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Robert Young
General Physician
Auckland City Hospital

Saturday, June 10, 2017
7:00 - 7:55 GlaxoSmithKline Breakfast Session - COPD
New approaches in the management of COPD

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Associate Professor
Consultant Physician
Disclosures and disclaimer

• I am not being paid an honorarium for this presentation

• I am not a GSK employee and do not hold shares in GSK

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• I have previously received honoraria for presentations sponsored by GlaxoSmithKline and Astra Zeneca on topics related to COPD and it’s management

• I received honoraria for participation on an advisory board for GSK
Commonly asked questions from New Zealand GP’s about COPD

✓ What are the new types of inhaler devices now available?

✓ Can we have clarification around Special Authority criteria for the dual bronchodilators; duration of assessment of mono bronchodilator before adding a dual bronchodilator?

✓ What are the changes to the new 2017 GOLD Strategy Update?:

  o Is the 2017 GOLD Strategy saying I should be managing my patients with co-morbid asthma with a LAMA/LABA (rather than treating as asthma)?

  o Eosinophils are not generally recommended as a biomarker in clinical practice. Why do you think this is?

  o Do you have any recommendations on if/how to withdraw ICS/LABA?
New Approaches in COPD management: Agenda

1. Overview of treatments available for COPD in NZ

2. The changing landscape of COPD
   • Summary of changes to the 2017 GOLD strategy update
   • FEV₁ for diagnosis and prognosis
   • Pharmacologic treatment updates including new place for LAMA/LABA
   • Patients most suitable for ICS/LABA
   • Importance of inhaler delivery

3. Non-pharmacological treatment for COPD
Burden of COPD in New Zealand - Key Statistics

- Affects an estimated 15% of adults over 45 yrs old (200,000 New Zealanders)
- Approximately 87 per 100,000 people with a new diagnosis per year = 3,500 new cases per year
- However studies show that as much as 70% of patients with COPD go undiagnosed

15% of Kiwis over 45 have COPD

That's 200,000 people

Most cases of COPD are linked to smoking

Overview of treatments available for COPD in NZ
The changing landscape of COPD treatments in NZ

Introduction of new COPD therapies

- ICS/LABA
- LAMA
- LAMA/LABA

Changes to 2017 GOLD Strategy Update

2016

March

November

1 X new ICS/LABA = Breo Ellipta
2 X new LAMA = Incruse Ellipta and Spiriva in Respimat
3 X new dual bronchodilators*
  = Anoro Ellipta, Spiolto Respimat, Ultibro Breezhaler

* SPECIAL AUTHORITY REQUIREMENTS:
LAMA monotherapy prior to LAMA/LABA

LABAs have been left out to simplify schematic
ICS = inhaled corticosteroid; LABA = long acting beta2 agonist; LAMA = long acting muscarinic antagonist
Overview of inhalers available for COPD in NZ

ICS/LABA
- Symbicort Turbuhaler
- Relpax
- Seretid Accuhaler
- Rimhaler
- Seretid Accuhaler (fluticasone with salmeterol)
- Symbicort Turbuhaler (fluticasone with salmeterol)

LABA/LAMA
- Onbrez Breo inhaler
- Serenvent Accuhaler
- Ona Turbohaler
- Foradil Accuhaler
- Seebri Breo inhaler
- Spiriva Handihaler
- Spiriva Risperidone
- Incensa Ellipta


ICS = inhaled corticosteroid; LABA = long acting beta2 agonist; LAMA = long acting muscarinic antagonist
The changing landscape of COPD
Summary of changes to the 2017 GOLD strategy update
Maintenance therapy for stable COPD: Where do we stand today?

We have clear treatment goals **that have not changed**

**Reduce symptoms**
- Relieve symptoms
- Improve exercise tolerance
- Improve health status

**Reduce risk**
- Prevent & treat exacerbations
- Prevent disease progression*
- Reduce mortality*

*These goals should be achieved with minimal side effects*

*To date, no pharmacotherapy has been proven to prevent disease progression or reduce mortality in COPD*

Summary of changes to the 2017 GOLD strategy update - 1

- Lung function is no longer included in the treatment classification grid, but remains important for diagnosis and prognosis

- Greater emphasis on individualised treatment and individualised treatment choices (co-existing asthma)

- Greater guidance on treatment options, with escalation (and de-escalation) strategies now suggested

- Greater emphasis on the use of LAMA/LABA for appropriate patients
Summary of changes to the 2017 GOLD strategy update - 2

• Triple Therapy is recommended for patients who have a high burden of symptoms and/or exacerbations despite initial maintenance therapy

• ICS/LABAs are recommended for patients (1) with co-existing asthma or ACOS, (2) with a higher blood eosinophil count, and (3) where patients are unable to access newer treatment classes

• There is a significant relationship between poor inhaler technique and symptom control in patients with COPD; therefore, inhaler technique needs to be assessed regularly

The changing landscape of COPD
FEV₁ for diagnosis and prognosis
FEV₁ is a poor predictor of individual disease severity
Weak correlation between disease outcome parameters and FEV₁
GOLD 2011-2016: Patients stratified based on risk (airflow limitation + exacerbation history) and symptoms

Stratification to guide pharmacologic treatment algorithm

<table>
<thead>
<tr>
<th>Risk (GOLD Classification of Airflow Limitation)</th>
<th>Symptoms</th>
<th>Breathlessness</th>
</tr>
</thead>
<tbody>
<tr>
<td>CAT &lt;10</td>
<td>mMRC 0-1</td>
<td>0</td>
</tr>
<tr>
<td>CAT ≥10</td>
<td>mMRC ≥2</td>
<td>≥1 leading to hospital admission OR &gt;1 leading to hospital admission</td>
</tr>
</tbody>
</table>

- **(A)**: high risk, less symptoms
- **(B)**: high risk, more symptoms
- **(C)**: low risk, less symptoms
- **(D)**: low risk, more symptoms

NEW GOLD 2017: Patients stratified based on risk (exacerbation history) and symptoms

Stratification to guide pharmacologic treatment algorithm

<table>
<thead>
<tr>
<th>Risk</th>
<th>Symptoms</th>
<th>CAT</th>
<th>mMRC</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥2 OR &gt;1</td>
<td>(C)</td>
<td>&lt;10</td>
<td>0-1</td>
</tr>
<tr>
<td>1, not leading</td>
<td>(D)</td>
<td>≥10</td>
<td>≥2</td>
</tr>
<tr>
<td>to hospital admission</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(A) low risk
   less symptoms
   CAT <10
   mMRC 0-1

(B) low risk
   more symptoms
   CAT ≥10
   mMRC ≥2

NEW 2017 GOLD: FEV$_1$ informs diagnosis and prognosis

Assessment of airflow limitation (severity + prognosis)

- FEV$_1$/FVC < 0.7

<table>
<thead>
<tr>
<th>Grade</th>
<th>FEV$_1$ (% pred.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>≥80</td>
</tr>
<tr>
<td>2</td>
<td>50-79</td>
</tr>
<tr>
<td>3</td>
<td>30-49</td>
</tr>
<tr>
<td>4</td>
<td>&lt;30</td>
</tr>
</tbody>
</table>
NEW 2017 GOLD: FEV$_1$ informs diagnosis and prognosis but not treatment recommendations

NEW 2017 GOLD: Patients stratified based on risk (exacerbation history) and symptoms

Stratification to guide pharmacologic treatment algorithm

- **Risk (Exacerbation history)**
  - 0, 1, not leading to hospital admission
  - 1, 2 leading to hospital admission

- **Symptoms**
  - CAT <10
  - CAT ≥10
  - mMRC 0-1
  - mMRC ≥2

Stratification to guide pharmacologic treatment algorithm:

- **(A)** low risk, less symptoms
  - CAT <10
  - mMRC 0-1

- **(B)** low risk, more symptoms
  - CAT ≥10
  - mMRC ≥2

- **(C)** high risk, less symptoms
  - CAT <10
  - mMRC 0-1

- **(D)** high risk, more symptoms
  - CAT ≥10
  - mMRC ≥2

Assessment of symptoms: The CAT questionnaire (www.catestonline.org)

- Cough
  - I never cough
  - I cough all the time
- Phlegm
  - I have no phlegm (mucus) in my chest at all
  - My chest is full of phlegm (mucus)
- Tight
  - My chest does not feel tight at all
  - My chest feels very tight
- SOB
  - When I walk up a hill or one flight of stairs I am not breathless
  - When I walk up a hill or one flight of stairs I am very breathless
- Activity
  - I am not limited doing any activities at home
  - I am very limited doing activities at home
- Confidence
  - I am confident leaving my home despite my lung condition
  - I am not at all confident leaving my home because of my lung condition
- Sleep
  - I sleep soundly
  - I don't sleep soundly because of my lung condition
- Energy
  - I have lots of energy
  - I have no energy at all

COPD Self Assessment Test

Score/40
- mild 0-10
- mod 10-15
- severe 15-25
- very severe 25-40

Basis on which to establish
- overall disability
- specific disabilities and
- response to treatments

www.catestonline.org
Assessment of symptoms: Modified MRC Breathlessness Score

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description of Breathlessness</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>I only get breathless with strenuous exercise.</td>
</tr>
<tr>
<td>1</td>
<td>I get short of breath when hurrying on level ground or walking up a slight hill.</td>
</tr>
<tr>
<td>2</td>
<td>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.</td>
</tr>
<tr>
<td>3</td>
<td>I stop for breath after walking about 100 yards or after a few minutes on level ground.</td>
</tr>
<tr>
<td>4</td>
<td>I am too breathless to leave the house or I am breathless when dressing.</td>
</tr>
</tbody>
</table>

Exercise, exercise tolerance and COPD

The changing landscape of COPD
Pharmacologic treatment updates including new place for LAMA/LABA
Maintenance therapy for stable COPD: Where do we stand today?

We have clear treatment goals that have not changed

Reduce symptoms
- Relieve symptoms
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Reduce risk
- Prevent & treat exacerbations
- Prevent disease progression*
- Reduce mortality*

These goals should be achieved with minimal side effects

* To date, no pharmacotherapy has been proven to prevent disease progression or reduce mortality in COPD

Changes for Management of Stable COPD:
Summary of new pharmacologic treatment algorithms by 2017 GOLD
Update

Preferred treatment pathway=
A bronchodilator evaluate effect
Continue, stop or try alternative class of bronchodilator

Further exacerbation(s)

LAMA

LABA/ICS

C

LABA/ICS

A long-acting bronchodilator (LABA or LAMA)

B

Further exacerbation(s)

A long-acting bronchodilator (LABA or LAMA)

A bronchodilator

Risk (Increasing Exacerbations)

Increasing Symptoms

D

ICS/LABA

LAMA

LAMA/LABA

ICS/LABA

LAMA/LABA

LAMA/LABA/ICS

Persistent symptoms

Further exacerbation(s)

Consider roflumilast if FEV₁ <50% predicted and patient has chronic bronchitis
Consider macrolide

Persistent symptoms/further exacerbation(s)

ICS/LABA

ICS/LABA

ICS/LABA

ICS/LABA

The 2017 GOLD strategy update
Group A: Low level of symptoms and low risk of exacerbation

Stratification to guide pharmacologic treatment algorithm

Preferred treatment pathway=

The 2017 GOLD strategy update
Group B: High level of symptoms and low risk of exacerbation
Stratification to guide pharmacologic treatment algorithm

A SAMA and/or SABA bronchodilator or long-acting bronchodilator (LAMA)

A long-acting bronchodilator (LABA or LAMA)

Consider roflumilast if FEV₁ <50% predicted and patient has chronic bronchitis

Consider macrolide

Persistent symptoms/further exacerbation(s)

Further exacerbation(s)

Persistent symptoms/further exacerbation(s)

ICS/LABA

ICS/LABA

LABA/ICS

LABA/ICS

LAMA/LABA

LAMA/LABA

LAMA/LABA/ICS

LAMA/LABA/ICS

LAMA

LAMA

LABA

The 2017 GOLD strategy update
Group C: Low level of symptoms and high risk of exacerbation

Stratification to guide pharmacologic treatment algorithm

A bronchodilator

Evaluate effect

Persistent symptoms

A long-acting bronchodilator (LABA or LAMA)

Consider roflumilast if FEV₁ < 50% predicted and patient has chronic bronchitis

Consider macrolide

A bronchodilator

Evaluate effect

Continue, stop or try alternative class of bronchodilator

A long-acting bronchodilator (LABA or LAMA)

Persistent symptoms

LAMA/LABA

LABA/ICS

Further exacerbation(s)

LAMA

LABA

ICS/LABA

ICS/LABA

LAMA/LABA/ICS

Further exacerbation(s)

Persistent symptoms/further exacerbation(s)

Consider roflumilast if FEV₁ < 50% predicted and patient has chronic bronchitis

Consider macrolide

Risk (Increasing Exacerbations)

(IDC)

Increasing Exacerbations


The 2017 GOLD strategy update

Group D: High level of symptoms and high risk of exacerbation

Stratification to guide pharmacologic treatment algorithm

Preferred treatment pathway=

Changes for Management of Stable COPD: Summary of new pharmacologic treatment algorithms in 2017 GOLD

**Group A:** SABA and/or SAMA or LAMA (or LABA)*

**Group B:** Initial therapy should consist of LAMA or LABA progressing to LAMA/LABA if patient has persistent symptoms

**Group C:** Initial therapy should consist of LAMA, progressing to LAMA/LABA (preferred) or ICS/LABA (alternative) if patient has persistent exacerbations

**Group D:**
- Initial therapy should consist of LAMA/LABA (preferred) or ICS/LABA in ACOS patients or those with high EOS
- If patient develops further exacerbations, LAMA/LABA/ICS is recommended
- If patient develops further exacerbations, roflumilast (not registered in NZ), macrolide or stopping ICS could be considered in certain patients

*Gold states that long acting bronchodilators are preferred over short acting alternatives, with the exception being when patients only have occasional dyspnoea.

'It should be noted that there is a lack of direct evidence supporting therapeutic recommendations for patients in groups C and D. These recommendations will be re-evaluated as additional data become available.'
Group A: Low symptom level and low risk of exacerbation

Short-acting and long-acting mono-bronchodilators available in NZ

ICS = inhaled corticosteroid; LABA = long acting beta2 agonist; LAMA = long acting muscarinic antagonist

The prescriber must provide written endorsement that the patient has been diagnosed as having COPD using spirometry to access subsidy.

Anoro Ellipta demonstrates significant improvement of trough FEV$_1$ compared with monotherapy and placebo


Benefit of LABA when added to LAMA

Benefit of LAMA when added to LABA

Vilanterol mono-therapy is unlicensed in COPD
Incruse Ellipta (umeclidinium) offers improvements in lung function vs tiotropium

LS mean change from baseline in trough FEV$_1$ at Day 85

Difference = 53 mL [95% CI: 25, 81 mL], p<0.001; Intention to Treat Population

Special Authority Criteria

INITIAL APPLICATION:

- Patient has been stabilised on a LAMA
- Prescriber considers that patient would receive additional benefit from switching to a combination product

LAMA = long-acting muscarinic antagonists; LABA = long-acting beta₂ agonists


Combination LAMA/LABAs available in New Zealand

GLYCOPYRRONIUM + INDACATEROL
One inhalation, once daily

GLYCOPYRRONIUM + INDACATEROL
One inhalation, once daily

UMECLIDINUM + VILANterol
One inhalation, once daily

UMECLIDINUM + VILANterol
One inhalation, once daily

OLODATEROL + TIOTROPIUM
Two puffs, once daily. MDI delivered as a mist (non-propellant).
Dual bronchodilators may provide optimal bronchodilation through complementary mechanisms\(^1,2\)

LAMA: inhibits \(M_3\) muscarinic receptors in the lungs

- Reduces airway smooth muscle contraction
- Prevents bronchoconstriction

LABA: stimulates \(\beta_2\) adrenergic receptors in airway smooth muscle

- Relaxes airway smooth muscle
- Stimulates bronchodilation

Optimal bronchodilation

“Combining bronchodilators with different mechanisms and durations of action may increase the degree of bronchodilation with a lower risk of side effects compared to increasing the dose of a single bronchodilator”

- GOLD 2017\(^3\)

References:
Anoro Ellipta significantly improved trough FEV$_1$ compared with tiotropium

Immediate, sustained, significant improvement in trough FEV$_1$

Results of 24-week, randomised, double-dummy, active-controlled, blinded, multi-centre, parallel-group studies that compared the efficacy and safety of Anoro Ellipta with tiotropium in subjects with COPD.

‘Distilling’ the 2017 GOLD strategy update

Group C, D and E (ACOS)

LAMA/LABA, ICS/LABA and/or LAMA
The changing landscape of COPD
Patients most suitable for ICS/LABA
Which of my COPD patients would benefit from an ICS?

**GOLD 2017 recommendations:**

In GOLD D patients, ICS/LABA as initial therapy may be the first choice in:

- Those patients who may co-existing asthma or a history and/or findings that are suggestive of asthma-COPD overlap syndrome
- Patients with high eosinophil counts may also be considered as a parameter to support the use of ICS-containing therapy

ACOS subgroup of COPD spectrum

- Recommendations are based on expert opinion and not RCTs (ACOS usually excluded from COPD trials)

- Features of ACOS
  - History of asthma (childhood or 20+ years of asthma) and smoking
  - History of atopy, allergic rhinitis or high IgE
  - High serum eosinophilia (>2%)
  - Highly variable PEFR or FEV₁ (>15% variability)

- About 20% of all COPD cohorts, suffer frequent exacerbations, moderate-severe GOLD grade (GOLD phenotype C and D)

- Assumed to
  - Gain greater benefit from ICS use with reduction in exacerbations
  - Have greater responsiveness to ICS with regards bronchodilator benefits
The effect of adding fluticasone furoate to vilanterol (Breo Ellipta) by blood eosinophils

Distribution of patients by a 2% eosinophil cut-off point

Randomised Clinical Trials (Seretide, Flixitotide, Breo Ellipta)

Generally, 50%-70% of COPD patients have Eos measurements ≥ 2% or ≥ 150/mm³

Di Santostefano et al; AJRCCM 2015;192; A2868 (poster presentation); NHANES; http://www.cdc.gov/nchs/nhanes/about_nhanes.htm
ICS/LABA therapy significantly reduces the exacerbation risk

Results of two large Cochrane meta-analyses

**ICS/LABA vs Placebo**¹

<table>
<thead>
<tr>
<th>Arm</th>
<th>Odds ratio and 95% CI</th>
<th>Heterogeneity</th>
</tr>
</thead>
<tbody>
<tr>
<td>FP/Sal, BDF (7 studies) (n=7495)</td>
<td></td>
<td>$I^2=0%$</td>
</tr>
<tr>
<td>FP/Sal (3 studies) (n=4255)</td>
<td></td>
<td>$I^2=0%$</td>
</tr>
<tr>
<td>BDF (4 studies) (n=3240)</td>
<td></td>
<td>$I^2=0%$</td>
</tr>
</tbody>
</table>

**ICS/LABA vs LABA**²

<table>
<thead>
<tr>
<th>Arm</th>
<th>Odds ratio and 95% CI</th>
<th>Heterogeneity</th>
</tr>
</thead>
<tbody>
<tr>
<td>FP/Sal, BDF (9 studies) (n=9921)</td>
<td></td>
<td>$I^2=68%$</td>
</tr>
<tr>
<td>FP/Sal (5 studies) (n=6391)</td>
<td></td>
<td>$I^2=82%$</td>
</tr>
<tr>
<td>BDF (4 studies) (n=2622)</td>
<td></td>
<td>$I^2=0%$</td>
</tr>
</tbody>
</table>

BDF, budesonide/formoterol; CI, confidence intervals; FP, fluticasone propionate; ICS, inhaled corticosteroid; LABA, long-acting beta₂ agonist; Sal, salmeterol

² Nannini et al. Combined corticosteroid and long-acting B-agonist in one inhaler vs LABA for COPD (Review). Cochrane 2012
Combining ICS/LABA and LAMA therapy provides dual bronchodilation while maintaining exacerbation control\(^1\)–\(^3\)

ICS\(^1\)
- Potentiates LABA effect in airway smooth muscle
- Anti-inflammatory effect in the airways

LABA\(^{2,3}\)
- Stimulates beta\(_{2}\) adrenergic receptors
- Relax airway smooth muscle
- Stimulates bronchodilation

LAMA\(^{2,3}\)
- Inhibits M\(_3\) muscarinic receptors
- Reduce airway smooth muscle contraction
- Prevents bronchoconstriction

Bronchodilation and exacerbation rate reduction

When would you consider withdrawing an ICS?

ICS "step-down" (de-escalation/substitution if:
- Not ACOS
- No exacerbations or chest infections in last 1-2 years and stable dyspnoea
- Recent pneumonia (CXR confirmed) or other ICS-related complications
- "Low" blood serum eosinophil count (<300 μL⁻¹ or ≤4%)

ICS "step-up" (escalation) based on:
- Recent "exacerbation" or chest infection history
- Symptom score (CAT > 10) or persistent SOB
- Low or highly variable expiratory flow rates (FEV₁ <50% or ≥15% or ≥400 mL)
- "High" blood serum eosinophil count (>300 μL⁻¹ or ≥6%)
Importance of inhaler delivery
2107 GOLD Update states:

- On average more than two thirds of patients make at least one error in using an inhalation device
- Observational studies have shown a significant relationship between poor inhaler use and symptom control in patients with COPD
- Key determinants of poor inhaler technique include use of multiple devices, older age and lack of previous education on inhaler technique
- GOLD recognise the importance of education and training in inhaler technique
Significantly fewer COPD patients made inhaler errors after reading the patient information leaflet.

Proportion of participants who made at least one critical error after reading the patient information leaflet.

Van der Palen et al. Primary Care Respir Med 26: 16079 (2016)
Non-pharmacological treatment for COPD
Non-pharmacological treatment for COPD

- Vaccinations – Influenza and pneumococcal

- Regular Exercise – optimise physical “fitness” or condition (anti-inflammatory)

- Pulmonary rehabilitation (post hospital discharge or after significant exacerbation) – physical conditioning, confidence and inhaler optimisation

- Diet – Diet high in fruit, vegetables and fibre (Mediterranean Diet)

- Treat underlying **Coronary Artery Disease** risk factors
Questions Welcomed!
• Do you have any potential safety concerns with the introduction of the new medicines?

• Is there any difference between the different ICS available in NZ and the risk of pneumonia?

• What is the definition of severe breathlessness?

• Sometimes it’s hard to know when to refer patients with COPD. At what stage would you like to see COPD patients in your respiratory clinic?
Anoro® Ellipta® (umeclidinium bromide/vilanterol trifenate inhaler 62.5/25mcg per inhalation) is a fully funded medicine; Special Authority criteria apply. Maximum Daily Dose: One inhalation once daily. Prescription Medicine for long-term regular treatment to relieve symptoms in adult patients with Chronic Obstructive Pulmonary Disease (COPD). This medicine has risks and benefits.

Warnings and Precautions: Not recommended for use in patients with asthma or for relief of acute symptoms or an acute exacerbation. Use care when co-administering with strong CYP3A4 inhibitors (e.g. ketoconazole), beta-blockers and in patients with severe cardiovascular disease, narrow-angle glaucoma or urinary retention. Common Side Effects: Nasopharyngitis, oropharyngeal pain, sinusitis, pharyngitis, cough, urinary tract infection, constipation, dry mouth, hypertension. Paradoxical bronchospasm may occur. Before prescribing Anoro Ellipta, please review the Data Sheet at www.medsafe.govt.nz.

Incruse® Ellipta®: In addition to the Anoro Ellipta information above which also applies to Incruse Ellipta (umeclidinium bromide), Incruse is available in a 62.5mcg per inhalation in the Ellipta device. Incruse Ellipta is a fully funded medicine. The prescriber must provide written endorsement that the patient has been diagnosed as having COPD using spirometry to access subsidy. Before prescribing Incruse Ellipta, please review the Data Sheet at www.medsafe.govt.nz.
**Incruse® Ellipta®** (umeclidinium bromide inhaler 62.5mcg per inhalation) is a *Prescription Medicine.* Incruse Ellipta is indicated as a long-term maintenance bronchodilator treatment to relieve symptoms in adult patients with Chronic Obstructive Pulmonary Disease (COPD). Incruse Ellipta is a fully funded medicine. The prescriber must provide written endorsement that the patient has been diagnosed as having COPD using spirometry to access subsidy. **Maximum Daily Dose:** One inhalation once daily. **Contraindications:** Patients with severe milk-protein allergy or those who have hypersensitivity to umeclidinium or any excipients. **Side Effects:** Urinary tract infection, tachycardia, upper respiratory tract infection, nasopharyngitis, sinusitis, cough, dysgeusia. **Warnings and Precautions:** Not recommended for use in patients with asthma or for relief of acute symptoms or an acute exacerbation. Use care in patients with severe cardiovascular disease (particularly cardiac arrhythmias), narrow-angle glaucoma or urinary retention. Paradoxical bronchospasm may occur. Before prescribing Incruse Ellipta, please review the Data Sheet at [www.medsafe.govt.nz](http://www.medsafe.govt.nz).

Incruse and Ellipta are registered trade marks of the GlaxoSmithKline group of companies. Marketed by GlaxoSmithKline NZ Limited, Auckland. Adverse events involving GlaxoSmithKline products should be reported to GSK Medical Information on 0800 808 500.
**Breo® Ellipta®** (fluticasone furoate/vilanterol trifenate inhaler 100/25mcg per inhalation) is a fully funded medicine. **Breo Ellipta 200/25mcg** is a private purchase medicine (dose indicated in asthma only); a prescription charge will apply. **Maximum Daily Dose**: One inhalation once daily. **Maintenance Dose**: Titrate to lowest effective dose. **Prescription Medicine** for the regular treatment of asthma (12 years of age and older) (100/25 and 200/25mcg) and/or COPD (100/25mcg) with a FEV1<70% predicted normal (post-bronchodilator) in patients with an exacerbation history. This medicine has risks and benefits. **Warnings and Precautions**: Not for relief of acute symptoms or an acute exacerbation. Do not discontinue abruptly. Use care when co-administering with strong CYP3A4 inhibitors (e.g. ketoconazole, ritonavir) or in patients with hepatic impairment, severe cardiovascular disease, pulmonary tuberculosis or chronic or untreated infections. **Common Side Effects**: Candidiasis of mouth and throat, headache, nasopharyngitis, oropharyngeal pain, sinusitis, pharyngitis, rhinitis, cough, dysphonia, upper respiratory tract infection, bronchitis, influenza, abdominal pain, arthralgia, back pain, pyrexia. Paradoxical bronchospasm may occur. Physicians should remain vigilant for the possible development of pneumonia in patients with COPD as the clinical features of such infections overlap with the symptoms of COPD exacerbations. The incidence of pneumonia in patients with asthma was uncommon. Avoid beta-blockers if possible. Before prescribing **Breo Ellipta**, please review the Data Sheet at www.medsafe.govt.nz.

**Anoro**, **Incruse**, **Breo** and **Ellipta** are registered trade marks of the GlaxoSmithKline group of companies. **Anoro and Breo Ellipta** were developed in collaboration with Theravance Inc. Marketed by GlaxoSmithKline NZ Limited, Auckland. **Adverse events involving GlaxoSmithKline products should be reported to GSK Medical Information on 0800 808 500.**
**Seretide®** (fluticasone propionate/salmeterol xinafoate inhaler 50/25 or 125/25mcg per actuation and Accuhaler® 100/50, 250/50mcg per actuation) is a fully funded medicine. **Seretide 250/25mcg inhaler is a private purchase medicine; a prescription charge will apply.** Maximum Daily Dose: MDI 2 puffs twice daily, Accuhaler 1 inhalation twice daily. **Maintenance Dose:** Titrate to lowest effective dose 1-2 times daily. **Prescription Medicine** for the treatment of reversible obstructive airway disease (ROAD) including asthma, and for the treatment of chronic obstructive pulmonary disease (COPD). This medicine has risks and benefits. **Warnings and Precautions:** Not for relief of acute symptoms. Do not discontinue abruptly. Use care when co-administering strong CYP3A4 inhibitors (e.g. ketoconazole) or in patients with pulmonary tuberculosis or thyrotoxicosis. **Common Side Effects:** Hoarseness/dysphonia, throat irritation, headache, oral candidiasis and palpitations. Paradoxical bronchospasm may occur. Avoid beta-blockers if possible. Before prescribing Seretide, please review the Data Sheet at www.medsafe.govt.nz. **Seretide and Accuhaler are registered trade marks of the GlaxoSmithKline group of companies.** Marketed by GlaxoSmithKline NZ Limited, Auckland. **Adverse events involving GlaxoSmithKline products should be reported to GSK Medical Information on 0800 808 500.**