Drug Benefit Council (DBC) Recommendation and Reasons for Recommendation

FINAL

Drugs for Chronic Obstructive Pulmonary Disease
AstraZeneca Canada Inc.
Novartis Pharmaceuticals Canada Inc.
Boehringer Ingelheim Canada
GlaxoSmithKline Inc.

Description:

The current PharmaCare coverage status and limited coverage criteria of inhalers used to treat Chronic Obstructive Pulmonary Disease (COPD) needs to be updated as they do not align with the recommended approach to pharmacologic therapies in current guidelines. A therapeutic review was initiated to assess coverage criteria to potentially improve patients' outcomes and safety and assess the efficient use of the PharmaCare budget.

In their review, the DBC considered the following:

- Internal documents, including: PharmaNet data on COPD Patient Utilization; and a University of British Columbia Faculty of Pharmaceutical Sciences presentation titled "The 'guideline utopia' and 'real world' of COPD medications."
- Comparative evidence reports, including: a February 2017 BC Provincial Academic Detailing (PAD) Service COPD Update; reports from the Therapeutics Initiative (TI) on the COPD hierarchy of outcomes; a September 2018 TI report including a summary of guidelines; and a February 2019 TI Update of PAD Literature Review: Inhaled medications for treatment of COPD.
- Guidelines, including: the February 2017 BC Guidelines on COPD Diagnosis and Management; the 2017 Canadian Thoracic Society (CTS) position statement on Pharmacotherapy in patients with COPD—An update; the 2019 Global Initiative for Chronic Obstructive Lung Disease report on the Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease (GOLD 2019); the 2018 National Institute for Health and Care Excellence (NICE) guideline on Chronic obstructive pulmonary disease in over 16s: diagnosis and management; and a NICE visual algorithm summary of the recommendations on non-

Property of the Ministry of Health
May not be used, divulged, published, or otherwise disclosed
without consent of the Ministry of Health

pharmacological management of chronic obstructive pulmonary disease and use of inhaled therapies in people over 16.

- Reports from other health technology assessment agencies, including: the 2017 Australian Pharmaceutical Benefits Scheme Post-market Review of COPD Medicines; the Ontario Drug Policy Research Network (ODPRN) review of ICS+LABA Combination Products for Asthma and COPD; the ODPRN recommendations on Select Drug Therapies for the Treatment of Chronic Obstructive Pulmonary Disease and Asthma; the Singapore Agency for Care Effectiveness (ACE) Appropriate Care Guide on managing stable chronic obstructive pulmonary disease, focusing on inhalers; and the ACE guidance on LAMA monotherapy and combination therapy with LAMA/LABA.
- Clinical Practice Reviews from two specialists and a GP; manufacturer input from AstraZeneca, Boehringer-Ingelheim, GSK, Novartis and Teva Pharmaceuticals; and Patient Input from 19 patients, 14 caregivers and 3 patient groups.

Dosage Forms:

Long Acting Muscarinic Antagonists (LAMAs)
Aclidinium (Tudorza Genuair), glycopyrronium (Seebri Breezhaler), tiotropium (Spiriva HandiHaler, Spiriva Respimat), umeclidinium (Incruse Ellipta)

Long Acting Beta2 Agonists (LABAs)
Formoterol (Foradil Aerolizer), indacaterol (Onbrez Breezhaler), salmeterol (Serevent Diskhaler, Serevent Diskus)

Inhaled Corticosteroids (ICS)
Beclomethasone dipropionate (QVAR), budesonide (Pulmicort Turbuhaler), ciclesonide (Alvesco), fluticasone furoate (Arnuity Ellipta), fluticasone propionate (Flovent HFA, Flovent Diskus), mometasone furoate (Asmanex Twisthaler)

Combination Therapies: (LAMA-LABA)
Aclidinium-formoterol (Duaklir Genuair), glycopyrronium-indacaterol (Ultibro Breezhaler), tiotropium-olodaterol (Inspiolto Respimat), umeclidinium-vilanterol (Anoro Ellipta)

Combination Therapies: (ICS-LABA)
Budesonide-formoterol (Symbicort Turbuhaler), fluticasone furoate-vilanterol (Breo Ellipta), fluticasone propionate-salmeterol (Advair, Advair Diskus)

Property of the Ministry of Health
May not be used, divulged, published, or otherwise disclosed
without consent of the Ministry of Health

Combination Therapies: (ICS-LAMA-LABA)
Fluticasone furoate-umeclidinium-vilanterol (Trelegy Ellipta)

The DBC was asked the following questions for consideration:

Based on the clinical evidence provided, should the coverage of the COPD inhalers be changed to the following:

Monotherapies:
1) Should LAMAs become the first-line therapies for the treatment of COPD?
    a. If so, should LAMAs be listed as regular benefits or Limited Coverage drugs with criteria?
2) Should LABAs be delisted?
    a. If so, should current patients on LABAs be grandfathered?

Dual therapies:
1) Should LAMA-LABAs Limited Coverage criteria be changed to provide access as second-line therapies tiered behind monotherapies (LAMAs or LABAs)?
2) Should LABA-ICS Limited Coverage criteria be changed to provide access to a defined subset of the COPD population?
    a. If so, how should that population be defined?
    b. Should discontinuation criteria be implemented?

Triple therapies:
1) Should criteria for the usage of triple therapies (as multiple inhalers or as a single inhaler) be implemented limiting the usage of ICS-LAMA-LABA as third-line therapies tiered behind dual therapies (ICS-LABA or LAMA-LABA)?
    a. Should discontinuation criteria be implemented?

Recommendations:

Monotherapies (LAMA or LABA):

1) The DBC recommends that LAMAs be listed for the treatment of COPD with the following criteria:
    - Patient has a diagnosis of COPD;
    - Patient is not adequately controlled on optimal therapy with a short acting bronchodilator (SABA, SAMA or SAMA-SABA combination product).
2) The DBC recommends that LABAs be listed for the treatment of COPD with the following criteria:

Property of the Ministry of Health
May not be used, divulged, published, or otherwise disclosed
without consent of the Ministry of Health

- Patient has a diagnosis of COPD;
- Patient is not adequately controlled on optimal therapy with a short acting bronchodilator (SABA, SAMA or SAMA-SABA combination product); AND
- Patient is not adequately controlled on optimal therapy with a long acting muscarinic antagonist (LAMA) OR has a contraindication to OR an intolerance to a LAMA.

Dual Therapies (LAMA-LABA or ICS-LABA combination products)

1) The DBC recommends that LAMA-LABA combination products be listed for the treatment of COPD with the following criteria:
   a. When prescribed by a General Practitioner (GP):
      - Patient has a diagnosis of moderate to severe COPD as defined by spirometry when available or by clinical presentation if spirometry is not available;
      - Patient is not adequately controlled after an adequate trial on optimal therapy with a long acting bronchodilator (a LAMA or a LABA).
   b. When prescribed by a respirologist:
      - Patient is not adequately controlled after an adequate trial on optimal therapy with a long acting bronchodilator (a LAMA or a LABA).

2) The DBC recommends that the ICS-LABA combination products should be listed for the treatment of COPD with the following criteria:
   - When prescribed by a respirologist;
   - Patient has a diagnosis of moderate to severe COPD as defined by spirometry when available or by clinical presentation if spirometry is not available;
   - Restricted for COPD GOLD D group patients at diagnosis as per the GOLD 2019 guidelines definition;
   - Patient is not adequately controlled on optimal therapy with a LAMA and LABA combination.

Of note:

- The COPD GOLD D group definition is a history of ≥2 moderate exacerbations in the previous year or ≥1 serious exacerbation leading to hospitalization and mMRC ≥2, or CAT™ ≥10.
- The Ministry should consider that ICS monotherapy be listed with Limited Coverage criteria to prevent inappropriate access for COPD treatment.
- A de-escalation of ICS strategy should be considered for renewal requests when no improvements are shown and when continuation of the ICS therapy puts the patients at higher risks than potential benefits.

Property of the Ministry of Health
May not be used, divulged, published, or otherwise disclosed
without consent of the Ministry of Health

- PharmaCare patients currently receiving an ICS monotherapy or in combination with other inhalers for the treatment of COPD should be re-evaluated for coverage and will not be grandfathered for any ICS products.
- The Ministry should consider granting coverage for a LAMA-LABA combination product for patients on ICS-LABA combination products.

Triple Therapies (ICS-LAMA-LABA combination products)

1) The DBC recommends that triple therapies be listed for the treatment of COPD with the following criteria:
    - When prescribed by a respirologist;
    - Patient has a diagnosis of moderate to severe COPD as defined by spirometry when available or by clinical presentation if spirometry is not available;
    - Restricted for COPD GOLD D group patients at diagnosis as per the GOLD 2019 guidelines definition;
    - Patient is not adequately controlled on optimal ICS-LABA therapy for COPD.

Of note:
- The Ministry should consider providing an indefinite Special Authority approval for Triple Therapy requests.

Reasons for the Recommendation:

1. Summary
- There is evidence to use single long-acting bronchodilator monotherapy as preferred initial therapy for COPD patients.
- There is some limited comparative evidence favouring LAMAs over LABAs in reducing the risk of exacerbations in a subset of patients with COPD.
- There is an absence of high quality evidence regarding the effect of intensifying inhaled therapy (e.g. progressing to a LAMA-LABA or an ICS-LAMA-LABA combination) on health-related quality of life and on the risk of exacerbation in people with COPD.
- There is evidence the LAMA-LABA combinations result in fewer exacerbations relative to the ICS-LABA combinations, a lower risk of pneumonia, and more frequent improvement in quality of life.
- There is evidence from systematic reviews and guidelines that ICS-containing regimens should be reserved only for patients at high risk of exacerbations (e.g. GOLD D patients) who do not show a reduction in exacerbations while on LAMAs or LAMA-LABAs.

Property of the Ministry of Health
May not be used, divulged, published, or otherwise disclosed
without consent of the Ministry of Health

- The DBC acknowledges the importance for patients to have access to different long-acting bronchodilator therapies based on preferences, different adverse event profiles, and drug interaction profiles.
- Comments from patients, clinical experts and manufacturers indicated that access to respirologists and spirometry testing may be limited in some areas of the province.

2. Clinical Efficacy

- There is evidence from guidelines that short- or long-acting bronchodilators should be used as initial treatment in COPD GOLD A patients.
- Comparative evidence reports found there is similar safety and efficacy for the LABAs and LAMAs, with the exception of the limited evidence favoring LAMAs over LABAs in terms of exacerbation rates in some patients with COPD.
- Evidence from the Cochrane Collaboration systematic review found that, in the treatment of COPD, the LAMA-LABA combinations result in fewer exacerbations relative to the ICS-LABA combinations, a lower risk of pneumonia, and more frequent improvement in quality of life.

3. Safety

- The long-term use of ICS-containing treatment regimens increases the risk of side effects such as pneumonia, oropharyngeal candidiasis, etc.

4. Economic Considerations

- At list prices, the LAMAs are, with some exceptions, generally less expensive than the LABAs. The LAMA-LABA combination products are generally less expensive than either a LAMA or a LABA when combined as separate products.
- The ICS-LABA combination products are more expensive than the LAMA-LABA combination products.
- The triple-therapy combination fluticasone furoate-umeclidinium-vilanterol (Trelegy Ellipta) is priced slightly lower than an ICS-LABA plus a LAMA combined as separate products.
- Based on a PharmaCare budget impact assessment of the treatments for COPD, the ICS-LABA combination products currently have the most significant budget impact.

5. Of Note

- The DBC considered patient input from 19 patients, 14 caregivers and 3 patient groups. Patients had tried most COPD medications in various combinations. Patients broadly supported access to therapies as recommended by the guideline documents, and particularly supported better access to long-acting bronchodilators. Patients also consistently noted issues with access to respirologists and spirometry testing.

Property of the Ministry of Health
May not be used, divulged, published, or otherwise disclosed
without consent of the Ministry of Health