

# Drug Class Review: Inhaled corticosteroids (ICS) + long-acting beta-agonists (LABA) combination products for treatment of chronic obstructive pulmonary disease (COPD)

Comprehensive Research Plan: Pharmacoepidemiology Unit

January 10, 2014

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**Objective:** To examine trends in COPD drug therapies across Canada, to describe characteristics of patients prescribed ICS/LABA combination products, and to investigate course of therapy and compliance.

### Objective 1: National and provincial trends in COPD Therapies

**Study Design:** Design: Time series analysis with quarterly time intervals  
Study period:

- *National and provincial trends (IMS Compuscript):* October 2009 to September 2013
- *Ontario trends among publically funded prescriptions (ODB):* January 2000 to March 2013

Population: All provinces  
Data Sources:

- *IMS Compuscript:* aggregated data for all prescriptions dispensed at retail pharmacies across Canada
- *Ontario Drug Benefit Database (ODB):* individual level data for all publically funded prescriptions dispensed in Ontario.

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**Study Population:** **Inclusion Criteria:**

- All privately and publically-funded prescriptions dispensed in Canada for treatment of COPD, including:
  - ICS/LABA combination products
  - Other Therapies (Inhaled corticosteroids, Long-acting beta agonists, Short-acting beta agonists, Inhaled anticholinergics)

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<b>Outcome(s) of Interest:</b>	<p>Measured over entire study period (quarterly):</p> <ul style="list-style-type: none"><li>• Number of prescriptions dispensed</li><li>• Total cost of prescriptions</li><li>• Number of users (Ontario public drug plan only)</li></ul> <p>Report:</p> <ul style="list-style-type: none"><li>• Overall rates of use by province</li><li>• National rates of use by drug</li><li>• Distribution of prescriptions by payer (public, private, cash, NIHB)</li><li>• Distribution of prescriptions by age (&lt;65, 65+; Ontario public drug plan only)</li></ul>
<b>Limitations:</b>	<ul style="list-style-type: none"><li>• Information for privately funded prescriptions is only available at the prescription and unit level.</li></ul>

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## Objective 2: Trends in Indication of Use of ICS/LABA Combination Products

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<b>Study Design:</b>	<p><u>Design:</u> Time series analysis with annual time intervals</p> <p><u>Study period:</u> April 2000 to March 2013</p> <p><u>Data Source:</u></p> <ul style="list-style-type: none"><li>• Ontario Drug Benefit Database (ODB)</li></ul>
<b>Study Population:</b>	<p><b>Inclusion Criteria:</b></p> <ul style="list-style-type: none"><li>• All publically-funded prescriptions for ICS/LABA combination products dispensed in Ontario</li><li>• Adults aged 35+ at time of ICS/LABA dispensing</li></ul>

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**Outcome(s) of Interest:** Measured over entire study period (quarterly)

- Prevalence of ICS/LABA use among disease cohorts:
  - COPD + Asthma
  - COPD only
  - Asthma only
  - Neither asthma nor COPD
- Proportion of ICS/LABA prescriptions by indication (i.e. diagnosis)

Stratify all analyses by:

- Drug
  - Age (<65, 65+)
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**Limitations:**

- COPD and Asthma diagnosis defined via validated datasets developed at ICES. Although these datasets have 85% and 84% sensitivity and 78% and 76% specificity, respectively, there may be some misclassification.
- COPD database is only created for those aged 35 and older.

### Objective 3: Characteristics of COPD Patients treated with ICS/LABA Combination Products in Ontario

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**Study Design:**

Design: Cross-sectional analysis

Study period: April 2012 to March 2013

Data Sources:

- Ontario Drug Benefit Database (ODB)
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**Study Population:**

Inclusion Criteria:

- All publically-funded beneficiaries of Ontario with a diagnosis of COPD who are prescribed an ICS/LABA combination product
  - Cohort #1: Adults aged 36+ at time of ICS/LABA dispensing
  - Cohort #2: Adults aged 66+ at time of ICS/LABA dispensing
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For each cohort, measure:

- Variable(s) of Interest:**
- Number of patients
  - Number of new ICS/LABA users
  - Age
  - Gender
  - History of asthma
  - COPD Severity
  - Residence in LTC
  - Drug plan coverage (Seniors, Ontario Disability Support Program, Ontario Works, Long-Term Care, Homes for Special Care, Trillium, Home Care, Special Drugs Program, Other)
  - Urban vs. rural residents
  - Socioeconomic status
  - Average cost of ICS/LABA prescriptions per person
  - Average number of micrograms of ICS/LABA products dispensed per person
  - Past COPD maintenance therapy (1 year)
  - Past treatment for COPD exacerbations (1 year)

Stratify by:

- Type of ICS/LABA combination product

#### Objective 4:

- a. Compliance to therapy between those treated with combination ICS/LABA products and those treated with dual therapy of individual ICS and LABA components
- b. Typical course of therapy through COPD drugs in Ontario

#### Study Design:

Design: Cohort Study

Study period: April 2008 to March 2013

- Accrual period: April 2008 to March 2012
- Maximum follow-up date: March 2013 (*1 year minimum follow-up*)

Data Sources:

- Ontario Drug Benefit Database (ODB)
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**Study Population:**

## Inclusion Criteria:

- All publically-funded beneficiaries of Ontario with COPD who initiate ICS/LABA therapy.
    - New users defined as those with no prescription for an ICS/LABA combination product or dual therapy in the past 365 days
  - Adults aged 66+ at time of ICS/LABA dispensing
  - Restrict to those with COPD diagnosis prior to drug initiation
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**Outcomes of Interest:** Duration of ICS/LABA Therapy:

Definition 1: RELAXED DEFINITION OF ADHERENCE Define ongoing use of ICS/LABA therapy according to receipt of a subsequent prescription within 180 days of the prior prescription.

## DEFINITION 2: STRICT CLINICAL COMPLIANCE

Define ongoing use of ICS/LABA therapy according to receipt of a subsequent prescription within 1.5 times the days supply of the prior prescription.

For each definition:

- Discontinuation of combination therapy defined as:
    - Reducing to single agent therapy
    - Discontinuation of combination product
  - Censor on:
    - End of study period
    - Death
    - For analysis stratified by ICS/LABA combination, censor on switch between products
  - Report the following:
    - Median duration of therapy
    - Cost of therapy
    - Stratify by:
      - Combination products vs. Dual Therapy
      - Type of ICS/LABA combination initiated (among those on combination therapy only)
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<b>Outcomes of interest (continued):</b>	<p><u>Course of Therapy:</u></p> <ul style="list-style-type: none"> <li>• In the 1 year prior to start of ICS/LABA therapy, report any prior COPD medications: <ul style="list-style-type: none"> <li>○ No prior use of any COPD medications</li> <li>○ Use of LABA single agents</li> <li>○ Use of ICS single agents</li> <li>○ Use of SABAs</li> <li>○ Use of anticholinergics</li> </ul> </li> <li>• Over period of ongoing use: <ul style="list-style-type: none"> <li>○ Number of different ICS/LABA combinations prescribed (among those on combination therapy only)</li> <li>○ Concomitant use of other COPD treatment options</li> <li>○ Median duration on combination therapy prior to escalation to triple therapy (where applicable)</li> </ul> </li> </ul>
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<b>Limitations:</b>	<ul style="list-style-type: none"> <li>• Due to unavailability of eligibility information, this analysis is restricted to patients aged 66 and older. Therefore, these findings may not be generalizable to the younger population.</li> </ul>
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**Objective 5: To summarize any observational studies evaluating the comparative effectiveness of ICS/LABA combination products**

<b>Objective:</b>	Review of population-based studies investigating comparative effectiveness and/or safety of ICS/LABA combination products among patients with COPD
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<b>Study Population</b>	Adults with COPD
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<b>Study Design:</b>	<p>Observational studies</p> <ul style="list-style-type: none"> <li>• Comparative effectiveness studies</li> <li>• Safety studies</li> </ul>
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<b>Study Inclusion Criteria</b>	1. English Language 2. Published in last 10 years
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<b>Interventions</b>	ICS/LABA combination products (as single combination products)
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<b>Comparators</b>	ICS/LABA combination products (either as a single product or dual therapy)
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<b>Outcomes</b>	Any reported outcomes
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