Inhaler Device Techniques

Dr Toby Capstick  (toby.capstick@nhs.net)
Lead Respiratory Pharmacist
Leeds Teaching Hospitals NHS Trust
Chair: UKCPA Respiratory Group
This is a Chiesi Meeting

@tcapper78
Declarations of Interest

- Payment received for educational events and conference sponsorship from:
  - Almirall
  - AstraZeneca
  - Boehringer Ingelheim
  - Chiesi
  - GSK
  - Novartis
  - Pfizer
  - Teva
# Prescription Cost Analysis - England, 2013

<table>
<thead>
<tr>
<th></th>
<th>Drug</th>
<th>Quantity Supplied</th>
<th>Expenditure</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Tiotropium 18mcg</td>
<td>4,194,787</td>
<td>£164,216,890</td>
</tr>
<tr>
<td>2</td>
<td>Seretide™ 250 MDI</td>
<td>2,164,820</td>
<td>£158,597,260</td>
</tr>
<tr>
<td>3</td>
<td>Symbicort® 200/6 Turbohaler</td>
<td>1,940,600</td>
<td>£95,381,230</td>
</tr>
<tr>
<td>4</td>
<td>Seretide™ 500 Accuhaler</td>
<td>1,951,720</td>
<td>£94,015,550</td>
</tr>
<tr>
<td>5</td>
<td>Seretide™ 125 MDI</td>
<td>1,590,810</td>
<td>£70,700,490</td>
</tr>
</tbody>
</table>

The Top 5 drugs in terms of overall expenditure in primary care are all inhaled medicines - accounting for £580 million per year in England.

**BUT, are we getting value for money?**
COPD Treatment: Cost-effectiveness

- **Foundations of management**
- **Inhaled therapy**

**Triple Therapy (LAMA/LABA/ICS)**
- ICS-LABA combination
- LABA £8,000/QALY
- LAMA* £7,000/QALY
- Pulmonary Rehabilitation £2,000-8,000/QALY
- Stop Smoking Support with pharmacotherapy £2,000/QALY
- Flu vaccination £1,000/QALY in "at risk" population

*Costing calculations based on Tiotropium*

Adapted from: IMPRESS Guide to the relative value of COPD interventions.
http://www.impressresp.com/index
<table>
<thead>
<tr>
<th>Drug</th>
<th>Mild %</th>
<th>Moderate %</th>
<th>Severe %</th>
<th>v. Severe %</th>
</tr>
</thead>
<tbody>
<tr>
<td>SABA</td>
<td>84.6</td>
<td>77.3</td>
<td>91.7</td>
<td>85.7</td>
</tr>
<tr>
<td>SAMA</td>
<td>7.7</td>
<td>21.2</td>
<td>8.3</td>
<td>4.8</td>
</tr>
<tr>
<td>LABA</td>
<td>0.0</td>
<td>6.1</td>
<td>8.3</td>
<td>4.8</td>
</tr>
<tr>
<td>LAMA</td>
<td>46.2</td>
<td>33.3</td>
<td>50.0</td>
<td>57.1</td>
</tr>
<tr>
<td>LABA/ICS</td>
<td>30.8</td>
<td>45.5</td>
<td>62.5</td>
<td>66.7</td>
</tr>
<tr>
<td>LABA/ICS (as DPI)</td>
<td>7.7</td>
<td>9.1</td>
<td>25.0</td>
<td>19.1</td>
</tr>
</tbody>
</table>

**Over-prescribing**
- Majority use of unlicensed preparation
- Not Cost-effective

**Under-prescribing**
- Low use of effective bronchodilators
- Lack of use of cost-effective therapy

New respiratory drugs and devices
# Asthma & COPD: Inhalers in 2010

## Bronchodilators

- **SABAs**
  - Salbutamol (7+ devices)
  - Terbutaline (1 device)

- **SAMAs**
  - Ipratropium (2 devices)

- **LABAs**
  - Formoterol (3 devices)
  - Salmeterol (2 devices)

- **LAMAs**
  - Tiotropium (2 devices)

## Corticosteroids

- **ICS**
  - Beclometasone (3 devices)
  - Beclometasone fine particle (1 device)
  - Budesonide (3 devices)
  - Ciclesonide (1 device)
  - Fluticasone propionate (2 devices)

- **ICS/LABA**
  - Fostair (beclometasone/formoterol) (1 device)
  - Seretide (2 devices)
  - Symbicort (1 device)
Asthma & COPD: Increasing Complexity

**Bronchodilators**

- **SABAs**
  - Salbutamol (7+ devices)
  - Terbutaline (1 device)

- **SAMAs**
  - Ipratropium (2 devices)

- **LABAs**
  - Formoterol (3 devices)
  - Salmeterol (2 devices)
  - Indacaterol (1 device)
  - Olodaterol (1 device)
  - Vilanterol (planned 1 device)

- **LAMAs**
  - Aclidinium (1 device)
  - Glycopyrronium (1 device)
  - Tiotropium (2 devices + ‘generics’...)
  - Umeclidinium (1 device)

- **LABA/LAMAs**
  - Anoro ® (umeclidinium/vilanterol) (1 device)
  - Duaklir ® (aclidinium/formoterol) (1 device)
  - Ultibro ® (glycopyrronium/indacaterol) (1 device)

**Corticosteroids**

- **ICS**
  - Beclometasone (3 devices)
  - Beclometasone fine particle (1 device)
  - Budesonide (3 devices)
  - Ciclesonide (1 device)
  - Fluticasone propionate (2 devices)
  - Fluticasone furoate (planned 1 device)

- **ICS/LABA**
  - Bufomix (planned 1 device)
  - DuoResp ® (1 device)
  - Fostair (2 devices)
  - Relvar ® (1 device)
  - Seretide (2 devices + ‘generics’...)
  - Symbicort (planned 2 devices)

...And don’t forget other future generics
Treatment approaches in Adult Asthma

There are now two treatment approaches for the use of Fostair pMDI in adult patients (≥18 years) with asthma:

A. **Maintenance therapy:**
   - Fostair pMDI is taken as regular maintenance treatment with a separate as-needed rapid-acting bronchodilator
   - 1 or 2 inhalations twice daily. The maximum daily dose is 4 inhalations.

B. **Maintenance and reliever therapy (MART):**
   - Fostair pMDI is taken as regular maintenance treatment and as-needed in response to symptoms
   - MART should be considered for patients with:
     - Not fully controlled asthma and in need of reliever medication
     - Asthma exacerbations in the past requiring medical intervention
   - 1 inhalation twice daily (one in the morning and one in the evening) and additional as-needed inhalations; maximum daily dose of 8 inhalations*.

Reference 1 Fostair. pMDI Summary of Product Characteristics. Chiesi Ltd. October 2014

* Fostair pMDI MART® dosing is different to that for Symbicort SMART.
How do I tell my patients to use Fostair pMDI in COPD?

Beclometasone dipropionate 100micrograms and formoterol fumarate 6micrograms per actuation pressurised inhalation solution (pMDI)

Chronic Obstructive Pulmonary Disease (COPD):

• Only to be used by adults (aged 18 years and above)
• The dose is 2 inhalations twice a day
• For symptomatic treatment of patients with severe COPD (FEV$_1$ < 50% predicted normal) and a history of repeated exacerbations, who have significant symptoms despite regular therapy with long-acting bronchodilators

New LAMAs & LABAs

- **LABAs**
  - Formoterol (Aerolizer®, Easyhaler®, Turbohaler®)
  - Salmeterol (Accuhaler™ pMDI)
  - Indacaterol (Breezhaler®)
  - *Olodaterol* (Respimat®)
  - *Vilanterol* (Ellipta®)

- **LAMAs**
  - Aclidinium (Genuair®)
  - Glycopyrronium (Breezhaler)
  - Tiotropium (HandiHaler®)
  - *Umeclidinium* (Ellipta)

- **LABA/LAMAs**
  - *Anoro* (*umeclidinium/vilanterol*) (Ellipta)
  - *Duaklir* (aclidinium/formoterol) (Genuair)
  - *Ultibro* (glycopyrronium/indacaterol) (Breezhaler)
Effect on Trough FEV$_1$ in COPD Patients.

1. Umeclidinium ($\pm$ICS)

- Placebo
- UMEC 62.5 $\mu$g
- UMEC 125 $\mu$g

Day 85: $+127$ mL $(p<0.001)$

2. Olodaterol ($\pm$ICS, LAMA, SAMA, theophylline)

3. Anoro ($\pm$ICS)

- Placebo
- UMEC 62.5
- VI 25
- UMEC/VI 62.5/25

Day 169:
- Anoro $+167$ mL $(p<0.001)$
- Vi $+72$ mL $(p<0.01)$
- Umec $+115$ mL $(p<0.001)$

Week 12: $+91$ mL $(p<0.0001)$ & $+47$ mL $(p<0.05)$

Effect on SGRQ in COPD Patients

1. Umeclidinium

- Day 84: -7.9 (p<0.001)

2. Olodaterol

- Week 24: -2.8 (p<0.005)

3. Anoro (umeclidinium + vilanterol)

- Day 168:
  - Anoro -5.51 (p≤0.001);
  - Vi -5.19 (p≤0.01);
  - Umec -4.69 (p≤0.001)

References:
Effect on TDI in COPD Patients

1. **Umeclidinium**
   - Placebo
   - UMEC 62.5 μg
   - UMEC 125 μg
   - **Day 84**: +1.0 (p=0.05)

2. **Olodaterol**
   - **Day 168**:
     - Anoro +1.2 (p≤0.001);
     - Vi +0.9 (p≤0.001);
     - Umec +1.0 (p≤0.001)

3. **Anoro (umeclidinium + vilanterol)**
   - LS mean (95% CI)
   - Change from baseline
   - **Day 24**: +0.3 (p=0.17)

References:
New ICS/LABAs

- *Bufomix* (planned Easyhaler)
- *DuoResp* (Spiromax)
- *Fostair* (beclometasone/formoterol) *(NEXThaler, pMDI)*
- *Relvar* (Ellipta)
- *Seretide* (Accuhaler, pMDI)
- *Symbicort* (Turbohaler (+planned pMDI?))
Fostair NEXThaler Indication

• Fostair NEXThaler is indicated in the regular treatment of adult asthma where use of a combination product (ICS/LABA) is appropriate:
  • patients not adequately controlled with ICS and 'as needed' inhaled SABA or
  • patients already adequately controlled on both ICS and LABA.

• Fostair NEXThaler is indicated for adult patients (18 and over).
• Fostair NEXThaler is not indicated for the treatment of acute asthma attacks.
• Fostair NEXThaler is not indicated for Maintenance & Reliever Therapy
• Fostair NEXThaler is not indicated for COPD
**COPD: Effect on Lung Function**

1. **Relvar**

   - Day 84: \( \text{wm FEV}_1 \) Relvar vs. Seretide = 22mL (\( p=0.282 \))

2. **Fostair pMDI**

   - Week 48: vs Baseline: Fostair pMDI 77ml, Symbicort 80ml, Formoterol 26ml.
     - Fostair pMDI vs.: Symbicort -2ml (\( p=0.52 \)); vs. formoterol 51ml (\( p=0.046 \))

---

2. Calverley PMA. *Resp Med* 2010;104:1858-68.
COPD: Effect on SGRQ

1. Relvar

Day 84: mean difference Relvar vs. Seretide = -1.3

2. Fostair pMDI

Week 48: Change from baseline all p<0.01).
Mean difference Fostair pMDI vs. comparators (ns)

2. Callverley PMA. *Resp Med* 2010;104:1858-68.
COPD: Effect on Exacerbations

1. Relvar

Relvar vs. Vilanterol = 27% reduction (p<0.0001)

2. Fostair pMDI

Exac. Rate per patient per year at week 48:
Fostair pMDI (0.414) vs. Symbicort 0.423 (p=0.597) vs. Formoterol 0.431 (p=0.607)

2. Calverley PMA. *Resp Med* 2010;104:1858-68.
New ICS/LABAs in Asthma: Lung Function

1. Relvar Ellipta

   Week 24:
   - Relvar vs. FF: 193ml (p<0.001)
   - Relvar vs. FP: 210ml ml (p<0.001)
   - FF vs. FP: 18ml (ns)

2. Fostair NEXThaler

   Change from baseline to entire treatment period average trough PEF:
   - NEXThaler vs. Fostair pMDI: -1.84 (ns)
   - NEXThaler vs. BDP DPI: 9.96 (p<0.001)
   - Fostair pMDI vs. BDP DPI: 11.81 (p<0.001)

Relvar: Asthma Exacerbations

Time to first severe exacerbation
Relvar vs. FF: HR 0.795 (p=0.036)
Relvar: Safety

Week 6 treatment ratios to placebo:
Relvar 92/22: 0.99
Relvar 184/22: 0.97
Prednisolone (7 days): 0.34

**Relvar: COPD pneumonia risk**

<table>
<thead>
<tr>
<th>Adverse Events</th>
<th>25 µg vilanterol (n=818)</th>
<th>50 µg fluticasone furoate+25 µg vilanterol (n=820)</th>
<th>100 µg fluticasone furoate+25 µg vilanterol (n=806)</th>
<th>200 µg fluticasone furoate+25 µg vilanterol (n=811)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>General adverse events</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any adverse event</td>
<td>575 (70.3%)</td>
<td>620 (75.6%)</td>
<td>621 (77.0%)</td>
<td>622 (76.7%)</td>
</tr>
<tr>
<td>Any adverse event leading to discontinuation or withdrawal</td>
<td>45 (5.5%)</td>
<td>53 (6.5%)</td>
<td>62 (7.7%)</td>
<td>61 (7.5%)</td>
</tr>
<tr>
<td>Any serious adverse event</td>
<td>126 (15.4%)</td>
<td>136 (16.6%)</td>
<td>123 (15.3%)</td>
<td>124 (15.3%)</td>
</tr>
<tr>
<td>Any on-treatment or post-treatment fatal adverse event</td>
<td>13 (1.6%)</td>
<td>16 (2.0%)</td>
<td>10 (1.2%)</td>
<td>14 (1.7%)</td>
</tr>
<tr>
<td><strong>Adverse events of specific interest</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Local corticosteroid effects</td>
<td>96 (11.7%)</td>
<td>142 (17.3%)</td>
<td>121 (15.0%)</td>
<td>140 (17.3%)</td>
</tr>
<tr>
<td>Cardiovascular effects</td>
<td>99 (12.1%)</td>
<td>108 (13.2%)</td>
<td>97 (12.0%)</td>
<td>85 (10.5%)</td>
</tr>
<tr>
<td>Lower-respiratory-tract infection (excluding pneumonia)</td>
<td>64 (7.8%)</td>
<td>57 (7.0%)</td>
<td>60 (7.4%)</td>
<td>63 (7.8%)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>27 (3.3%)</td>
<td>48 (5.9%)</td>
<td>51 (6.3%)</td>
<td>55 (6.8%)</td>
</tr>
<tr>
<td>Hypersensitivity</td>
<td>26 (3.2%)</td>
<td>38 (4.6%)</td>
<td>37 (4.6%)</td>
<td>29 (3.6%)</td>
</tr>
<tr>
<td>Bone disorders (including fractures)</td>
<td>9 (1.1%)</td>
<td>24 (2.9%)</td>
<td>27 (3.3%)</td>
<td>21 (2.6%)</td>
</tr>
<tr>
<td>Effects on glucose</td>
<td>14 (1.7%)</td>
<td>18 (2.2%)</td>
<td>15 (1.9%)</td>
<td>22 (2.7%)</td>
</tr>
<tr>
<td>Ocular events</td>
<td>9 (1.1%)</td>
<td>7 (0.9%)</td>
<td>12 (1.5%)</td>
<td>7 (0.9%)</td>
</tr>
<tr>
<td>Effects on potassium</td>
<td>8 (1.0%)</td>
<td>5 (0.6%)</td>
<td>1 (0.1%)</td>
<td>2 (0.2%)</td>
</tr>
<tr>
<td>Tremor</td>
<td>3 (0.4%)</td>
<td>1 (0.1%)</td>
<td>2 (0.2%)</td>
<td>2 (0.2%)</td>
</tr>
</tbody>
</table>

Data are n (%).

New Devices
Inhaler Devices

- Accuhaler
- Autohaler
- Breezhaler / Aeroliser
- Clickhaler
- Diskhaler
- Easi-Breathe
- Easyhaler
- Ellipta
- Genuair / Novoliser
- HandiHaler
- NEXThaler
- pMDI
- Pulvinal
- Respimat
- Spiromax
- Turbohaler
Which Device do Patients Want?

Meeting the needs of patients with COPD: patients’ preference for the Diskus inhaler compared with the Handihaler

Preference for novel soft mist inhaler over pMDI in patients with COPD

Comparison of Patient Preference and Ease of Teaching Inhaler Technique for Pulmicort Turbuhaler® versus Pressurized Metered-Dose Inhalers

MICHAEL J. WELCH, M.D.,1 HAROLD S. NELSON, M.D.,2 GAIL SHAPIRO, M.D.,3 GEORGE W. BENSCH, M.D.,4 WILLIAM N. SOKOL, M.D.,5 JOSEPH A. SMITH, M.D.,6 and BHASH M. PARASURAMAN, Ph.D.6

1Allergy & Asthma Medical Group and Research Center, San Diego, California.
2National Jewish Medical & Research Center, Denver, Colorado.
4Private practice, Stockton, California.
5Health Research Institute, Newport Beach, California.
6AstraZeneca LP, Wilmington, Delaware.
New Devices

• Claimed easier / simpler devices. But...
  • Often industry sponsored studies

“Of the 29 studies, 23 were sponsored by the pharmaceutical industry, and 83% of the sponsored trials favoured the device manufactured by the sponsoring company.”

• Increased patient choice
• Education required
  • Healthcare professionals
  • Patients
3-item Feedback:
1. Click on inhalation (activation of BAM – Breath-actuated mechanism)
2. Dose Counter
3. Taste
   • Dose counter does not count down if dose is not inhaled
   • 6-month expiry out of foil.
NEXThaler

- Low resistance device: $0.036 \text{kPa}^{1/2} \text{l/min}$ corresponding to a flow rate of 55 l/min at 4 kPa.\(^1\)
- Consistent emitted FPF Dose released only when IFR >35L/min\(^1\)

2-item Feedback:
1. Dose Counter
2. Taste

- Dose counter counts as cover open (clicks).
- Lose dose if cover closed before exhalation
- Six-week expiry
Ellipta

• Low resistance device: $0.0286 \text{kPa}^{1/2} \text{l/min.}$

• Asthma patients and COPD (moderate to v. severe) could all achieve PIFR $>43 \text{ L/min.}$

• Consistent dosing with IFRs $43.5 – 130 \text{ L/min.}$

• Correct technique assessed in 2 Anoro Ellipta crossover exercise studies:
  • After initial instruction: 98% (n=632).
  • At 6-weeks 99% (n=587).

Spiromax

- No Phase 3 clinical efficacy or safety studies (not required)
- MA is based on the demonstration of pharmacokinetic equivalence to Symbicort.
- Lack of PK study for low strength (80/4.5) – application withdrawn
- 2-item Feedback:
  1. Dose Counter
  2. Taste
- Dose counter counts as cover open (clicks).
- Retains dose if cover closed before exhalation, but dose counter moves on
- 6-month expiry out of foil.
Spiromax – Practical Aspects

1. CHMP Assessment Report
3. Teva R&D in Focus – Respiratory: Webinar. 8th October 2013

• “Patients achieved faster IF and greater positive change in pressure with Spiromax versus Turbuhaler.”

![Graphs showing spirometers' performance](http://www.google.co.uk/url?sa=t&rct=j&q=&esrc=s&source=web&cd=1&ved=0CCMQFjAA&url=http%3A%2F%2Fwww.phx.corporate-ir.net%2FExternal.File%3Fitem%3DUGFyZW50SUQ9MjA1NDExfENoaWxkSUQ9LTF8VHlwZT0z%26t%3D1&ei=XXcsVPKfG8Su7Ab6_YDgAw&usg=AFQjCNEebI3ug0hMLkxSJ2kbXiII7-Xi2X&sig2=n1WkSacZCsd KwL8h4dc9Q&bvm=bv.76477589,d.ZGU&cad=rja)

GFK Research, August 2013 (market study conducted in EU, sponsored by Teva)

- Preference: Spiromax® vs. Diskus®
  - 65%
- Preference: Spiromax® vs. Turbuhaler®
  - 71%

"Patients achieved faster IF and greater positive change in pressure with Spiromax versus Turbuhaler."

1. Patients achieved faster IF and greater positive change in pressure with Spiromax versus Turbuhaler.
‘Generic’ Prescribing

- Budesonide/formoterol
- Salbutamol Breath-actuated
- Beclometasone/formoterol
Switching Inhaler Devices: Effect of unconsented switch

Treatment Success OR:
0.29 [95% CI: 0.19, 0.44; p<0.001]

Implications for Practice
Cost Data – LABA & LAMA

NHS price

- Duaklir (Aclidinium/Formoterol) Genuair TWICE daily
  - TBC
- Anoro (Umeclidinium/Vilanterol) Ellipta ONCE daily
  - £32.50
- Salmeterol pMDI / Accuhaler 50mcg TWICE daily
  - £29.26
- Olodaterol 2.5mcg Respimat 2p ONCE daily
  - £26.35
- Indacaterol 150mcg/300mcg Breezhaler ONCE daily
  - £29.26
- Formoterol 12mcg Easyhaler 12mcg TWICE daily
  - £11.88
- Formoterol 6mcg/12mcg Turbohaler 12mcg...
  - £49.60
- Umeclidinium 55mcg Ellipta ONCE daily
  - £27.50
- Tiotropium 18mcg HandiHaler ONCE daily
  - £34.87
- Tiotropium 2.5mcg Respimat 2p ONCE daily
  - £33.50
- Glycopyrronium 44mcg Breezhaler ONCE daily
  - £27.50
- Aclidinium 322mcg Genuair TWICE daily
  - £28.60

NHS List Price (Sept 2014)
Cost Data – ICS/LABA (DPIs)
(by BTS/SIGN Asthma management – Steps 3 to 5)

NHS Price

- Fostair 100/6 Nexthaler 1p TWICE daily: £14.66
- DuoResp 200/6 Spiromax 1p TWICE daily: £14.99
- Relvar 92/22 1p ONCE daily: £27.80
- Symbicort 100/6 Turbolizer 2p TWICE daily: £33.00
- Seretide 100 Accuhaler 1p TWICE daily: £18.00
- Fostair 100/6 Nexthaler 2p TWICE daily: £29.32
- DuoResp 200/6 Spiromax 2p TWICE daily: £29.97
- Relvar 92/22 Ellipta 1p TWICE daily: £27.80
- Symbicort 200/6 Turbohaler 2p TWICE daily: £38.00
- Seretide 250 Accuhaler 1p TWICE daily: £35.00
- DuoResp 400/12 Spiromax 2p TWICE daily: £59.94
- Relvar 184/22 Ellipta 1p ONCE daily: £38.87
- Symbicort 400/12 Turbohaler 2p TWICE daily: £40.92
- Seretide 500 Accuhaler 1p TWICE daily: £76.00

Prices range from £14.66 to £76.00.
Cost Data – ICS/LABA (MDIs)
(by BTS/SIGN Asthma management – Steps 3 to 5)

NHS Price

- Fostair 100/6 MDI 1p TWICE daily: £14.66
- Flutiform 50/5 MDI 2p TWICE daily: £18.00
- Seretide 50 MDI 2p TWICE daily: £18.00
- Fostair 100/6 MDI 2p TWICE daily: £29.32
- Flutiform 125/5 MDI 2p TWICE daily: £29.26
- Seretide 125 MDI 2p TWICE daily: £35.00
- Flutiform 250/10 MDI 2p TWICE daily: £45.56
- Seretide 250 MDI 2p TWICE daily: £59.48

NHS List Price (Sept 2014)
GOLD (2014) Recommendations for the Management of COPD

www.goldcopd.org

- **Assessment of COPD:**
  - **Assess symptoms**
    - COPD Assessment Test (CAT)
    - mMRC Dyspnoea Scale
  - Assess degree of airflow limitation using spirometry
  - Assess risk of exacerbations

*Combine these assessments for the purpose of improving management of COPD*
# Manage Stable COPD: The Leeds “Preferred Formulary” Approach

(assuming local approval Feb 2015)

## CATEGORY A
**Low symptoms (mMRC 0 or 1; CAT<10) & low risk (predicted FEV₁ >50%, exacerbations of COPD <2 per year none leading to hospital admission)**

<table>
<thead>
<tr>
<th>First-line: SABA</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st Choice DPI: Salbutamol 100microgram Easyhaier 2 puffs PRN</td>
</tr>
<tr>
<td>1st Choice MDI: Salbutamol 100microgram MDI 2 puffs PRN</td>
</tr>
<tr>
<td>2nd Choice: Salbutamol 100microgram Easi-Breathe 2 puffs PRN</td>
</tr>
</tbody>
</table>

## CATEGORY B
**High symptoms (mMRC 2.3 or 4; CAT≥10) & low risk (predicted FEV₁ >50%, exacerbations of COPD <2 per year none leading to hospital admission)**

<table>
<thead>
<tr>
<th>First-line: LAMA/LABA (as a combination inhaler)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st Choice: Anoro 55/22 Ellipta 1 puff once daily</td>
</tr>
<tr>
<td>2nd Choice: Duakir 340/12 Genuair 1 puff twice daily</td>
</tr>
</tbody>
</table>

## CATEGORY C
**Low symptoms (mMRC 0 or 1; CAT<10) & High risk (predicted FEV₁ <50% and/or exacerbations of COPD ≥2 per year or at least 1 leading to hospital admission)**

- **Group 1:** FEV₁ <50% predicted and exacerbations of COPD <2 per year none leading to hospital admission
- **Group 2:** Any FEV₁ and exacerbations of COPD ≥2 per year or at least 1 leading to hospital admission

<table>
<thead>
<tr>
<th>First-line: LAMA/LABA</th>
<th>First-line: ICS/LABA</th>
<th>First-line: ICS/LABA + LAMA</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st Choice: Anoro 55/22 Ellipta 1 puff once daily</td>
<td>1st Choice: Relvar 92/22 Ellipta 1 puff once daily</td>
<td>1st Choice: Relvar 92/22 Ellipta 1 puff once daily + Umeclidinium 55micrograms Ellipta 1 puff once daily</td>
</tr>
<tr>
<td>2nd Choice: Duakir 340/12 Genuair 1 puff twice daily</td>
<td>2nd Choice: Fostair 100/6 MDI 2 puffs twice daily</td>
<td>2nd Choice: Fostair 100/6 MDI 2 puffs twice daily + Acindium 322micrograms Genuair 1 puff twice daily</td>
</tr>
</tbody>
</table>

## CATEGORY D
**High symptoms (mMRC 2.3 or 4; CAT≥10) & high risk (predicted FEV₁ <50% and/or exacerbations of COPD ≥2 per year or at least 1 leading to hospital admission)**

<table>
<thead>
<tr>
<th>First-line: ICS/LABA</th>
<th>First-line: ICS/LABA + LAMA</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st Choice: Relvar 92/22 Ellipta 1 puff once daily</td>
<td>1st Choice: Relvar 92/22 Ellipta 1 puff once daily + Umeclidinium 55micrograms Ellipta 1 puff once daily</td>
</tr>
<tr>
<td>2nd Choice: Fostair 100/6 MDI 2 puffs twice daily</td>
<td>2nd Choice: Fostair 100/6 MDI 2 puffs twice daily + Acindium 322micrograms Genuair 1 puff twice daily</td>
</tr>
</tbody>
</table>

Adapted from: Global Initiative for Chronic Obstructive Lung Disease 2014
Inhaler Technique
Examples of ‘Poor’ Technique
How Frequently are Patients able to Use Inhaler Devices?

<table>
<thead>
<tr>
<th>Device</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>pMDI</td>
<td>79%</td>
</tr>
<tr>
<td>pMDI + Volumatic</td>
<td>87%</td>
</tr>
<tr>
<td>Easi-Breathe</td>
<td>91%</td>
</tr>
<tr>
<td>Autohaler</td>
<td>91%</td>
</tr>
<tr>
<td>Turbohaler</td>
<td>87%</td>
</tr>
<tr>
<td>Accuhaler</td>
<td>90%</td>
</tr>
</tbody>
</table>

Definition of Errors in Inhaler Technique

• Correct and incorrect inhaler technique for all devices – determines how much drug reaches the lung
• Incorrect technique involves “Crucial” and “non-crucial” errors
• CRUCIAL ERRORS:
  • Likely to result in *no* drug reaching the lungs
• NON-CRUCIAL ERRORS:
  • Likely to result in *less* drug reaching the lungs
# How Frequently do Patients make Errors Using Inhaler Devices?

<table>
<thead>
<tr>
<th></th>
<th>Accuhaler (n = 894), %</th>
<th>pMDI (n = 552), %</th>
<th>Turbohaler (n = 868), %</th>
</tr>
</thead>
<tbody>
<tr>
<td>At least one error</td>
<td>49</td>
<td>76</td>
<td>54</td>
</tr>
<tr>
<td>At least one critical error</td>
<td>11</td>
<td>28</td>
<td>32</td>
</tr>
<tr>
<td>GPs opinion that the patient inhaled the correct dose</td>
<td>75</td>
<td>50</td>
<td>70</td>
</tr>
<tr>
<td>Overestimation of good inhalation by GPs</td>
<td>9</td>
<td>6</td>
<td>24</td>
</tr>
</tbody>
</table>

Misuse of Inhalers is Associated with Decreased Asthma Stability

AIS = Asthma Instability Score
- 0: best asthma stability
- 9: worst asthma stability

Frequency distribution of the number of errors in inhalation technique (left axis)

Asthma Instability Score (right axis)

Can Healthcare Professionals use pMDIs?

- 150 Hospital doctors, hospital nurses, general practitioners, practice nurses, hospital and community pharmacy staff

Can we improve Inhaler Technique?...
...and does it help?
How Should We Teach Inhaler Technique?

Turbohaler Technique Score

<table>
<thead>
<tr>
<th></th>
<th>Pre n=8</th>
<th>Post n=7</th>
<th>Pre n=9</th>
<th>Post n=8</th>
<th>Pre n=9</th>
<th>Post n=9</th>
</tr>
</thead>
<tbody>
<tr>
<td>Verbal</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Augmented Verbal</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Augmented Verbal + Physical</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Unsatisfactory
- Satisfactory
- Optimal

Impact of “Show and Tell” Inhaler Technique Counselling Service

- Assess Technique using Placebos
- “Show and Tell” training method
- Re-assess technique
- Complete Inhaler Technique Labels
- Repeat at frequent intervals
Impact of “Show and Tell” Inhaler Technique Counselling Service

Basheti IA et al. Patient Education and counseling 2008;72:26-33
Impact of “Show and Tell” Inhaler Technique Counselling Service

Basheti IA et al. Patient Education and counseling 2008;72:26-33
SO....WHAT IS ‘GOOD’ INHALER TECHNIQUE???

*HANDS ON SESSION*
1. Turn the DIAL to select the inhaler resistance

(Diskus / Accuhaler)  
Multiple-dose powder inhaler

(Common pMDI)  
Metered Dose Inhaler and MDI spacers with low resistance (e.g. AbleSpacer)

(Easibreathe)  
Automatic pMDI

(Turbuhaler)  
Turbulent flow inhaler

(Autohaler)  
Automatic pMDI
Trademark Acknowledgements

Accuhaler™ Anoro™ Ellipta® Evohaler™ Flixotide™ Incruse™ Relvar® Seretide™ Serevent™ Ventolin™ Volumatic™
COPD Assessment Test (CAT)™ are Registered Trademarks of Glaxo Group Limited

Bricanyl® Oxis® Pulmicort® Symbicort® Symbicort SMART® Turbohaler® are Registered Trademarks of AstraZeneca AB

Flutiform® is a Registered Trademark of Jagotec AG

Nasonex® Singulair® is a Registered Trademark of Merck Sharp & Dohme Corp

Asthma Control Test™ is a Registered Trademark of QualityMetric Incorporated

AeroChamber® Plus is a Registered Trademark of Trudell Medical International

Airomir® Qvar® DuoResp Spiromax® are Registered Trademarks of IVAX International B.V.

Aatrovent® Combivent® HandiHaler® Respimat® Spiriva® are Registered Trademarks of Boehringer Ingelheim Pharma GmbH & Co. KG

Easyhaler® Bufomix® is a Registered Trademark of Orion Corporation

Breezhaler® Onbrez® Seebri® Ultibro® Aerolizer® are Registered Trademarks of Novartis AG

Eklira® Duaklir® Genuair® Novolizer® are Registered Trademarks of Almirall, S.A.

Autohaler® is a Registered Trademark of 3M Company

Easi-Breathe® Salamol® are Registered Trademarks of Norton Healthcare Limited

Easyhaler® is a Registered Trademark of Orion Corporation

Clickhaler® is a Registered Trademark of Tianjin Kinnovata Pharmaceutical Company Limited

Daxas® is a Registered Trademark of Takeda GmbH

Uniphyllin® is a Registered Trademark of Mundipharma AG

Foradil® is Registered Trademark of Astellas Pharma Inc

Twisthaler® is Registered Trademark of MSD International Holdings GmbH

Asmabec® is Registered Trademark of Celltech Pharma Europe Limited
Fostair 100/6 mcg pressurised metered dose inhaler (Beclometasone dipropionate/formoterol fumarate dihydrate)

Please refer to the full Summary of Product Characteristics (SmPC) before prescribing.

Prescribing information

Presentation Each metered dose contains 100 micrograms (mcg) of beclometasone dipropionate (BDP) and 6mcg of formoterol fumarate dihydrate. Indications Asthma: Regular treatment of asthma in patients ≥18 years who are not adequately controlled on inhaled corticosteroids (ICS) and ‘as needed’ rapid acting beta₂-agonist or patients who are adequately controlled on both ICS and long-acting beta₂-agonists (LABA), where the use of an ICS/LABA combination is appropriate. COPD: Symptomatic treatment of patients with severe COPD (FEV₁ <50% predicted normal) and a history of repeated exacerbations, who have significant symptoms despite regular therapy with long-acting bronchodilators.

Dosage and administration For inhalation in adult patients (≥18 years). BDP in Fostair is characterised by an extrafine particle size distribution which results in a more potent effect than formulations of BDP with a non-extrafine particle size distribution (100mcg of BDP extrafine in Fostair are equivalent to 250mcg of BDP in a non-extrafine formulation). Therefore the total daily dose of BDP administered in Fostair should be lower than the total daily dose of BDP administered in a non-extrafine BDP formulation. Asthma: Fostair may be used as a maintenance therapy (with a separate rapid-acting bronchodilator as needed) or as a maintenance and reliever therapy (taken as a regular maintenance treatment and as needed in response to asthma symptoms). Maintenance therapy: 1–2 inhalations twice daily. The maximum daily dose is 4 inhalations. Patients should receive the lowest dose that effectively controls their symptoms. Maintenance and reliever therapy: 1 inhalation twice daily (morning/evening) plus one additional inhalation as needed in response to symptoms. If symptoms persist after a few minutes, an additional inhalation is recommended. The maximum daily dose is 8 inhalations. COPD: 2 inhalations twice daily. Can be used with the AeroChamber Plus® spacer device. Contraindications Hypersensitivity to the active substances or to any of the excipients (HFA-134a, ethanol anhydrous, hydrochloric acid). Warnings and precautions Use with caution in patients with cardiac arrhythmias, aortic stenosis, hypertrophic obstructive cardiomyopathy, severe heart disease, occlusive vascular diseases, arterial hypertension, aneurysm, thyrotoxicosis, diabetes mellitus, phaeochromocytoma and untreated hypokalaemia. Caution should also be used when treating patients with known prolongation of the QTc interval (QTc > 0.44 seconds). Formoterol itself may induce QTc prolongation. Potentially serious hypokalaemia may result from beta₂-agonist therapy which may be potentiated by concomitant treatments and increase the risk of arrhythmias. Formoterol may cause a rise in blood glucose levels. As Fostair contains a corticosteroid, it should be administered with caution in patients with pulmonary tuberculosis or fungal/viral airway infections. Fostair treatment should not be stopped abruptly. Treatment should not be initiated during exacerbations or deteriorating asthma. Fostair treatment should be discontinued immediately if the patient experiences a paradoxical bronchospasm. Systemic effects: Systemic effects of ICS may occur, particularly at high doses for long periods, but less likely than with oral steroids. These include Cushing’s syndrome, Cushingoid features, adrenal suppression, decrease in bone mineral density, cataract and glaucoma and more rarely, a range of psychological or behavioural effects including psychomotor hyperactivity, sleep disorders, anxiety, depression and aggression. Prolonged treatment with high doses of inhaled corticosteroids may result in adrenal suppression and/or acute adrenal crisis. Interactions Beta-blockers should be avoided. Concomitant administration of other beta-adrenergic drugs may potentiate the adverse reactions of Fostair. Concomitant treatment with quinidine, disopyramide, procainamide, phenothiazines, antihistamines, monoamine oxidase inhibitors and tricyclic antidepressants can prolong the QTc interval and increase the risk of ventricular arrhythmias. L-dopa, L-thyroxine, oxytocin and alcohol can impair cardiac tolerance towards beta₂-sympathomimetics. Hypertensive reactions may occur following co-administration with monoamine oxidase inhibitors. Concomitant treatment with beta₂-agonists and xanthine derivatives, steroids or diuretics may potentiate hypokalaemic effects. Hypokalaemia may increase the likelihood of arrhythmias in patients receiving digitalis glycoiides. Fertility, pregnancy and lactation Fostair should only be used during pregnancy or breast-feeding if the expected benefits outweigh the potential risks. Effects on driving and operating machinery Fostair is unlikely to have any effect on the ability to drive or operate machinery. Side effects Common: pharyngitis, headache, dysphonia, hypokalaemia, tremor, palpitations, cough, muscle spasms, prolongation of QTc interval, oral candidiasis and throat irritation. Serious side effects: hypersensitivity reactions, granulocytopenia, thrombocytopenia, adrenal suppression, hyperglycaemia, hypokalaemia, psychomotor hyperactivity, behavioural changes, glaucoma, cataract, tachyarrhythmias, angina pectoris, asthmatic crisis, decrease in bone mineral density and growth retardation in children and adolescents, pneumonia, influenza (Refer to SmPC for full list of side effects). Legal category POM Packs and prices £29.32 1x120 actuations. Marketing authorisation number PL 08829/0156. Marketing authorisation holder Chiesi Limited, Cheadle Royal Business Park, Highfield, Cheadle, SK8 3GY, United Kingdom. Date of preparation April 2014.

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Chiesi Limited. (address as above) Tel: 01

0161 488 5555
Prescribing Information – Fostair NEXThaler

FOSTAIR NEXTHALER 100/6 dry powder inhaler
Beclometasone dipropionate/formoterol fumarate dihydrate
Please refer to Summary of Product Characteristics (SmPC) before prescribing

Prescribing information

Presentation Each metered dose contains 100mcg of beclometasone dipropionate (BDP) and 6mcg of formoterol fumarate dihydrate. **Indication** Regular treatment of asthma in patients ≥18 years who are not adequately controlled on inhaled corticosteroids and ‘as needed’ rapid acting beta₂-agonist or patients who are already adequately controlled on both ICS and long-acting beta₂-agonists. Fostair NEXThaler is not indicated for the treatment of acute asthma attacks. **Dosage and administration** For inhalation in adult patients (≥18 years). 1 or 2 inhalations twice daily. The maximum daily dose is 4 inhalations. Fostair NEXThaler has an extrafine particle size distribution; therefore, dose adjustment is required when patients are transferred from a formulation with a non-extrafine particle size distribution. When switching patients from previous treatments, it should be considered that the recommended total daily dose of BDP for Fostair NEXThaler is lower than that for non-extrafine BDP containing products and should be adjusted to the needs of the individual patient. However, patients who are transferred to Fostair NEXThaler from Fostair pressurised inhalation solution do not need dose adjustment. **Contraindications** Hypersensitivity to the active substances or to any of the excipients (lactose monohydrate and magnesium stearate). **Warnings and precautions** Use with caution in patients with cardiac arrhythmias, aortic stenosis, hypertrophic obstructive cardiomyopathy, ischemic heart disease, severe heart failure, severe arterial hypertension, aneurysm, thyrotoxicosis, diabetes mellitus, phaeochromocytoma and untreated hypokalaemia. Caution should also be used when treating patients with prolongation of the QTc interval (QTc > 0.44 seconds). Formoterol itself may induce QTc prolongation. Potentially serious hypokalaemia may result from beta₂-agonist therapy which may be potentiated by concomitant treatments (e.g. xanthine derivatives, steroids and diuretics) and increase the risk of arrhythmias. Formoterol may cause a rise in blood glucose levels. Fostair NEXThaler should not be administered for at least 12 hours before the start of anaesthesia, if halogenated anaesthetics are planned. When treatment with Fostair NEXThaler is discontinued the dose should be tapered, treatment should not be stopped abruptly. Treatment should not be initiated during exacerbations or acutely deteriorating asthma. Treatment should be discontinued immediately if the patient experiences a paradoxical bronchospasm. Use with caution in patients with pulmonary tuberculosis or fungal/viral airway infections. **Systemic effects:** Systemic effects of ICS may occur, particularly at high doses for long periods, but less likely than with oral steroids. These include Cushing’s syndrome, Cushingoid features, adrenal suppression, decrease in bone mineral density, cataract and glaucoma and more rarely a range of psychological or behavioural effects including psychomotor hyperactivity, sleep disorders, anxiety, depression and aggression. Prolonged treatment with high doses of inhaled corticosteroids may result in adrenal suppression and/or acute adrenal crisis. Lactose contains small amounts of proteins, which may cause allergic reactions. **Interactions** Beta-blockers should be avoided in asthmatic patients. Concomitant administration of other beta-adrenergic drugs may potentiate the effects of Fostair NEXThaler. Concomitant treatment with quinidine, disopyramide, procainamide, phenothiazines, certain antihistamines (e.g. terfenadine), monoamine oxidase inhibitors and tricyclic antidepressants can prolong the QTc interval and increase the risk of ventricular arrhythmias. L-dopa, L-thyroxine, oxytocin and alcohol can impair cardiac tolerances towards beta₂-sympathomimetics. Hypertensive reactions may occur following co-administration with monoamine oxidase inhibitors including agents with similar properties (e.g. furazolidone, procarbazine). Concomitant treatment with beta₂-agonists and xanthine derivatives, steroids or diuretics may potentiate hypokalaemic effects. Hypokalaemia may increase the likelihood of arrhythmias in patients receiving digitalis glycosides. **Fertility, pregnancy and lactation** Fostair NEXThaler should only be used during pregnancy or breast-feeding if the expected benefits outweigh the potential risks. **Effects on driving and operating machinery** Fostair NEXThaler has no or negligible influence on the ability to drive and use machines. **Side effects** Common: Tremor **Uncommon or of unknown frequency, but potentially serious, side effects include:** Tachycardia, angina pectoris, myocardial ischaemia, asthma exacerbation, electrocardiogram QT prolonged, Cushing’s syndrome, adrenal suppression, glaucoma, atrial fibrillation, tachyarrhythmia, hypokalaemia, hypersensitivity reactions, angioedema, paradoxical bronchospasm. (Refer to SmPC for full list of side effects). Legal category POM **Pack and price** £29.32 1x120 actuations **Marketing authorisation number** PL 08829/0173 **Marketing authorisation holder** Chiesi Limited, Cheadle Royal Business Park, Highfield, Cheadle, SK8 3GY, United Kingdom. **Date of preparation** August 2014

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Chiesi Limited (address as above) Tel: 0161 488 5555.