommendations of inhalers for COPD, bearing in mind that inappropriate dosing may lead to adverse effects and drug wastage. This is of particular concern with combination ICS/LABA inhaler devices where the ICS-to-LABA ratio may differ between inhaler devices.

This document contains information regarding the acquisition costs of available inhaled drugs and inhaler devices as of 20 July 2018 and provides a useful tool for prescribers for selecting cost-effective inhaler options for their patients with COPD.

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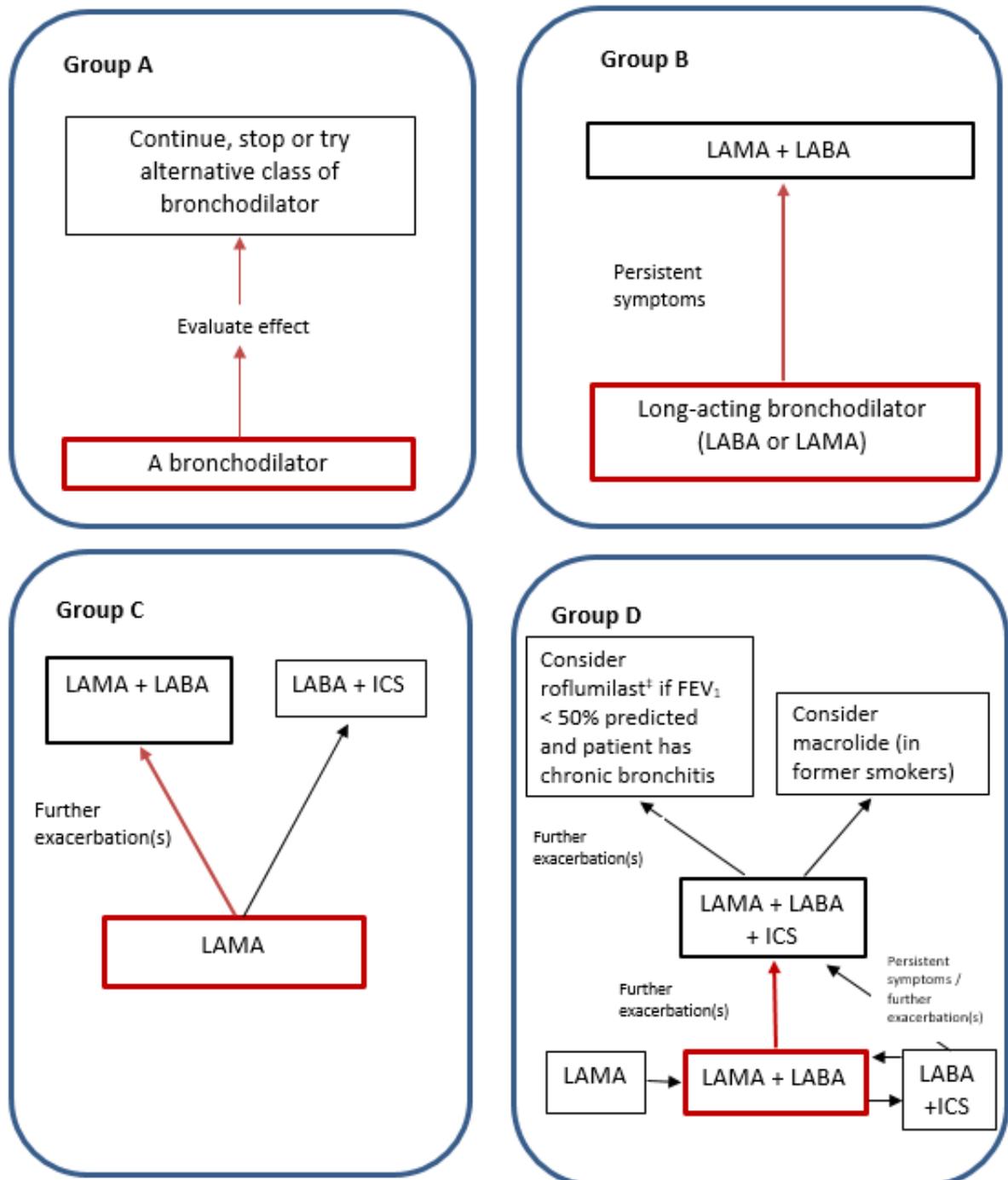
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### Appendix 1. Pharmacological treatment algorithms by GOLD patient group classification<sup>1</sup>

The red boxes indicate the preferred option for initiation of treatment within the GOLD patient groups. The red arrows indicate the preferred option for escalation of treatment; the black arrows indicate alternative treatment options.



<sup>‡</sup> Roflumilast: This is an oral phosphodiesterase-4 inhibitor. It is not reimbursed by the HSE.

## Appendix 2. Practice Points – Management of COPD

### Practice Points – Management of COPD



- Regular treatment with long-acting inhaled bronchodilators is more effective and convenient than treatment with short-acting bronchodilators.
- Combination bronchodilator therapy (long-acting beta<sub>2</sub> agonist + long-acting muscarinic agonist [LABA + LAMA]) may increase the degree of bronchodilation with fewer associated side-effects.
- Inhaled corticosteroid (ICS) monotherapy is not recommended in the long-term treatment of COPD. ICS use is associated with an increased risk of non-fatal pneumonia.
- Where appropriate, consider a stepwise reduction of the ICS dose whilst maintaining treatment with a long-acting bronchodilator, or a combination of long-acting bronchodilators.
- A patient's ability to use an inhaler correctly is crucial when prescribing an inhaler device:
  - ✓ Some COPD patients may have difficulty using a DPI, which often involves loading the dose, and a pMDI, breath-actuated MDI or soft mist inhaler may be considered. A spacer device, e.g. Volumatic®, may be useful when coordinating actuation and inhalation is a problem.
  - ✓ If patient compliance / technique is good with a particular inhaler device, use the same type of device if possible for any additional inhaler therapy that is required.
  - ✓ Stop any additional inhaler therapy that does not lead to any benefit after three months despite appropriate inhaler technique.

### Appendix 3. COPD - Summary of Inhaler Costs

Drug and device	Strength	Doses per device	Cost per device €	Cost per actuation € (cost per day where standard dose is once or twice daily)
<b>Short-acting beta<sub>2</sub>-agonists (SABA)</b>				
<b>Salbutamol</b>				
Salamol <sup>®</sup> CFC-free inhaler (pMDI)	100 mcg	200	2.96	0.01
Salbutamol <sup>®</sup> CFC-free inhaler (pMDI)	100 mcg	200	3.00	0.02
Ventamol <sup>®</sup> CFC-free inhaler (pMDI)	100 mcg	200	2.95	0.01
Salbul <sup>®</sup> Inhalation Suspension (pMDI)	100 mcg	200	3.01	0.02
Ventolin <sup>®</sup> Evohaler (pMDI)	100 mcg	200	2.72	0.01
Salamol <sup>®</sup> Easi-breathe CFC-free inhaler (BA MDI)	100 mcg	200	7.95	0.04
Novolizer <sup>®</sup> Salbutamol (BA MDI)	100 mcg	200	8.90	0.04
Ventolin <sup>®</sup> Diskus (DPI)	200 mcg	60	4.48	0.07
<b>Terbutaline</b>				
Bricanyl <sup>®</sup> Turbohaler (DPI)	500 mcg	100	5.79	0.06
<b>Short-acting muscarinic antagonists (SAMA)</b>				
<b>Ipratropium</b>				
Atrovent <sup>®</sup> CFC-free inhaler (pMDI)	20 mcg	200	2.67	0.01
<b>Long-acting muscarinic antagonists (LAMA)</b>				
<b>Aclidinium bromide</b>				
Eklira <sup>®</sup> Genuair (DPI) ▼	322 mcg	60	33.22	0.55 (1.11)
<b>Glycopyrronium</b>				
Seebri <sup>®</sup> Breezhaler (DPI) ▼	44 mcg	30	33.29	1.11 (1.11)
<b>Tiotropium</b>				
Spiriva <sup>®</sup> Handihaler (DPI)	18 mcg	30	33.40	1.11 (1.11)
Spiriva <sup>®</sup> Respimat (SMI)	2.5 mcg	60	32.14	0.54 (1.07)
<b>Umeclidinium bromide</b>				
Incruse <sup>®</sup> Ellipta (DPI) ▼	55 mcg	30	31.34	1.04 (1.04)
<b>Long-acting beta<sub>2</sub>-agonists (LABA)</b>				
<b>Formoterol</b>				
Foradil <sup>®</sup> Aerolizer (DPI)	12 mcg	60	22.42	0.37
Oxis <sup>®</sup> Turbohaler (DPI)	12 mcg	60	20.11	0.34
Oxis <sup>®</sup> Turbohaler (DPI)	6 mcg	60	16.55	0.28
<b>Indacaterol</b>				
Onbrez <sup>®</sup> Breezhaler (DPI)	150 mcg	30	31.53	1.05 (1.05)
Onbrez <sup>®</sup> Breezhaler (DPI)	300 mcg	30	31.24	1.04 (1.04)

Costs listed reflect the reimbursed price. Private/DP scheme patients may pay significantly more than the reimbursed price.

▼ This medicinal product is subject to additional monitoring by the European Medicines Agency. This will allow quick identification of new safety information.

BA MDI – Breath-actuated metered dose inhaler, pMDI – Pressurised metered dose inhaler, DPI – Dry powder inhaler, SMI – Soft mist inhaler, mcg = microgram

Drug and device	Strength	Doses	Cost per device €	Cost per actuation € (cost per day where standard dose is once or twice daily)	
<b>Long-acting beta<sub>2</sub>-agonists (LABA) (continued)</b>					
<b>Olodaterol</b>					
Striverdi Respimat <sup>®</sup> (SMI) ▼	2.5 mcg	60	28.20	0.47 (0.94)	
<b>Salmeterol</b>					
Salmeterol Neolab <sup>®</sup> (pMDI)	25 mcg	120	26.37	0.22	
Serevent <sup>®</sup> Evohaler (pMDI)	25 mcg	120	23.91	0.20	
Serevent <sup>®</sup> Diskus (DPI)	50 mcg	60	24.03	0.40	
<b>Combined long-acting beta<sub>2</sub>-agonist/long-acting muscarinic antagonist (LABA/LAMA)</b>					
<b>Indacaterol/Glycopyrronium</b>					
Ultibro <sup>®</sup> Breezhaler (DPI) ▼	85/43 mcg	30	47.31	1.58 (1.58)	
<b>Umeclidinium/Vilanterol</b>					
Anoro <sup>®</sup> Ellipta (DPI) ▼	55/22 mcg	30	43.15	1.44 (1.44)	
<b>Acidinium bromide/Formoterol</b>					
Brimica <sup>®</sup> Genuair (DPI) ▼	340/12 mcg	60	45.36	0.76 (1.51)	
<b>Tiotropium/Olodaterol</b>					
Spiolto <sup>®</sup> Respimat (SMI)	2.5/2.5 mcg	60	44.82	0.75 (1.49)	
<b>Inhaled corticosteroids (ICS) [monotherapy not indicated in long-term management of COPD]</b>					
<b>Budesonide</b>					
Pulmicort <sup>®</sup> Turbohaler (DPI)	400 mcg	50	12.84	0.26	
<b>Fluticasone propionate</b>					
Flixotide <sup>®</sup> Diskus (DPI)	500 mcg	60	29.78	0.50	
Flixotide <sup>®</sup> Evohaler (pMDI)	250 mcg	120	27.36	0.23	
<b>Combined inhaled corticosteroid/long-acting beta<sub>2</sub>-agonist (various strengths)</b>					
<b>Budesonide/Formoterol</b>					
Bufomix <sup>®</sup> Easyhaler (BA MDI)*	160/4.5 mcg	120	31.86	0.27 (1.06)	EQUIVALENT DOSES
DuoResp <sup>®</sup> Spiromax (BA MDI)	160/4.5 mcg	120	37.58	0.31 (1.25)	
Symbicort <sup>®</sup> Turbohaler (DPI)*	200/6 mcg	120	38.62	0.32 (1.29)	EQUIVALENT DOSES
Bufomix <sup>®</sup> Easyhaler (BA MDI)*	320/9 mcg	60	31.86	0.53 (1.06)	
DuoResp <sup>®</sup> Spiromax (BA MDI)	320/9 mcg	60	36.85	0.61 (1.22)	
Symbicort <sup>®</sup> Turbohaler (DPI)*	400/12 mcg	60	36.67	0.61 (1.22)	
<b>Fluticasone propionate/Salmeterol</b>					
Aerivio <sup>®</sup> Spiromax (DPI)	500/50 mcg	60	33.85	0.56 (1.13)	EQUIVALENT DOSES
AirFluSal <sup>®</sup> Forspiro (DPI)	500/50 mcg	60	41.41	0.69 (1.38)	
Seretide <sup>®</sup> Diskus (DPI)	500/50 mcg	60	38.23	0.64 (1.28)	
<b>Fluticasone furoate/Vilanterol</b>					
Relvar <sup>®</sup> Ellipta (DPI) ▼	92/22 mcg	30	32.59	1.09 (1.09)	
<b>Combined inhaled long-acting beta<sub>2</sub>-agonist/long-acting muscarinic antagonist/inhaled corticosteroid</b>					
<b>Fluticasone furoate/Umeclidinium/Vilanterol</b>					
Trelegy <sup>®</sup> Ellipta (DPI) ▼	92/55/22mcg	30	59.35	1.98	
* Fixed-dose combinations of budesonide and formoterol have been shown to be bioequivalent with regard to total systemic exposure and exposure via the lungs.					

**Appendix 4. COPD Assessment Test (CAT) and Modified Medical Research Council Questionnaire (mMRC)**

**COPD Assessment Test (CAT):** Determine whether the patient has less symptoms (<10) or more symptoms (>10).

	Score (0 – 5)					
I never cough	1	2	3	4	5	I cough all the time
I have no phlegm (mucus) in my chest at all	1	2	3	4	5	My chest is full of phlegm (mucus)
My chest does not feel tight	1	2	3	4	5	My chest feels very tight
When I walk up a hill or one flight of stairs I am not breathless	1	2	3	4	5	When I walk up a hill or one flight of stairs I am very breathless
I am not limited doing any activities any home	1	2	3	4	5	I am very limited doing activities at home
I am confident leaving my home despite my lung condition	1	2	3	4	5	I am not at all confident leaving my home because of my lung condition
I sleep soundly	1	2	3	4	5	I don't sleep soundly because of my lung condition
I have lots of energy	1	2	3	4	5	I have no energy at all

**Modified Medical Research Council Questionnaire (mMRC):** Determine if the patient has less breathlessness (0 -1) or more breathlessness (≥2).

mMRC Score	Description of breathlessness
0	I only get breathlessness with strenuous exercise
1	I get short of breath when hurrying on level ground or walking up a slight hill
2	On level ground, I walk slower than people of the same age because of breathlessness, or have to stop for breath when walking at my own pace
3	I stop for breath after walking about 100 yards or after a few minutes on level ground
4	I am too breathless to leave the house or I am breathless when dressing or undressing

#### **Appendix 5. New in this update - version 1.4**

- Content updated to reflect GOLD Report 2018
- Treatment pathways included for inhaled medicines for stable COPD
- Ellipta pathway recommended as the preferred option for patients with COPD
- Cost prices have been updated to July 2018 prices
- Section on deprescribing included in guidance